PHARMACY & THERAPEUTICS COMMITTEE

Tuesday, March 18th, 2025
5:00pm – 7:00pm

Alameda Alliance for Health
1240 South Loop Road
Alameda, CA 94502

Location: Microsoft Teams
Meeting ID: 222 078 790 80
Password: wfXzdp

YOU MAY SUBMIT COMMENTS ON ANY AGENDA ITEM OR ON ANY ITEM NOT ON THE AGENDA, IN WRITING VIA MAIL TO "ATTN: ALLIANCE PHARMACEUTICAL AND THERAPEUTICS COMMITTEE" 1240 SOUTH LOOP ROAD, ALAMEDA, CA 94502; OR THROUGH E-COMMENT AT bochoa@alamedaalliance.org . YOU MAY WATCH THE MEETING LIVE BY LOGGING IN VIA COMPUTER AT THE FOLLOWING LINK: Microsoft Teams Meeting OR MAY LISTEN TO THE MEETING BY CALLING IN TO THE FOLLOWING TELEPHONE NUMBER: +1 510-210-0967,80299282#. IF YOU USE THE LINK AND PARTICIPATE VIA COMPUTER, YOU MAY, THROUGH THE USE OF THE CHAT FUNCTION, REQUEST AN OPPORTUNITY TO SPEAK ON ANY AGENDIZED ITEM, INCLUDING GENERAL PUBLIC COMMENT. YOUR REQUEST TO SPEAK MUST BE RECEIVED BEFORE THE ITEM IS CALLED ON THE AGENDA. IF YOU PARTICIPATE BY TELEPHONE, YOU MAY SUBMIT ANY COMMENTS VIA THE E-COMMENT EMAIL ADDRESS DESCRIBED ABOVE OR PROVIDE COMMENT DURING THE MEETING AT THE END OF EACH TOPIC.

PLEASE NOTE: THE ALAMEDA ALLIANCE FOR HEALTH IS MAKING EVERY EFFORT TO FOLLOW THE SPIRIT AND INTENT OF THE BROWN ACT AND OTHER APPLICABLE LAWS REGULATING THE CONDUCT OF PUBLIC MEETINGS, IN ORDER TO MAXIMIZE TRANSPARENCY AND PUBLIC ACCESS. DURING EACH AGENDA ITEM, YOU WILL BE PROVIDED A REASONABLE AMOUNT OF TIME TO PROVIDE PUBLIC COMMENT. THE COMMMITTEE WOULD APPRECIATE, HOWEVER, IF COMMUNICATIONS OF PUBLIC COMMENTS RELATED TO ITEMS ON THE AGENDA, OR ITEMS NOT ON THE AGENDA, ARE PROVIDED PRIOR TO THE COMMENCEMENT OF THE MEETING.

AGENDA

ITEM	DESCRIPTION	TIME	VOTE
I)	**Call to order** *Donna Carey, MD, Chief Medical Officer – Alameda Alliance* • Conflict of Interest Check/Disclosure • Agenda Overview	2 min	-
II)	**Informational Updates** *Donna Carey, MD, Chief Medical Officer – Alameda Alliance* *Nora Tomassian, PharmD, Interim Pharmacy Director – Alameda Alliance* • 2025 Joint DHCS and DMHC Audit • Recruitment for permanent director of Pharmacy Services • D-SNP P&P updates (listed in e-voting section) • Carveout Drug SOP - Pharmacy - P&T (non-voting item)	15 min	-
III)	**Pharmacy Utilization Reports (Quarter 4, 2024)** *Nora Tomassian, PharmD, Interim Pharmacy Director – Alameda Alliance* • Top 50 Drugs by Cost • Top 50 PA Reviewed Drugs	2 min	-

ADJOURN TO CLOSED SESSION *(Pursuant to California Government Code Title 5, §54954.5(h))*

Discussion will Concern: *Review and Recommendations to changes to the AAH Formulary and utilization management for selected drug classes*

Estimated Date of Public Disclosure: 03/18/2025 *(formulary changes only; no trade secrets will be disclosed)*

IV) E-Voting Material/Consent Agenda

The following items have been sent to the voting committee for review via E-voting

Nora Tomassian, PharmD, Interim Pharmacy Director – Alameda Alliance

Benita Ochoa, CPhT, Lead Pharmacy Technician – Alameda Alliance

(All matters listed on the Consent Calendar are to be approved with one motion unless a member of the P&T Committee removes an item for separate action. Any consent calendar item for which separate action is requested shall be heard as the next Agenda item in closedsession.)

Monographs/Class Reviews	**Changes**
Alcohol Use Disorder Agents Class Review	• No changes
Direct Oral Anticoagulants Class Review	• No changes
Fluoride Dental Preparations Class Review	• No changes
Inhaled Corticosteroids Class Review	• No changes
Leukotriene Inhibitors Class Review	• No changes
Methergine Monograph	• No changes
Medication Request Guidelines	**Changes**
Angiotensin II Receptor Blockers and Renin Inhibitors	• No changes
Atovaquone (Mepron)	• No changes
Tadalafil (Cialis) for BPH	• No changes
Corlanor (ivabradine)	• No changes
Injectable Anticoagulants	• No changes
Elmiron (pentosane polysulfate sodium)	• No changes
Ezetimibe (Zetia)	• No changes
Inhaled Corticosteroids/Long-Acting Beta-Agonists (ICS/LABA) Combinations	• Remove discontinued AirDuo Digihaler
Altoprev (lovastatin ER) and Fluvastatin, Fluvastatin ER	• No changes
Symlin (pramlintide)	• No changes
Histamine H2 Receptor Antagonists	• No changes
Brilinta (ticagrelor) tablet	• No changes
GLP-1 Agonists	• No changes

10 min EV

DPP-4 Inhibitors and Combinations	• No changes
SGLT2 inhibitors and Combinations	• No changes, grammatical correction
Parkinson's Disease Agents	• No changes
PCSK-9 Monoclonal Antibodies (mAbs)	• Add preferred NDCs
Linezolid	• No changes
Pyridostigmine (Mestinon)	• No changes
Long-Acting Muscarinic /Long-Acting Beta Agonist/ Corticosteroid inhaled Triple Combination Products	• No changes
Corticosteroid Preparations to Treat Hemorrhoids	• No changes
Savella (milnacipran) tablet	• No changes
Travoprost (Travatan Z) ophthalmic drops	• No changes
Arikayce (amikacin)	• No changes
Antifibrotic Respiratory Tract Agents	• Update naming convention to reflect generic availability of Esbriet as pirfenidone
Biologic Agents for Nasal Polyposis	• Update naming of referenced policies
Verquvo	• No changes
Siklos (hydroxyurea)	• No changes
Presbyopia Agents	• No changes
Zurzuvae	• No changes
Dificid	• No changes
Physician Administered Drug (PAD) Guidelines	**Changes**
Emergency Use Authorization (EUA)	• No changes
Primary Hyperoxaluria Agents	• No changes, minor formatting correction
Tzield	• No changes
Gene Therapy for Regular Red Blood Cell (RBC) Transfusion Dependent Beta-Thalassemia	• No changes, minor formatting correction
Pompe Disease Agents	• No changes
Adzynma	• No changes
Interim Formulary Updates	
• See p. 158 in packet	
Summary of Physician Administered Drug (PAD) Updates	
• See p. 159 in packet	

Pharmacy Policy & Procedure Updates	
• RX – 001 Pharmaceutical Operating Processes Summary	• Update RxNova to Darwin claims system
• RX – 002 PA Review Process	• Q1 2025 Annual Review
• RX – 003 Exception Review Process	• Update external exception review process language
• RX – 004 Formulary Management	• Add language to support AB 1842 (4 category coverage requirement)
• RX – 005 P&T Committee Roles and Scope	• Update DUR reporting language to align w/QI Program Description
• RX – 006 Pharmacy Services Staff Description	• Q1 2025 Annual Review
• RX – 007 Pharmaceutical Patient Safety	• Q1 2025 Annual Review
• RX – 008 PBM Delegated Audit Oversight	• Q1 2025 Annual Review
• RX – 009 Emergency Supply Provision	• Q1 2025 Annual Review
• RX – 010 Drug Utilization Management	• DUR Reports to UM and BOG alignment update
• RX – 011 Decision and Notification Requirements	• Q1 2025 Annual Review
• RX – 012 DU Policies – Pharmacy Portal UD Access	• Q1 2025 Annual Review
• RX-013 Medical Benefit Physician Facility-Administered Drugs (PAD) Prior Authorization Review Process	• Q1 2025 Annual Review
• RX-014 Physician Facility-Administered Drugs (PAD) Prior Authorization List Management	• Q1 2025 Annual Review
• RX-015 Pharmaceutical Safe Use Monitoring of Physician Administered Drugs	• Q1 2025 Annual Review
• Rx-016 Self-Administered Drugs Requested Under Medical Benefit	• NEW Policy
D-SNP P&Ps (5 New)	
• Continuity of Care	
• Medicare Part D Hospice	
• Medicare Part D Medication Therapy Management (MTM)	
• PBM Delegated Function Oversight and Monitoring	
• Vaccine Benefit	

ED Oversight
• None
90 Day Maintenance List updates
• Q1 2025 Annual Review
P&T Meeting Minutes
• P&T Meeting Minutes Q4 December 17, 2024

- **New Business**

Timothy Tong, PharmD, Pharmacist – Alameda Alliance
Iryna Makukh, PharmD, Pharmacist – PerformRx

New Rx Policy

- Rx-016 Self-Administered Drugs Requested Under Medical Benefit

New MRG

- Niemann-Pick Disease Type C
- Vyalev
- Zepbound for Moderate to Severe Obstructive Sleep Apnea

New PAD

- Vyalev

Benchmark Analysis

- **Class Reviews, Monographs, and Recommendations**

Iryna Makukh, PharmD, Pharmacist – PerformRx

- Multiple Sclerosis Agents Class Review
- Second Generation Antihistamines Class Review
- Alyftrek Monograph

45 min V

- **Medication Request Guidelines**

Rahel Negash, PharmD, Pharmacist – Alameda Alliance

- Corticosteroids for Duchenne Muscular Dystrophy (DMD)
- Agents for Atopic Dermatitis
- Thrombocytopenia Agents
- Pulmonary Biologics for Asthma and Eosinophilic Conditions
- Anti-Obesity Medications

V) Physician Administered Drug (PAD) Policies — 10 min — V
Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Rituximab
2. Ophthalmic indications for bevacizumab
3. Immunoglobulin Therapy (IVIG)
4. Reblozyl
5. Zulresso

VI) Informational Updates on New Developments in Pharmacy — 2 min — V
Iryna Makukh, PharmD, Pharmacist – PerformRx

- New Product Review

VII) Old Business — 2 min — -
Liza Rosendale, PharmD, CPM – PerformRx

- Pharmacists to prescribe Naloxone at POS

RECONVENE IN OPEN SESSION

VIII) Public Comment

IX) Adjournment

-

ACTION / FOLLOW-UP ITEMS

ITEM	DUE DATE	RESPONSIBLE

FUTURE P&T MEETINGS	
NEXT MEETING	**2025 P&T MEETINGS**
June 17, 2025	September 16, 2025 December 16, 2025

The Alameda Alliance for Health Pharmacy & Therapeutics Committee welcomes you to its meetings and your interest is appreciated. If you wish to speak on a matter on the agenda, you will have the opportunity to do so in the order determined by the Chair. If you wish to speak on a matter not on the agenda, please wait until the Chair asks for public comments at the end of the regular agenda. Please be brief and limit your comments to the specific subject under discussion.

Note: Only matters within the jurisdiction of the Alameda Alliance for Health Pharmacy & Therapeutics Committee may be addressed. If necessary, the Chair may limit the total time to be devoted to public comment on any item, and the time allotted to individual speakers, to ensure sufficient time for the consideration of all matters on the agenda.

This meeting is wheelchair accessible. Please contact Rahel Negash at 510-747-6108 rnegash@alamedaalliance.org at least 72 hours before the meeting to request agenda materials in an alternative format, or any other reasonable disability-related accommodations or services that may be necessary for you to participate in and enjoy the benefits of the meeting.

ALAMEDA Alliance FOR HEALTH Health care you can count on. Service you can trust.	**Standard Operating Procedure (SOP)**	Medi-Cal Carveout Drugs

SOP Title	Medi-Cal Carveout Drugs		
SOP ID	XXX		
Department	Pharmacy, Healthcare Services		
Functional Areas	Pharmacy, UM, Claims, Config, Communications and Outreach, Provider Services		
Effective Date	1/1/2025	Last Revision Date	
Line of Business	☐ All ☒ Medi-Cal ☐ Medicare(Non D-SNP) ☐ Medicare D-SNP ☐ Group ☐ Other		
Approved By / Title	Nora Tomassian, Interim Pharmacy Director	Date Approved	1/1/2025

1. PROCEDURE PURPOSE

Outline the process in how carveout drugs are identified and managed for Medi-Cal Members. Carveout drugs defined as the drugs that belong to the following drug class

a. Antivirals (HIV/AIDS/Hepatitis B) Drugs
b. Alcohol and Heroin Detoxification and Dependency Treatment Drugs
c. Blood Factor: Clotting Factor Disorder Treatment Drugs
d. Psychiatric/Antipsychotic Drugs

Carved out drugs are not covered by the Alliance and are to billed to Medi-Cal fee-for-service as described in APL 16-004.

Carved out drugs requested as pharmacy benefit are to be managed by Medi-Cal Rx and if requested as medical benefit are to be managed by Medi-Cal's FFS Fiscal Intermediary.

2. INTENDED USERS

Pharmacy

3. ADDITIONAL RESOURCES

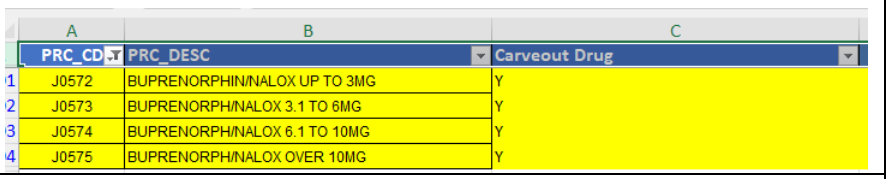
https://www.dhcs.ca.gov/provgovpart/Documents/MRx-Scope-09-04-2020.pdf
https://mcweb.apps.prd.cammis.medi-cal.ca.gov/assets/11F02F0E-1773-4278-90B3-B934358F0D45/mcpsingle.pdf?access_token=6UyVkRRfByXTZEWIh8j8QaYylPyP5ULO
https://www.dhcs.ca.gov/formsandpubs/Documents/MMCDAPLsandPolicyLetters/APL2016/APL16-004.pdf

4. ACRONYMS AND DEFINITIONS

Term	Definition
HIV	Human immunodeficiency virus
AIDS	Acquired immunodeficiency syndrome

5. WORK PROCESS

Step #	Title of Position	Process (Step by Step Instructions)
1.	AAH Configuration Department	AAH Configuration team will email the Pharmacy Department at distgrpPharmacy@alamedaalliance.org to inform there is a new monthly file to review to identify carveout drugs saved in W:\Pharmacy\PAD
2.	AAH Pharmacist	AAH Pharmacy will review file and identify any drugs that fall under

Step #	Title of Position	Process (Step by Step Instructions)
		a. Antivirals (HIV/AIDS/Hepatitis B) Drugs b. Alcohol and Heroin Detoxification and Dependency Treatment Drugs c. Blood Factor: Clotting Factor Disorder Treatment Drugs d. Psychiatric/Antipsychotic Drugs Create Column "Carveout Drug" and enter Y for Carveout Drug on column C. Ex. 
3.	AAH Pharmacist	After review is complete save the file into W:\Pharmacy\PAD\Completed Review
4.	AAH Pharmacist	AAH Pharmacy will notify configuration team when file review is complete and if any new codes need to be configured for Carveout
5.	AAH Technician	Update and add new codes to K:\Unit - Pharmacy Services\PAD\Data\Carveout\CarveoutDrugs Save new file with date and archive old file.

6. CROSS REFERENCES

(P&Ps, regs, other workflows, etc.)

7. DOCUMENTATION AND ATTACHMENTS

MCP Single Plan: Capitated and Non-Capitated Drugs
APL 16-004
Medi-Cal Rx Scope

8. REVISION HISTORY

Document Changes	References/Changes	Changes Approved By	Date

636 IHSS Top 50 Drugs by Cost for 4th Quarter 2024

- The top 50 drugs accounted for **1,404 claims** for **839 members** and cost **$1,589,451,** which is a decrease of $101,770 in spend from the previous quarter.
- Biktarvy remains at number one, claims having gone down by 3, and there is one more member since the previous quarter.
- Ozempic is at numbers 2, 4 and 6, with 272 total claims for 137 members. There was an increase of 4 claims and of 20 members from the previous quarter.
- Vemlidy is up to number 3 with 55 claims for 23 members. This medication is managed via the Hepatitis B MRG.
- Rezurock is up to number 5 with 2 claims for 1 member. This medication is managed via the Agents for graft versus host disease MRG.

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
1	201625	Biktarvy Oral Tablet 50-200-25 MG	32	12	$123,152.99
2	221271	Ozempic (0.25 or 0.5 MG/DOSE) Subcutaneous Solution Pen-injector 2 MG/3ML	117	62	$108,793.10
3	195609	Vemlidy Oral Tablet 25 MG	55	23	$90,284.19
4	218338	Ozempic (2 MG/DOSE) Subcutaneous Solution Pen-injector 8 MG/3ML	81	35	$75,554.57
5	215662	Rezurock Oral Tablet 200 MG	2	1	$70,327.34
6	209911	Ozempic (1 MG/DOSE) Subcutaneous Solution Pen-injector 4 MG/3ML	74	40	$68,954.20
7	214809	Skyrizi Pen Subcutaneous Solution Auto-injector 150 MG/ML	3	2	$61,968.24
8	170343	Jakafi Oral Tablet 5 MG	3	1	$59,266.14
9	177191	Eliquis Oral Tablet 5 MG	76	34	$42,483.69
10	202548	Humira (2 Syringe) Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	3	1	$40,327.71
11	215133	Wegovy Subcutaneous Solution Auto-injector 2.4 MG/0.75ML	30	10	$38,899.63
12	193035	Ocaliva Oral Tablet 10 MG	4	1	$37,778.04
13	223809	Cosentyx UnoReady Subcutaneous Solution Auto-injector 300 MG/2ML	5	2	$36,199.27
14	223302	Zejula Oral Tablet 100 MG	1	1	$35,392.95

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
15	122702	Januvia Oral Tablet 100 MG	63	27	$33,834.45
16	198848	Nerlynx Oral Tablet 40 MG	5	1	$32,623.40
17	207961	Rybelsus Oral Tablet 7 MG	32	18	$29,799.69
18	199758	Verzenio Oral Tablet 100 MG	2	1	$29,733.88
19	224365	Comirnaty Intramuscular Suspension Prefilled Syringe 30 MCG/0.3ML	165	165	$28,891.18
20	207962	Rybelsus Oral Tablet 14 MG	28	13	$26,108.52
21	215135	Wegovy Subcutaneous Solution Auto-injector 0.25 MG/0.5ML	20	14	$25,952.37
22	120500	Dasatinib Oral Tablet 20 MG	2	1	$25,947.42
23	192096	Odefsey Oral Tablet 200-25-25 MG	7	3	$24,642.84
24	190802	Genvoya Oral Tablet 150-150-200-10 MG	6	3	$23,421.97
25	182336	Farxiga Oral Tablet 10 MG	42	17	$23,305.72
26	184848	Jardiance Oral Tablet 10 MG	39	19	$22,721.99
27	197146	Cosentyx Sensoready (300 MG) Subcutaneous Solution Auto-injector 150 MG/ML	3	2	$21,826.26
28	229051	Trulicity Subcutaneous Solution Auto-injector 1.5 MG/0.5ML	23	9	$21,666.31
29	224366	Spikevax Intramuscular Suspension Prefilled Syringe 50 MCG/0.5ML	120	119	$21,523.93
30	201116	Steglatro Oral Tablet 5 MG	53	23	$20,799.56
31	217440	Apretude Intramuscular Suspension Extended Release 600 MG/3ML	5	3	$19,220.23
32	184849	Jardiance Oral Tablet 25 MG	34	15	$18,789.04
33	201117	Steglatro Oral Tablet 15 MG	56	25	$18,766.49
34	203127	Symtuza Oral Tablet 800-150-200-10 MG	4	1	$18,532.40

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
35	204204	Shingrix Intramuscular Suspension Reconstituted 50 MCG/0.5ML	85	73	$18,327.06
36	215134	Wegovy Subcutaneous Solution Auto-injector 0.5 MG/0.5ML	14	10	$18,207.75
37	182488	Glatiramer Acetate Subcutaneous Solution Prefilled Syringe 40 MG/ML	3	1	$16,013.49
38	217569	Adbry Subcutaneous Solution Prefilled Syringe 150 MG/ML	4	2	$15,072.88
39	199759	Verzenio Oral Tablet 150 MG	1	1	$14,866.94
40	218737	Radicava ORS Oral Suspension 105 MG/5ML	1	1	$13,674.31
41	205122	Actemra ACTPen Subcutaneous Solution Auto-injector 162 MG/0.9ML	3	1	$13,136.35
42	212379	Cabenuva Intramuscular Suspension Extended Release 600 & 900 MG/3ML	2	1	$12,997.36
43	187839	Cresemba Oral Capsule 186 MG	2	1	$12,129.90
44	197463	Dupixent Subcutaneous Solution Prefilled Syringe 300 MG/2ML	3	1	$11,318.97
45	170142	Xarelto Oral Tablet 20 MG	21	9	$11,279.30
46	171646	Eliquis Oral Tablet 2.5 MG	20	9	$11,268.02
47	193353	Orencia ClickJect Subcutaneous Solution Auto-injector 125 MG/ML	2	1	$11,246.62
48	182335	Farxiga Oral Tablet 5 MG	20	10	$11,062.49
49	122700	Januvia Oral Tablet 50 MG	20	8	$10,886.52
50	215132	Wegovy Subcutaneous Solution Auto-injector 1 MG/0.5ML	8	6	$10,473.10
TOTAL			**1,404**	**839**	**$1,589,450.77**

Medi-Cal Top 50 Drugs by Cost for 4th Quarter 2024

- The top 50 drugs accounted for **42,049 claims** for **36,406 members** and cost **$58,117,376.51**, which is an increase of **$1,795,296.87** in spend from the previous quarter.
- **The last quarter'stotal cost increase relative to the one before was over 3 million dollars**
- **Biktravy** remains at the number 1 spot with **889** claims for **727** members. An decrease of **28** claims from last quarter, although 37 more members filled the medication in the quarter
- **Ozempic** also remains at the number 2 spot, with **2,141** claims for **1,601** members. This is an decrease of **171** claims from last quarter.
- **Jardiance** is still at number 3 for the 25 mg strength with **1903** claims for **1759** members, but also at number 4 for the 10mg strength with **1952** claims for **1748** members. Total Jardiance claims for the 25mg strength has increased by **91** claims from last quarter and the total Jardiance claims for the 10mg strength has increased by **97** claims. This increased utilization reflects the expanded indication for Jardiance (Type 2 diabetes, prophylaxis heart failure in diabetes and non diabetes patients and reduction of risk of GFR decline in ESRD patients). **86** more members are using Jardiance 25mg relative to the previous quarter and **67** more members are using Jardiance 10mg relative to the previous quarter.
- **Skyrizi** is at the number 5 spot down from number 5, with **102** claims in **94** members, same number of claims as last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	44426	BIKTARVY 50-200-25 MG TABLET	889	727	$6,519,177.42
2	53536	OZEMPIC 0.25-0.5 MG/DOSE PEN	1970	1601	$2,681,828.22
3	36723	JARDIANCE 25 MG TABLET	1903	1759	$2,607,142.41
4	36716	JARDIANCE 10 MG TABLET	1952	1748	$2,545,477.14
5	49591	SKYRIZI 150 MG/ML PEN	102	94	$2,253,542.21
6	48208	OZEMPIC 1 MG/DOSE (4 MG/3 ML)	1239	996	$1,967,276.80
7	43506	HUMIRA(CF) PEN 40 MG/0.4 ML	118	94	$1,842,243.55
8	52125	OZEMPIC 2 MG/DOSE (8 MG/3 ML)	998	792	$1,731,113.17
9	49754	WEGOVY 2.4 MG/0.75 ML PEN	786	596	$1,711,384.93
10	48277	DUPIXENT 300 MG/2 ML PEN	191	159	$1,548,694.67
11	28159	STELARA 90 MG/ML SYRINGE	38	32	$1,466,173.10

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
12	42624	VEMLIDY 25 MG TABLET	464	380	$1,423,705.48
13	49748	WEGOVY 0.25 MG/0.5 ML PEN	931	835	$1,341,292.72
14	49099	CABENUVA ER 600 MG-900 MG SUSP	158	137	$1,264,249.30
15	27418	INVEGA SUSTENNA 234 MG/1.5 ML	206	148	$1,234,873.45
16	33935	ELIQUIS 5 MG TABLET	1113	891	$1,222,943.99
17	49752	WEGOVY 1 MG/0.5 ML PEN	769	637	$1,195,062.34
18	49753	WEGOVY 1.7 MG/0.75 ML PEN	656	527	$1,171,586.56
19	40133	TAGRISSO 80 MG TABLET	42	31	$1,167,736.77
20	97400	JANUVIA 100 MG TABLET	794	717	$1,126,303.23
21	49749	WEGOVY 0.5 MG/0.5 ML PEN	773	661	$1,111,621.65
22	34394	FARXIGA 10 MG TABLET	709	627	$962,142.76
23	97724	ENBREL 50 MG/ML SURECLICK	77	67	$956,467.51
24	44014	HUMIRA(CF) PEN 80 MG/0.8 ML	23	19	$905,552.49
25	46965	RYBELSUS 7 MG TABLET	431	398	$890,272.58
26	47136	TRIKAFTA 100-50-75 MG/150 MG	14	13	$877,969.31
27	46966	RYBELSUS 14 MG TABLET	369	337	$806,670.03
28	40953	DESCOVY 200-25 MG TABLET	235	189	$792,463.67
29	56163	COMIRNATY 2024-25(12Y UP) SYRG	4372	4368	$772,794.39
30	43968	SYMTUZA 800-150-200-10 MG TAB	105	80	$772,587.96
31	98637	BASAGLAR 100 UNIT/ML KWIKPEN	1445	1224	$734,394.92
32	47586	TEPEZZA 500 MG VIAL	8	5	$697,894.02

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
33	49468	COSENTYX UNOREADY 300 MG PEN	35	28	$691,747.45
34	25200	FREESTYLE LITE TEST STRIP	3966	3816	$677,556.78
35	49487	APRETUDE ER 600 MG/3 ML VIAL	133	113	$677,372.65
36	38702	INVEGA TRINZA 819 MG/2.63 ML	61	58	$626,274.67
37	37682	ABILIFY MAINTENA ER 400 MG SYR	126	85	$590,369.38
38	94200	DEXCOM G7 SENSOR	527	482	$578,698.03
39	40092	GENVOYA TABLET	78	63	$557,433.34
40	54456	FERRIPROX 1,000 MG TAB(2X/DAY)	9	9	$547,226.25
41	22913	ALBUTEROL HFA 90 MCG INHALER	12323	10099	$547,136.29
42	97005	HUMIRA PEN 40 MG/0.8 ML	39	29	$525,563.54
43	37789	COSENTYX SNRDY 300MG DOSE-2PEN	31	25	$518,172.75
44	43699	MAVYRET 100-40 MG TABLET	29	29	$516,782.29
45	37788	COSENTYX 300 MG DOSE-2 SYRINGE	24	19	$486,247.58
46	43924	ENBREL 50 MG/ML MINI CARTRIDGE	29	24	$475,007.65
47	43116	ELOCTATE 5,000 UNIT NOMINAL	6	1	$461,787.76
48	30819	XARELTO 20 MG TABLET	410	348	$452,175.97
49	37171	TRULICITY 1.5 MG/0.5 ML PEN	285	239	$446,896.12
50	43222	DUPIXENT 300 MG/2 ML SYRINGE	58	50	$438,289.26
TOTAL			**42,049**	**36,406**	**$58,117,376.51**

636 IHSS Top 50 Prior Authorization Requests by Volume for 4th Quarter 2024

- Top 50 PA requests = 209. There were 316 total PA requests for quarter 4.
  - 82 requests (39%) were approved. This approval rate is lower by 3% than it was observed last quarter.
  - 122 requests (59%) were denied or partially approved.
- Wegovy is at numbers 1, 6, 13 and 19 with 59 total requests and 17 approvals (29%).
  - Wegovy to reduce excess body weight requires a diagnosis of obesity or BMI ≥27 and at least one weight-related comorbidity (diabetes, hypertension, hyperlipidemia) or history of heart attack, despite diet and exercise, and trial and failure or inability to use Qsymia and Contrave.
  - Wegovy to reduce the risk of major adverse cardiovascular events requires a documentation that the patient is obese or has BMI ≥27, has an established cardiovascular disease (prior myocardial infarction, stroke or symptomatic peripheral arterial disease), patient is on standard of care treatment for CVD and does not have diabetes.
- Lidocaine 5% patch is at number 2 with 17 requests and 3 approvals (18%).
  - Lidocaine requires a diagnosis of neuropathic pain and a trial and failure of gabapentin or pregabalin and one other formulary alternative (e.g., duloxetine, venlafaxine, amitriptyline) used for neuropathic pain or morphine MME ≧ 50/day for 3 months.
- Vemlidy is at number 3 with 13 requests. There were 6 approvals (46%).
  - Vemlidy requires a diagnosis of Hepatitis B, and trial and failure of, intolerance to, or inability to use entecavir tablets.
- Jardiance is at numbers 4 & 5 with 18 total requests and 4 approvals (22%).
  - Jardiance requires trial and failure of one of the following: metformin, branded/generic drug containing metformin, branded angiotensin receptor/neprilysin inhibitor (ARNi), generic angiotensin-converting enzyme inhibitor (ACEi), generic angiotensin receptor blocker (ARB), generic mineralocorticoid receptor antagonist (MRA), or generic beta blocker.

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
1	Wegovy Subcutaneous Solution Auto-injector 0.25 MG/0.5ML	45	8	17.78%	36	80.00%	1	2.22%
2	Lidocaine External Patch 5 %	17	3	17.65%	13	76.47%	0	0.00%
3	Vemlidy Oral Tablet 25 MG	13	6	46.15%	5	38.46%	2	15.38%
4	Jardiance Oral Tablet 25 MG	9	1	11.11%	5	55.56%	2	22.22%
5	Jardiance Oral Tablet 10 MG	9	3	33.33%	6	66.67%	0	0.00%
6	Wegovy Subcutaneous Solution Auto-injector 2.4 MG/0.75ML	8	6	75.00%	1	12.50%	0	0.00%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
7	Ozempic (0.25 or 0.5 MG/DOSE) Subcutaneous Solution Pen-injector 2 MG/3ML	8	3	37.50%	5	62.50%	0	0.00%
8	Zepbound Subcutaneous Solution Auto-injector 2.5 MG/0.5ML	8	2	25.00%	6	75.00%	0	0.00%
9	cycloSPORINE Ophthalmic Emulsion 0.05 %	7	6	85.71%	0	0.00%	1	14.29%
10	Xiidra Ophthalmic Solution 5 %	6	1	16.67%	4	66.67%	0	0.00%
11	Tyrvaya Nasal Solution 0.03 MG/ACT	4	2	50.00%	2	50.00%	0	0.00%
12	Prolia Subcutaneous Solution Prefilled Syringe 60 MG/ML	4	4	100.00 %	0	0.00%	0	0.00%
13	Wegovy Subcutaneous Solution Auto-injector 0.5 MG/0.5ML	4	2	50.00%	2	50.00%	0	0.00%
14	Phentermine HCl Oral Tablet 37.5 MG	4	4	100.00 %	0	0.00%	0	0.00%
15	Brilinta Oral Tablet 90 MG	3	2	66.67%	1	33.33%	0	0.00%
16	Trelegy Ellipta Inhalation Aerosol Powder Breath Activated 100-62.5-25 MCG/ACT	3	1	33.33%	2	66.67%	0	0.00%
17	CONTRAVE Tablet ER 12HR 8/90/MG	3	1	33.33%	2	66.67%	0	0.00%
18	Tretinoin External Cream 0.025 %	3	1	33.33%	2	66.67%	0	0.00%
19	Wegovy Subcutaneous Solution Auto-injector 1 MG/0.5ML	2	1	50.00%	0	0.00%	1	50.00%
20	VUMERITY Capsule DR 231MG	2	1	50.00%	1	50.00%	0	0.00%
21	valGANciclovir HCl Oral Tablet 450 MG	2	1	50.00%	0	0.00%	1	50.00%
22	Adbry Subcutaneous Solution Prefilled Syringe 150 MG/ML	2	0	0.00%	0	0.00%	2	100.00 %
23	Betamethasone Dipropionate Aug External Ointment 0.05 %	2	2	100.00 %	0	0.00%	0	0.00%
24	QSYMIA Capsule ER 24HR 7.5/46/MG	2	1	50.00%	1	50.00%	0	0.00%
25	Lisdexamfetamine Dimesylate Oral Capsule 20 MG	2	0	0.00%	2	100.00 %	0	0.00%
26	TACROLIMUS Ointment 0.1%	2	1	50.00%	1	50.00%	0	0.00%
27	Icosapent Ethyl Oral Capsule 1 GM	2	2	100.00 %	0	0.00%	0	0.00%
28	Calcium Carb-Cholecalciferol Oral Tablet 500-10 MG-MCG	2	0	0.00%	2	100.00 %	0	0.00%
29	Vyvanse Oral Capsule 60 MG	2	2	100.00 %	0	0.00%	0	0.00%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
30	TRETINOIN Cream 0.1%	2	1	50.00%	1	50.00%	0	0.00%
31	Zoryve External Foam 0.3 %	2	2	100.00 %	0	0.00%	0	0.00%
32	Mirabegron ER Oral Tablet Extended Release 24 Hour 50 MG	2	1	50.00%	1	50.00%	0	0.00%
33	Bumetanide Oral Tablet 1 MG	2	1	50.00%	1	50.00%	0	0.00%
34	Doxycycline Hyclate Oral Tablet 100 MG	2	0	0.00%	2	100.00 %	0	0.00%
35	Praluent Subcutaneous Solution Auto-injector 150 MG/ML	2	0	0.00%	1	50.00%	1	50.00%
36	UBRELVY Tablet 100MG	2	1	50.00%	1	50.00%	0	0.00%
37	ZTlido External Patch 1.8 %	2	0	0.00%	1	50.00%	1	50.00%
38	REZUROCK Tablet 200MG	1	1	100.00 %	0	0.00%	0	0.00%
39	CARISOPRODOL Tablet 350MG	1	0	0.00%	1	100.00 %	0	0.00%
40	SUTAB Tablet 1479;225;188MG	1	1	100.00 %	0	0.00%	0	0.00%
41	Estradiol Transdermal Gel 0.75 MG/1.25 GM (0.06%)	1	1	100.00 %	0	0.00%	0	0.00%
42	XDEMVY Solution 0.25%	1	1	100.00 %	0	0.00%	0	0.00%
43	Estring Vaginal Ring 7.5 MCG/24HR	1	0	0.00%	1	100.00 %	0	0.00%
44	SCOPOLAMINE Patch 72HR 1MG/3DAYS	1	1	100.00 %	0	0.00%	0	0.00%
45	Ezetimibe Oral Tablet 10 MG	1	1	100.00 %	0	0.00%	0	0.00%
46	CAPECITABINE Tablet 500MG	1	0	0.00%	0	0.00%	0	0.00%
47	EZETIMIBE Tablet 10MG	1	0	0.00%	1	100.00 %	0	0.00%
48	Voquezna Dual Pak Oral Therapy Pack 500-20 MG	1	1	100.00 %	0	0.00%	0	0.00%
49	Farxiga Oral Tablet 10 MG	1	1	100.00 %	0	0.00%	0	0.00%
50	REPATHA SURECLICK Soln Auto-inj 140MG/ML	1	1	100.00 %	0	0.00%	0	0.00%
TOTAL		**209**	**82**	**39%**	**110**	**53%**	**12**	**6%**

Medi-Cal Top 50 Claims by Volume for 4th Quarter 2024

- The top 50 drugs accounted for **211,954 claims** for **189,479 members** and cost of **$5,148,097.19.** This is an increase of **4,500** claims from last quarter and an increase of **of $154.474.78** compared to last quarter.
- **Albuterol** remains at the number 1 spot with **12,323** claims for **10,099** members. This is an **increase of 1,356** claims from last quarter.
- **Ibuprofen** is at number 2, with **9,573** claims for **8,656** members .This is **a decrease of 182** claims compared to the previous quarter.
- Diclofenac gel has risen from 5th spot to number **3** with **8,964 claims** for **7709 members.** This is an increase of 1,314 claims compared to last quarter and an upward trend for this topical product.
- **Aspirin** is back on the 4th spot with **8,784** claims and **8,118** unique members. This is a decrease of 290 claims compared to last quarter.
- **Fluticasone** has dropped from the number 4 to the number 5 spot with **8,076** claims for **7,213** members. There was a **decrease of 287** claims from last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	22913	ALBUTEROL HFA 90 MCG INHALER	12323	10099	$547,136.29
2	35742	IBUPROFEN 600 MG TABLET	9573	8656	$136,726.18
3	45680	DICLOFENAC SODIUM 1% GEL	8964	7709	$263,237.16
4	00161	ASPIRIN EC 81 MG TABLET	8784	8118	$97,965.87
5	62263	FLUTICASONE PROP 50 MCG SPRAY	8076	7213	$179,727.47
6	16965	ACETAMINOPHEN 500 MG CAPLET	7624	6884	$102,397.47
7	49291	CETIRIZINE HCL 10 MG TABLET	6149	5628	$102,596.75
8	43721	ATORVASTATIN 20 MG TABLET	5928	5523	$89,679.94
9	02683	AMLODIPINE BESYLATE 5 MG TAB	5833	5234	$81,513.09
10	60563	LORATADINE 10 MG TABLET	5713	5051	$93,386.64
11	43722	ATORVASTATIN 40 MG TABLET	5568	5130	$92,750.68
12	02682	AMLODIPINE BESYLATE 10 MG TAB	5171	4658	$73,992.41
13	10857	METFORMIN HCL 1,000 MG TABLET	4930	4528	$81,946.44

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
14	86212	POLYETHYLENE GLYCOL 3350 POWD	4475	4145	$116,285.87
15	46430	FAMOTIDINE 20 MG TABLET	4382	3870	$64,620.44
16	56163	COMIRNATY 2024-25(12Y UP) SYRG	4372	4368	$772,794.39
17	10810	METFORMIN HCL 500 MG TABLET	4366	3888	$67,828.48
18	00781	GABAPENTIN 300 MG CAPSULE	4319	3527	$80,677.39
19	04348	OMEPRAZOLE DR 20 MG CAPSULE	4266	3683	$66,635.54
20	25200	FREESTYLE LITE TEST STRIP	3966	3816	$677,556.78
21	20045	ONDANSETRON ODT 4 MG TABLET	3945	3639	$57,934.33
22	00223	VITAMIN D3 25 MCG TABLET	3823	3616	$46,654.29
23	99882	VITAMIN D3 50 MCG SOFTGEL	3777	3589	$49,620.72
24	40120	PANTOPRAZOLE SOD DR 40 MG TAB	3629	3042	$57,125.01
25	43720	ATORVASTATIN 10 MG TABLET	3589	3336	$53,682.54
26	94422	VITAMIN D2 1.25MG(50,000 UNIT)	3549	3299	$54,791.39
27	16965	ACETAMINOPHEN 500 MG TABLET	3509	3212	$34,847.79
28	09101	DOCUSATE SODIUM 100 MG SOFTGEL	3288	2942	$44,862.50
29	97503	FERROUS GLUCONATE 324 MG TAB	3091	2822	$43,708.55
30	35793	NAPROXEN 500 MG TABLET	3001	2617	$49,368.80
31	94781	FOLIC ACID 1 MG TABLET	2990	2550	$49,215.38
32	14851	LOSARTAN POTASSIUM 50 MG TAB	2950	2673	$45,611.09
33	39661	AMOXICILLIN 500 MG CAPSULE	2933	2766	$40,352.33

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
34	48191	TAMSULOSIN HCL 0.4 MG CAPSULE	2754	2359	$47,009.61
35	16964	ACETAMINOPHEN 325 MG TABLET	2730	2574	$28,852.23
36	35744	IBUPROFEN 800 MG TABLET	2690	2340	$42,536.42
37	14850	LOSARTAN POTASSIUM 25 MG TAB	2667	2401	$39,086.41
38	35930	CHILDREN IBUPROFEN 100 MG/5 ML	2625	2466	$50,236.49
39	16391	TRAZODONE 50 MG TABLET	2621	2021	$42,099.00
40	29189	SYSTANE BALANCE 0.6% EYE DROP	2620	2460	$90,015.10
41	39802	CEPHALEXIN 500 MG CAPSULE	2540	2383	$36,210.37
42	70330	HYDROCODONE-ACETAMIN 10-325 MG	2509	1059	$51,817.64
43	29840	BENZONATATE 100 MG CAPSULE	2509	2306	$35,732.63
44	94200	FREESTYLE 28G LANCETS	2444	2400	$44,279.24
45	35741	IBUPROFEN 400 MG TABLET	2437	2341	$33,435.98
46	30370	CLOTRIMAZOLE 1% TOPICAL CREAM	2423	2234	$37,946.46
47	34824	HYDROCHLOROTHIAZIDE 25 MG TAB	2418	2187	$34,879.74
48	94444	MONTELUKAST SOD 10 MG TABLET	2387	2150	$40,130.50
49	13943	HYDROXYZINE HCL 25 MG TABLET	2380	1829	$38,724.66
50	14853	LOSARTAN POTASSIUM 100 MG TAB	2344	2138	$37,874.71
TOTAL			**211,954**	**189,479**	**$5,148,097.19**

Alcohol Use Disorder

Executive Summary

Class Overview

Alcohol use disorder (AUD), or alcohol dependence, is characterized by a problematic pattern of alcohol use leading to clinically significant impairment, as manifested by multiple psychosocial, behavioral, or physiologic features. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines AUD and alcohol dependence as one disorder with mild, moderate, and severe sub-classifications. The pathogenesis of AUD is not known, but its development may be due to several factors such as genetics, environmental influences, specific personality, and cognitive functioning. It is estimated that 29 million Americans (aged 12 years or older) have AUD. In the United States, the 12-month prevalence of AUD is estimated to be 13.9%, and lifetime prevalence is estimated to be 29.1%, with about half of those with lifetime AUD having a severe disorder. Unhealthy alcohol use has been often associated with psychological consequences and may have a serious impact on social well-being. AUD increases the risk of suicide, criminal activity (including domestic violence), overdose deaths, and the transmission of HIV and other sexually transmitted infections. Alcohol dependence can also be a significant contributing factor to many medical conditions including cardiovascular disease, liver disease, gastritis, esophagitis, pancreatitis, chronic infectious diseases, depressive disorders, and sleep disturbances. While psychosocial interventions are effective treatment for some individuals, as many as 70% of individuals have recurrence of symptoms after psychosocial treatment alone. Several medications can be used to treat alcohol dependence leading to reduced heavy drinking and increased days of abstinence. Disulfiram is an aversive agent that does not directly influence motivation to drink, but instead discourages drinking by causing an unpleasant physiologic reaction when alcohol is consumed. Acamprosate works to balance the neurotransmitters in the brain to help patients stay abstinent. Naltrexone is used to help patients who have strong cravings for alcohol. Naltrexone and acamprosate are the two medications most strongly supported by clinical trial evidence in AUD and are generally considered to be first-line treatment options according to clinical guidelines. Despite the high prevalence of AUD and the availability of effective treatments (non-pharmacologic and pharmacologic), AUD remains an undertreated condition. Barriers to treatment include challenges associated with comorbid psychiatric disorders and/or substance abuse, lack of patient awareness of treatment options, and the inability of providers to connect patients with adequate psychosocial cointerventions.

Utilization Findings

There were 10 claims for 5 members, for a total cost of $440.07 and an average cost per claim of $44.01. The most highly utilized medication was Naltrexone 50 mg oral tablet with 10 claims. There were no prior authorization requests.

Recommendations

- No changes

Clinical Summary

According to the DSM-5, AUD or alcohol dependence is characterized by a problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by multiple psychosocial, behavioral, or physiologic features. It is estimated that 29 million Americans (aged 12 years or older) have AUD. More than 170,000 deaths a year in the United States are directly attributed to alcohol use, with the annual economic cost of alcohol use estimated to be over $250 billion. The pathogenesis of AUD is not known, but its development may be due to result of several factors such as genetics, environmental influences, specific personality, and cognitive functioning.

Symptoms or behaviors displayed by patients with AUD include recurrent drinking in failure to fulfill obligations, evidence of tolerance, evidence of alcohol withdrawal, persistent desire, unsuccessful attempts to stop or reduce drinking, continued drinking despite knowledge of physical or psychological problems, and alcohol craving. Signs and symptoms of acute intoxication vary with severity and can include slurred speech, disinhibited behavior, incoordination, hypotension, tachycardia, memory impairment, stupor, or coma. Unhealthy alcohol use has been often associated with psychological consequences and may have a serious impact on social well-being. Alcohol dependence can also be a significant contributing factor to many medical conditions including cardiovascular disease, liver disease, gastritis, esophagitis, pancreatitis, chronic infectious diseases, depressive disorders, and sleep disturbances.
All patients with AUD should be encouraged to participate in some type of psychosocial treatment, most commonly, some form of alcohol counseling and participation in a mutual help group. While psychosocial interventions are effective for some individuals as treatment, as many as 70% of individuals have recurrence of symptoms after psychosocial treatment alone.

Several medications can be used to treat alcohol dependence leading to reduced heavy drinking and increased days of abstinence. Disulfiram is an aversive agent that does not directly influence motivation to drink, but instead discourages drinking by causing an unpleasant physiologic reaction when alcohol is consumed. For this reason, disulfiram should only be used by abstinent patients with the goal of maintaining abstinence. Acamprosate should also be started once abstinence is achieved and works to balance the neurotransmitters in the brain to help patients stay abstinent. As a result, patients may notice less of a desire to return to drinking. Naltrexone can be started while the patient is still an active drinker and is used to help patients who have strong cravings for alcohol. This allows for treatment to be initiated at the point of maximum crisis without the need for enforced abstinence or medically supervised withdrawal. Naltrexone is available as both an oral tablet and as an extended-release subcutaneous injection (Vivitrol®). Naltrexone and acamprosate are the two medications most strongly supported by placebo-controlled clinical trials in AUD and are generally considered to be first-line treatment options according to clinical guidelines. Topiramate and gabapentin are also supported by guidelines, but these agents are used off-label. Patients with AUD who successfully maintain abstinence or experience an adequate reduction in heavy drinking should continue psychosocial treatments for at least 6 months and ideally for 12 months. Medication treatment should ideally be continued for at least a year, a duration associated with a lower risk of recurrence, or longer if well tolerated and appears to be beneficial.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
Anti-Alcoholic Preparations		
Disulfiram	Alcohol use disorder	Initial: 250 to 500 mg orally once daily for 1 to 2 weeks Average maintenance dose: 250 mg orally once daily (range: 125 to 500 mg/day)
Acamprosate		666 mg orally 3 times a day Lower doses may be considered in patients weighing <60kg
Opioid Antagonists		
Naltrexone	Alcohol use disorder Opioid Dependence	50 mg orally once daily Some patients may require doses up to 100 mg/day. Alternative maintenance regimens may be used and include: 50 mg on weekdays with a 100 mg dose on Saturday; 100 mg every other day; or 150 mg every 3 days.
Vivitrol® (naltrexone)		380 mg intramuscularly once every 4 weeks

Boxed Warnings and Contraindications

Medication	Boxed Warnings	Contraindications
Disulfiram	**Alcohol Intoxication:** Disulfiram should never be administered to a patient who is in a state of alcohol intoxication, or without their full knowledge. Physicians should instruct relatives accordingly.	Hypersensitivity to thiuram derivatives used in pesticides and rubber vulcanization Patients receiving or using alcohol, metronidazole, paraldehyde, or alcohol-containing preparations (e.g., cough syrup, tonics) Psychosis Severe myocardial disease or coronary occlusion
Acamprosate	None	Hypersensitivity to acamprosate or any component of the formulation Severe renal impairment (CrCl ≤30 mL/minute)
Naltrexone Vivitrol® (naltrexone)	None	Hypersensitivity to naltrexone or any component of the formulation Opioid dependence or current use of opioid analgesics (including partial opioid agonists) Acute opioid withdrawal Failure to pass naloxone challenge or positive urine screen for opioids

Warnings/Precautions

Medication	Warnings/Precautions
Disulfiram	Concerns related to adverse effects: - Disulfiram reaction: Ingesting alcohol, even in small amounts, during treatment with disulfiram may result in flushing, throbbing in head and neck, nausea, copious vomiting, respiratory difficulty, diaphoresis, thirst, chest pain, palpitation, dyspnea, hyperventilation, tachycardia, hypotension, syncope, marked uneasiness, weakness, vertigo, blurred vision and confusion. Severe reactions may involve respiratory depression, cardiovascular collapse, arrhythmias, myocardial infarction, acute congestive heart failure, unconsciousness, seizure and death. The intensity of the reaction is generally proportional to the amounts of disulfiram and alcohol ingested. Patients should avoid alcohol consumption for >12 hours prior to administration; disulfiram reactions can occur up to 14 days after taking disulfiram if alcohol is consumed. - Hepatotoxicity: Severe (sometimes fatal) hepatitis and/or hepatic failure resulting in transplantation have been associated with use; may occur in patients with or without prior history of abnormal hepatic function. Disease-related concerns: - Cerebral damage - Contact dermatitis: Evaluate patients with a history of rubber contact dermatitis for hypersensitivity to thiuram derivatives. - Diabetes - Hepatic impairment - Hypothyroidism - Nephritis - Seizures Concurrent drug therapy issues: - Drug-drug interactions Other warnings/precautions: - Alcohol intoxication: Should never be administered to a patient who is in a state of alcohol intoxication, or without their full knowledge. - Patient information: Patients must receive appropriate counseling, including information on the disulfiram reaction, “disguised” forms of alcohol (e.g., tonics, mouthwashes, cough mixtures, sauces, vinegars, aftershave lotions, back rubs) and the duration of drug activity (up to 14 days).
Acamprosate	Concerns related to adverse effects: - CNS depression: May cause CNS depression, which may impair physical or mental abilities.

Medication	Warnings/Precautions
	- Suicidal thinking/behavior: Attempted and completed suicides have occurred in acamprosate-treated patients. Monitor for depression and/or suicidal thinking. Disease-related concerns: - Alcohol use disorder: Should be used as part of a comprehensive program to treat alcohol use disorder. Treatment should be initiated as soon as possible following the period of alcohol withdrawal, when the patient has achieved abstinence. Acamprosate does not eliminate or diminish the symptoms of alcohol withdrawal. - Renal impairment: Use with caution and reduce dose in patients with moderate renal impairment (CrCl 30 to 50 mL/minute). Use is contraindicated in patients with severe renal impairment (CrCl ≤30 mL/minute). Dosage form specific issues: - Sulfites: Traces of sulfites may be present.
Naltrexone Vivitrol® (naltrexone)	Concerns related to adverse effects: - Accidental opioid overdose: Patients who had been treated with naltrexone may respond to lower opioid doses than previously used. This could result in potentially life-threatening opioid intoxication. Patients should be aware that they may be more sensitive to lower doses of opioids after naltrexone treatment is discontinued, after a missed dose, or near the end of the dosing interval. Patients should be warned that any attempt to overcome opioid blockade during naltrexone therapy, could potentially lead to fatal opioid overdose. - Acute opioid withdrawal: May precipitate symptoms of acute withdrawal in opioid-dependent patients, including pain, hypertension, sweating, agitation, and irritability - Eosinophilic pneumonia: Cases of eosinophilic pneumonia have been reported and should be considered in patients presenting with progressive hypoxia and dyspnea. - Hepatocellular injury: Dose-related hepatocellular injury is possible. Clinicians should note that elevated transaminases may be a result of pre-existing alcoholic liver disease, hepatitis B and/or C infection, or concomitant use of other hepatotoxic drugs. - Hypersensitivity reactions: Hypersensitivity, including urticaria, angioedema, and anaphylaxis, have been reported. - Injection site reactions (Vivitrol® only): Serious injection site reactions (e.g., cellulitis, induration, hematoma, abscess, necrosis) have been reported with use, including severe cases requiring surgical debridement. Females appear to be at a higher risk. For IM use only in the gluteal muscle; incorrect administration may increase the risk of injection site reactions.

Medication	Warnings/Precautions
	- Suicidal thoughts/depression: Suicidal thoughts, attempted suicide, and depression have been reported post-marketing. Disease-related concerns: - Bleeding disorders (Vivitrol® only): Use IM injection with caution in patients thrombocytopenia or any bleeding disorder (including hemophilia and severe hepatic failure), or patients on anticoagulant therapy; bleeding/hematoma may occur from IM administration. - Hepatic impairment: Use is not recommended in acute hepatitis or hepatic failure - Renal impairment Dosage form specific issues: - Injection (Vivitrol® only): Vehicle used in the injectable naltrexone formulation (polylactide-co-glycolide microspheres) has rarely been associated with retinal artery occlusion in patients with abnormal arteriovenous anastomosis following injection of other drug products that also use the polylactide-co-glycolide microspheres vehicle. Other warnings/precautions: - Emergency pain management: In naltrexone-treated patients requiring emergency pain management, consider alternatives to opioid therapy (e.g., regional analgesia, non-opioid analgesics, general anesthesia). If opioid therapy is required for pain therapy, patients should be under the direct care of a trained anesthesia provider. - Surgery: In patients treated with naltrexone for opioid addiction who requiring surgery, discontinue oral naltrexone at least 72 hours before scheduled elective surgery if opioid use is anticipated; extended-release IM naltrexone should be discontinued at least 30 days prior to scheduled surgery.

Practice Guidelines

US Department of Veterans Affairs VA/DoD Clinical Practice Guidelines. Management of Substance Use Disorder (SUD) (2021).

- For patients with moderate-severe alcohol use disorder, we recommend offering one of the following medications: naltrexone (oral or extended-release), or topiramate. (Strong for; Not reviewed, Amended).
- For patients with moderate-severe alcohol use disorder, we suggest offering one of the following medications: acamprosate or disulfiram. (Weak for; Not reviewed, Amended).
- For patients with moderate-severe alcohol use disorder for whom first-line pharmacotherapy is contraindicated or ineffective, we suggest offering gabapentin. (Weak for, Not reviewed, Not changed).
- For patients with alcohol use disorder, we suggest one or more of the following interventions, considering patient preference and availability: behavioral couples therapy, cognitive behavioral therapy, community reinforcement approach, motivational enhancement therapy, 12-step facilitation. (Weak for, Not reviewed, Amended).

Recommendation Definitions

Recommendation Strength and Direction	General Corresponding Text
Strong for	We recommend …
Weak for	We suggest …
Neither for nor against	There is insufficient evidence to recommend for or against …
Weak against	We suggest against …
Strong against	We recommend against …

Evidence Reviewed	Recommendation Category	Definition
Reviewed	New-added	New recommendation.
	New-replaced	Recommendation from previous clinical practice guideline (CPG) was carried forward and revised
	Not changed	Recommendation from previous CPG was carried forward but not changed
	Amended	Recommendation from the previous CPG was carried forward with a nominal change
	Deleted	Recommendation from the previous CPG was deleted
Not Reviewed	Not changed	Recommendation from previous CPG was carried forward but not changed
	Amended	Recommendation from the previous CPG was carried forward with a nominal change
	Deleted	Recommendation from the previous CPG was deleted

Reus VI, Fochtmann LJ, Bukstein O, et al. The American Psychiatric Association (APA) Practice Guideline for the Pharmacological Treatment of Patients with Alcohol Use Disorder. Am J Psychiatry. 2018;175(1):86-90.

Selection of a Pharmacotherapy

- APA recommends (1B) that naltrexone or acamprosate be offered to patients with moderate to severe alcohol use disorder who:
    - Have a goal of reducing alcohol consumption or achieving abstinence
    - Prefer pharmacotherapy or have not responded to nonpharmacological treatments alone
    - Have no contraindications to the use of these medications

- APA suggests (2C) that disulfiram be offered to patients with moderate to severe alcohol use disorder who:
    - Have a goal of achieving abstinence
    - Prefer disulfiram or are intolerant to or have not responded to naltrexone and acamprosate
    - Aare capable of understanding the risks of alcohol consumption while taking disulfiram
    - Have no contraindications to the use of this medication
- APA suggests (2C) that topiramate or gabapentin be offered to patients with moderate to severe alcohol use disorder who:
    - Have a goal of reducing alcohol consumption or achieving abstinence
    - Prefer topiramate or gabapentin or are intolerant to or have not responded to naltrexone and acamprosate
    - Have no contraindications to the use of these medications

Recommendations Against Use of Specific Medications

- APA recommends (1B) that antidepressant medications not be used for treatment of alcohol use disorder unless there is evidence of a co-occurring disorder for which an antidepressant is an indicated treatment.
- APA recommends (1C) that in individuals with alcohol use disorder, benzodiazepines not be used unless treating acute alcohol withdrawal or unless a co-occurring disorder exists for which a benzodiazepine is an indicated treatment.
- APA recommends (1C) that for pregnant or breastfeeding women with alcohol use disorder, pharmacological treatments not be used unless treating acute alcohol withdrawal with benzodiazepines or unless a co-occurring disorder exists that warrants pharmacological treatment.
- APA recommends (1C) that acamprosate not be used by patients who have severe renal impairment.
- APA recommends (1C) that for individuals with mild to moderate renal impairment, acamprosate not be used as a first-line treatment and, if used, the dose of acamprosate be reduced compared with recommended doses in individuals with normal renal function.
- APA recommends (1C) that naltrexone not be used by patients who have acute hepatitis or hepatic failure.
- APA recommends (1C) that naltrexone not be used as a treatment for alcohol use disorder by individuals who use opioids or who have an anticipated need for opioids.

Treatment of Alcohol Use Disorder and Co-occurring Opioid Use Disorder

- APA recommends (1C) that in patients with alcohol use disorder and co-occurring opioid use disorder, naltrexone be prescribed to individuals who:
    - Wish to abstain from opioid use and either abstain from or reduce alcohol use and
    - Are able to abstain from opioid use for a clinically appropriate time prior to naltrexone initiation.

Recommendation Definitions

Recommendation Rating	Phrasing	Definition
1	Recommendation	Indicates confidence that the benefits of the intervention clearly outweigh harms.
2	Suggestion	Although the benefits of the statement are still viewed as outweighing the harms, the balance of benefits and harms is more difficult to judge, or either the benefits or the harms may be less clear. With a suggestion, patient values and preferences may be more variable, and this can influence the clinical decision that is ultimately made
Evidence Rating	**Definition**	

A	High-category evidence defined as being derived from well-conducted, randomized, controlled trials and meta-analyses.
B	Moderate-category evidence defined as being derived from nonrandomized studies (i.e. case series, retrospective cohort studies).
C	Low-category evidence that was formed from expert opinion.

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. JAMA. 2014;311(18):1889-900.	Systematic review and meta-analysis of the benefits and harms of medications for adults with alcohol use disorders. Literature search was conducted by searching PubMed, Cochrane Library, PsycINFO, CINAHL, EMBASE, FDA website, and clinical trials registries for literature published between January 1, 1970, to March 1, 2014. Studies that were included were RCTs with least 12 weeks' duration that reported eligible outcomes and head-to-head prospective cohort studies reporting health outcomes or harms. A total of 122 RCTs were included with 22,803 patients.	• Primary endpoints: Alcohol consumption (return to drinking), return to heavy drinking, drinking days, heavy drinking days (≥4 drinks per day for women; ≥5 for men), drinks per drinking day, accidents (i.e., motor vehicle crashes), injuries, quality of life, function, and mortality
Results: The number needed to treat (NNT) to prevent return to any drinking for acamprosate was 12 (95% CI 8 to 26; risk difference [RD] −0.09; 95% CI, −0.14 to −0.04) and was 20 (95% CI 11 to 500; RD −0.05; 95% CI −0.10 to −0.002) for oral naltrexone (50 mg/day). The NNT to prevent return to heavy drinking was 12 (95% CI 8 to 26; RD −0.09; 95% CI −0.13 to −0.04) for oral naltrexone. Meta-analyses of trials comparing acamprosate to naltrexone found no statistically significant difference between them for return to any drinking (RD 0.02; 95% CI −0.03 to 0.08) or heavy drinking (RD 0.01; 95% CI −0.05 to 0.06). For injectable naltrexone, meta-analyses found no association with return to any drinking (RD −0.04; 95% CI −0.10 to 0.03) or heavy drinking (RD −0.01; 95% CI −0.14 to 0.13) but found an association with reduction in heavy drinking days (weighted mean difference [WMD] −4.6%; 95% CI −8.5% to −0.56%). Among medications used off-label, moderate evidence supports an association with improvement in some consumption outcomes for topiramate. For naltrexone, numbers needed to harm (NNH) for withdrawal from trials due to adverse events were 48 (95% CI 30 to 112) and 12 (95% CI 7 to 50), respectively; risk was not significantly increased for acamprosate or topiramate. **Conclusion**: Both acamprosate and oral naltrexone were associated with reduction in return to drinking. When directly compared with one another, no significant differences were found between acamprosate and naltrexone for controlling alcohol consumption. Factors such as dosing frequency, potential adverse events, and availability of treatments may guide medication choice.		
Citation	**Design**	**Endpoints**
Miller PM, Book SW, Stewart SH. Medical treatment of alcohol dependence: a systematic review. Int J	Systematic review performed by searching MEDLINE, SCOPUS, CINAHL, Embase, and PsychINFO in August 2010. A search was conducted for RCTs published between January 1960 and August 2010 on pharmacologic treatments for alcohol dependence alone and in combination with brief	• Primary endpoint: Number of abstinence days

Psychiatry Med. 2011;42(3):227-66.	psychosocial therapies that may be feasible for primary care and specialty medical settings. A total of 85 RCTs were included with 18,937 patients.	

Results: The evidence base for oral naltrexone (6% more days abstinent than placebo in the largest study) and topiramate (e.g., 26.2% more days abstinent than placebo in study) is positive but modest. Acamprosate shows modest efficacy with recently abstinent patients, with European studies showing better results than U.S. ones. The evidence-base for disulfiram is equivocal. Depot naltrexone shows efficacy (25% greater reduction in rate of heavy drinking vs. placebo, in one of the largest studies) in a limited number of studies. Some studies suggest that patients do better with extensive psychosocial treatments added to medications while others show that brief support can be equally effective.
Conclusion: Although treatment effects are modest, medications for alcohol dependence, in conjunction with either brief support or more extensive psychosocial therapy, can be effective in primary and specialty care medical settings.

Citation	Design	Endpoints
Rösner S, Hackl-herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. Cochrane Database Syst Rev. 2010;(9):CD004332.	Systematic review performed by searching Cochrane Drugs and Alcohol Group (CDAG) Specialized Register, PubMed, EMBASE and CINAHL in January 2009. A search was conducted of all double-blind RCTs which compared the effects of acamprosate with placebo or active control on drinking-related outcomes. A total of 24 RCTs were included with 6,915 patients.	• Primary endpoints: Risk of any drinking, cumulative abstinence duration • Secondary endpoints: Heavy drinking days, gamma-glutamyltransferase

Results: Compared to placebo, acamprosate was shown to significantly reduce the risk of any drinking (RR 0.86 [95% CI 0.81 to 0.91]; NNT 9.09 [95% CI 6.66 to 14.28]) and to significantly increase the cumulative abstinence duration (10.94 [95% CI 5.08 to 16.81]), while secondary outcomes (gamma-glutamyltransferase, heavy drinking) did not reach statistical significance. Diarrhea was the only side effect that was more frequently reported under acamprosate than placebo.
Conclusion: Acamprosate appears to be an effective and safe treatment strategy for supporting continuous abstinence after detoxification in alcohol dependent patients. Even though the sizes of treatment effects appear to be rather moderate in their magnitude, they should be valued against the background of the relapsing nature of alcoholism and the limited therapeutic options currently available for its treatment.

Citation	Design	Endpoints
Rösner S, Hackl-herrwerth A, Leucht S, Vecchi S,	Systematic review performed by searching Cochrane Drugs and Alcohol Group (CDAG) Specialized Register, PubMed, EMBASE and CINAHL in January 2010. A	• Primary endpoints: Risk of heavy drinking, number of drinking days

Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database Syst Rev. 2010;(12):CD001867.	search was conducted of all double-blind randomized controlled trials (RCTs) which compared the effects of naltrexone with placebo or active control on drinking-related outcomes. A total of 50 RCTs were included with 7,793 patients.	• Secondary endpoints: Heavy drinking days, consumed amount of alcohol, gamma-glutamyltransferase, return to any drinking
Results: Naltrexone reduced the risk of heavy drinking to 83% of the risk in the placebo group (RR 0.83 [95% CI 0.76 to 0.90]) and decreased drinking days by about 4% (-3.89 [95% CI -5.75 to -2.04]). Significant effects were also demonstrated for heavy drinking days (- 3.25 [95% CI -5.51 to -0.99]), consumed amount of alcohol, (- 10.83 [95% CI -19.69 to -1.97]) and gamma-glutamyltransferase, (- 10.37 [95% CI -18.99 to -1.75]), while effects on return to any drinking missed statistical significance (RR 0.96 [95% CI 0.92 to 1.00]). Side effects of naltrexone were mainly gastrointestinal problems (e.g. nausea) and sedative effects (e.g. daytime sleepiness). **Conclusion**: Naltrexone appears to be an effective and safe strategy in alcoholism treatment. Even though the sizes of treatment effects might appear moderate in their magnitudes, these should be valued against the background of the relapsing nature of alcoholism and the limited therapeutic options currently available for its treatment.		

Formulary Placement, Utilization and Cost Experience (10-01-2024 to 12-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Anti-Alcoholic Preparations								
Disulfiram 250 mg, 500 mg oral tablets	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Acamprosate 333 mg delayed release (DR) oral tablet	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Opioid Antagonists								
Naltrexone 50 mg oral tablet	10	5	$440.07	$44.01	0	0 (0%)	F	No change
Vivitrol® (naltrexone) 380 mg intramuscular injection	0	0	$0.00	$0.00	0	0 (0%)	F	No change
TOTAL	10	5	$440.07	$44.01	0	0 (0%)		

Key (as applicable) F = Formulary, no restrictions; F-QL = Formulary, quantity limit applies; F-AL = Formulary, age limit applies; F-ST = Formulary, step therapy applies; F-PA = Formulary, PA required; NF = Non-formulary; X = Excluded

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Direct Oral Anticoagulants

Executive Summary

Class Overview

The direct oral anticoagulants (DOACs), sometimes referred to as non-vitamin K oral anticoagulants (NOACs), include the factor Xa inhibitors Xarelto® (rivaroxaban), Eliquis® (apixaban), and Savaysa® (edoxaban), along with the direct thrombin inhibitor Dabigatran (Pradaxa®). The terms DOAC and NOAC are used interchangeably in this document. The acronym DOAC is used preferentially, but the acronym NOAC is used when it was also used in the related guideline or study. All carry indications for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and reduction in the risk of stroke in non-valvular atrial fibrillation (NVAF). Additionally, rivaroxaban, apixaban, and dabigatran are indicated for the secondary prevention of venous thromboembolism (VTE) and thromboprophylaxis after hip or knee replacement surgery. Rivaroxaban also has additional indications for prophylaxis of VTE in acutely ill medical patients at risk for thromboembolic complications not at high risk of bleeding and for the long-term prevention of major adverse cardiovascular events in patients with coronary artery disease (CAD) and peripheral artery disease (PAD). Only rivaroxaban and dabigatran can be used in pediatric patients, specifically for VTE treatment and to reduce the risk of recurrent VTE. Rivaroxaban has an additional pediatric indication for thromboprophylaxis in children ages 2 years and older with congenital heart disease who have undergone the Fontan procedure.

The DOACs do not require bridging or routine dose adjustments based on lab values, but most are not recommended for use in renal failure and many require dose adjustment based on renal function. Dabigatran has an antidote called Praxbind® (idarucizumab), while Andexxa® (andexanet alfa) is an emergency reversal agent for rivaroxaban and apixaban.

A multitude of guidelines has been published related to oral anticoagulation. Guidelines authored by four different societies are included herein.

Utilization Findings

There were 134 claims for 61 members, for a total cost of $72,855.91 and an average cost per claim of $543.70. The most highly utilized medication was Eliquis, with 97 claims, followed by Xarelto with 32 claims. There were no prior authorization requests.

Recommendations

- No changes

Clinical Summary

The DOACs block major procoagulant activities involved in the generation of a fibrin clot, either through the inhibition of thrombin (which cleaves fibrinogen to fibrin, activates other procoagulant factors and activates platelets) or factor Xa (which works directly upstream to thrombin in the clotting cascade and cleaves prothrombin to thrombin). These products inactivate both circulating and clot-bound activated coagulation factors, and do not carry monitoring requirements or dietary restrictions like warfarin, which can make them a more convenient option for both prescribers and patients. However, they are not always the preferred option over more traditional agents such as warfarin or heparins (i.e., patients with prosthetic heart valves, pregnancy, and renal impairment) and still carry risks for major bleeding events like warfarin. The risk of bleeding episodes overall with warfarin and DOACs are low, and these agents may carry a slightly lesser risk of fatal bleeding events when compared to warfarin. In terms of efficacy, DOACs appear to be comparably effective (non-inferior) to warfarin and heparin products. The efficacy and safety of DOACs have never been compared directly with each other in a prospective, randomized clinical trial. Systematic reviews and retrospective observational data suggest similar efficacy between the DOACs, but apixaban may hold a safety advantage due to fewer observed bleeding episodes.

The American College of Chest Physicians (CHEST) has published various guidelines. In the treatment of VTE (DVT of the leg or PE) DOACs are preferred over warfarin. The same recommendation applies for the prevention of VTE in patients with atrial fibrillation (AF). The American Society of Clinical Oncology (ASCO) recommends DOACs as an option for anticoagulation in cancer care. The American Heart Association (AHA)/ American College of Cardiology (ACC)/Heart Rhythm Society (HRS) guidelines for the management of AF recommend NOACs over warfarin in eligible patients. American Society of Hematology (ASH) has also published several guidelines related to the management of VTE disease with oral anticoagulation. ASH guidelines suggest using DOACs over warfarin for the treatment of DVT/PE. In the prevention of VTE in patients undergoing total hip arthroplasty (THA) or total knee arthroplasty (TKA), DOACs are preferred over low-molecular-weight heparin (LMWH). ASH has also published VTE prophylaxis guidelines, however, they do not recommend the use of DOACs over LMWH.

There are a couple agents in the pipeline that are in Phase 3 trials, however, it's unclear when a new drug application (NDA) will be submitted for them. The first is tecarfarin, which is similar to warfarin, but is metabolized through the esterase pathway thereby avoiding the CYP-450 drug interactions which complicate warfarin management and is touted to potentially have a flatter dose-response curve than warfarin. Additionally, there are two factor XIa inhibitors, milvexian and asundexian that are in Phase 3 trials. Factor XIa inhibitors are a new class of drug. Early studies show that inhibiting factor XIa seems to provide the same anticoagulant properties of current DOACs and may have a reduced risk for bleeding. Finally, abelacimab is a dual-acting monoclonal antibody targeting both factor XI and factor XIa and also has the potential of exhibiting a minimal effect on hemostasis or risk for bleeding.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
Factor Xa Inhibitors		
Eliquis® (apixaban)	To reduce the risk of stroke and systemic embolism (SE) in patients with NVAF	5 mg orally twice daily; reduce dose to 2.5 mg orally twice daily if patient has at least 2 of the following characteristics: - Age ≥ 80 years - Body weight ≤ 60 kg - Serum creatinine ≥ 1.5 mg/dL
	DVT and/or PE treatment	10 mg orally twice daily for 7 days, followed by 5 mg orally twice daily
	Reduction in the risk of recurrent DVT and/or PE following initial therapy	2.5 mg orally twice daily after at least 6 months of treatment for DVT and/or PE
	Prophylaxis of DVT, which may lead to PE in patients who have undergone hip or knee replacement surgery	Knee replacement: 2.5 mg orally twice daily for 12 days Hip replacement: 2.5 mg orally twice daily for 35 days
Xarelto® (rivaroxaban)	To reduce the risk of stroke and SE in patients with NVAF	20 mg orally once daily with evening meal; if CrCl ≤ 50 mL/min reduce dose to 15 mg orally once daily with evening meal
	DVT and/or PE treatment	15 mg orally twice daily with food for 21 days, followed by 20 mg orally once daily with food For patients <18 years of age dosing varies based on weight and ranges from 2.4 mg to 20 mg per day; use is not recommended in children less than 6 months of age with any of the following: - Less than 37 weeks of gestation at birth - Less than 10 days of oral feeding - Body weight of less than 2.6 kg
	Reduction in the risk of recurrence of DVT and/or PE in adults at continued risk after completion of initial 6-month treatment	10 mg orally once daily after at least 6 months of standard anticoagulant treatment
	Prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery	Knee replacement: 10 mg orally once daily for 12 days Hip replacement: 10 mg orally once daily for 35 days
	Prophylaxis of VTE and VTE-related death during hospitalization and post hospital discharge in adults admitted for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and	10 mg orally once daily in hospital and after hospital discharge, for a total recommended duration of 31 to 39 days

Medication	Indications	Dosing/Administration
	other risk factors for VTE and not at high risk of bleeding	
	To reduce the risk of major cardiovascular (CV) events (CV death, myocardial infarction [MI] and stroke) in patients with CAD	2.5 mg orally twice daily in combination with aspirin (ASA) 75-100 mg once daily
	To reduce the risk of major thrombotic vascular events (myocardial infarction, ischemic stroke, acute limb ischemia, and major amputation of a vascular etiology) in patients with PAD, including patients who have recently undergone a lower extremity revascularization procedure due to symptomatic PAD	2.5 mg orally twice daily in combination with ASA 75-100 mg once daily; when starting therapy after a successful lower extremity revascularization procedure, initiate once hemostasis has been established
	Reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years after at least 5 days of initial parenteral anticoagulant treatment	Dosing varies by weight and ranges from 2.4 mg to 20 mg per day; use is not recommended in children less than 6 months of age with any of the following: - Less than 37 weeks of gestation at birth - Less than 10 days of oral feeding - Body weight of less than 2.6 kg
	Thromboprophylaxis in pediatric patients aged 2 years and older with congenital heart disease who have undergone the Fontan procedure	Dosing varies by weight and ranges from 2.2 mg to 20 mg per day
Savaysa® (edoxaban)	To reduce the risk of stroke and SE in patients with NVA	60 mg orally once daily in patients with CrCl >50 to ≤ 95 mL/min; reduce dose to 30 mg orally once daily in patients with CrCl 15 to 50 mL/min; do not use in patients with CrCl > 95 mL/min
	DVT and/or PE treatment following 5 to 10 days of initial therapy with a parenteral anticoagulant	60 mg orally once daily in patients with CrCl >50 to ≤ 95 mL/min; reduce dose to 30 mg orally once daily for patients with CrCl 15 to 50 mL/min, patients who weigh ≤ 60 kg, or patients who use certain P-gp inhibitors
Direct Thrombin Inhibitors		
Dabigatran (Pradaxa®)	To reduce the risk of stroke and systemic embolism (SE) in patients with NVAF	150 mg orally twice daily for patients with CrCl > 30 mL/min; 75 mg orally twice daily for patients with CrCl 15 to 30 mL/min
	DVT and/or PE treatment in patients who have been treated with a parenteral anticoagulant for 5-10 days	150 mg orally twice daily after 5-10 days of parenteral anticoagulation for patients with CrCl >30 mL/min For patients ≥3 months to <18 years of age dosing varies based on weight

Medication	Indications	Dosing/Administration
	To reduce the risk of recurrence of DVT and PE in previously treated patients	150 mg orally twice daily after previous treatment for patients with CrCl >30 mL/min For patients ≥3 months to <18 years of age dosing varies based on weight
	Prophylaxis of DVT and PE in patients who have undergone hip replacement surgery	110 mg orally on first day, then 220 mg orally once daily for patients with CrCl >30 mL/min

Boxed Warnings and Contraindications

Medication	Boxed Warnings	Contraindications
Factor Xa Inhibitors		
Eliquis® (apixaban) Xarelto® (rivaroxaban)	**Premature Discontinuation:** Increased risk of thrombotic events with premature discontinuation **Spinal/Epidural Hematomas:** Spinal or epidural hematomas may occur with neuraxial anesthesia or spinal puncture in patients who are anticoagulated resulting in long-term or permanent paralysis	- Active pathological bleeding - Severe hypersensitivity to product
Savaysa® (edoxaban)	**Reduced Efficacy in NVAF Patients with CrCl >95 mL/minute:** Edoxaban should not be used in patients with CrCl >95 mL/minute; an increased rate of ischemic stroke with edoxaban 60 mg compared to warfarin was observed **Premature Discontinuation:** Increased risk of ischemic events with premature discontinuation **Spinal/Epidural Hematomas:** Spinal or epidural hematomas may occur with neuraxial anesthesia or spinal puncture in patients who are anticoagulated resulting in long-term or permanent paralysis	
Direct Thrombin Inhibitors		
Dabigatran (Pradaxa®)	**Premature Discontinuation:** Increased risk of thrombotic events with premature discontinuation **Spinal/Epidural Hematomas:** Spinal or epidural hematomas may occur with neuraxial anesthesia or spinal puncture in patients who are anticoagulated resulting in long-term or permanent paralysis	- Active pathological bleeding - History of serious hypersensitivity reaction to product - Mechanical prosthetic heart valve

Warnings/Precautions

Medication	Warnings/Precautions
Factor Xa Inhibitors	
Eliquis® (apixaban)	- Bleeding: Apixaban can cause serious, potentially fatal, bleeding; promptly evaluate signs and symptoms of blood loss; an agent to reverse the anti-factor Xa activity of apixaban is available - Prosthetic heart valves: Apixaban use not recommended - Increased risk of thrombosis in patients with triple-positive antiphospholipid syndrome: Apixaban use not recommended
Xarelto® (rivaroxaban)	- Risk of bleeding: Rivaroxaban can cause serious and fatal bleeding; an agent to reverse the activity of rivaroxaban is available - Pregnancy-related hemorrhage: Use rivaroxaban with caution in pregnant women due to the potential for obstetric hemorrhage and/or emergent delivery - Prosthetic heart valves: Rivaroxaban use not recommended - Increased risk of thrombosis in patients with triple-positive antiphospholipid syndrome: Rivaroxaban use not recommended
Savaysa® (edoxaban)	- Bleeding: Serious and potentially fatal bleeding; promptly evaluate signs and symptoms of blood loss - Mechanical heart valves or moderate to severe mitral stenosis (MS): Edoxaban use not recommended - Increased risk of thrombosis in patients with triple-positive antiphospholipid syndrome: Edoxaban use not recommended
Direct Thrombin Inhibitors	
Dabigatran (Pradaxa®)	- Bleeding: Dabigatran can cause serious and fatal bleeding - Bioprosthetic heart valves: Dabigatran use not recommended - Increased risk of thrombosis in patients with triple-positive antiphospholipid syndrome: Dabigatran use not recommended

Practice Guidelines

American College of CHEST Physicians

Stevens SM, Woller SC, Kreuziger LB, et al. Antithrombotic therapy for VTE disease: second update of the chest guideline and expert panel report. Chest. 2021;160(6):e545-e608.

- In patients with VTE (DVT of the leg or PE) we recommend apixaban, dabigatran, edoxaban, or rivaroxaban over VKA as treatment-phase (first 3 months) anticoagulant therapy (Strong recommendation, moderate quality evidence).
- In patients with acute VTE in the setting of cancer (cancer-associated thrombosis) we recommend an oral Xa inhibitor (apixaban, edoxaban, rivaroxaban) over LMWH for the initiation and treatment phases of therapy (Strong recommendation, moderate quality evidence).
- In patients with confirmed antiphospholipid syndrome being treated with anticoagulant therapy, we suggest adjusted dose VKA (target INR 2.5) over DOAC therapy during the treatment phase (Weak recommendation, low quality evidence).
- In patients with superficial venous thrombosis (SVT) who refuse or are unable to use parenteral anticoagulation, we suggest rivaroxaban 10 mg daily as a reasonable alternative for fondaparinux 2.5 mg daily (Weak recommendation, low quality evidence).
- In patients with VTE diagnosed in the absence of transient risk factor (unprovoked VTE or provoked by a persistent risk factor) who cannot receive a DOAC, we suggest offering extended-phase anticoagulation with a VKA (Weak recommendation, moderate quality evidence).
- In patients offered extended-phase anticoagulation, we suggest the use of reduced-dose apixaban or rivaroxaban over full-dose apixaban or rivaroxaban (Weak recommendation, very low quality evidence).
- In patients offered extended-phase anticoagulation, we recommend reduced-dose DOAC over aspirin or no therapy (Strong recommendation, low quality evidence) and suggest rivaroxaban over aspirin (Weak recommendation, moderate quality evidence).

Recommendation Definitions- Table 1

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Strength of Supporting Evidence	Implications
Strong recommendation, high quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	We are very confident that the true effect lies close to that of the estimate of the effect	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Recommendation can apply to most patients in most circumstances. Higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect	Recommendation can apply to most patients in many circumstances. Higher quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate

Grade of Recommendation	Benefit vs. Risk and Burdens	Methodologic Strength of Supporting Evidence	Implications
Strong recommendation, very low quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect	Recommendation can apply to most patients in many circumstances. Higher quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak (conditional) recommendation, high quality evidence	Benefits closely balanced with risks and burden	We are very confident that the true effect lies close to that of the estimate of the effect	The best action may differ depending on circumstances or patients' or societal values. Further research is very unlikely to change our confidence in the estimate of effect
Weak (conditional) recommendation, moderate quality evidence	Benefits closely balanced with risks and burden	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Best action may differ depending on circumstances or patients' or societal values. Higher quality research may well have an important impact on our confidence in the estimate of effect and may change the estimate
Weak (conditional) recommendation, low quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk and burden may be closely balanced	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect	Other alternatives may be equally reasonable. Higher quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Weak (conditional) recommendation, very low quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk and burden may be closely balanced	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect	Other alternatives may be equally reasonable. Higher quality research is likely to have an important impact on our confidence in the estimate of effect and may well change the estimate
Ungraded Consensus Based Statement	Uncertainty due to lack of evidence but expert opinion that benefits outweigh risk and burdens or vice versa	Insufficient evidence for a graded recommendation	Future research may well have an important impact on our confidence in the estimate of effect and may change the estimate

Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. Chest. 2018 Nov;154(5):1121-1201. doi: 10.1016/j.chest.2018.07.040.

- For patients with AF, we recommend against antiplatelet therapy alone (monotherapy or ASA in combination with clopidogrel) for stroke prevention alone, regardless of stroke risk (Strong recommendation, moderate quality evidence).
- In patients with AF who are eligible for oral anticoagulation (OAC), we recommend NOACs over vitamin K antagonist (VKA) (Strong recommendation, moderate quality evidence).
- In patients with prior unprovoked bleeding, warfarin-associated bleeding, or at high risk of bleeding, we suggest using apixaban, edoxaban, or dabigatran 110 mg (where available) as all demonstrate significantly less major bleeding compared with warfarin (Weak recommendation, very low quality evidence).
- For patients with AF of > 48 h or unknown duration undergoing elective electrical or pharmacologic cardioversion, we recommend therapeutic anticoagulation with well-managed VKA (INR 2-3) or an NOAC using dabigatran, rivaroxaban, edoxaban, or apixaban for at least 3 weeks before cardioversion or a transesophageal

echocardiography (TEE)-guided approach with abbreviated anticoagulation before cardioversion rather than no anticoagulation (Strong recommendation, moderate quality evidence).

- For patients with AF of > 48 hours or unknown duration undergoing elective electrical or pharmacologic cardioversion, we recommend therapeutic anticoagulation (with VKA or NOAC) for at least 4 weeks after successful cardioversion to sinus rhythm rather than no anticoagulation, regardless of the baseline risk of stroke (Strong recommendation, moderate quality evidence).
- For patients with AF and hemodynamic instability undergoing urgent cardioversion (electrical or pharmacologic), after successful cardioversion to sinus rhythm, we suggest therapeutic anticoagulation (with VKA or full adherence to NOAC therapy) for at least 4 weeks rather than no anticoagulation, regardless of baseline stroke risk (Weak recommendation, low quality evidence).
- In AF patients requiring OAC undergoing elective percutaneous coronary intervention (PCI)/stenting,
    - where bleeding risk is low (HAS-BLED 0-2) relative to risk for recurrent acute coronary syndrome (ACS) and/or stent thrombosis, we suggest triple therapy for 1-3 months, followed by dual therapy with OAC plus single antiplatelet (preferably clopidogrel) until 12 months, following which OAC monotherapy can be used (Weak recommendation, low quality evidence).
    - where bleeding risk is high (HAS-BLED ≥ 3), we suggest triple therapy for 1 month, followed by dual therapy with OAC plus single antiplatelet (preferably clopidogrel) for 6 months, following which OAC monotherapy can be used (Weak recommendation, low quality evidence).
    - where bleeding risk is unusually high and thrombotic risk relatively low, we suggest use of OAC plus single antiplatelet (preferably clopidogrel) for 6 months, following which OAC monotherapy can be used (Weak recommendation, low quality evidence).
- In AF patients requiring OAC presenting with an ACS, undergoing PCI/stenting,
    - where bleeding risk is low (HAS-BLED 0-2) relative to risk for ACS or stent thrombosis, we suggest triple therapy for 6 months, followed by dual therapy with OAC plus single antiplatelet (preferably clopidogrel) until 12 months, following which OAC monotherapy can be used (Weak recommendation, low quality evidence).
    - where bleeding risk is high (HAS-BLED ≥ 3), we suggest triple therapy for 1-3 months, followed by dual therapy with OAC plus single antiplatelet (preferably clopidogrel) up to 12 months, following which OAC monotherapy can be used (Weak recommendation, low quality evidence).
    - where bleeding risk is unusually high and thrombotic risk low, we suggest OAC plus single antiplatelet (preferably clopidogrel) for 6-9 months, following which OAC monotherapy can be used (Weak recommendation, low quality evidence).
- In AF patients with ACS or undergoing PCI in whom OAC is recommended, we suggest using VKA with time in therapeutic range (TTR) > 65-70% (INR range 2.0-3.0), or to use an NOAC at a dose licensed for stroke prevention in AF (Weak recommendation, low quality evidence)
- In AF patients in which ASA is concomitantly used with OAC, we suggest a dose of 75-100 mg QD with concomitant use of proton pump inhibitor (PPI) to minimize gastrointestinal (GI) bleeding (Weak recommendation, low quality evidence).
- In AF patients in which a P2Y12 inhibitor is concomitantly used with OAC, we suggest the use of clopidogrel (Weak recommendation, low quality evidence).
- For patients with AF and stable coronary artery disease (e.g., no ACS within the previous year) and who choose oral anticoagulation, we suggest OAC with either an NOAC or adjusted dose VKA therapy alone (target INR range, 2.0-3.0) rather than the combination of OAC and ASA (Weak recommendation, low quality evidence).

- In AF patients with acute stroke without contraindications, we recommend that long-term oral anticoagulation is indicated as secondary prevention (Strong recommendation, high quality evidence).
- In patients with AF and high ischemic stroke risk, we suggest anticoagulation with an NOAC after acute spontaneous intracranial hemorrhage (ICH) (which includes subdural, subarachnoid, and intracerebral hemorrhages) after careful consideration of the risks and benefits (Ungraded consensus-based statement).
- In patients with AF and symptomatic carotid stenosis (> 50%), we suggest carotid revascularization with endarterectomy or stenting in addition to OAC as indicated (Weak recommendation, moderate quality evidence).
- In patients with AF and carotid stenosis treated with revascularization, we suggest OAC therapy, without long-term antiplatelet therapy (Ungraded consensus-based statement).
- In patients with AF, we suggest prescription of oral anticoagulants could be considered as a result of an individualized clinical assessment taking into account overall atrial high-rate episode (AHRE) burden (in the range of hours rather than minutes) and specifically, the presence of AHRE > 24 h, individual stroke risk (using CHA_2DS_2-VASc), predicted risk benefit of oral anticoagulation and informed patient preferences (Ungraded consensus-based statement).
- For patients with atrial flutter, we suggest that antithrombotic therapy decisions follow the same risk-based recommendations as for AF (Ungraded consensus-based statement).
- For women receiving OAC for prevention of stroke/thromboembolism (TE) in AF who become pregnant, we suggest discontinuation of OAC with a VKA between weeks 6 and 12 and replacement by LMWH BID (with dose adjustment according to weight and target antiXa level 4-6 h post-dose 0.8-1.2 U/mL), especially in patients with a warfarin dose required of > 5 mg/day. OAC should then be discontinued and replaced by adjusted-dose LMWH (target anti-Xa level 4-6 h post-dose 0.8-1.2 U/mL) in the 36th week of gestation (Ungraded consensus-based statement).
- For women on treatment with long-term VKAs who are attempting pregnancy and are candidates for LMWH substitution, we suggest performing frequent pregnancy tests and use LMWH instead of VKA when pregnancy is achieved rather than switching to LMWH while attempting pregnancy (Ungraded consensus-based statement).
- For pregnant women, we suggest avoiding the use of NOACs (Ungraded consensus-based statement).
- For lactating women using warfarin or unfractionated heparin (UFH) who wish to breast-feed, we suggest continuing the use of warfarin, LMWH, or UFH (Ungraded consensus-based statement).
- For breast-feeding women, we suggest alternative anticoagulants rather than NOACs (Ungraded consensus-based statement).
- For moderate CKD (Stage III, CrCl 30-59 mL/min), we suggest oral anticoagulation in patients with a CHA_2DS_2-VASc ≥ 2 with label-adjusted NOACs or dose-adjusted VKAs (Weak recommendation, very low quality evidence).
- In severe non-dialysis CKD (Stage IV CrCl 15-30 mL/min), we suggest using VKAs and selected NOACs (rivaroxaban 15 mg QD, apixaban 2.5 mg BID, edoxaban 30 mg QD, and dabigatran 75 mg BID) with caution, based on pharmacokinetic data (Ungraded consensus-based statement).
- In end-stage renal disease (CrCl < 15 mL/min or dialysis-dependent, we suggest using well-managed VKA with TTR > 65-70% (Ungraded consensus-based statement).
  Remark: NOACs should generally not be used, although in USA, apixaban 5 mg BID is approved for use in AF patients receiving hemodialysis.
  Remark: In patients with CKD who initiate OAC, concomitant antiplatelet therapy including low-dose ASA is likely to substantially elevate bleeding risk and should be used very judiciously.

- In AF patients at risk of ischemic stroke undergoing cardiac surgery, we suggest surgical exclusion of the left atrial appendage for stroke prevention, but the need for long-term OAC is unchanged (Weak recommendation, low quality evidence).

Recommendation Definitions – see Table 1

American Society of Clinical Oncology (ASCO)

Key NS, Khorana AA, Kuderer NM, et al. Venous Thromboembolism Prophylaxis and Treatment in Patients with Cancer: ASCO Guideline Update. J Clin Oncol. 2023;41(16):3063-3071.

- High-risk outpatients with cancer (Khorana score ≥ 2 prior to starting a new systemic chemotherapy regimen) may be offered thromboprophylaxis with apixaban, rivaroxaban, or LMWH provided there are no significant risk factors for bleeding and no drug interactions. Consideration of such therapy should be accompanied by a discussion with the patient about the relative benefits and harms, drug cost, and duration of prophylaxis in this setting (Type: Evidence based; Evidence quality: Intermediate to High for apixaban and rivaroxaban, Intermediate for LMWH; Strength of recommendation: Moderate).
- Initial anticoagulation may involve LMWH, UFH, fondaparinux, rivaroxaban, or apixaban. For patients initiating treatment with parenteral anticoagulation, LMWH is preferred over UFH for the initial 5-10 days of anticoagulation for the patient with cancer with newly diagnosed VTE who does not have severe renal impairment (defined as creatinine clearance <30 mL/min; Type: Evidence based; Evidence quality: High; Strength of recommendation: Strong).
- For long-term anticoagulation, LMWH, edoxaban, rivaroxaban, or apixaban for at least 6 months are preferred over VKAs because of improved efficacy. VKAs may be used if LMWH or direct factor Xa inhibitors are not accessible. There is reduction in recurrent thrombosis but an increase in clinically relevant nonmajor bleeding risk with direct factor Xa inhibitors compared with LMWH. Caution with direct factor Xa inhibitors is warranted in GI and genitourinary malignancies and other settings with high risk for mucosal bleeding. Drug-drug interaction should be checked before using a direct factor Xa inhibitor (Type: Evidence based; Evidence quality: High; Strength of recommendation: Strong).
- Anticoagulation with LMWH, direct factor Xa inhibitors, or VKAs beyond the initial 6 months should be offered to select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy. Anticoagulation beyond 6 months needs to be assessed on an intermittent basis to ensure a continued favorable risk-benefit profile (Type: Informal consensus; Evidence quality: Low; Strength of recommendation: Weak to Moderate).
- For patients with primary or metastatic central nervous system (CNS) malignancies and established VTE, anticoagulation as described for other patients with cancer should be offered, although uncertainties remain about choice of agents and selection of patients most likely to benefit (Type: Informal consensus; Quality of evidence: Low; Strength of recommendation: Moderate).

Recommendation Definitions- Table 2A

Type of Recommendation	Definition
Evidence Based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal Consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., “strong,”

Type of Recommendation	Definition
	"moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in an online data supplement.
Informal Consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No Recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Recommendation Definitions- Table 2B

Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on: a) strong evidence for a true net effect (e.g., benefits exceed harms); b) consistent results, with no or minor exceptions; c) minor or no concerns about study quality; and/or d) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on: a) good evidence for a true net effect (e.g., benefits exceed harms); b) consistent results, with minor and/or few exceptions; c) minor and/or few concerns about study quality; and/or d) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on: a) limited evidence for a true net effect (e.g., benefits exceed harms); b) consistent results, but with important exceptions; c) concerns about study quality; and/or d) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Recommendation Definitions- Table 2C

Quality of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (e.g., balance of benefits versus harms) and further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Intermediate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect, however it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change the magnitude and/or direction of this net effect
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. Reliance on consensus opinion of experts may be reasonable to provide guidance on the topic until better evidence is available.

American College of Cardiology (ACC)/American Heart Association (AHA)/Heart Rhythm Society (HRS)

January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. Circulation. 2019 Jul 9;140(2):e125-e151.

Risk-Based Anticoagulant Therapy Recommendations

- Patients with AF and an elevated CHA_2DS_2-VASc score ≥ 2 in men and ≥ 3 in women, oral anticoagulants are recommended. Options include: warfarin (Class 1 Level A), dabigatran, rivaroxaban, apixaban (Class I, Level B), or edoxaban (Class I, Level B-R)
- NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe MS or a mechanical heart valve) (Class I, Level A)
- Patients with AF who have mechanical heart valves, warfarin is recommended (Class I, Level B)
- Patients with AF (except with moderate-to-severe MS or a mechanical heart valve) who are unable to maintain a therapeutic INR level, use of a DOAC is recommended. (Class I, Level C-EO)
- Patients with AF who have a CHA_2DS_2-VASc score of ≥ 2 in men or ≥ 3 in women and who have end-stage CKD or on dialysis, it might be reasonable to prescribe warfarin or apixaban (Class IIb, Level B-NR)
- Dabigatran, rivaroxaban, and edoxaban are not recommended in patients with AF and end-stage CKD or on dialysis (Class III: No benefit, Level C-EO).
- Dabigatran should not be used in patients with AF and a mechanical heart valve (Class III: Harm, Level B-R).

Specific Patient Groups and AF

- In patients with AF at increased risk of stroke (based on CHA_2DS_2-VASc risk score of ≥ 2) who have undergone PCI with stenting for acute coronary ACS, double therapy with P2Y12 inhibitors (clopidogrel) and low-dose rivaroxaban 15 mg daily is reasonable to reduce the risk of bleeding as compared with triple therapy. (Class IIa, Level B-R)
- In patients with AF at increased risk of stroke (based on CHA_2DS_2-VASc risk score of ≥ 2) who have undergone PCI with stenting for ACS, double therapy with a P2Y12 inhibitor (clopidogrel) and dabigatran 150 mg BID is reasonable to reduce the risk of bleeding as compared with triple therapy. (Class IIa, Level B-R)

Recommendation Definitions-Table 3A

Class (Strength) of Recommendation (COR)		Recommendation Phrases

Class I (Strong)	Benefit >>> Risk	• Is recommended
		• Is indicated/useful/effective/beneficial
		• Should be performed/administered/other
		• Comparative-effectiveness phrases†
		  ○ Treatment/strategy A is recommended/indicated in preference to treatment B
		  ○ Treatment A should be chosen over treatment B

Class IIa (Moderate)	Benefit >> Risk	• Is reasonable
		• Can be useful/effective/beneficial
		• Comparative-effectiveness phrases†
		  ○ Treatment/strategy A is probably recommended/indicated in preference to treatment B
		  ○ It is reasonable to choose treatment A over treatment B

Class (Strength) of Recommendation (COR)		Recommendation Phrases
Class IIb (Weak)	Benefit ≥ Risk	• May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain
Class III: No benefit (Moderate) (*Generally, LOE A or B use only*)	Benefit = Risk	• Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other
Class III: Harm (Moderate)	Risk > Benefit	• Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other

Recommendation Definitions-Table 3B

Level (Quality) of Evidence‡ (LOE)	Definition
Level A	• High-quality evidence‡ from more than 1 randomized controlled trial (RCT) • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies
Level B-R (Randomized)	• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs
Level B-NR (Non-randomized)	• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies
Level C-LD (Limited data)	• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects
Level C-EO (Expert opinion)	• Consensus of expert opinion based on clinical experience

COR and LOE are determined independently

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinic consensus that a particular test or therapy is useful or effective.

**The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).*

†For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews the incorporation of an Evidence Review Committee.

Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021; 143(5):e35-e71.

- Anticoagulation with a VKA is indicated for patients with rheumatic MS and AF. (Class I, Level C-EO)
- For patients with new-onset AF ≤3 months after surgical or transcatheter biprosthetic valve replacement, anticoagulation with VKA is reasonable. (Class IIa, Level B-NR)
- It is reasonable to use a DOAC as an alternative to a VKA in patients with AF and native valve disease and should be administered on the basis of the patient's CHA2DS2-VASc score. (Class I, Level A)

Recommendation Definitions – see Table 3A and Table 3B

American Society of Hematology (ASH)

Ortel TL, Neumann I, Ageno W, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv. 2020;4(19):4693-4738.

- For patients with DVT and/or PE, the ASH guideline panel suggests using DOACs over VKA (conditional recommendation, moderate certainty in the evidence of effects ⨁⨁⨁◯).
- For patients with DVT and/or PE, the ASH guideline panel does not suggest 1 DOAC over another (conditional recommendation, very low certainty in the evidence of comparative effects ⨁◯ ◯ ◯).
- For patients with DVT and/or PE who have completed primary treatment and will continue with a DOAC for secondary prevention, the ASH guideline panel suggests using a standard-dose DOAC or a lower-dose DOAC (conditional recommendation, moderate certainty in the evidence of effects ⨁⨁⨁◯).
- For patients with breakthrough DVT and/or PE during therapeutic VKA treatment, the ASH guideline panel suggests using LMWH over DOAC therapy (conditional recommendation, very low certainty in the evidence of effects ⨁◯ ◯ ◯).

Recommendation Definitions- Table 4A

Strength of Recommendation	Interpretation
Strong	• For patients: Most individuals in this situation would want the recommended course of action, and only a small proportion would not. • For clinicians: Most individuals should follow the recommended course of action. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences. • For policy makers: The recommendation can be adopted as policy in most situations. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. • For researchers: The recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide important information that alters the recommendations.
Conditional	• For patients: The majority of individuals in this situation would want the suggested course of action, but many would not. Decision aids may be useful in helping patients to make decisions consistent with their individual risks, values, and preferences. • For clinicians: Different choices will be appropriate for individual patients, and clinicians must help each patient arrive at a management decision consistent with the patient's values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their individual risks, values, and preferences. • For policy makers: Policy-making will require substantial debate and involvement of various stakeholders. Performance measures should assess whether decision-making is duly documented. • For researchers: This recommendation is likely to be strengthened (for future updates or adaptation) by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations) that determined the conditional (rather than strong) recommendation will help identify possible research gaps.

Recommendation Definitions-Table 4B

Quality of Evidence	Symbol	Definition^
High	⨁⨁⨁⨁	Further research is very unlikely to change our confidence in the estimate of effect

Quality of Evidence	Symbol	Definition^
Moderate	⨁⨁⨁◯	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	⨁⨁◯◯	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	⨁◯◯◯	Any estimate of effect is very uncertain

^From the GRADE series of papers.

Witt DM, Nieuwlaat R, Clark NP, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy. Blood Adv (2018) 2 (22): 3257-3291.

- For patients requiring administration of inhibitors or inducers of P-glycoprotein (P-gp) or strong inhibitors or inducers of CYP-450 enzymes, the ASH guideline panel suggests using an alternative anticoagulant (such as VKA or LMWH) rather than a DOAC for the treatment of VTE (conditional recommendation, low certainty in the evidence about effects ⨁◯ ◯ ◯).
- For patients receiving DOAC therapy for the treatment of VTE, the ASH guideline panel suggests against measuring the DOAC anticoagulant effect during management of bleeding (conditional recommendation, very low certainty in the evidence about effects ⨁◯ ◯ ◯).
- For patients transitioning from DOAC to VKA, the ASH guideline panel suggests overlapping DOAC and VKA therapy until the INR is within the therapeutic range over using LMWH or UFH “bridging therapy” (conditional recommendation, very low certainty in the evidence about effects ⨁◯ ◯ ◯).

Recommendation Definitions – see Table 4A and Table 4B

Anderson DR, Morgano GP, Bettett C, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. Blood Adv (2019) 3 (23): 3898–3944.

- For patients undergoing total hip arthroplasty or total knee arthroplasty in which anticoagulants are used, the ASH guideline panel suggests using DOACs over LMWH (conditional recommendation, moderate certainty in the evidence of effects ⨁⨁⨁◯).
- For patients undergoing surgery, the ASH guideline panel suggests using any of the DOACs approved for use (conditional recommendation, low certainty in the evidence of effects ⨁⨁◯◯).
- For patients undergoing total hip arthroplasty or total knee arthroplasty, if a DOAC is not used, the ASH guideline panel suggests using LMWH rather than warfarin (conditional recommendation based on very low certainty in the evidence of effects ⨁◯◯◯).
- For patients undergoing total hip arthroplasty or total knee arthroplasty, if a DOAC is not used, the ASH guideline panel suggests using LMWH rather than UFH (strong recommendation, moderate certainty in the evidence of effects ⨁⨁⨁◯).

Recommendation Definitions – see Table 4A and Table 4B

Schünemann HJ, Cushman M, Burnett AE, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. Blood Adv (2018) 2 (22): 3198-3225.

- In acutely ill hospitalized medical patients, the ASH guideline panel *recommends* using LMWH over DOACs for VTE prophylaxis (strong recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯).
- In acutely ill hospitalized medical patients, the ASH guideline panel recommends inpatient VTE prophylaxis with LMWH only, rather than inpatient and extended-duration outpatient VTE prophylaxis with DOACs (strong recommendation, moderate certainty in the evidence of effects ⊕⊕⊕◯). Remark: If patients are on a DOAC for other reasons, this recommendation may not apply.

Recommendation Definitions – see Table 4A and Table 4B

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Ingason AB, Hreinsson JP, Ágústsson AS, et al. Rivaroxaban is associated with higher rates of gastrointestinal bleeding than other direct oral anticoagulants: a nationwide propensity score-weighted study. Ann Intern Med. 2021;174(11):1493-1502.	Nationwide population-based cohort study to compare rates of gastrointestinal bleeding (GIB) among apixaban, dabigatran, and rivaroxaban. Study population consisted of patients in the Icelandic Medicine Registry who filled a prescription for apixaban, dabigatran, or rivaroxaban from 1 March 2014 to 28 February 2019. Patients were excluded from the study if they had filled an oral anticoagulant prescription in the preceding 12 months, had end-stage renal disease, a mechanical heart valve, or mitral valve stenosis, had permanent residence outside Iceland, or were receiving 2.5 mg of rivaroxaban. Overall, 2157 patients receiving apixaban, 494 patients receiving dabigatran, and 3217 patients receiving rivaroxaban were compared.	• Clinically relevant GIB, defined as bleeding leading to medical intervention, unscheduled physician contact, or temporary treatment cessation • Clinically relevant upper or lower GIB • Major GIB
Results: For all patients, rivaroxaban had higher overall rates of GIB (3.2 vs. 2.5 events per 100 person-years; hazard ratio [HR], 1.42 [95% CI, 1.04 to 1.93]) and major GIB (1.9 vs. 1.4 events per 100 person-years; HR, 1.50 [95% CI, 1.00 to 2.24]) compared with apixaban. Rivaroxaban also had higher GIB rates than dabigatran, with similar point estimates, although the CIs were wider and included the possibility of a null effect. When only patients with atrial fibrillation were included, rivaroxaban was associated with higher rates of overall GIB than apixaban (HR, 1.40 [95% CI, 1.01 to 1.94]) or dabigatran (HR, 2.04 [95% CI, 1.17 to 3.55]). Dabigatran was associated with lower rates of upper GIB than rivaroxaban in both analyses. **Conclusion:** Rivaroxaban was associated with higher GIB rates than apixaban and dabigatran regardless of treatment indication.		
Citation	**Design**	**Endpoints**
Van Ganse E, Danchin N, Mahé I, et al. Comparative safety and effectiveness of oral anticoagulants in nonvalvular atrial fibrillation: the NAXOS study. Stroke. 2020;51(7):2066-2075.	Observational study using French National Health System claims data to compare the safety, effectiveness, and mortality of apixaban with VKAs, rivaroxaban, and dabigatran, in oral anticoagulant-naive patients with NVAF. Study population consisted of all patients aged ≥18 years with ≥1 reimbursement for oral anticoagulant treatments (VKAs, apixaban, rivaroxaban, or dabigatran) between January 2014 and December 2016. Patients with several oral anticoagulant treatments, multiple doses or multiple prescribers at the initiation date, and patients possibly treated for indications other than stroke prevention in NVAF were excluded. Overall, 321,501 patients were analyzed, of whom 35.0%, 27.2%, 31.1%, and 6.6% initiated VKAs, apixaban, rivaroxaban, and dabigatran, respectively.	• Major bleeding events leading to hospitalization (safety) • Stroke and systemic thromboembolic events (efficacy) • All-cause mortality
Results: Apixaban was associated with a lower risk of major bleeding compared with VKAs (HR, 0.43 [95% CI, 0.40–0.46]) and rivaroxaban (HR, 0.67 [95% CI, 0.63–0.72]), but not dabigatran (HR, 0.93 [95% CI, 0.81–1.08]). Apixaban was associated with a lower risk of stroke and systemic thromboembolic event compared with VKAs (HR, 0.60 [95% CI, 0.56–0.65]), but not rivaroxaban (HR, 1.05 [95% CI, 0.97–1.15]) or dabigatran (HR, 0.93 [95% CI, 0.78–1.11]). All-cause mortality was lower with apixaban than with VKAs, but not lower than with rivaroxaban or dabigatran.		

Conclusion: Apixaban was associated with superior safety, effectiveness, and lower mortality than VKAs. It was also associated with superior safety than rivaroxaban and similar safety to dabigatran along with similar effectiveness when compared with rivaroxaban or dabigatran. These observational data suggest potentially important differences in outcomes between direct oral anticoagulants, which should be explored in randomized trials.		
Citation	**Design**	**Endpoints**
Dawwas GK, Brown J, Dietrich E, Park H. Effectiveness and safety of apixaban versus rivaroxaban for prevention of recurrent venous thromboembolism and adverse bleeding events in patients with venous thromboembolism: a retrospective population-based cohort analysis. Lancet Haematol. 2019;6(1):e20-e28.	Retrospective cohort analysis of data from the Truven Health MarketScan commercial and Medicare Supplement claims databases in the US to compare the effectiveness and safety of apixaban and rivaroxaban in prevention of recurrent VTE and major bleeding events in patients with VTE. Adult patients with newly diagnosed VTE (DVT or PE) who were new users of apixaban or rivaroxaban between January 2014 and December 2016. Patients who did not initiate the study drugs within 30 days of their diagnosis, those without 12 months of continuous enrolment in medical and pharmacy benefits, and those who used other anticoagulants during the baseline period were excluded. A total of 15, 254 patients were included in the cohort analysis (3,091 apixaban users and 12,163 rivaroxaban users).	• Incidence of recurrent VTE (efficacy) • Incidence of major bleeding events (safety)
Results: The crude incidence of recurrent VTE was three per 100 person-years in the apixaban group and seven per 100 person-years in the rivaroxaban group. The incidence of major bleeding was three per 100 person-years in the apixaban group and six per 100 person-years in the rivaroxaban group. In multivariable Cox regression models, the use of apixaban compared with rivaroxaban was associated with decreased risk of recurrent VTE (HR, 0.37 [95% CI, 0.24-0.55]; p<0.0001) and major bleeding events (HR, 0.54 [95% CI, 0.37-0.82]; p=0.0031). **Conclusion:** Based on our findings, apixaban seems to be more effective than rivaroxaban in preventing the development of recurrent VTE and major bleeding events.		
Citation	**Design**	**Endpoints**
Lewis S, Glen J, Dawoud D, et al. Venous thromboembolism prophylaxis strategies for people undergoing elective total knee replacement: a systematic review and network meta-analysis. Lancet Haematol. 2019;6(10):e530-e539.	A systemic review and meta-analyses of RCTs to assess relative efficacy and safety of VTE prophylaxis strategies for people undergoing elective total knee replacement 25 RCTs (DVT, N=23; major bleeding, N=19; PE, N=12) were included.	Relative risk (RR) for the following outcomes of interest: • DVT (symptomatic and asymptomatic) • PE • Major bleeding
Results: For DVT, rivaroxaban (RR 0.12 [95% credible interval (CrI) 0.06-0.22]), followed by apixaban (RR 0.15[95% CrI 0.07-0.26]), then LMWH high prophylactic dose for standard duration (10-14 days; RR 0.18 [95% CrI 0.10-0.30]) were the top three interventions. For PE, LMWH at standard prophylactic dose for an extended duration (28-35 days; RR 0.02 [95% CrI 0.00-3.86]), followed by rivaroxaban (RR 0.08 [95% CrI 0.00-6.65]), then IPCDs (RR 0.20 [95% CrI 0.00-8.53]) were the top three interventions. For major bleeding, LMWH low prophylactic dose for standard duration (10-14 days; RR 0.08 [95% CrI 0.00-1.76], followed by LMWH at standard dose for an extended duration (28-35 days; RR 0.21 [95% CrI 0.00 10.41]), then VKA (RR 0.52 [95% CrI 0.08-2.89]) were the top three interventions for prevention. The major bleeding and PE results were determined to be highly uncertain.		

Conclusion: Single prophylaxis strategies are more effective in prevention of DVT in the elective total knee replacement population than combination strategies. Rivaroxaban ranked first for DVT prophylaxis in elective total knee replacement. There is no conclusive evidence on what treatment option is preferred for PE and major bleeding prophylaxis due to limited data.		
Citation	**Design**	**Endpoints**
Cohen AT, Hill NR, Luo X, et al. A systematic review of network meta-analyses among patients with nonvalvular atrial fibrillation: A comparison of efficacy and safety following treatment with direct oral anticoagulants. Int J Cardiol. 2018;269:174-181.	Systematic literature review that summarizes the evidence on stroke/SE bleeding events, mortality, and other adverse events from network meta-analyses (NMAs) that reported indirect comparisons of DOACs. Searches were conducted in PubMed, Embase, and the Cochrane Database of Systematic Reviews to identify NMAs published between January 2010 and March 2017. NMAs were eligible for inclusion if they included RCTs that evaluated stroke/SE and/or major bleeding and evaluated DOACs and VKAs. Patient populations in eligible NMAs were required to include ≥90% of patients with NVAF or report results for NVAF populations separately. A total of 22 NMAs were included in the final summary.	• Major bleeding • Stroke/SE • Mortality
Results: No statistically significant differences were observed for apixaban compared with any DOAC in the NMAs that assessed stroke/SE. Apixaban was associated with a lower risk for major bleeding compared with rivaroxaban in 16 of 20 NMAs and dabigatran 150 mg in 13 of 16 NMAs. Four of 6 NMAs showed lower risk for GI bleeding for apixaban compared with rivaroxaban and dabigatran 150 mg; however, this outcome was not assessed by most NMAs. **Conclusion:** This systematic literature review of network meta analyses showed varying levels of bleeding risk among DOACs, with apixaban generally having a lower risk than rivaroxaban and dabigatran 150 mg.		
Citation	**Design**	**Endpoints**
Almutairi AR, Zhow L, Gellad WF, et al. Effectiveness and Safety of Non-vitamin K Antagonist Oral Anticoagulants for Atrial Fibrillation and Venous Thromboembolism: A Systematic Review and Meta-analyses. Clin Ther. 2017 Jul;39(7):1456-1478.e36.	A systematic review and meta-analysis which examined efficacy and safety comparing DOACs and VKAs for AF and VTE. Both phase III randomized controlled trials and observational studies were simultaneously examined and analyzed comparative safety/efficacy by disease, study design, and individual DOAC agent. 13 RCTs and 27 observational studies (AF, N=32; VTE, N=8) were included.	• The primary outcomes were stroke/ SE for AF; recurrent VTE/fatal PE for VTE; and major bleeding for both conditions.
Results: A total of 13 RCTs and 27 observational studies (AF, n = 32; VTE, n = 8) were included. For AF, dabigatran and VKAs were comparable for stroke/SE risk in 1 RCT (HR, 0.77 [95% CI, 0.57-1.03]) and 6 observational studies (HR, 1.03 [95% CI, 0.83-1.27]). Rivaroxaban had a 20% decreased risk of stroke/SE in 3 RCTs (HR, 0.80 [95% CI, 0.67-0.95]) compared with VKA, but the effect was nonsignificant in 3 observational studies (HR, 0.78 [95% CI, 0.59-1.04]). Apixaban decreased stroke/SE risk (HR, 0.79 [95% CI, 0.66-0.95]) compared with VKA in 1 RCT, but edoxaban was comparable to VKA (HR, 0.99 [95% CI, 0.77-1.28]) in 1 RCT (no observational studies available for apixaban/edoxaban). Dabigatran, apixaban, and edoxaban decreased the risk of hemorrhagic stroke, mortality, major bleeding, and ICH by 10% to 71% compared with VKAs but not rivaroxaban. For VTE, NOACs and VKAs were comparable for recurrent VTE/fatal PE/DVT/PE risk in 7 RCTs and 1 observational study. The 7 RCTs demonstrated a 32% to 69% decreased risk		

of major bleeding for dabigatran, rivaroxaban, and apixaban compared with VKAs. No difference was shown in 1 rivaroxaban observational study (HR, 0.77 [95% CI, 0.40-1.49]) and 1 edoxaban RCT (HR, 0.84 [95% CI, 0.59-1.20]). Except for dabigatran, the NOACs had a 61% to 86% decreased risk of ICH and GI bleeding. **Conclusion**: DOACs and warfarin have similar efficacy and safety profiles. Data may slightly favor the DOAC agents, especially in regards to safety endpoints.		
Citation	**Design**	**Endpoints**
Lopez-Lopez JA, Sterne JAC, Thom HHZ, et al. Oral anticoagulants for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis, and cost effectiveness analysis. BMJ. 2017 Nov 28;359:j5058.	A systematic review, network meta-analysis, and cost effectiveness analysis for DOACs for patients with AF. Phase II or III RCTs comparing either a DOAC, VKA, or antiplatelet regimen for prevention of stroke in NVAF were included. Trials including warfarin comparators were only included if study targets were within therapeutic ranges (INR 2.0-3.0). 23 randomized trials involving 94,656 patients were analyzed.	• Outcomes extracted included all stroke, stroke or SE, ischemic stroke, hemorrhagic stroke, myocardial infarction, all-cause mortality, all bleeding, minor bleeding, major bleeding, intracranial bleeding, GI bleeding, and clinically relevant bleeding.
Results: Apixaban 5 mg BID (odds ratio 0.79, 95% confidence interval 0.66 to 0.94), dabigatran 150 mg BID (0.65, 0.52 to 0.81), edoxaban 60 mg QD (0.86, 0.74 to 1.01), and rivaroxaban 20 mg QD (0.88, 0.74 to 1.03) reduced the risk of stroke or SE compared with warfarin. The risk of stroke or SE was higher with edoxaban 60 mg QD (1.33, 1.02 to 1.75) and rivaroxaban 20 mg QD (1.35, 1.03 to 1.78) than with dabigatran 150 mg BID. The risk of all-cause mortality was lower with all DOACs than with warfarin. Apixaban 5 mg BID (0.71, 0.61 to 0.81), dabigatran 110 mg BID (0.80, 0.69 to 0.93), edoxaban 30 mg QD (0.46, 0.40 to 0.54), and edoxaban 60 mg QD (0.78, 0.69 to 0.90) reduced the risk of major bleeding compared with warfarin. The risk of major bleeding was higher with dabigatran 150 mg BID than apixaban 5 mg BID (1.33, 1.09 to 1.62), rivaroxaban 20 mg BID than apixaban 5 mg BID (1.45, 1.19 to 1.78), and rivaroxaban 20 mg BID than edoxaban 60 mg QD (1.31, 1.07 to 1.59). The risk of intracranial bleeding was substantially lower for most DOACs compared with warfarin, whereas the risk of GI bleeding was higher with some DOACs than warfarin. Apixaban 5 mg BID was ranked the highest for most outcomes, and was cost effective compared with warfarin. **Conclusion**: This SR/NMA suggests superior efficacy and safety profiles of most DOAC agents when compared directly to warfarin. Head-to-head trials comparing DOAC agents are needed.		
Citation	**Design**	**Endpoints**
Eikelboom JW, Connolly SJ, Bosch J, et al. for the COMPASS Investigators. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med 2017; 377:1319-1330.	A phase III, randomized, double-blind, controlled trial including 27,395 participants with stable atherosclerotic vascular disease which compared treatment with rivaroxaban 2.5 mg BID plus ASA 100 mg QD, rivaroxaban 5 mg BID, or 100 mg QD. In another randomized comparison (still ongoing), pantoprazole is being compared with placebo in patients participating in the trial who are not receiving a proton-pump inhibitor. Inclusion criteria: CAD or PAD, age ≥ 65 years, or age < 65 years and documented atherosclerosis or revascularization involving at least 2 vascular bets, or at least 2 additional risk factors.	• The primary efficacy outcome was a composite of cardiovascular death, stroke, or myocardial infarction. The primary safety outcome was major bleeding occurrence.

	Exclusion criteria: need for dual antiplatelet therapy, other non-ASA antiplatelet therapy or oral anticoagulant therapy, stroke within 1 month or any history of hemorrhagic or lacunar stroke, severe heart failure with known ejection fraction <30% or New York Heart Association (NYHA) class III or IV symptoms, estimated glomerular filtration rate (eGFR)<15 mL/min.	
Results: The study was stopped early due to superiority of the rivaroxaban + ASA arm. Rivaroxaban 2.5 mg BID + daily ASA 100 mg showed a significant 24% reduction of the risk of major CV events in patients with chronic CAD and/or PAD, compared to ASA alone. This finding was driven by a 42% reduction in stroke (significant), 22% reduction in CV death (significant) and 14% reduction in heart attack (not significant). The risk of major bleeding was significantly higher in patients taking the rivaroxaban/ASA regimen compared to ASA alone, with no significant increase in fatal or intracranial bleeds. Most of the major bleeding was into the GI tract. A reduction in composite MACE was shown with the rivaroxaban 5 mg dose, but was not statistically significant. **Conclusion**: Rivaroxaban 2.5 mg BID plus daily ASA therapy showed significant benefits toward reducing patient risk of MACE including CV death in those with chronic, stable CAD/PAD.		
Citation	**Design**	**Endpoints**
Weitz JI, et al. Rivaroxaban or aspirin for extended treatment of venous thromboembolism for the EINSTEIN CHOICE Investigators. N Engl J Med 2017; 376(13):1211-1222.	Randomized, double-blind, phase III study enrolled 3,396 participants were randomized to receive either once-daily rivaroxaban (at 10 or 20 mg) or ASA 100 mg. Inclusion criteria: Adult patients with symptomatic proximal DVT or PE; had been treated for 6 to 12 months with an anticoagulant agent, including a vitamin K antagonist or a direct oral anticoagulant agent such as dabigatran, rivaroxaban, apixaban, or edoxaban; and had not interrupted therapy for more than 7 days before randomization. Exclusion criteria: contraindication to continued anticoagulant therapy or if they required extended anticoagulant therapy at therapeutic doses or antiplatelet therapy, CrCl < 30 ml/min, hepatic disease with coagulopathy.	• Primary efficacy outcome was symptomatic recurrent fatal or nonfatal VTE. The principal safety outcome was major bleeding.
Results: The primary efficacy outcome occurred in 17 of 1107 patients (1.5%) receiving 20 mg of rivaroxaban and in 13 of 1127 patients (1.2%) receiving 10 mg of rivaroxaban, as compared with 50 of 1131 patients (4.4%) receiving ASA (hazard ratio for 20 mg of rivaroxaban vs. ASA, 0.34; 95% CI, 0.20 to 0.59; hazard ratio for 10 mg of rivaroxaban vs. ASA, 0.26; 95% CI, 0.14 to 0.47; P<0.001 for both comparisons). Rates of major bleeding were 0.5% in the group receiving 20 mg of rivaroxaban, 0.4% in the group receiving 10 mg of rivaroxaban, and 0.3% in the ASA group; the rates of clinically relevant non-major bleeding were 2.7%, 2.0%, and 1.8%, respectively. The incidence of adverse events was similar in all three groups. **Conclusion:** Among patients with VTE needing continued anticoagulation, the risk of a recurrent event was significantly lower with rivaroxaban at either a treatment dose (20 mg) or a prophylactic dose (10 mg) than with ASA, without a significant increase in bleeding rates.		
Citation	**Design**	**Endpoints**

Schulman S, Kakkar AK, Goldhaber SZ et al. Treatment of acute venous thromboembolism with dabigatran or warfarin and pooled analysis. Circulation. 2014;129(7):764.	Randomized, double-blind, double-dummy trial included 2589 patients with acute VTE treated with LMWH or unfractionated heparin for 5-11 days. Dabigatran 150 mg BID was compared with warfarin in these patients. Inclusion Criteria: Adults with acute, symptomatic, objectively verified proximal DVT of the legs or PE and for whom 6 months of anticoagulant therapy was considered to be an appropriate treatment. Exclusion Criteria: duration of symptoms longer than 14 days, PE with hemodynamic instability or requiring thrombolytic therapy, another indication for warfarin therapy, recent unstable cardiovascular disease, a high risk of bleeding, liver disease, CrCl < 30 ml/min, a life expectancy of less than 6 months, a contraindication to heparin, pregnancy or risk of becoming pregnant, or a requirement for long-term antiplatelet therapy.	• The primary outcome was recurrent symptomatic VTE and related deaths during 6 months of treatment. The safety endpoint was major bleeding.
Results: The primary efficacy outcome occurred in 30 patients (2.3%) treated with dabigatran compared with 28 patients (2.2%) treated with warfarin. Major bleeding occurred in 15 patients (1.2%) treated with dabigatran and 22 patients (1.7%) treated with warfarin. **Conclusion:** Dabigatran has similar effects on VTE recurrence and lower risk of bleeding in comparison to warfarin.		
Citation	**Design**	**Endpoints**
Agnelli G, Buller HR, Cohen A, et al. Oral apixaban for the treatment of acute venous thromboembolism. N Engl J Med. 2013;369(9):799.	Randomized, double-blind study included 5,395 patients with acute VTE and compared apixaban (10 mg BID for 7 days, followed by 5 mg BID for 6 months) to conventional therapy with enoxaparin followed by warfarin. Inclusion Criteria: Adults with confirmed, symptomatic proximal DVT or PE (with or without DVT). Exclusion Criteria: Active bleeding or a high risk of bleeding; if they had cancer and long-term treatment with low-molecular-weight heparin was planned; if less than 6 months of anticoagulant treatment was planned; or if they had another indication for long-term anticoagulation therapy, dual antiplatelet therapy, treatment with ASA at a dose of more than 165 mg daily, or treatment with potent inhibitors of cytochrome P-450 3A4.	• The primary efficacy outcome was recurrent symptomatic VTE or death related to VTE. Primary safety outcomes were major bleeding alone and major bleeding plus clinically relevant non-major bleeding.
Results: Primary efficacy outcome occurred in 59 of 2,609 patients (2.3%) in the apixaban group compared with 71 of 2,635 (2.7%) in the conventional therapy group. Apixaban was non-inferior to conventional therapy. Major bleeding occurred in 0.6% of patients using apixaban compared to 1.8% of patients using conventional therapy. The composite outcome of major bleeding and clinically relevant non-major bleeding occurred in 4.3% of the patients treated with apixaban compared with 9.7% of those in the conventional-therapy group.		

Conclusion: Apixaban alone was non-inferior to conventional therapy for the treatment of acute VTE. Apixaban was associated with significantly less major bleeding than conventional therapy.		
Citation	**Design**	**Endpoints**
Hokusai-VTE Investigators. Edoxaban versus warfarin for the treatment of symptomatic venous thromboembolism. N Engl J Med. 2013;369(15):1406.	Randomized, double-blind, non-inferiority study of 4,921 patients with DVT and 3,319 patients with PE, who were initially treated with heparin, were randomly assigned to receive edoxaban (60 mg daily or 30 mg daily) or to receive warfarin. Inclusion Criteria: Adult patients with objectively diagnosed, acute, symptomatic DVT involving the popliteal, femoral, or iliac veins or acute, symptomatic PE (with or without DVT). Exclusion Criteria: contraindications to heparin or warfarin, cancer for which long-term treatment with low-molecular-weight heparin was anticipated, had another indication for warfarin therapy, continued to receive treatment with ASA at a dose of more than 100 mg daily or dual antiplatelet therapy, or had CrCl < 30 mL/min.	• The primary efficacy outcome was recurrent symptomatic VTE. The primary safety outcome was major or clinically relevant non-major bleeding.
Results: Edoxaban was non-inferior to warfarin regarding the primary efficacy outcome. The primary efficacy outcome occurred in 130 patients (3.2%) receiving edoxaban and in 146 patients (3.5%) receiving warfarin. The safety outcome occurred in 349 patients (8.5%) in the edoxaban group and 423 patients (10.3%) in the warfarin group. **Conclusion:** Edoxaban administered after heparin was non-inferior to standard therapy with warfarin. Edoxaban was associated with significantly less bleeding.		
Citation	**Design**	**Endpoints**
EINSTEIN–PE Investigators. Oral rivaroxaban for the treatment of symptomatic pulmonary embolism. N Engl J Med. 2012;366(14):1287. Epub 2012 Mar 26.	Randomized, open-label, event-driven, non-inferiority trial included 4,832 with acute symptomatic PE with or without DVT. The study compared rivaroxaban (15 mg BID for 3 weeks followed by 20 mg daily) with standard therapy of enoxaparin followed by VKA for 3, 6, or 12 months. Inclusion criteria: cute, symptomatic, objectively confirmed proximal DVT, without symptomatic PE. Exclusion criteria: another indication for a vitamin K antagonist; a CrCl < 30 mL/min; clinically significant liver disease; bacterial endocarditis; active bleeding or a high risk of bleeding, contraindicating anticoagulant treatment; systolic blood pressure greater than 180 mm Hg or diastolic blood pressure greater than 110 mm Hg; childbearing potential without proper contraceptive measures, pregnancy, or breast-feeding; concomitant use of strong cytochrome P-450 3A4 inhibitors or inducers.	• The primary efficacy outcome was symptomatic recurrent VTE. The primary safety outcome was major or clinically relevant non-major bleeding.

Results: Rivaroxaban was non-inferior to standard therapy for the primary efficacy outcome with 50 events vs. 44 events. The primary safety outcome occurred in 10.3% of patients in the rivaroxaban group compared with 11.4% of those in the standard-therapy group. Major bleeding was observed in 26 patients (1.1%) treated with rivaroxaban and 52 patients (2.2%) treated with standard-therapy. **Conclusion**: Rivaroxaban alone was non-inferior to standard therapy for both initial and long-term treatment of PE and demonstrated potentially improved benefit-risk profile.		
Citation	**Design**	**Endpoints**
ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365(10):883. Epub 2011 Aug 10.	Double-blind randomized trial of 14,264 patients with NVAF and at increased risk of stroke were randomized to receive rivaroxaban 20 mg daily or dose-adjusted warfarin. Per-protocol, as-treated primary analysis was designed to determine if rivaroxaban was non-inferior to warfarin for the primary endpoint of stroke or SE. Inclusion Criteria: Adults with NVAF, as documented on electrocardiography, who were at moderate-to-high risk for stroke. Exclusion Criteria: Prosthetic heart valve, planned cardioversion, active endocarditis, active bleeding, planned invasive procedure, sustain uncontrolled hypertension, treatment with ASA > 100 mg daily, indication for anticoagulant therapy for other condition.	• Primary endpoint was occurrence of stroke or SE.
Results: The primary endpoint occurred in 188 patients (1.7% per year) in the rivaroxaban-treated group and 241 patients (2.2% per year) in the warfarin-treated group. Major and non-major clinically relevant bleeding occurred in 1475 patients in the rivaroxaban group (14.9% per year) and in 1449 in the warfarin group (14.5% per year). There were significant reductions in intracranial hemorrhage (0.5% vs 0.7%) and fatal bleeding (0.2% vs 0.5%) in the rivaroxaban treated group. **Conclusion:** Rivaroxaban was non-inferior to warfarin for prevention of stroke and SE in patients with AF. There were no significant differences between groups in the risk of major bleeding. Intracranial and fatal bleeding occurred less frequently in rivaroxaban group.		
Citation	**Design**	**Endpoints**
ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365(11):981.	Randomized, double-blind trial, compared apixaban (5 mg BID) with warfarin in 18,201 patients with AF and at least one additional risk factor for stroke. The trial was designed to test non-inferiority. It tested superiority of the primary outcome and rates of major bleeding and deaths. Inclusion Criteria: Adults with AF or flutter plus at least one additional risk factor for stroke. Exclusion criteria: AF due to a reversible cause, moderate or severe MS, conditions other than AF that required anticoagulation, stroke within the previous 7 days, a need	• Primary outcome was ischemic or hemorrhagic stroke or SE.

	for ASA at a dose of >165 mg a day or for both ASA and clopidogrel, and severe renal insufficiency.	
Results: The rate of primary outcome was 1.27% per year in the apixaban group compared with 1.60% per year in the warfarin group. The rate of major bleeding was 2.13% per year in the apixaban group compared with 3.09% per year in the warfarin group. The rate of hemorrhagic stroke was 0.24% per year in the apixaban group compared with 0.47% per year in the warfarin group. Rate of ischemic or uncertain type of stroke was 0.97% per year in apixaban group and 1.05% per year in the warfarin group. **Conclusion:** In patients with AF, apixaban was superior to warfarin in preventing stroke or SE.		
Citation	**Design**	**Endpoints**
EINSTEIN Investigators. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med. 2010;363(26):2499.	Open-label, randomized, event-driven, non-inferiority study included 3,449 patients and compared oral rivaroxaban alone (15 mg BID for 3 weeks followed by 20 mg daily) with subcutaneous enoxaparin followed by a vitamin k antagonist for 2, 5 or 12 months in patients with acute symptomatic DVT. In parallel, a double-blind, randomized, event-driven superiority trail compared rivaroxaban alone (20 mg QD) with placebo for an additional 6 or 12 months in patients who completed 6 or 12 months of treatment. Inclusion criteria: acute, symptomatic, objectively confirmed proximal DVT, without symptomatic PE. Exclusion criteria: another indication for a vitamin K antagonist; a CrCl < 30 mL/min; clinically significant liver disease; bacterial endocarditis; active bleeding or a high risk of bleeding, contraindicating anticoagulant treatment; systolic blood pressure greater than 180 mm Hg or diastolic blood pressure greater than 110 mm Hg; childbearing potential without proper contraceptive measures, pregnancy, or breast-feeding; concomitant use of strong cytochrome P-450 3A4 inhibitors or inducers.	• Primary efficacy outcome was recurrent VTE. Primary safety outcomes were major bleeding or clinically relevant non-major bleeding in the initial-treatment study and major bleeding in the continued-treatment study.
Results: Rivaroxaban had non-inferior efficacy with respect to the primary outcome (36 events vs. 51 events with enoxaparin-VKA). The primary safety outcome occurred in 8.1% of the patients in each group. In the continued-treatment study, rivaroxaban showed superior efficacy compared to placebo with 8 events vs. 42 events with placebo. **Conclusion**: Rivaroxaban is a single-drug approach to both short term and continued treatment of VTE.		

Formulary Placement, Utilization and Cost Experience (10-01-2024 to 12-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Factor Xa Inhibitors								
Eliquis® (apixaban) 2.5 mg, 5 mg tablets	97	44	$54,323.31	$560.03	0	0 (0%)	F	No change
Eliquis® (apixaban) 5 mg tablet dose pack	1	1	$708.26	$708.26	0	0 (0%)	F	No change
Xarelto® (rivaroxaban) 2.5 mg, 10 mg, 15 mg, 20 mg tablets	32	15	$17,230.98	$538.47	0	0 (0%)	F	No change
Xarelto® (rivaroxaban) 15 mg-20 mg tablet dose pack	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Xarelto® (rivaroxaban) 1 mg/ml oral suspension	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Savaysa® (edoxaban) 15 mg, 30 mg, 60 mg tablets	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Direct Thrombin Inhibitors								
Dabigatran (Pradaxa®) 75 mg, 110 mg, 150 mg capsules	4	1	$593.36	$148.34	0	0 (0%)	F	No change
Pradaxa® (dabigatran) 20 mg, 30 mg, 40 mg, 50 mg, 110 mg, 150 mg pellet packets	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	134	61	$72,855.91	$543.70	0	0 (0%)		

Key (as applicable) F = Formulary, no restrictions; F-QL = Formulary, quantity limit applies; F-AL = Formulary, age limit applies; F-ST = Formulary, step therapy applies; F-PA = Formulary, PA required; NF = Non-formulary; X = Excluded

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Fluoride Dental Preparations

Utilization Findings

There was no utilization and no prior authorization requests.

Recommendations

- No changes

Formulary Placement, Utilization and Cost Experience (10-01-2024 to 12-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Subcategory A								
Sodium fluoride 0.25, 0.5, 1 mg chewable tablet	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Sodium fluoride (SoluVita) 0.5 mg/ml oral drops	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Floriva™ (fluoride-vitamin D3) 0.25 mg/ml oral drops	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sodium fluoride (PreviDent®) 0.2% dental solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sodium fluoride (Denta® 5000 Plus, PreviDent® 5000 Plus, SF 5000 Plus) 1.1% dental cream	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sodium fluoride (DentaGel, Fraiche 5000, PreviDent®, SF) 1.1% dental gel	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sodium fluoride (PreviDent®) 1.1% dry mouth dental paste	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sodium fluoride (Clinpro® 5000, Fluoridex Daily Defense®, FluoriMax™ 5000, Just Right® 5000, PreviDent® 5000 Booster Plus, PreviDent® 5000 Ortho Defense, PreviDent® 5000 Kids) 1.1% dental paste	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
PerioMed™ (stannous fluoride) 0.63% dental rinse	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Gel-Kam® (stannous fluoride) 0.4% dental gel	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fraiche 5000 (sodium fluoride-hydroxyapatite) 1.1%-4.5% gel	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

Sodium fluoride-potassium nitrate (Denta 5000 Plus, Fluoridex® Sensitivity Relief, FluoriMax™, PreviDent® 5000 Enamel Protect, PreviDent® 5000 Sensitive) 1.1%-5% dental gel	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fraiche 5000 (sodium fluoride-hydroxyapatite) 1.1%-3% gel	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	0	0	$0.00	$0.00	0	0 (0%)		

Key (as applicable) F = Formulary, no restrictions; F-QL = Formulary, quantity limit applies; F-AL = Formulary, age limit applies; F-ST = Formulary, step therapy applies; F-PA = Formulary, PA required; NF = Non-formulary; X = Exclude

Inhaled Corticosteroids

Executive Summary

Class Overview

This review covers inhaled corticosteroids (ICS) for the treatment of asthma. Asthma is a chronic inflammatory disorder of the airways, characterized by bronchial hyper-responsiveness leading to intermittent cough, wheezing and shortness of breath. Mainstay treatment options include short-acting beta agonists (SABAs), ICS inhalers, ICS-LABA combinations, leukotriene receptor antagonists (LTRAs) and anticholinergic agents. Historically, treatment started with SABA products for those with mild or intermittent symptoms, although use of single maintenance and reliever therapy (MART/SMART) regimens are becoming increasingly recommended in the asthma treatment landscape.

Various single-ingredient ICS products are available. Selection of therapy is typically based on patient factors including age, preference, device ease of use, and previous experience in addition to insurance coverage. Recently, generic equivalents for Flovent HFA and Flovent Disk were released, but there do not appear to be other near-term generic product releases in this category at the current time. Several products have lost patent protection, but do not appear to have generated interest from generic manufacturers. Novel ICS products near term in the pipeline were not discovered; widespread adoption of combination inhaler products and significant generic availability across the class has likely stalled interest in development. Single ingredient ICS inhalers are still considered an important cornerstone of asthma management, especially in younger populations and those with milder asthma severity; there is currently insufficient evidence to recommend MART/SMART regimens across all age groups.

Utilization Findings

There were 42 claims for 30 members, for a total cost of $9,803.97 and an average cost per claim of $233.43. The most highly utilized medication was Qvar, with 19 claims, followed by Fluticasone propionate with 14 claims. There was 1 prior authorization request with 1 approval (100%).

Recommendations

- No changes

Clinical Summary

Asthma has classically been difficult to define in a manner acceptable to all disciplines (clinicians, physiologists and pathologists). The Expert Panel Report 3 (EPR-3) of the National Asthma Education and Prevention Program defines asthma as "a common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness, and an underlying inflammation. The interaction of these features of asthma determines the clinical manifestations and severity of asthma and the response to treatment." The Global Initiative for Asthma (GINA) defines asthma as "a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation."

Mainstay treatment options for mild to moderate asthma include short-acting or long-acting beta agonists, inhaled corticosteroids, leukotriene receptor antagonists (LTRAs) and anticholinergic agents. These different agents can be considered reliever therapies that ease bronchoconstriction (such as SABAs), or controller therapies which mediate the chronic inflammatory processes responsible for pulmonary remodeling (such as inhaled corticosteroids). Initial pharmacologic treatment of asthma depends largely on the severity and frequency of symptoms and intensifies in a stepwise fashion up or down depending on the level of response/control achieved by a given intervention. For intermittent asthma symptoms, single-ingredient therapy with short-acting beta agonists (SABAs) had long been the standard of care for bronchodilation in acute control situations. However, recent evidence demonstrates that SABA-only treatment increases the risk of severe exacerbations and death and that the addition of an ICS when reliever therapy is administered reduces those risks. Additionally, indirect evidence from a large, double-blind study in patients with mild asthma comparing budesonide-formoterol as needed (PRN) to SABA-only PRN and SABA PRN + regular ICS supports the use of low dose combination ICS-formoterol (the ICS being either budesonide or [BDP]). Accordingly, GINA guidelines for adults and adolescents 12+ years have been updated to recommend ICS-formoterol as both the preferred “controller” and “reliever” regimens, a treatment regimen commonly known as MART or SMART [maintenance and reliever therapy]. GINA guidelines also recommend ICS-formoterol MART regimens in children 6-11 years as a preferred management option in step 3 and 4 of the treatment algorithm. Notably, this PRN use is not an FDA-approved, labeled use of ICS-formoterol products. Beyond clinical outcomes, GINA guidelines emphasize use of a single inhaler for controller and reliever therapy is advantageous from the perspective of a more simplified regimen for the patient to follow.

Asthma guidelines published by the National Asthma Education and Prevention Program (NAEPP) Expert panel report IV (EPR-4) have also recently updated pursuant to the new evidence, and MART therapy with ICS-formoterol is the recommended regimen for ages 5 and older in step 3 and step 4 of the asthma treatment guidelines. PRN use of SABA agents is still recommended in the NAEPP guidelines in mild asthma across age groups, taking a more traditional line than the GINA guidelines. Another notable update to both NAEPP and GINA guidelines includes adding on long-acting muscarinic agents (LAMAs) for later-line therapy in certain patients whose asthma is severe and uncontrolled. Further specifics regarding the applicable age groups and agents used can be found in individual guidelines.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
Alvesco® (ciclesonide)	Maintenance treatment of asthma as prophylactic therapy	Age ≥ 12 years: In patients who received bronchodilators alone – 1 inhalation (80 mcg) BID; do not exceed 160 mcg BID In patients who received ICSs – 1 inhalation (80 mcg) BID; do not exceed 320 mg BID In patients who received oral corticosteroids – 320 mcg BID; do not exceed 320 mg BID
Arnuity® Ellipta® (fluticasone furoate)		Age 5-11 years: 1 inhalation (50 mcg) once daily (QD) Age ≥ 12 years: 1 inhalation (100 mcg or 200 mcg) QD (based on prior asthma therapy and disease severity)
Asmanex® HFA (mometasone furoate)		Age 5-11 years: 2 inhalations (50 mcg) BID Age ≥ 12 years: In patients who received medium dose ICSs – (100 mcg inhaler) 2 inhalations (200 mcg) BID In patients who received high dose ICSs or oral corticosteroids – (200 mcg inhaler) 2 inhalations (400 mcg) BID
Asmanex® Twisthaler® (mometasone furoate)		Age 4-11 years: (110 mcg inhaler) 1 inhalation (110 mcg) once every evening Age ≥ 12 years: In patients who received bronchodilators alone or ICSs – (220 mcg inhaler) 1 inhalation (220 mcg) once every evening In patients who received oral corticosteroids – (220 mcg inhaler) 2 inhalations (440 mcg) BID
fluticasone propionate (Flovent® Diskus®)		Age 4-11 years: Initial therapy for patients not on an ICS – 50 mcg BID; increase to a maximum of 100 mcg BID as needed (PRN) Age ≥ 12 years: Initial therapy for patients not on an ICS – 100 mcg BID; increase to a maximum of 1,000 mcg BID PRN
Fluticasone propionate (Flovent® HFA)		Age 4-11 years: 88 mcg BID Age ≥ 12 years: Initial therapy for patients not on an ICS – 88 mcg BID; increase to a maximum of 880 mcg BID PRN

Medication	Indications	Dosing/Administration
Budesonide (Pulmicort Respules®)		Age 12 months - 8 years: In patients who previously received bronchodilators alone – 0.5 mg QD or 0.25 mg BID; maximum 0.5 mg daily In patients who previously received ICSs – 0.5 mg QD or 0.25 mg BID; maximum 0.5 mg BID In patients who previously received oral corticosteroids – 0.5 mg BID or 1 mg QD; maximum 1 mg daily
Pulmicort Flexhaler™ (budesonide)		Age 6-17 years: Initial – 180 mg BID (360 mcg BID may be appropriate in some patients); maximum 360 mcg BID Age ≥ 18 years: Initial – 360 mg BID (180 mcg BID may be appropriate in some patients); maximum 720 mcg BID
Qvar® RediHaler™ HFA (beclomethasone dipropionate)		Age 4-11 years: Initial therapy for patients not on an ICS – 40 mcg BID; maximum 80 mcg BID Age ≥ 12 years: Initial therapy for patients not on an ICS – 40 to 80 mcg BID; maximum 320 mcg BID

Boxed Warnings and Contraindications

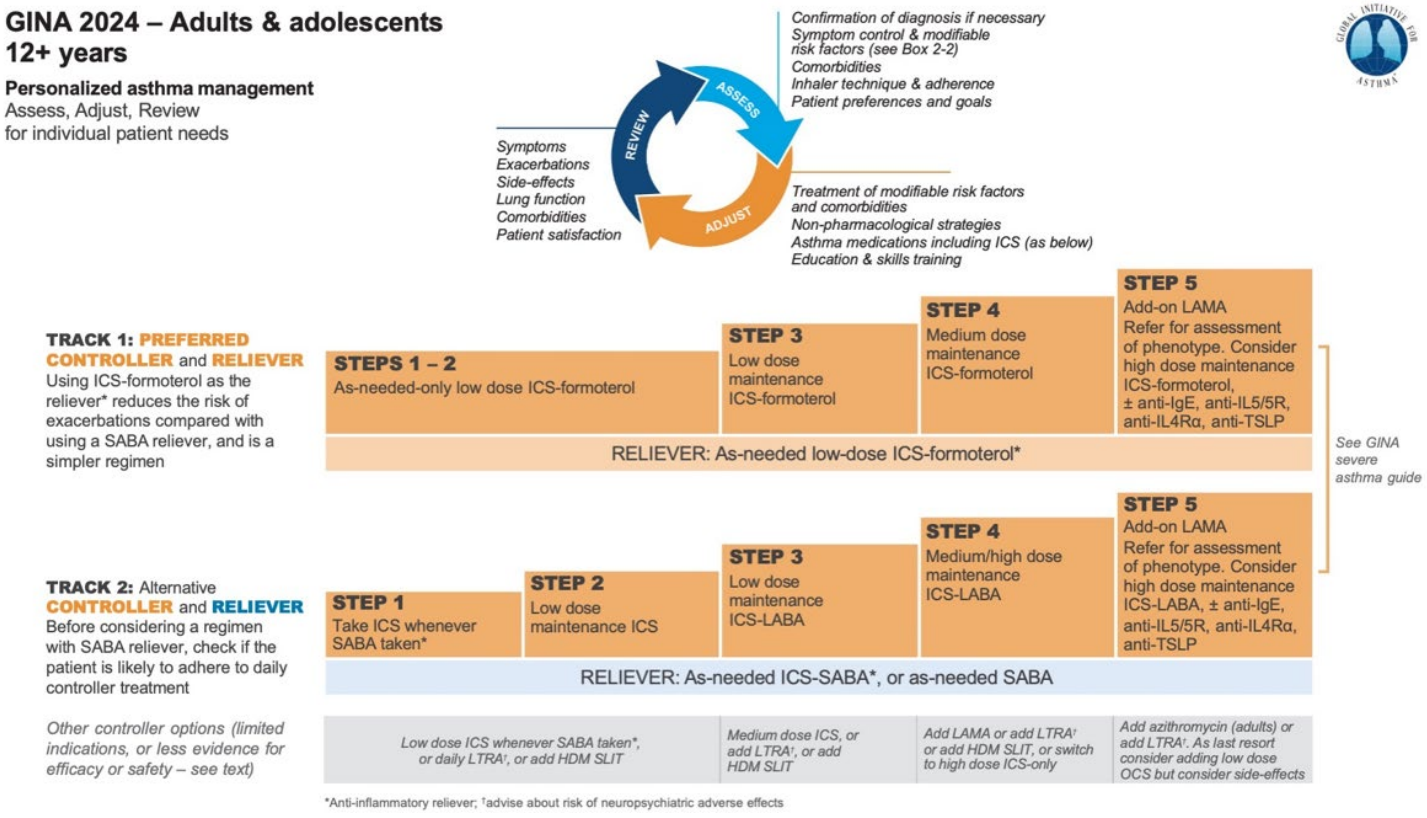
Medication	Boxed Warnings	Contraindications
Alvesco® (ciclesonide) Asmanex® HFA (mometasone furoate) Fluticasone propionate (Flovent® HFA) Budesonide (Pulmicort Respules®) Qvar® RediHaler™ HFA (beclomethasone dipropionate)	None	Patients with status asthmaticus or other acute episodes of asthma where intensive measures are required. Hypersensitivity to component ingredients.
Arnuity® Ellipta® (fluticasone furoate) Asmanex® Twisthaler® (mometasone furoate) Fluticasone propionate (Flovent® Diskus®) Pulmicort Flexhaler™ (budesonide)		Patients with status asthmaticus or other acute episodes of asthma where intensive measures are required. Known or severe hypersensitivity to milk proteins or component ingredients.

Warnings/Precautions

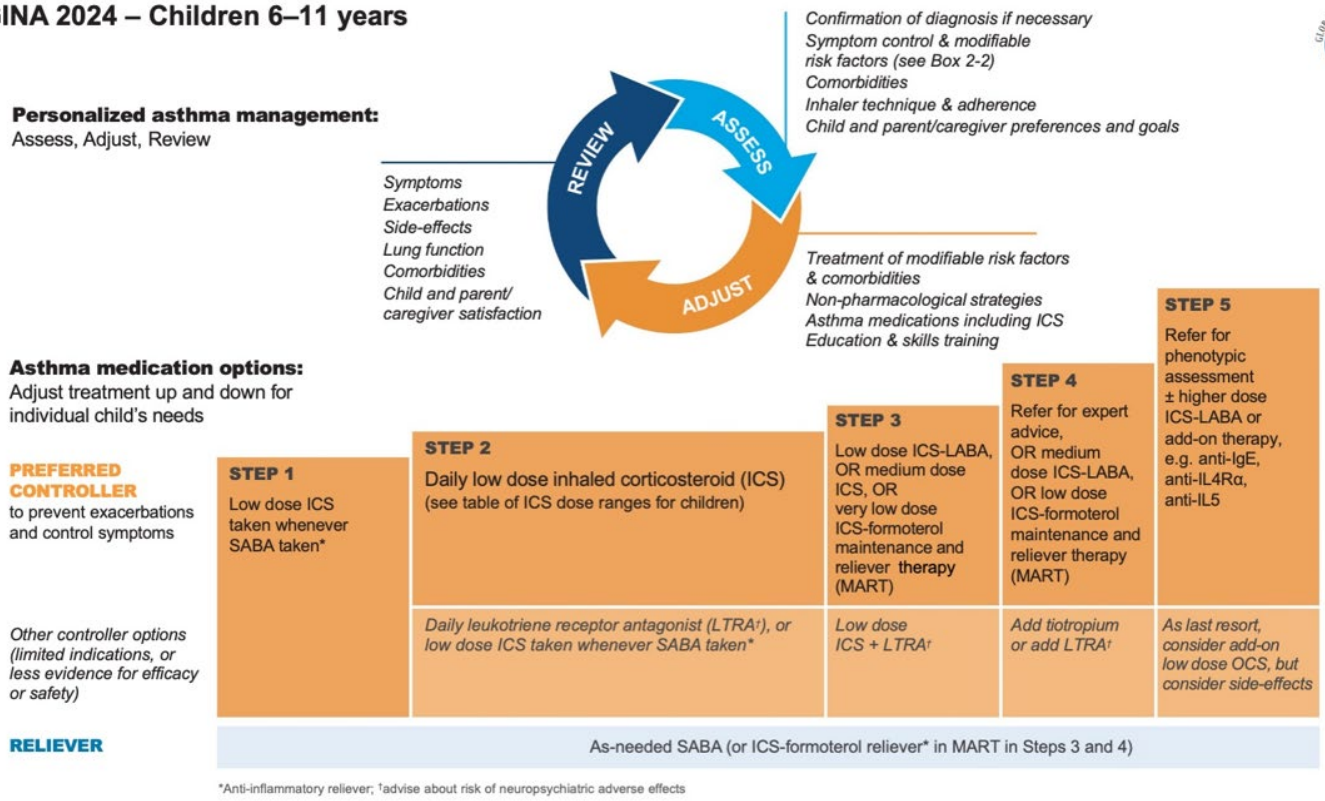
Medication	Warnings/Precautions
Alvesco® (ciclesonide) Arnuity® Ellipta® (fluticasone furoate) Asmanex® HFA (mometasone furoate) Asmanex® Twisthaler® (mometasone furoate) Fluticasone propionate (Flovent® Diskus®, Flovent® HFA) Budesonide (Pulmicort Respules®) Pulmicort Flexhaler™ (budesonide) Qvar® RediHaler™ HFA (beclomethasone dipropionate)	Hypercortisolism or suppression of hypothalamic-pituitary-adrenal (HPA) axis, bronchospasm, immunosuppression with prolonged use, Kaposi's sarcoma with prolonged use, psychiatric disturbances may occur Use with caution in patients with HF, diabetes, GI diseases, hepatic impairment, myasthenia gravis, glaucoma and/or cataracts, osteoporosis, renal impairment, seizure disorders, or following acute MI Orally inhaled corticosteroids may cause a reduction in growth velocity in pediatrics

Practice Guidelines

Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma 2024 Report (GINA). Available at www.ginasthma.org.

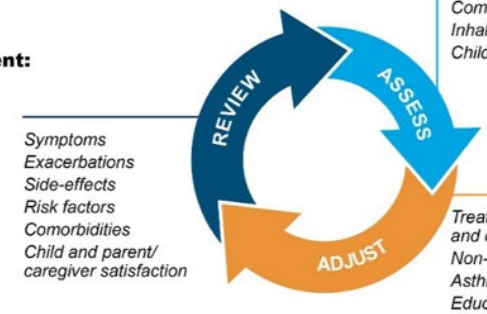


GINA 2024 – Children 6–11 years



GINA 2024 – Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response



Exclude alternative diagnoses
Symptom control & modifiable risk factors
Comorbidities
Inhaler technique & adherence
Child and parent/caregiver preferences and goals

Symptoms
Exacerbations
Side-effects
Risk factors
Comorbidities
Child and parent/ caregiver satisfaction

Treat modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE	*(Insufficient evidence for daily controller)*	Daily low dose inhaled corticosteroid (ICS) (see Box 11-3 for ICS dose ranges for pre-school children)	Double 'low dose' ICS *(See Box 11-3)*	Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*	*Daily leukotriene receptor antagonist (LTRA†), or intermittent short course of ICS at onset of respiratory illness*	*Low dose ICS + LTRA† Consider specialist referral*	*Add LTRA†, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral.	Asthma diagnosis, and asthma not well-controlled on low dose ICS	Asthma not well-controlled on double ICS
		Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

*†Advise about risk of neuropsychiatric adverse effects

US National Heart Lung and Blood Institute 2020 Focused Updates to the Asthma Management Guidelines: Clinician's Guide. Available at: https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/clinician-guide-2020-focused-updates-asthma-management-guidelines

AGES 0–4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0–4 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily low-dose ICS-LABA and PRN SABA▲ or Daily low-dose ICS + montelukast,* or daily medium-dose ICS, and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA
			For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5–11 Years diagram.			

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 4–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; SABA, inhaled short-acting beta$_2$-agonist; RTI, respiratory tract infection; PRN, as needed

▲ Updated based on the 2020 guidelines.

* Cromolyn and montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a Boxed Warning for montelukast in March 2020.

NOTES FOR INDIVIDUALS AGES 0–4 YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment. • Consider short course of oral systemic corticosteroid if exacerbation is severe or individual has history of previous severe exacerbations.

Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲

Notes	• If clear benefit is not observed within 4–6 weeks and the medication technique and adherence are satisfactory, the clinician should consider adjusting therapy or alternative diagnoses.

Abbreviations	EIB, exercise-induced bronchoconstriction; SABA, inhaled short-acting beta$_2$-agonist. ▲Updated based on the 2020 guidelines. ‡ Refers to mice and cockroaches, which were specifically examined in the Agency for Healthcare Research and Quality systematic review.

AGES 5–11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5–11 Years				
Treatment	**STEP 1**	**STEP 2**	**STEP 3**	**STEP 4**	**STEP 5**	**STEP 6**
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS +Theophylline,* and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA or Daily medium-dose ICS + LTRA* or daily medium-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider Omalizumab**▲	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

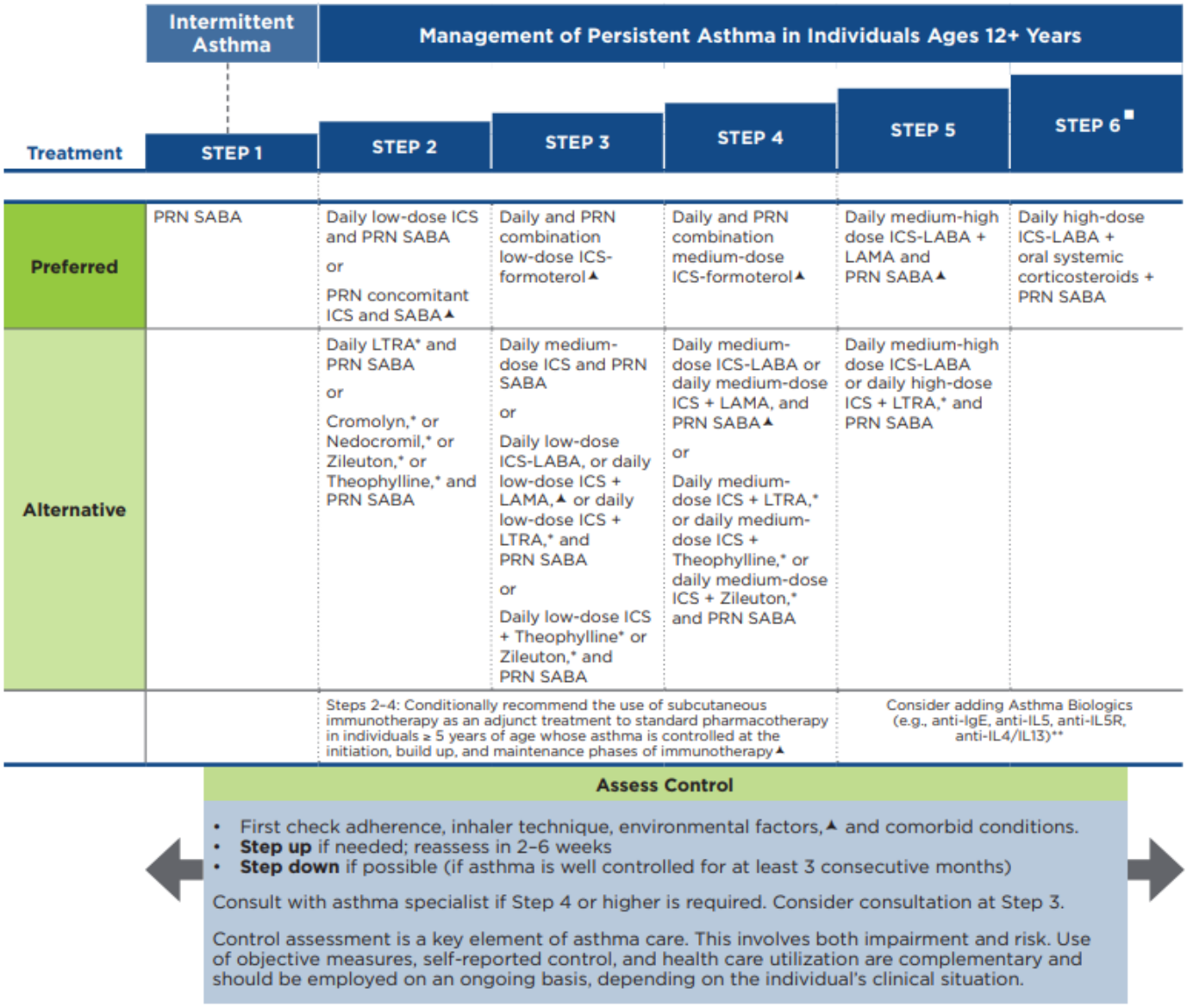
▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including montelukast, and Theophylline were not considered in this update and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** Omalizumab is the only asthma biologic currently FDA-approved for this age range.

NOTES FOR INDIVIDUALS AGES 5–11 YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • In Steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 8 puffs (36 mcg).▲ • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• The terms ICS-LABA and ICS-formoterol indicate combination therapy with both an ICS and a LABA, usually and preferably in a single inhaler. • Where formoterol is specified in the steps, it is because the evidence is based on studies specific to formoterol. • In individuals ages 5–11 years with persistent allergic asthma in which there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry, FeNO measurement is conditionally recommended as part of an ongoing asthma monitoring and management strategy that includes frequent assessment.
Abbreviations	EIB (exercise-induced bronchoconstriction); FeNO (fractional exhaled nitric oxide); ICS (inhaled corticosteroid); LABA (long-acting $beta_2$-agonist); SABA (inhaled short-acting $beta_2$-agonist). ▲Updated based on the 2020 guidelines. ‡ Refers to mice and cockroaches, which were specifically examined in the Agency for Healthcare Research and Quality systematic review.



Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6 ■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including Zileuton and montelukast, and Theophylline were not considered for this update, and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** The AHRQ systematic reviews that informed this report did not include studies that examined the role of asthma biologics (e.g. anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13). Thus, this report does not contain specific recommendations for the use of biologics in asthma in Steps 5 and 6.

■ Data on the use of LAMA therapy in individuals with severe persistent asthma (Step 6) were not included in the AHRQ systematic review and thus no recommendation is made.

NOTES FOR INDIVIDUALS AGES 12+ YEARS DIAGRAM

Quick-relief medications	• Use SABA as needed for symptoms. The intensity of treatment depends on the severity of symptoms: up to 3 treatments at 20-minute intervals as needed. • In steps 3 and 4, the preferred option includes the use of ICS-formoterol 1 to 2 puffs as needed up to a maximum total daily maintenance and rescue dose of 12 puffs (54 mcg).▲ • **Caution:** Increasing use of SABA or use >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and may require a step up in treatment.
Each step: Assess environmental factors, provide patient education, and manage comorbidities▲	• In individuals with sensitization (or symptoms) related to exposure to pests‡: conditionally recommend integrated pest management as a single or multicomponent allergen-specific mitigation intervention.▲ • In individuals with sensitization (or symptoms) related to exposure to identified indoor allergens, conditionally recommend a multi-component allergen-specific mitigation strategy.▲ • In individuals with sensitization (or symptoms) related to exposure to dust mites, conditionally recommend impermeable pillow/mattress covers only as part of a multicomponent allergen-specific mitigation intervention, but not as a single component intervention.▲
Notes	• The terms ICS-LABA and ICS-formoterol indicate combination therapy with both an ICS and a LABA, usually and preferably in a single inhaler. • Where formoterol is specified in the steps, it is because the evidence is based on studies specific to formoterol. • In individuals ages 12 years and older with persistent allergic asthma in which there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry, FeNO measurement is conditionally recommended as part of an ongoing asthma monitoring and management strategy that includes frequent assessment. • Bronchial thermoplasty was evaluated in Step 6. The outcome was a conditional recommendation against the therapy.
Abbreviations	EIB, exercise-induced bronchoconstriction; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroid; LABA, long-acting $beta_2$-agonist; SABA, inhaled short-acting $beta_2$-agonist. ▲Updated based on the 2020 guidelines. ‡ Refers to mice and cockroaches, which were specifically examined in the Agency for Healthcare Research and Quality systematic review.

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Beasley R, Holliday M, Reddel HK, Braithwaite I, Ebmeier S, Hancox RJ, et al. Controlled trial of budesonide-formoterol as needed for mild asthma. N Engl J Med. 2019;380:2020–30.	A randomized, open-label, parallel-group 52-week controlled trial conducted at 16 trial centers. Patients were randomized in a 1:1:1 ratio. Patients in the albuterol group received albuterol (Ventolin, GlaxoSmithKline), 100 µg, with two inhalations from a pressurized metered-dose inhaler PRN for symptom relief. Patients in the budesonide maintenance group received budesonide (Pulmicort Turbuhaler, AstraZeneca), 200 µg, one inhalation twice daily, plus albuterol (Ventolin), 100 µg, two inhalations from a pressurized metered-dose inhaler PRN for symptom relief. Patients in the budesonide–formoterol group received budesonide–formoterol (Symbicort Turbuhaler, AstraZeneca), 200 µg of budesonide and 6 µg of formoterol, one inhalation PRN for symptom relief. Inclusion criteria:18-75 years of age with a diagnosis of asthma; the use of SABA as the sole asthma therapy in the previous 3 months; patient report of the use of SABA on at least 2 occasions in the previous month Randomized to receive: Albuterol 100 µg MDI Budesonide 200 µg plus PRN albuterol Budesonide-formoterol 200 µg/6 µg	• Primary endpoints: annualized rate of asthma exacerbations
Results: The analysis included 668 of 675 patients who underwent randomization. The annualized exacerbation rate in the budesonide–formoterol group was lower than that in the albuterol group (absolute rate, 0.195 vs. 0.400; relative rate, 0.49; 95% confidence interval [CI], 0.33 to 0.72; P<0.001) and did not differ significantly from the rate in the budesonide maintenance group (absolute rate, 0.195 in the budesonide–formoterol group vs. 0.175 in the budesonide maintenance group; relative rate, 1.12; 95% CI, 0.70 to 1.79; P=0.65). The number of severe exacerbations was lower in the budesonide–formoterol group than in both the albuterol group (9 vs. 23; relative risk, 0.40; 95% CI, 0.18 to 0.86) and the budesonide maintenance group (9 vs. 21; relative risk, 0.44; 95% CI, 0.20 to 0.96). The mean (±SD) dose of inhaled budesonide was 107±109 µg per day in the budesonide–formoterol group and 222±113 µg per day in the budesonide maintenance group. The incidence and type of adverse events reported were consistent with those in previous trials and with reports in clinical use. **Conclusion**: The authors concluded in an open-label trial involving adults with mild asthma, budesonide–formoterol used as needed was superior to albuterol used as needed for the prevention of asthma exacerbations.		
Citation	**Design**	**Endpoints**

Sobieraj DM, Weeda ER, Nguyen E, et al. Association of Inhaled Corticosteroids and Long-Acting β-Agonists as Controller and Quick Relief Therapy With Exacerbations and Symptom Control in Persistent Asthma: A Systematic Review and Meta-analysis. JAMA. 2018 Apr 10;319(14):1485-1496. doi: 10.1001/jama.2018.2769.	Meta-analyses of RCTs or observational studies evaluating the use of single product combination ICSs + LABAs as the controller together with quick relief SABA therapy, termed single maintenance and reliever therapy (SMART), vs ICSs +/- LABAs used as the controller therapy and quick relief SABA therapy for patients aged 5 years or older with persistent asthma using a random-effects model Databases MEDLINE (via OVID), EMBASE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews were searched from database inception through August 2016 and updated through November 28, 2017 N = 16 RCTs evaluating 22,748 patients	• Primary: Risk ratio (RR) and risk difference (RD) of asthma exacerbation
Results: Among patients aged 12 years or older, SMART was associated with a reduced risk of asthma exacerbations compared with the same dose of ICS + LABA as the controller therapy (RR, 0.68 [95% CI, 0.58 to 0.80]; RD, -6.4% [95% CI, -10.2% to -2.6%]) and a higher dose of ICS + LABA as the controller therapy (RR, 0.77 [95% CI, 0.60 to 0.98]; RD, -2.8% [95% CI, -5.2% to -0.3%]). Similar results were seen when SMART was compared with ICSs alone as the controller therapy. Among patients aged 4 to 11 years, SMART was associated with a reduced risk of asthma exacerbations compared with a higher dose of ICS as the controller therapy (RR, 0.55 [95% CI, 0.32 to 0.94]; RD, -12.0% [95% CI, -22.5% to -1.5%]) or the same dose of ICS + LABA as the controller therapy (RR, 0.38 [95% CI, 0.23 to 0.63]; RD, -23.2% [95% CI, -33.6% to -12.1%]). **Conclusion:** In patients 12 years of age and older, the use of SMART compared with ICSs as the controller therapy (with or without a LABA) and SABA as the relief therapy was associated with a lower risk of asthma exacerbations. Evidence for patients aged 4 to 11 years was limited.		

Citation	Design	Endpoints
O'Byrne PM, FitzGerald JM, Bateman ED, Barnes PJ, Zhong N, Keen C, et al. Inhaled combined budesonide-formoterol as needed in mild asthma. N Engl J Med. 2018 May 17;378(20):1865-1876. doi: 10.1056/NEJMoa1715274.	A randomized, parallel 52-week, double-blind, phase 3 trial involving patients 12 years of age or older with mild asthma Patients were randomly assigned to one of three groups: 1. Twice-daily placebo plus terbutaline (terbutaline Turbuhaler, AstraZeneca) 0.5 mg used PRN (terbutaline group) 2. Twice-daily placebo plus budesonide–formoterol (Symbicort Turbuhaler, AstraZeneca) 200 µg of budesonide and 6 µg of formoterol used PRN (budesonide–formoterol group) 3. Twice-daily budesonide (Pulmicort Turbuhaler, AstraZeneca), 200 µg plus terbutaline (terbutaline Turbuhaler, AstraZeneca) used PRN (budesonide maintenance group). Inclusion criteria: 12 years of age and older with a documented diagnosis of asthma for ≥ 6 months prior to visit 1. Patients who are in need of Step 2 treatment according to the GINA guidelines. Patients treated with PRN inhaled short-acting bronchodilator only should have a pre-bronchodilator FEV_1 ≥ 60% pf predicted normal (PN) and post-	Primary endpoints: Electronically recorded well-controlled asthma weeks (eWCAW) defined as the fulfillment both of the following 1. Two or more of: a. ≤ 2 days with a daily asthma symptom score >1 b. ≤ 2 days of PRN medication use c. Morning PEF ≥ 80 % of predicted normal everyday 2. Both of the following: a. No nighttime awakenings due to asthma

	bronchodilator $FEV_1 \geq 80\%$. To be randomized patients must have used Bricanyl Turbuhaler PRN on at least 3 separate days during the last week of the run in period.	• No additional inhaled and or systemic glucocorticosteroid treatment due to asthma
Results: Of the 5721 patients who were enrolled, 3849 underwent randomization: 1280 patients were assigned to the terbutaline group, 1279 to the budesonide–formoterol group, and 1290 to the budesonide maintenance group. 3836 patients had data that could be evaluated for the full analysis and safety data sets, and 3363 patients (87.4%) completed the trial. Budesonide–formoterol used PRN was superior to terbutaline used PRN with regard to the primary outcome of the mean percentage of electronically recorded weeks with well-controlled asthma per patient (34.4% vs. 31.1% of weeks; odds ratio, 1.14; 95% confidence interval [CI], 1.00 to 1.30; P=0.046). Budesonide-formoterol was inferior to budesonide maintenance therapy (34.4% and 44.4%, respectively; odds ratio, 0.64; 95% CI, 0.57 to 0.73) The odds of having a week with well-controlled asthma during the 52-week trial period were 14% higher in the budesonide–formoterol group than in the terbutaline group. Adverse events were more frequent in the terbutaline group than the budesonide-formoterol group or the budesonide maintenance group. No notable differences between the adverse effects were seen except that more adverse events led to discontinuation in the terbutaline group. **Conclusion**: Budesonide-formoterol used PRN was a more effective treatment than terbutaline alone in patients with mild asthma. Budesonide-formoterol used PRN was superior to terbutaline for both symptom control and prevention of moderate to severe exacerbations, based on the patients electronically recorded weeks. Budesonide-formoterol used PRN was inferior to budesonide maintenance therapy in achieving electronically recorded well controlled asthma. A strength of this trial was that it included a 1 year duration and a high rate of 80% adherence was observed (with twice daily reminders). One limitation of this trial could be that the patients had to input into their own electric diary and this could be very subjective.		

Formulary Placement, Utilization and Cost Experience (10-01-2024 to 12-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Inhaled Corticosteroids								
Alvesco® (ciclesonide) 80 mcg, 160 mcg aerosol	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Arnuity® Ellipta® (fluticasone furoate) 50 mcg, 100 mcg, 200 mcg DPI	7	5	$1,789.24	$255.61	0	0 (0%)	F	No change
Asmanex® HFA (mometasone furoate) 50 mcg, 100 mcg, 200 mcg aerosol	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Asmanex® Twisthaler® (mometasone furoate) 110 mcg (30 doses); 220 mcg (14, 30, 60, 120 doses) aerosol	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fluticasone propionate (Flovent® Diskus®) 50 mcg, 100 mcg, 250 mcg DPI	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Fluticasone propionate (Flovent® HFA) 44 mcg, 110 mcg, 220 mcg aerosol	14	11	$2,213.54	$158.11	0	0 (0%)	F	No change
Budesonide (Pulmicort Respules®) 0.25 mg/2 mL, 0.5 mg/2 mL, 1 mg/2 mL inhalation suspension	2	1	$299.24	$149.62	1	1 (100%)	F-PA	No change
Pulmicort Flexhaler® (budesonide) 90 mcg, 180 mcg DPI	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Qvar® RediHaler® (beclomethasone dipropionate) 40 mcg, 80 mcg aerosol	19	13	$5,501.95	$289.58	0	0 (0%)	F	No change
TOTAL	**42**	**30**	**$9,803.97**	**$233.43**	**1**	**1 (100%)**		

Key (as applicable) F = Formulary, no restrictions; F-QL = Formulary, quantity limit applies; F-AL = Formulary, age limit applies; F-ST = Formulary, step therapy applies; F-PA = Formulary, PA required; NF = Non-formulary; X = Excluded

Prior Authorization Criteria

No changes

Budesonide Nebulization Solution (Pulmicort Respules)	
Therapeutic Classes (AHFS)	ORALLY INHALED PREPARATIONS (STEROIDS)
Medications	Budesonide nebulization solution (Pulmicort Respules)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	○ Documentation as to why the member cannot use a preferred formulary corticosteroid via inhaler ○ Total daily dose should not exceed 2 mg. Doses beyond 2 mg/day should be reviewed for medical necessity.
Criteria Statement	Budesonide nebulization solution (Pulmicort Respules) are reserved for members who have used (or cannot/should not use) a preferred formulary corticosteroid via inhaler at doses that do not exceed 2mg per day.
Last P&T Review Date	~~12/2024~~3/2025

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Leukotriene Inhibitors

Executive Summary

Class Overview

Leukotrienes are proinflammatory mediators implicated in a variety of disease states. Currently, three leukotriene modifiers are available in the United States. Montelukast and zafirlukast are classified as leukotriene receptor antagonists, while zileuton is classified as a 5-lipoxygenase inhibitor. Guidelines group these agents together as leukotriene receptor antagonists (LTRA) or leukotriene modifiers. Montelukast, zafirlukast, and zileuton are all indicated for the treatment of asthma, while montelukast carries additional indications for prevention of exercise-induced bronchospasm and treatment of allergic rhinitis. These agents are available in oral formulations. LTRAs are generally used as an alternative treatment to inhaled glucocorticoids in mild persistent asthma, or as an add-on agent for moderate to severe persistent asthma management. For the treatment of allergic rhinitis, nasal glucocorticoids or second-generation antihistamines are typically preferred, with leukotriene inhibitors being considered a less effective and more costly alternative option. Leukotriene inhibitors may be used as an alternative to short-acting beta agonists in exercise-induced bronchospasm prevention. It is imperative the patient understands LTRA are not for relief of emergent episodes of bronchoconstriction, and short-acting beta agonist treatment should still be available in these circumstances. All three of the available LTRAs (except the immediate-release form of zileuton) are available generically.

Utilization Findings

There were 51 claims for 41 members, for a total cost of $2,165.52 and an average cost per claim of $42.46. The most highly utilized medication was Montelukast 10mg tablet with 51 claims. There were no prior authorization requests.

Recommendations

- No changes

Clinical Summary

Asthma has classically been difficult to define in a manner acceptable to all disciplines (clinicians, physiologists and pathologists). The Expert Panel Report 3 (EPR-3) of the National Asthma Education and Prevention Program defines asthma as "a common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyperresponsiveness, and an underlying inflammation. The interaction of these features of asthma determines the clinical manifestations and severity of asthma and the response to treatment." The Global Initiative for Asthma (GINA) defines asthma as "a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness, and cough that vary over time and in intensity, together with variable expiratory airflow limitation."

Mainstay treatment options for mild to moderate asthma include short-acting or long-acting beta agonists (SABAs or LABAs), inhaled corticosteroids (ICS), LTRAs, and anticholinergic agents. These different agents can be considered reliever therapies that ease bronchoconstriction (such as SABAs), or controller therapies which mediate the chronic inflammatory processes responsible for pulmonary remodeling (such as ICS). Initial pharmacologic treatment of asthma depends largely on the severity and frequency of symptoms and intensifies in a stepwise fashion up or down depending on the level of response/control achieved by a given intervention. For intermittent asthma symptoms, single-ingredient therapy with short-acting beta agonists (SABAs) had long been the standard of care for bronchodilation in acute control situations. However, recent evidence demonstrates that SABA-only treatment increases the risk of severe exacerbations and death and that the addition of an ICS when reliever therapy is administered reduces those risks. Additionally, indirect evidence from a large, double-blind study in patients with mild asthma comparing budesonide-formoterol as needed (PRN) to SABA-only PRN and SABA PRN + regular ICS supports the use of low dose combination ICS-formoterol (the ICS being either budesonide or [BDP]). Accordingly, GINA guidelines for adults and adolescents 12+ years have been updated to recommend ICS-formoterol as both the preferred “controller” and “reliever” regimens, a treatment regimen commonly known as MART or SMART [maintenance and reliever therapy]. GINA guidelines also recommend ICS-formoterol MART regimens in children 6-11 years as a preferred management option in step 3 and 4 of the treatment algorithm. Notably, this PRN use is not an FDA-approved, labeled use of ICS-formoterol products. Beyond clinical outcomes, GINA guidelines emphasize use of a single inhaler for controller and reliever therapy is advantageous from the perspective of a more simplified regimen for the patient to follow. LTRAs are not usually the first line of treatment for asthma but are used when symptoms are not fully controlled with other medications. The decision to add an LTRA depends on the patient’s individual characteristics, such as allergies and response to other therapies.

Allergic rhinitis is characterized by sneezing, rhinorrhea, nasal obstruction, and itching of the eyes, nose, and mouth. It is also associated with postnasal drip, cough, and fatigue and occurs in 10-30% of individuals in the United States, with the prevalence increasing particularly in urban areas. First-line treatment for allergic rhinitis consists of intranasal corticosteroids and second-generation antihistamines. LTRAs are not recommended as first line due to their inferior efficacy and increased cost as compared to intranasal steroids and antihistamines. There are exceptions to these guideline recommendations, such as when a patient with allergic rhinitis has a concurrent diagnosis of asthma.

There do not appear to be any new drug entities in the pipeline for the LTRA class of drugs.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
Zafirlukast (Accolate®)	Prophylaxis and chronic treatment of asthma in adults and children 5 years of age and older	Adults and children ≥12 yrs: 20 mg twice daily Children 5-11 yrs: 10 mg twice daily
Montelukast (Singulair®)	• Prophylaxis and chronic treatment of asthma in patients 12 months of age and older • Acute prevention of exercise-induced bronchoconstriction (EIB) in patients 6 years of age and older • Relief of symptoms of allergic rhinitis (AR): seasonal allergic rhinitis (SAR) in patients 2 years of age and older, and perennial allergic rhinitis (PAR) in patients 6 months of age and older	Administration (by indications): ○ Asthma: Once daily in the evening for patients 12 months and older. ○ Acute prevention of EIB: One tablet at least 2 hours before exercise for patients 6 years of age and older. ○ Seasonal allergic rhinitis: Once daily for patients 2 years and older. ○ Perennial allergic rhinitis: Once daily for patients 6 months and older. Dosage (by age): ○ 15 years and older: one 10-mg tablet. ○ 6 to 14 years: one 5-mg chewable tablet. ○ 2 to 5 years: one 4-mg chewable tablet or one packet of 4-mg oral granules. ○ 6 to 23 months: one packet of 4-mg oral granules.
Zileuton (Zyflo®, Zyflo CR®)	Prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older	One 600-mg immediate-release tablet four times a day, or two 600 mg extended-release tablets twice daily.

Boxed Warnings and Contraindications

Medication	Boxed Warnings	Contraindications
Zafirlukast (Accolate®)	None	• Hypersensitivity to zafirlukast or any of its inactive ingredients • Patients with hepatic impairment including hepatic cirrhosis
Montelukast (Singulair®)	None	Hypersensitivity to any component of this product
Zileuton (Zyflo®, Zyflo CR®)	None	• Active liver disease or transaminase elevations greater than or equal to three times the upper limit of normal (≥3xULN) • Hypersensitivity to zileuton or any of its inactive ingredients

Warnings/Precautions

Medication	Warnings/Precautions
Zafirlukast (Accolate®)	Hepatotoxicity, bronchospasm, concomitant warfarin administration, eosinophilic conditions, neuropsychiatric events, drug interactions, nursing mothers
Montelukast (Singulair®)	Acute asthma, concomitant corticosteroid use, aspirin sensitivity, neuropsychiatric events, eosinophilic conditions, phenylketonuria
Zileuton (Zyflo®, Zyflo CR®)	Acute asthma, drug interactions, hepatotoxicity, neuropsychiatric events

Practice Guidelines

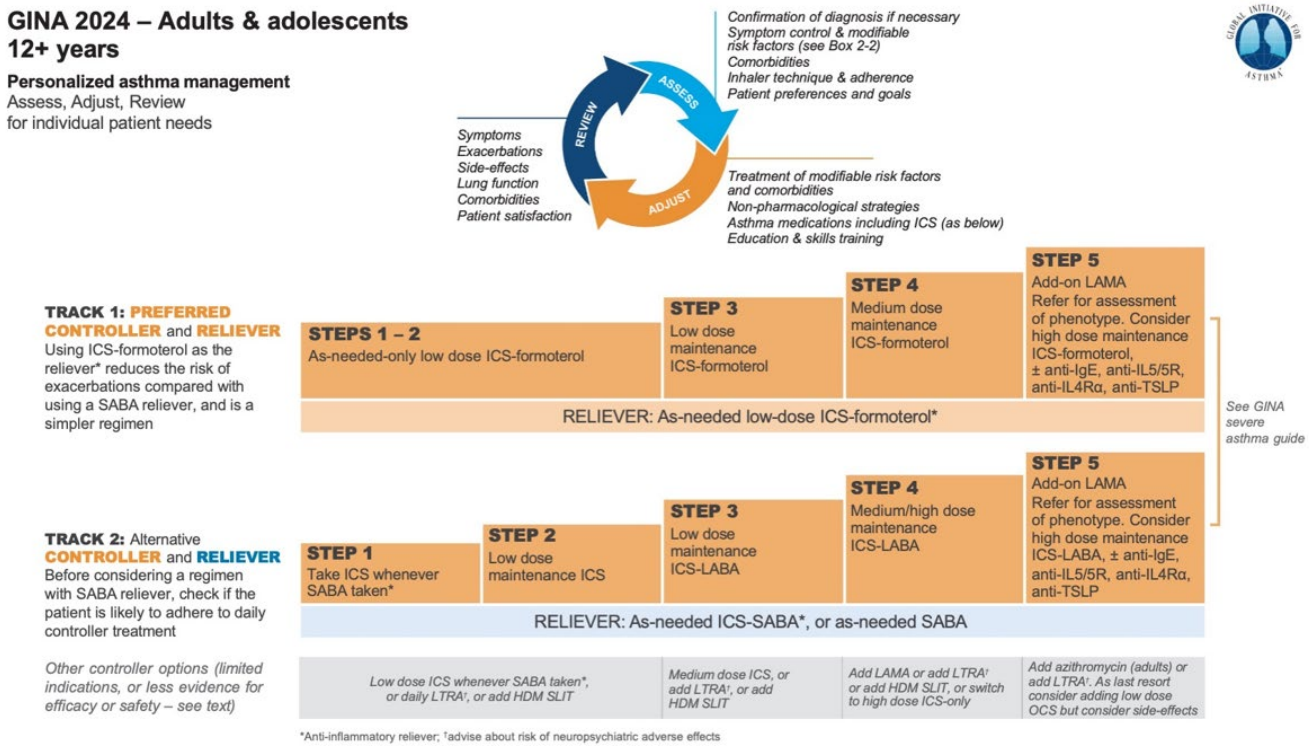
Global Strategy for Asthma Management and Prevention, Global Initiative for Asthma 2024 Report (GINA).

- Other Step 1 or 2 treatment options (Tracks 1 and 2): Leukotriene receptor antagonists (LTRAs) are less effective than ICS, particularly for exacerbations (Evidence A).
- Other Step 3 treatment options (Tracks 1 and 2): Other less efficacious options are low-dose ICS-containing therapy plus either LTRA (Evidence A for lower efficacy than ICS) or low-dose, sustained released theophylline (lack of efficacy, and safety concerns).
- Other Step 4 treatment options (Tracks 1 and 2): Other options for adults or adolescents that can be added to a medium or high-dose ICS, but that are less efficacious than adding LABA, include LTRA (Evidence A), or low-dose sustained release theophylline (Evidence B).

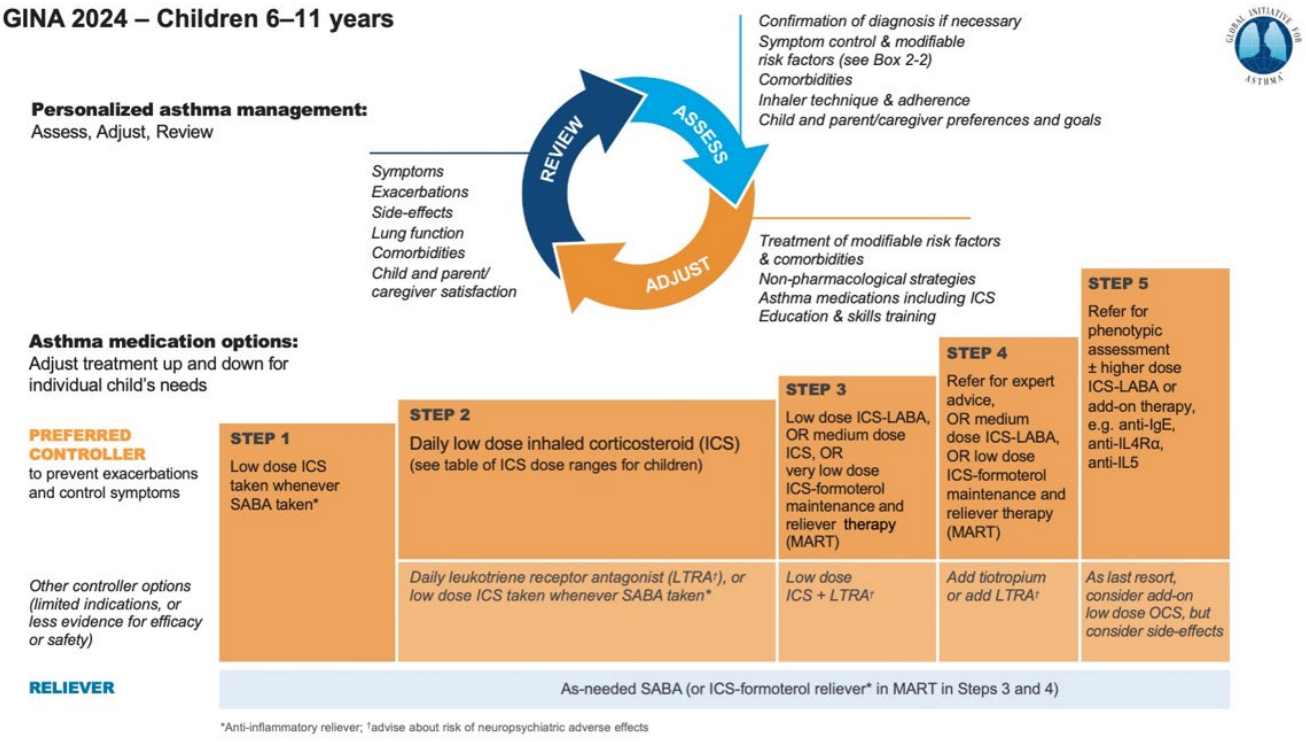
Recommendation Definitions

Class/Level	Sources of evidence	Definition
A	Randomized controlled trials (RCTs), systematic reviews, observational evidence. Rich body of data	Evidence is from endpoints of well-designed RCTs, systematic reviews of relevant studies or observational studies that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires

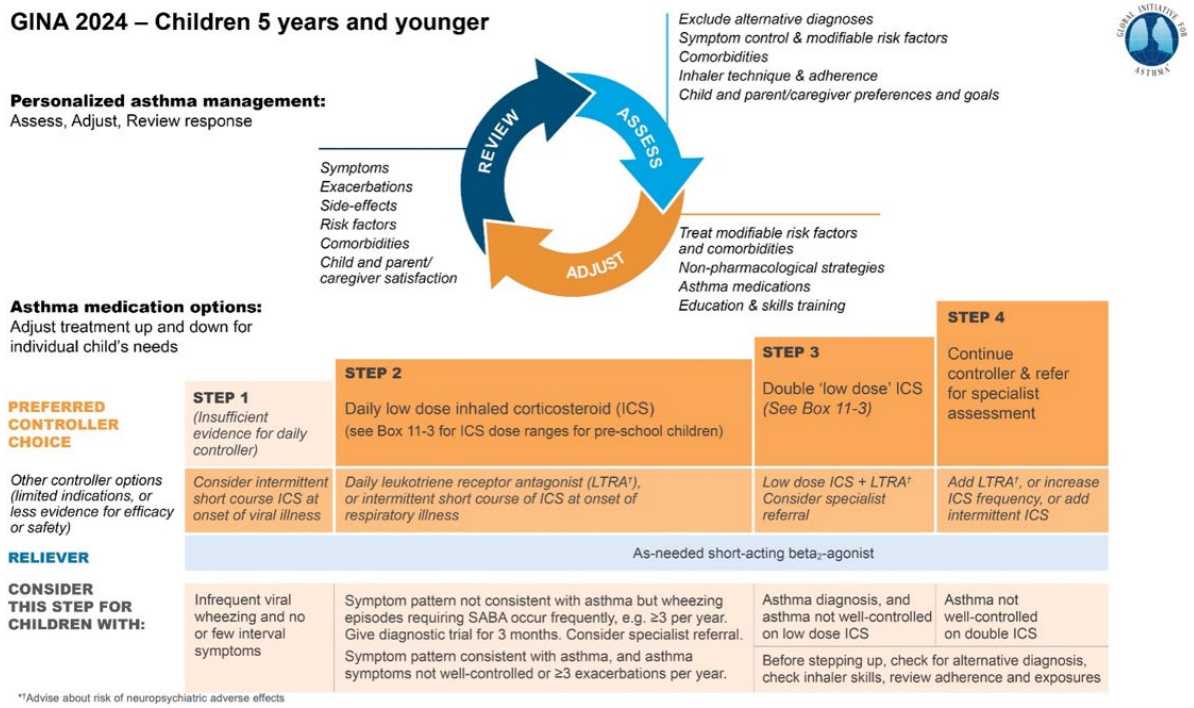
Class/Level	Sources of evidence	Definition
		substantial numbers of studies involving substantial numbers of participants.
B	Randomized controlled trials and systematic reviews. Limited body of data	Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of RCTs or systematic reviews of such RCTs. In general, Category B applies when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Nonrandomized trials or observational studies	Evidence is from non-randomized trials or observational studies.
D	Panel consensus judgement	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above listed criteria.



GINA 2024 – Children 6–11 years



GINA 2024 – Children 5 years and younger



Rhinitis 2020: A Practice Parameter Update. Journal of Allergy and Clinical Immunology.

- We suggest that the clinician not select the oral LTRA montelukast for the initial treatment of allergic rhinitis (AR) due to reduced efficacy when compared with that of other agents. Furthermore, serious neuropsychiatric events that may include suicidal thoughts or actions have been reported in some patients taking montelukast. As advised by the FDA, montelukast should be used to treat AR only in patients who are not treated effectively with or cannot tolerate other alternative therapies (conditional, very low).
- We recommend that the clinician not select an oral LTRA for the treatment of nonallergic rhinitis (NAR) (conditional, very low).
- Recommendation (level of evidence)

Recommendation Definitions

Class/Level	Definition
High	Further research is very unlikely to change our confidence in the estimate of effect. The recommendation is based on high-quality evidence, such as multiple highly rated randomized controlled trials, systematic reviews, or meta-analyses.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. The recommendation would likely be based on somewhat limited evidence, such as reduced number or quality of randomized controlled trials or controlled trials without randomization.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. The recommendation would likely be based on very weak evidence, such as nonexperimental studies, registries, or comparative studies.
Very low	Any estimate of effect is very uncertain. The recommendation is based largely on very low quality studies and/or on expert opinion.
Uncertainty	When there are either no published studies, or very limited and/or very weak evidence, a consensus statement without any category of certainty of evidence was developed. The degree of agreement by all JTFPP and work group members is indicated, with voting details provided if there were dissenting votes.

American Academy of Otolaryngology-Head and Neck Surgery Clinical Practice Guideline 2015: Allergic Rhinitis (reaffirmed April, 2020).

- Strong Recommendations:
  - Clinicians recommend intranasal steroids for patients with a clinical diagnosis of AR whose symptoms affect their quality of life.
  - Clinicians recommend oral second-generation/less sedating antihistamines for patients with AR and primary complaints of sneezing and itching.
- Recommendations **for**:
  - Clinicians should offer, or refer to a clinician who can offer, immunotherapy (sublingual or subcutaneous) for patients with AR who have inadequate response to symptoms with pharmacologic therapy with or without environmental controls.
- Recommendations **against**:
  - Clinicians offering oral leukotriene receptor antagonists as primary therapy for patient with AR.
    - Guideline points out increased cost of these agents vs. less expensive and more clinically effective first line agents such as intranasal corticosteroids and second-generation antihistamines. Exception: patients with concurrent diagnosis of asthma may benefit from this medicine as a first line therapy.
- Options:
  - Clinicians may offer intranasal antihistamines for patients with seasonal, perennial, or episodic AR.

- Clinicians may offer combination pharmacologic therapy in patients with AR who have inadequate response to pharmacologic monotherapy.

Recommendation Definitions

Class/Level	Definition	Implication
Strong Recommendation	The benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent (Grade A or B)[a]. In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The benefits exceed the harms (or that the harms exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (Grade B or C)[a]. In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Clinicians should also generally follow a recommendation but should remain alert to new information and sensitive to patient preferences.
Option	Either the quality of evidence that exists is suspect (Grade D)[a] or that well-done studies (Grade A, B, or C)[a] show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
No Recommendation	There is both a lack of pertinent evidence (Grade D)[a] and an unclear balance between benefits and harms.	Clinicians should feel little constraint in their decision making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role.

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Chauhan B, Jeyaraman M, Singh Mann A, et al. Addition of anti-leukotriene agents to inhaled corticosteroids for adults and adolescents with persistent asthma. Cochrane Database Syst Rev. 2017 Mar 16;3:CD010347. doi: 10.1002/14651858.CD010347.pub2.	A 2017 Cochrane Review of randomized controlled trials (RCTs) of adults and adolescents 12 years of age and older on a maintenance dose of ICS for whom investigators added anti-leukotrienes to the ICS and compared treatment with the same dose, an increased dose or a tapering dose of ICS for at least four weeks. Review included 37 studies and 6128 patients; zileuton was not included.	• Efficacy/safety of LIs added to ICS (compared to same dose, increased dose or tapering dose) in patients with persistent asthma 12 years and older. • To determine if the magnitude of response is influenced by treatments or characteristics of participants.
Results: LIs + ICS vs same-dose ICS: LIs given with ICS reduced the number of patients with exacerbations requiring oral steroids by half. Of the trial reporting adverse events, little difference between groups was noted. Between-group differences favored the addition of LIs for: morning peak expiratory flow rate (PEFR), forced expiratory volume in one second (FEV_1), asthma symptoms and night-time awakenings. **LIs + ICS vs higher dose of ICS:** no statistically significant difference in the number of patients with exacerbations requiring oral corticosteroids or in all adverse events between groups. No statistically significant differences in lung function tests or asthma control measures including use of rescue β_2-agonists or asthma symptom scores. **LIs + ICS vs tapering dose of ICS:** No statistically significant difference in % change from baseline ICS, number of participants with exacerbations requiring oral corticosteroids, or all adverse events. Serious adverse events occurred more frequently among those taking LIs + tapering ICS than in those on tapering doses of ICS alone, but deaths were too infrequent for researchers to draw any conclusions about mortality. Data showed no improvement in lung function or asthma control measures. **Conclusion**: IL agents have benefit in patients as an add-on therapy to an ICS for lung function and control if there are no plans to increase the ICS dose or contraindications/patient preference, but should not be thought of as a "corticosteroid sparing" agent. No conclusions were made as to whether addition of an LI is superior to, inferior to, or the same as increasing the ICS dose. Risk of adverse events was greater with LIs + tapering dose of ICS.		
Citation	**Design**	**Endpoints**
Miligkos M, Bannuru R, Alkofide H, et al. Leukotriene-receptor antagonists versus placebo in the treatment of asthma in adults and adolescents: a systematic review and meta-analysis. Ann Intern Med. 2015 Nov 17;163(10):756-67. doi: 10.7326/M15-1059. Epub 2015 Sep 22.	This SR/MA examined peer-reviewed, English-language, randomized, controlled trials in patients with asthma that reported the effect of LIs versus placebo on measures of asthma control through June 2015. 50 trials met eligibility criteria;	• Determining benefits and harms of LIs either as monotherapy or as combination therapy with ICS vs placebo in adults and adolescents with asthma.

Results: In six trials of LI monotherapy, LI's did show reduced risk for exacerbations of asthma by 40% (summary risk ratio [RR], 0.60 [95% CI, 0.44 to 0.81]). In four trials as add-on therapy to ICS, there was no statistically significant difference in the risk of exacerbations between the intervention groups (summary RR for exacerbation was 0.80 (CI, 0.60 to 1.07)). LIs either as monotherapy or as add-on therapy to ICS increased FEV1, but FEV1 percentage of predicted values was improved only in trials of LI monotherapy. For daytime symptoms, LI's significantly reduced symptoms when used as an add-on to ICS therapy but not as monotherapy. Adverse event rates were similar between intervention and comparator groups.
Conclusion: LIs improved asthma control significantly as monotherapy when compared to a placebo, but the results were not always significant when LIs were used as add-on therapy to ICS. The authors were unable to discern which patients with asthma are more likely to respond than others.

Citation	Design	Endpoints
Xu Y, Zhang J, Wang J. The efficacy and safety of selective H1-antihistamine versus leukotriene receptor antagonist for seasonal allergic rhinitis: a meta-analysis. PLoS One. 2014 Nov 10;9(11):e112815. doi: 10.1371/journal.pone.0112815.	An SR/MA examining eligible studies comparing efficacy and safety for SAH and LI for SAR up to September 2014. Studies had to be randomized, controlled trials or case-control studies. Nine studies including 5,781 subjects were included.	• Comparing the efficacy and safety of selective H1-antihistamines (SAH) and LIs for seasonal allergic rhinitis.

Results:

- SAH was better than LI for daytime eye symptoms score (MD = 0.06, 95% CI, 0.03 to 0.10, P = 0.000, I2 = 99%) and composite symptoms score (MD = 0.03, 95% CI, 0.01 to 0.05, P = 0.010, I2 = 98%).
- LIs were superior in night-time symptoms score (MD = -0.04, 95% CI, -0.05 to -0.02, P = 0.000, I2 = 97%).
- Subgroup analysis indicated factors such as gender, duration and dose might impact comparisons of the effects of these drugs on efficacy.

Conclusion: Authors suggest SAH may be more appropriate for daytime nasal symptoms, but LIs may be more appropriate for nighttime symptoms. Overall, the comparative safety and efficacy were very similar.

Formulary Placement, Utilization and Cost Experience (10-01-2024 to 12-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Leukotriene Receptor Antagonist								
Zafirlukast (Accolate®) 10 mg, 20 mg oral tablets	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Montelukast (Singulair®) 4 mg oral granules	0	0	$0.00	$0.00	0	0 (0%)	F- QL (30/30) AL>2yo	No change
Montelukast (Singulair®) 4 mg, 5 mg chewable tablets	0	0	$0.00	$0.00	0	0 (0%)	F-QL(30/30) AL >1 <5	No change
Montelukast (Singulair®) 10 mg oral tablets	51	41	$2,165.52	$42.46	0	0 (0%)	F-QL(30/30)	No change
5-Lipoxygenase Inhibitors								
Zyflo® (zileuton) 600 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Zileuton 600 mg extended release (ER) oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	51	41	$2,165.52	$42.46	0	0 (0%)		

Key (as applicable) F = Formulary, no restrictions; F-QL = Formulary, quantity limit applies; F-AL = Formulary, age limit applies; F-ST = Formulary, step therapy applies; F-PA = Formulary, PA required; NF = Non-formulary; X = Excluded

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Drug Name: Methylergonovine maleate (Methergine) **Manufacturer:** Novel Laboratories

Approval Date: November 19, 1946

Recommendation

- No changes
  - The current formulary status is F
  - There was 1 claim for 1 member for a total cost of $17.79 and no prior authorization requests from 10/1/2024 to 12/31/2024

Prescribing Information

Indication

Following delivery of placenta, for routine management of uterine atony, hemorrhage and subinvolution of the uterus. For control of uterine hemorrhage in the second stage of labor following delivery of the anterior shoulder.

Mechanism of Action

Methergine acts directly on the smooth muscle of the uterus and increases the tone, rate, and amplitude of rhythmic contractions. Thus, it induces a rapid and sustained tetanic uterotonic effect which shortens the third stage of labor and reduces blood loss.

Dosage and Administration

Oral dosing: 0.2 mg 3 or 4 times daily in the puerperium for a maximum of 1 week.

Black Box Warning

None

Adverse Reactions

Most common: Hypertension, headache, abdominal pain, nausea, and vomiting

Serious: Myocardial infarction and seizure

Use in Specific Populations, Pregnancy

Animal reproductive studies have not been conducted with methylergonovine. It is also not known whether methylergonovine maleate can cause fetal harm or can affect reproductive capacity. Use of methylergonovine is contraindicated during pregnancy because of its uterotonic effects.

Drug Interactions

CYP 3A4 Inhibitors: There have been rare reports of serious adverse events in connection with the coadministration of certain ergot alkaloid drugs (e.g., dihydroergotamine and ergotamine) and potent CYP 3A4 inhibitors (e.g., macrolide antibiotics and protease inhibitors), resulting in vasospasm leading to cerebral ischemia and/or ischemia of the extremities. Potent CYP 3A4 inhibitors should not be coadministered with Methergine.

CYP3A4 Inducers: Drugs that are strong inducers of CYP3A4 (e.g., nevirapine, rifampicin) are likely to decrease the pharmacological action of Methergine.

Beta-Blockers: Caution should be exercised when Methergine is used concurrently with beta-blockers. Concomitant administration with beta-blockers may enhance the vasoconstrictive action of ergot alkaloids.

Anesthetics: Anesthetics like halothan and methoxyfluran may reduce the oxytocic potency of Methergine.

Glyceryl Trinitrate and Other Antianginal Drugs: Methylergonovine maleate produces vasoconstriction and can be expected to reduce the effect of glyceryl trinitrate and other antianginal drugs.

How Supplied

Oral Tablets: 0.2 mg

Price

$221

(Per month, based on NADAC.)

Clinical Studies

Completed

Title	Reduction of Endometritis After Cesarean Section With the Routine Use of Methergine NCT: 00858832
Design	• Allocation: Randomized • Intervention Model: Parallel Assignment • Masking: None (Open Label) • Primary Purpose: Prevention
Population	N=80, patients 18 and older having singleton pregnancies without evidence of intra-amniotic infection that are undergoing a non-elective cesarean delivery with a normal blood pressure.

Arms	Patient were randomized to receive either: • Methergine 0.2 mg orally every 6 hours for two days, plus routine postpartum care • Routine postpartum care
Endpoint(s)	Number of participants who developed endometritis
Inclusion Criteria	• Female singleton gravidas • Patients receiving non-elective cesarean deliveries after trial of labor • No evidence of chorioamnionitis
Exclusion Criteria	• Diagnosis of chorioamnionitis • Elective cesarean section • Immunocompromised patients and those on antiretroviral drugs • Patients with known infection • Hypertension (two blood pressure readings greater than 140/90, six hours apart), including those with a past history, gestational or preeclampsia • Allergic to ergot alkaloids, including migraine medicine
Results	Fourteen patients (36%) in the control group and four patients (10%) in the Methergine group were diagnosed with endometritis (P<0.005; odds ratio, 5.2; 95% confidence interval, 1.5 to 17.5). Additionally, while the preoperative hemoglobin (Hb) values between the two groups were similar, the mean postoperative Hb level was 10.2 gm/dL in the control group and -11.2 gm/dL in the study group (P<0.001), showing that Methergine reduced postoperative blood loss. There were no significant demographic differences between the two groups.
Conclusion	N/A
Interpretation	While this was on open-label trial design which can introduce bias, Methergine appears to be a successful intervention as a preventative measure for endometritis. It also appears to conserve appropriate Hb levels postoperatively.

Title	The Effect of the Combined Use of Methylergonovine and Oxytocin during Caesarean Section in the Prevention of Post-partum Hemorrhage NCT: N/A PMID: 26449959
Design	Randomized, prospective trial
Population	N=1210, patients 18 to 40 years of age with gestation greater than 34 weeks, with gravida 1 to 3. The mean age of patients was about 31 years.

Arms	Two groups of patients undergoing caesarean section at the same clinic were randomized to receive either: • A combination of methylergonovine (given 0.2 mg IM in the first minute after delivery and post-operatively after 3 hours) and oxytocin (per IV infusion) during the intra-operative and post-operative periods (N=295) • Only oxytocin infusion in the intra-operative and post-operative periods (N=915)
Endpoint(s)	Mean reduction rates of Hb levels in the post-partum period
Inclusion Criteria	• Age 18–40 years • Gestation ≥34 weeks • Gravida 1–3; and all with indications for Caesarean
Exclusion Criteria	• Those with known pre-eclampsia, eclampsia and hypertensive disease • Patients with coagulation disorder • Patients who had been given blood transfusion • Those diagnosed with severe anemia (Hb<7 gr/dL) and polycythemia vera (Hb>16 gr/dL) • Patients with known ischemic heart disease, cerebrovascular disease or peripheral vascular disease, and with no post-partum uterine atony which would require additional medical therapy or blood transfusion due to change in Hb levels
Results	When pre-operative and post-operative Hb values of the patients administered and not administered with methylergonovine maleate were compared, no significant difference was found between the mean pre-operative Hb values of both groups (P=0.687). However, the mean post-operative Hb values of the group which received methylergonovine maleate were found to be statistically significantly higher (P=0.005). In the group administered with methylergonovine maleate, the mean reduction in Hb level of 0.85 ± 0.97 units, between the pre-operative and post-operative readings, was determined to be statistically significant (P=0.001). In the group not administered with methylergonovine maleate, the mean reduction in Hb level of 1.05 ± 0.95 units, between the pre-operative and post-operative readings, was also found to be statistically significant (P=0.001). It was determined that the extent of the reduction in postoperative Hb values compared to pre-operative Hb values demonstrated a highly significant difference between the two groups (P=0.002). The extent of the reduction in post-operative Hb values compared to pre-operative Hb values was found to be significantly greater in the group receiving oxytocin only, as compared with the group receiving the combined treatment.
Conclusion	Uterotonic treatment plays an important role in post-partum hemorrhage. Prophylactic methylergonovine treatments with oxytocin combination treatments were significantly more successful than treatments with oxytocin only for the patients in this study, without any evidence of

	adverse side effects. The authors call for larger scale studies for determination of a consensus in approach to post-partum hemorrhage prophylaxis.
Interpretation	Only healthy patients (with low cardiovascular risk) were included in the study, therefore potentially providing biased safety results in terms of the methylergonovine intervention.

Ongoing

There are no ongoing studies for oral Methergine currently. The following study is underway regarding IM/IV formulations of methylergonovine.

Guidelines

American College of Obstetrics and Gynecologists (ACOG) Practice Bulletin No. 183: Postpartum Hemorrhage. Obstet Gynecol. 2017;130(4):e168-e186.

ACOG does not make recommendations for oral use of Methergine for control of postpartum hemorrhage, but rather the use of IM methylergonovine. Uterotonic agents are considered first-line therapy, but specific agents are not given rank or preference due to a lack of data showing any one product's superiority over another.

Clinical Opinions

Methergine appears to have benefit as a second line agent for appropriately selected candidates for use in treatment of post-partum hemorrhage and in a prophylactic setting. Due to the fact that this medication has been on the market for several years, well-controlled clinical data (in particular pivotal data) is unavailable or potentially non-existent, and new research is scarce. Use of the IM formulation of the product is common in most settings where emergent control of bleeding is needed, as its desired effects are realized much more quickly than when taken orally. Oral use of Methergine should be limited, as less expensive options exist for management.

Alternatives

Drug Name^	Formulary Status	Dosage Form	Price*
Misoprostol (Cytotec)	F	100 mcg, 200 mcg oral tablets	$2 (for one-time 600 mcg dose)

Methylergonovine maleate injection	NF	0.2 mg/1 mL injection solution	$31 (per 1 mL vial)
Carboprost tromethamine (Hemabate)	NF	250 mcg/1 mL intramuscular solution	$319 (per 1 mL ampule)
Tranexamic acid (Cyklokapron)	NF	1000 mg/10 mL intravenous solution	$4 (per 10 mL vial)

^The manner in which the Drug Name is listed implies its availability. The generic name is listed first, with brand in parenthesis, if the product is available as a generic. The brand name is listed first, with the generic name in parenthesis, if the product is available as a brand only.

**Price per month unless otherwise noted. Pricing for multi-source generic medications based on National Average Drug Acquisition Cost (NADAC). Pricing for single-source branded medications and generic drugs without NADAC data based on Wholesale Acquisition Cost (WAC).*

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Alameda MRGs for review Q1 2025 P&T Consent Agenda

Recommendation: No changes

Angiotensin II Receptor Blockers and Renin Inhibitors	
Therapeutic Classes (AHFS)	Angiotensin II Receptor Inhibitors and Renin Inhibitors
Medications	**FORMULARY STATUS: Formulary, Pays at Point-of-Sale (first line)** Losartan (Cozaar) Tablets: 25 mg, 50 mg, 100 mg Losartan/Hydrochlorothiazide (Hyzaar) Tablets: 50mg/12.5mg, 100mg/12.5mg, 100mg/25mg Valsartan/Hydrochlorothiazide (Diovan-HCT) Tablets: 80mg/12.5mg, 160mg/12.5mg,160mg/25mg,320mg/12.5mg, 320mg/25mg Valsartan (Diovan) Tablets: 40 mg, 80mg, 160mg, 320mg Irbesartan (Avapro) Tablets: 75mg, 150mg, 300mg Irbesartan/Hydrochlorothiazide (Avalide) Tablets: 150mg/12.5mg, 300mg/12.5mg Telmisartan (Micardis) Tablets: 20mg, 40mg, 80mg Olmesartan Medoxomil (Benicar) Tablets: 5mg, 20mg, 40mg Olmesartan Medoxomil/ Hydrochlorothiazide (Benicar HCT) Tablets: 20mg/12.5mg, 40mg/12.5mg, 40mg/25mg Amlodipine Besylate/Valsartan (Exforge) Tablets: 5mg/160mg, 5mg/320mg, 10mg/160mg, 10mg/320mg **FORMULARY STATUS: Formulary, Requires Prior Authorization (second line)** Amlodipine Besylate/Olmesartan Medoxomil (Azor) Tablets: 5mg/20mg, 5mg/40mg, 10mg/20mg,10mg/40mg Telmisartan/Hydrochlorothiazide (Micardis-HCT) Tablets: 40mg/12.5mg, 80mg/12.5mg, 80mg/25mg Candesartan Cilexetil/ Hydrochlorothiazide (Atacand HCT) Tablets: 16mg/12.5mg, 32mg/12.5mg, 32mg/25mg Candesartan Cilexetil (Atacand) Tablets: 4mg, 8mg, 16mg, 32mg **FORMULARY STATUS: Formulary, Requires Prior Authorization (third line)** Edarbi (Azilsartan) Tablets: 40mg, 80mg Edarbyclor (Azilsartan/ Chlorthalidone) Tablets: 40mg/12.5mg, 40mg/25mg Aliskiren (Tekturna) Tablets: 150mg, 300mg Amlodipine/Valsartan/Hydrochlorothiazide (Exforge HCT) Tablets: 5mg/160mg/12.5mg, 5mg/160mg/25 mg, 10mg/160mg/12.5mg, 10mg/160mg/25mg, 10mg/320mg/25mg Olmesartan Medoxomil/Amlodipine/Hydrochlorothiazide (Tribenzor) Tablets: 20mg/5mg/12.5mg, 40mg/5mg/12.5mg, 40mg/5mg/25mg, 40mg/10mg/12.5mg, 40mg/10mg/25mg Telmisartan/Amlodipine (Twynsta) Tablets: 40mg/5mg, 40mg/10mg, 80mg/5mg, 80mg/10mg Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months

	If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**PA Criteria for approval (2nd line):** • Documented trial and failure or intolerance of two first line agents for at least 15 days of therapy within the previous 90 days. **PA Criteria for approval (3rd line):** • Documented trial and failure or intolerance of two first line agents for at least 15 days of therapy within the previous 90 days AND documented trial and failure or intolerance of one second line agent for at least 15 days of therapy within the previous 90 days
Criteria Statement	Second line medications are reserved for members who have used (or cannot/should not use) two first line medications. Third line medications are reserved for members who have used (or cannot/should not use) two first line medications and one second line medication.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Atovaquone (Mepron)	
Therapeutic Classes (AHFS)	Antiprotozoals, Miscellaneous
Medications	Formulary, PA required Atovaquone (Mepron)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Criteria for approval: • For prophylaxis or acute oral treatment of mild to moderate Pneumocystis jiroveci pneumonia (PCP) AND • Documented trial and failure, intolerance, inability to use, or contraindication to therapeutic doses of trimethoprim-sulfamethoxazole (TMP/SMX) (first-line therapy)
Criteria Statement	Atovaquone is reserved for members that have used (or cannot/should not use) trimethoprim-sulfamethoxazole (TMP/SMX)
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Tadalafil (Cialis) for BPH	
Therapeutic Classes (AHFS)	Phosphodiesterase type 5 inhibitor
Medications	Non-formulary Tadalafil (Cialis) 2.5, 5 mg
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	The following criteria must be met: • Patient has diagnosis of benign prostatic hyperplasia (BPH) • Documentation of trial and failure, intolerance, contraindication, or inability to use at least ONE alpha blocker • Drug is being requested at an FDA approved dose.
Criteria Statement	For benign prostatic hyperplasia (BPH), tadalafil (Cialis) 2.5 and 5 mg are reserved for members who have previously used (or cannot/should not use) at least one alpha blocker such as alfuzosin, terazosin, doxazosin, or tamsulosin.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Corlanor (ivabradine)	
Therapeutic Classes (AHFS)	Cardiac drugs, miscellaneous
Medications	Formulary, PA required: Corlanor (ivabradine)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Provider must be a cardiologist
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial authorization:** **All** of the following conditions must be met in adult patients: • Diagnosis of stable symptomatic chronic heart failure (NYHA Class II-IV) • Documented left ventricular ejection fraction less than or equal to 35% • Documentation (claims history or chart notes) patient is on maximally tolerated doses of beta-blockers or have contraindication to beta blocker use • Documentation that the patient has a resting heart rate greater than or equal to 70 bpm • Documentation that the patient has had a previous admission to a hospital for worsening heart failure within the past 12 months while on at least two medications from two different medication classes used in the treatment of heart failure with reduced ejection fraction • Documentation Corlanor is being used in combination with an angiotensin converting enzyme (ACE) inhibitor, an angiotensin II receptor blocker (ARB) or angiotensin II receptor blocker/ neprilysin inhibitor (ARNI) unless not tolerated or contraindicated. • Corlanor may **not** be approved if the request indicates **any** of the following: o Severe hypotension (less than 90/50 mmHg) o Severe hepatic impairment (Child-Pugh class C) o Patient's heart rate maintained exclusively by a pacemaker All of the following conditions must be met in pediatric patients. • Member has stable heart failure (NYHA/Ross functional class II-IV) due to dilated cardiomyopathy and a left ventricular ejection fraction ≤ 45% • Member is in sinus rhythm with an elevated resting heart rate **Reauthorization:** • The medication is being prescribed at an appropriate FDA approved dose and indication • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit).
Criteria Statement	Corlanor is reserved for adult members with heart failure and who have used (or cannot/should not use) beta blockers, and an angiotensin converting enzyme (ACE)

	inhibitor, an angiotensin II receptor blocker (ARB), or an angiotensin II receptor blocker/ neprilysin inhibitor (ARNI) and who have been hospitalized due to heart failure in the previous 12 months. Corlanor is reserved for pediatric members with heart failure and are in sinus rhythm with an elevated resting heart rate.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Injectable Anticoagulants	
Therapeutic Classes (AHFS)	Anticoagulants
Medications	**Preferred:** Formulary, with quantity limits Enoxaparin is formulary with quantity limits and will be approved automatically within these limits, the below criteria applies to those requests that exceed these limits. **Non-Preferred:** Non-formulary fondaparinux (Arixtra) Fragmin (dalteparin) Any newly marketed injectable anticoagulant
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	Member's current weight
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** For the use in venous thromboembolism (VTE):- up to a 31-day duration (unless greater duration of therapy is requested and medically necessary then will be approved for up to a 6 month duration). For use in pregnant members: up to 6 weeks past the patient's expected due date. For use in members with cancer: 6 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	If the request is for fondaparinux or Fragmin, documentation must be provided of trial and failure, intolerance, contraindication, or inability to use enoxaparin AND the following criteria must be met. PA CRITERIA FOR APPROVAL FOR USE IN VENOUS THROMBOEMBOLISM (VTE): • The medication is being prescribed for the prevention and/or treatment of VTE • The medication is being prescribed at a dose that is within FDA approved guidelines and/or is supported by the medical compendia. • The prescriber must provide a medical reason why the member cannot be treated with a preferred formulary oral anticoagulant (e.g. Eliquis). PA CRITERIA FOR APPROVAL FOR USE IN A PREGNANT MEMBER: • The medication is being prescribed for the prevention or treatment of a VTE while the member is pregnant. • Documentation of the expected due date (EDD). • The medication is being recommended and prescribed by an obstetrician or a hematologist at a dose that is within FDA approved guidelines and/or is supported by the medical compendia. PA CRITERIA FOR APPROVAL FOR USE IN MEMBER WITH CANCER:

Injectable Anticoagulants	
	• The medication is being prescribed for the prevention or treatment of a VTEfor a member with cancer. • The medication is being prescribed at a dose that is within FDA approved guidelines and/or is supported by the medical compendium as defined by the Social Security Act and/or per the National Comprehensive Cancer Network (NCCN) or American Society of Clinical Oncology (ASCO) standard of care guidelines. • The medication is being prescribed by an oncologist/hematologist • The prescriber must provide a medical reason why the member cannot be treated with a preferred formulary oral anti-coagulant (e.g. Eliquis). REAUTHORIZATION CRITERIA FOR APPROVAL FOR USE IN MEMBER WITH CANCER: • The medication is being used for the prevention and/or treatment of a VTE for a member with cancer. • The prescriber must provide a valid medical reason as to why the member needs to continue treatment and cannot be treated with a preferred formulary oral anticoagulant. • The medication is being prescribed an oncologist/hematologist The medication is being prescribed at a dose that is within FDA approved guidelines or is supported by the medical compendium as defined by the Social Security Act and/or per the National Comprehensive Cancer Network (NCCN) or American Society of Clinical Oncology (ASCO) standard of care guidelines.
Criteria Statement	For venous thromboembolism (VTE) treatment or prevention, enoxaparin is reserved for members who have used (or cannot/should not use) a preferred formularyoral anticoagulant (e.g. Eliquis). For pregnant members, enoxaparin is reserved for members who need treatment or prevention of venous thromboembolism (VTE) For members with cancer, enoxaparin is reserved for members who need treatment or prevention of venous thromboembolism (VTE) who have used (or cannot/should not use) a preferred formulary oral anticoagulant (e.g. Eliquis). Fragmin or fondaparinux are reserved for members who cannot/should not use enoxaparin.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Elmiron (pentosane polysulfate sodium)	
Therapeutic Classes (AHFS)	Protective agents
Medications	Formulary, limited to members age 16 years or older, #90 capsules per 30 days, and 6 fills per year Elmiron 100 mg capsule
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 6 months **Later Approvals** 6 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For requests exceeding 6 months of therapy, the following criteria must be met: • Documentation of medical necessity for therapy beyond 6 months is required. ○ Efficacy and safety of continued treatment after 6 months of therapy is unknown. • The medication is being prescribed at a dose that is within FDA approved guidelines.
Criteria Statement	Using Elmiron for more than 6 months is reserved for members who have a medical reason for using Elmiron for longer than 6 months.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Ezetimibe (Zetia)	
Therapeutic Classes (AHFS)	Cholesterol Absorption Inhibitors
Medications	Formulary, step therapy required Ezetimibe (Zetia) 10 mg tablet
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	The following criteria must be met: • Documented trial and failure, intolerance, contraindication, or inability to use, a formulary preferred statin in the previous 100 days OR • Diagnosis of homozygous sitosterolemia
Criteria Statement	Ezetimibe is reserved for members who have used or who cannot or should not use statin medications or for members with a diagnosis of homozygous sitosterolemia.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: Remove AirDuo Digihaler from the criteria as it was discontinued

Inhaled Corticosteroids/Long-Acting Beta-Agonists (ICS/LABA) Combinations	
Therapeutic Classes (AHFS)	Corticosteroids (respiratory tract)
Medications	**Formulary, PA required** Dulera (mometasone/formoterol) fluticasone/salmeterol (Advair HFA) fluticasone/vilanterol (Breo Ellipta) **Non-Formulary** ~~AirDuo Digihaler (fluticasone/salmeterol)~~ Airsupra (albuterol sulfate-budesonide) 90 mcg-80 mcg Inhaler Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Asthma • Documentation of adequate trial and failure, intolerance or inability to use formulary inhaled corticosteroid/long-acting beta agonist combination fluticasone/salmeterol (AirDuo) OR fluticasone/salmeterol (Advair Diskus/ Wixela Inhub) OR budesonide/formoterol (Symbicort) COPD • Documentation of adequate trial and failure, intolerance or inability to use formulary inhaled corticosteroid/long-acting beta agonist combination fluticasone/salmeterol (Advair Diskus/ Wixela Inhub) OR budesonide/formoterol (Symbicort)
Criteria Statement	Dulera, fluticasone/vilanterol (Breo Ellipta), ~~AirDuo Digihaler,~~ fluticasone/salmeterol (Advair HFA), or Airsupra are reserved for members who have used (or cannot/should not use) fluticasone/salmeterol (AirDuo) OR fluticasone/salmeterol (Advair Diskus/ Wixela Inhub) OR budesonide/formoterol (Symbicort), dependent on diagnosis.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Altoprev (lovastatin ER) and Fluvastatin, Fluvastatin ER	
Therapeutic Classes (AHFS)	Antihyperlipidemic – HMG CoA reductase inhibitors
Medications	Non-formulary (non-preferred, requires prior authorization): Altoprev (lovastatin ER) 20, 40, 60 mg capsules Fluvastatin 20, 40 mg capsule Fluvastatin ER 80 mg tablet
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Altoprev, fluvastatin, or fluvastatin ER are approved when the following criteria are met: • Documentation of a trial and failure, intolerance, contraindication, or inability to use ALL formulary alternative statins at maximally tolerated doses: simvastatin, lovastatin, pravastatin, atorvastatin, and rosuvastatin.
Criteria Statement	Altoprev, fluvastatin, or fluvastatin ER are reserved for members who have used (or cannot/should not use) ALL formulary alternative statins at highest allowed doses: simvastatin, lovastatin, pravastatin, atorvastatin, and rosuvastatin.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Symlin (pramlintide)	
Therapeutic Classes (AHFS)	Amylinomimetics
Medications	Formulary, PA required Symlin (pramlintide)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	None
Prescriber Restrictions	Prescriber is an endocrinologist
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	All of the following must be met: • Diagnosis of Type I or Type II diabetes • Patient requires the use of mealtime insulin (e.g. Humulin/Novolin, Apidra/Humalog/Novolog) • Patient unable to achieve blood glucose control despite optimal insulin therapy • Documentation patient's A1C is ≤ 9%
Criteria Statement	SymlinPen is reserved for members with uncontrolled type 1 or type 2 diabetes using mealtime insulin and A1C is 9% or lower.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Histamine H2 Receptor Antagonists	
Therapeutic Classes (AHFS)	Histamine H2 Receptor Antagonists
Medications	Formulary, step therapy required Cimetidine 200, 300, 400, 800 mg tablets
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Criteria for approval: Cimetidine tablets are approved when the following criteria is met: • Documentation of a trial and failure, intolerance, contraindication, or inability to use famotidine tablets.
Criteria Statement	Cimetidine tablets are reserved for members who have used (or cannot/should not use) famotidine tablets.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Brilinta (ticagrelor) tablet		
Therapeutic Classes (AHFS)	Platelet aggregation inhibitors	
Medications	Formulary, PA required Brilinta (ticagrelor) 60, 90 mg tablet	
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.	
Exclusion Criteria	N/A	
Required Clinical Information	See "**PA Review Criteria**" below	
Age Restrictions	N/A	
Prescriber Restrictions	N/A	
Coverage Duration	**Initial Approval**	For stable CAD, primary prevention: 12 months For ischemic stroke (NIHSS score ≤5) or high-risk transient ischemic attack (ABCD2 score ≥4), 30 days For ACS or history of MI: 12 months (for the 90mg twice daily dose only) during the first year after an ACS event
	Later Approvals	For stable CAD, primary prevention and ACS or history of MI: 12 months For ischemic stroke (NIHSS score ≤5) or high-risk transient ischemic attack (ABCD2 score ≥4), do not approve If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**Initial Approval**
	• For a diagnosis of coronary artery disease (stable) and high risk for ischemic cardiovascular events, primary prevention
	  ○ 60mg twice daily dose is used in combination with aspirin
	OR
	• For a diagnosis of minor ischemic stroke (NIHSS score ≤5) or high-risk transient ischemic attack (ABCD2 score ≥4)
	  ○ 90mg twice daily dose is used in combination with aspirin
	OR
	• For a diagnosis of acute coronary syndrome (ACS) OR a history of myocardial infarction (MI)
	  ○ 90mg twice daily dose is used in combination with aspirin
	  ○ Patient has trialed and failed clopidogrel AND prasugrel or documentation has been provided to show that there is a medical reason why ticagrelor should be preferred over clopidogrel (for example: the patient has diabetes, over 50% stenosis in more than one vessel, or is over the age of 60, etc.) AND prasugrel (for example: the patient is at high risk of bleeding complications, or has history of transient ischemic attack (TIA), or stroke).
	Later Approval	

	• For a diagnosis of coronary artery disease (stable) and high risk for ischemic cardiovascular events, primary prevention, the patient is stable and the provider recommends continuation of therapy • For a diagnosis of minor ischemic stroke (NIHSS score ≤5) or high-risk transient ischemic attack (ABCD2 score ≥4), continuation past 30 days is not indicated, do not approve • For a diagnosis of acute coronary syndrome (ACS) OR a history of myocardial infarction (MI), the patient is stable on the previous 90mg twice daily dose and converts to the 60mg twice daily dose after 12 months of therapy, unless the provider submits a reason why (e.g. the patient has an ongoing high ischemic risk) the 90mg twice daily dose continues to be necessary
Criteria Statement	Brilinta is reserved for members with a diagnosis of stable coronary artery disease with a high risk for cardiovascular events. Brilinta is reserved for members with a diagnosis of minor ischemic stroke (NIHSS score ≤5) or high-risk transient ischemic attack (ABCD2 score ≥4). Brilinta is reserved for patients who have either acute coronary syndrome or a past heart attack who have tried and failed or are unable to take clopidogrel AND prasugrel.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

GLP-1 Agonists	
Therapeutic Classes (AHFS)	GLP-1 Agonists
Medications	**Formulary, Step therapy required (prior use of metformin)** • Trulicity (dulaglutide) • Ozempic (semaglutide) • Rybelsus (semaglutide) • Mounjaro (tirzepatide) **Formulary, PA required** • Byetta, Bydureon, Bydureon Bcise (exenatide) • Victoza (liraglutide) Any other newly marketed incretin GLP-1 Agonist
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Criteria for Type 2 Diabetes** For formulary, step-therapy required medications, approve if: • Documentation of trial and failure, intolerance, contraindication, or inability to use metformin For formulary medications that require prior authorization, approve if: • The above criteria are met AND documentation of trial and failure, intolerance, contraindication or inability to use one preferred formulary step therapy required alternative
Criteria Statement	Preferred formulary, step therapy required medications <insert medication name> are reserved for members with type 2 diabetes who have used (or cannot/should not use) metformin. Medications that require prior authorization <insert medication name> are reserved for members with type 2 diabetes who have used (or cannot/should not use) metformin AND one preferred, formulary step therapy required medication.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

DPP-4 Inhibitors and Combinations	
Therapeutic Classes (AHFS)	Dipeptidyl Peptidase-4 (DPP-4) Inhibitors
Medications	**Formulary, Step therapy required (prior use of metformin)** • Alogliptin (Nesina) • Alogliptin/metformin (Kazano) • Alogliptin/pioglitazone (Oseni) • Januvia (sitagliptin) • Janumet, Janumet XR (sitagliptin/metformin) **Formulary, PA required/ Non-formulary** • Tradjenta (lingagliptin) • Jentadueto, Jentadueto XR (linagliptin/metformin) • Onglyza (saxagliptin) • Kombiglyze XR (saxagliptin/metformin) • Zituvio (sitagliptin) Any other newly marketed dipeptidyl peptidase-4 (DPP-4) inhibitor
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Criteria for Type 2 Diabetes** For formulary, step-therapy required medications, approve if: • Documentation of trial and failure, intolerance, contraindication, or inability to use metformin For formulary medications that require prior authorization, approve if: • The above criteria are met AND documentation of trial and failure, intolerance, contraindication or inability to use one preferred formulary step therapy required alternative
Criteria Statement	Preferred formulary, step therapy required medications <insert medication name> are reserved for members with type 2 diabetes who have used (or cannot/should not use) metformin. Medications that require prior authorization <insert medication name> are reserved for members with type 2 diabetes who have used (or cannot/should not use) metformin AND one preferred, formulary step therapy required medication
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes, correct grammar

SGLT2 inhibitors and Combinations	
Therapeutic Classes (AHFS)	Glucose Cotransport 2 Inhibitors (SGLT2 inhibitors)
Medications	**Formulary, step therapy required** • Steglatro (ertiugluiflozin) • Segluromet (ertiugluiflozin/metformin) • Farxiga (dapaglif<u>l</u>ozin) • Xigduo XR (dapagliflozin/metformin) **Formulary, PA required/Non-formulary** • Jardiance (empagliflozin) • Synjardy/Synjardy XR (empagliflozin/metformin) • Dapaglif<u>l</u>ozin (Farxiga) • Dapagliflozin/metformin (Xigduo XR) • Invokana (canaglif<u>l</u>ozin) • Invokamet (canagliflozin/metformin) • Steglujan (ertugliflozin/sitagliptin) • Trijardy XR (empagliflozin-linagliptin-metformin) • Glyxambi (empagliflozin/linagliptin) • Qtern (dapagliflozin/saxagliptin) • Inpefa (sotagliflozin) Any other newly marketed sodium glucose cotransport 2 inhibitor (SGLT2 inhibitor)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Formulary, step therapy required medications** For formulary, step-therapy required medications, approve if: • Trial and failure of one of the following: ○ Metformin, branded/generic drug containing metformin, branded angiotensin receptor/neprilysin inhibitor (ARNi), generic angiotensin-converting enzyme inhibitor (ACEi), generic angiotensin receptor blocker (ARB), generic mineralocorticoid receptor antagonist (MRA), or generic beta blocker **Formulary, PA required/Non-formulary medications** For medications that require prior authorization or are non-formulary, approve if:

	• The above criteria are met AND documentation of trial and failure, intolerance, contraindication or inability to use one preferred formulary step therapy medication
Criteria Statement	Preferred formulary, step therapy required medications <insert medication name> are reserved for members who have used (or cannot/should not use) one of the following medications: metformin, branded/generic drugs containing metformin, branded angiotensin receptor/neprilysin inhibitor (ARNi), generic angiotensin-converting enzyme inhibitor (ACEi), generic angiotensin receptor blocker (ARB), generic mineralocorticoid receptor antagonist (MRA), or generic beta blockers. Medications that require prior authorization or are non-formulary <insert medication name> are reserved for members who have used (or cannot/should not use) one of the following medications: metformin, branded/generic drugs containing metformin, branded angiotensin receptor/neprilysin inhibitor (ARNi), generic angiotensin-converting enzyme inhibitor (ACEi), generic angiotensin receptor blocker (ARB), generic mineralocorticoid receptor antagonist (MRA), or generic beta blockers AND one preferred, formulary step therapy required medication.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Parkinson's Disease Agents	
Therapeutic Classes (AHFS)	DOPAMINE PRECURSORS
Medications	**Formulary, Step Therapy Required** Carbidopa-levodopa-entacapone (Stalevo) oral tablet Entacapone (Comtan) oral tablet **Formulary, Prior Authorization** Tolcapone (Tasmar) Ongentys (opicapone)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 1 month for tolcapone (Tasmar)), 12 months for all other medications in this policy **Later Approvals** 12 months If criteria are not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	Formulary, step therapy required medications require trial and failure of carbidopa-levodopa INITIAL CRITERIA FOR AUTHORIZATION • Diagnosis of Parkinson's disease AND • Documentation patient is currently taking carbidopa and levodopa AND currently experiencing symptom fluctuations or "off" episodes AND not responding to or are not candidates for other adjunctive therapies (such as dopamine agonists [e.g., pramipexole or ropinirole] or monoamine oxidase B inhibitors [e.g., selegiline]) AND • Documented trial and failure, contraindication or intolerance to carbidopa-levodopa-entacapone (Stalevo). RENEWAL CRITERIA • Documentation of positive clinical response ○ If clinical improvement is not seen with tolcapone (Tasmar) after 3 weeks of use, tolcapone (Tasmar) should be discontinued. • Dosing is appropriate as per labeling or is supported by compendia or standard of care guidelines
Criteria Statement	Carbidopa-levodopa-entacapone and entacapone are reserved for members who are using carbidopa and levodopa and are still experiencing symptoms. Tolcapone (Tasmar) or Ongentys are reserved for members who are using carbidopa and levodopa and are still experiencing symptoms and have used (or cannot/should not use) carbidopa-levodopa-entacapone (Stalevo) and also other adjunctive therapies

	(such as dopamine agonists [e.g., pramipexole or ropinirole] or monoamine oxidase B inhibitors [e.g., selegiline])
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: Add preferred NDCs for Repatha and Praluent

PCSK-9 Monoclonal Antibodies (mAbs)	
Therapeutic Classes (AHFS)	PCSK9 Monoclonal Antibodies (mAbs)
Medications	Formulary, prior authorization Repatha (evolocumab) Preferred NDCs: 72511-0770-01, 72511-0750-01, 72511-0760-02, 72511-0760-01 Praluent (alirocumab) Preferred NDCs: 61755-0021-02, 61755-0020-02
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be cardiologist or a specialist in the treatment of lipid disorders.
Coverage Duration	**Initial Approval** 3 months **Later Approvals** 6 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**INITIAL AUTHORIZATION:** **For all requests** • Request is appropriate for member (e.g. age) as indicated in package labeling or standard of care guidelines • Patient has tried and failed simvastatin 40mg, atorvastatin 40mg-80mg, or rosuvastatin 20-40mg (consistently for 3 months via claim history or chart notes). If patient is not able to tolerate simvastatin, atorvastatin or rosuvastatin, documentation was provided that patient is taking another statin at the highest tolerated dose, or a medical reason was provided why the member is not able to use these therapies. • If prescriber indicates member is "statin intolerant", documentation was provided including description of the side effects, duration of therapy, "wash out", re-trial, and then change of agents. • Patient has tried and failed ezetimibe in combination with highest-tolerated intensity statin (if clinically appropriate) consistently for 3 months, OR, patient has an LDL-C that is >25% above goal LDL-C while adherent to treatment with highest-tolerated intensity statin (if clinically appropriate) consistently for 3 months • Documentation was provided indicating provider has counseled member on smoking cessation and following a "heart healthy diet". **Diagnosis of Familial Hypercholesterolemia (FH)** • Member has a diagnosis of familial hypercholesterolemia, as evidenced by one of the following: ○ Documentation provided, including two fasting lipid panel lab reports with abnormal baseline low density lipoprotein (LDL) levels ≥190 for FH in adults or ≥160 for FH in children. ○ Results of positive genetic testing for an LDL-C–raising gene defect (LDL receptor, apoB, or PCSK9) **Diagnosis of hyperlipidemia (Primary OR Secondary Prevention):** • If the diagnosis is primary severe hyperlipidemia (i.e. baseline LDL ≥ 190 mg/dL)

<table>
<tr><th colspan="2">PCSK-9 Monoclonal Antibodies (mAbs)</th></tr>
<tr><td></td><td>

LDL remains ≥ 100 mg/dL despite maximally tolerated LDL-lowering therapy

If the diagnosis is secondary atherosclerotic cardiovascular disease (ASCVD) prevention

The patient is “very high risk” (both of the following):

(i.e. a history of multiple major ASCVD <u>events</u> or 1 major ASCVD event and multiple high-risk <u>conditions</u>, see table below)

<table>
<tr><td rowspan="4">Major ASCVD Events</td><td>Recent ACS (within past 12 months)</td></tr>
<tr><td>History of MI (other than recent ACS event above)</td></tr>
<tr><td>History of ischemic stroke</td></tr>
<tr><td>Symptomatic PAD</td></tr>
<tr><td rowspan="8">High-risk Conditions</td><td>Age ≥ 65 years</td></tr>
<tr><td>Heterozygous familial hypercholesterolemia</td></tr>
<tr><td>History of prior CABG or PCI intervention outside the major ASCVD event(s)</td></tr>
<tr><td>DM</td></tr>
<tr><td>HTN</td></tr>
<tr><td>CKD (eGFR 15-59 mL/min/1.73 m2)</td></tr>
<tr><td>Current smoker</td></tr>
<tr><td>CHF</td></tr>
</table>
ACS – acute coronary syndrome; CABG – coronary artery bypass graft; CHF – congestive heart failure; CKD – chronic kidney disease; DM – diabetes mellitus; HTN – hypertension; MI – myocardial infarction; PAD – peripheral artery disease; PCI – percutaneous coronary intervention

LDL remains ≥ 55 mg/dL or non-HDL (i.e. total cholesterol minus HDL) ≥ 85 mg/dL despite maximally tolerated LDL-lowering therapy

The patient is not at very high risk:

LDL remains ≥ 70 mg/dL or non-HDL (i.e. total cholesterol minus HDL) ≥ 100 mg/dL despite maximally tolerated LDL-lowering therapy

If the above criteria are met, the request will be approved for up to a 3 month duration; if all of the above criteria are not met, the request will be sent to a clinical reviewer.
<u>REAUTHORIZATION CRITERIA FOR ALL INDICATIONS:</u>

Documentation submitted indicates that the member has obtained clinical benefit from the medication including repeat fasting lipid panel lab report, and the member has had a reduction in LDL from baseline, prior to starting PCSK9 inhibitor therapy
The patient’s claim history shows consistent therapy (i.e. monthly fills)

</td></tr>
<tr><td>Psck
Criteria Statement</td><td>For familial hypercholesterolemia, Repatha and Praluent are reserved for members who have used (or cannot/should not use) simvastatin 40 mg, atorvastatin 40 or 80 mg or rosuvastatin 20 or 40 mg tablets AND ezetimibe, are following a heart healthy diet, a non-smoker or trying to quit smoking, has two cholesterol tests with low density lipoprotein (LDL) ≥190 for adults or ≥160 for children or results of positive genetic testing for an LDL-C–raising gene defect.
For hyperlipidemia (primary or secondary prevention) Repatha and Praluent are reserved for members who have used (or cannot/should not use) simvastatin 40 mg, atorvastatin 40 or 80 mg or rosuvastatin 20 or 40 mg tablets AND ezetimibe, following a heart healthy diet, a non-smoker or trying to quit smoking. For primary severe hyperlipidemia, LDL that remains ≥ 100 mg/dL despite maximally tolerated LDL-</td></tr>
</table>

PCSK-9 Monoclonal Antibodies (mAbs)	
	lowering therapy. For secondary atherosclerotic cardiovascular disease (ASCVD), LDL remains ≥ 55 mg/dL or non-HDL (i.e. total cholesterol minus HDL) ≥ 85 mg/dL for those at very high risk, or LDL remains ≥ 70 mg/dL or non-HDL (i.e. total cholesterol minus HDL) ≥ 100 mg/dL for those not at very high risk, despite maximally tolerated LDL-lowering therapy.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Linezolid	
Therapeutic Classes (AHFS)	Oxazolidinone antibiotics
Medications	Formulary, Step Therapy Linezolid ****Please Note: If the request is for linezolid for the treatment of multi-drug resistant tuberculosis, refer to criteria for medications for the treatment of multi-drug resistant tuberculosis *****
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all of the criteria are met, approve up 1 fill up to FDA approved maximum dosing If the criteria is not met, the request will be referred to a clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for approval: • Appropriate diagnosis/indication AND • Appropriate dose of medication based on age (i.e. pediatric and elderly populations) and indication AND • Documented trial and failure or intolerance to up to two formulary antibiotics that are used to treat the documented diagnosis OR • No other formulary medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia. OR • Based on culture and sensitivity data, linezolid is the only treatment option.
Criteria Statement	Linezolid is reserved for members who have used (or cannot/should not use) up to two formulary medications with the same mechanism of action (if available) or that are used to treat the documented diagnosis based on patient-specific factors.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Pyridostigmine (Mestinon)	
Therapeutic Classes (AHFS)	Parasympathomimetic (cholinergic) agents
Medications	Formulary, PA required Pyridostigmine (Mestinon) (Regonol)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	None
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Criteria for initial authorization: • Used for the treatment of myasthenia gravis at FDA-approved doses. Criteria for re-authorization: • Patient is stable and continuing the medication AND • Medication is used for appropriate indication and at appropriate dose
Criteria Statement	Mestinon is reserved for members who have a diagnosis of myasthenia gravis and are using it at the recommended doses.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Long-Acting Muscarinic /Long-Acting Beta Agonist/ Corticosteroid inhaled Triple Combination Products	
Therapeutic Classes (AHFS)	Asthma/COPD Tx - Beta-adrenergic-Anticholinergic-Glucocorticoid combinations
Medications	Formulary, PA required Trelegy Ellipta (fluticasone/ umeclidinium/ vilanterol) Breztri Aerosphere (budesonide/ glycopyrrolate/ formoterol)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	The following criteria must be met: • Used for an FDA-approved dose and indication • The patient has been well controlled, for at least 3 months, on a regimen consisting of formulary/ preferred single/ combo agents of: an inhaled long-acting beta-agonist (LABA), AND inhaled long-acting antimuscarinic agent (LAMA), AND inhaled corticosteroid (ICS), or combinations thereof, however has compliance issues with multiple inhalers OR • The patient has tried and failed a regimen consisting of formulary/ preferred single/ combo agents consisting of: an inhaled long-acting beta-agonist (LABA), AND inhaled long-acting antimuscarinic agent (LAMA), AND inhaled corticosteroid (ICS), or combinations thereof
Criteria Statement	Trelegy Ellipta and Breztri Aerosphere are reserved for patients with a diagnosis of COPD or asthma who have been stable for at least 3 months on a regimen consisting of an inhaled long-acting beta-agonist (LABA), AND inhaled long-acting antimuscarinic agent (LAMA), AND inhaled corticosteroid (ICS) or combinations thereof, but has a compliance issue OR has used (or cannot/ should not use) a combination on a regimen consisting of multiple inhaled long-acting beta-agonist (LABA), AND inhaled long-acting antimuscarinic agent (LAMA), AND inhaled corticosteroid (ICS) or combinations thereof.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Corticosteroid Preparations to Treat Hemorrhoids	
Therapeutic Classes (AHFS)	Corticosteroids (skin, mucous membrane)
Medications	Formulary Hydrocortisone acetate (Anucort-HC) rectal suppository 25 Mg Hydrocortisone (Proctozone-HC) topical cream with perineal applicator 2.5 % Formulary, PA required Proctofoam HC (hydrocortisone/pramoxine) 1%-1% rectal foam Hydrocortisone acetate (Proctocort) rectal suppository 30mg
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial/ Re-Approval** 7 days If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	Initial criteria for authorization for formulary, PA-required medications: • Documented trial and failure, intolerance, inability to use, or contraindication to one preferred formulary medication Re-approval criteria for formulary, PA-required medications • For requests greater than 7 days of treatment, the provider must submit a medical reason of necessity for treatment longer than 7 days
	Proctofoam HC 1%-1% rectal foam and hydrocortisone acetate (Proctocort) rectal suppository 30mg are reserved for members are using the medications for 7 days or less and who have used (or cannot/ should not use) hydrocortisone acetate (Anucort-HC) rectal suppository 25 Mg or hydrocortisone (Proctozone-HC) topical cream with perineal applicator 2.5 %.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Savella (milnacipran) tablet	
Therapeutic Classes (AHFS)	Fibromyalgia Agents
Medications	Formulary, step therapy required Savella (milnacipran)tablet
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Reauthorization** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Savella tablet step therapy criteria: • Documentation of a trial and failure or intolerance to duloxetine required.
	Savella tablet is reserved for members who have used (or cannot/should not use) duloxetine.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Travoprost (Travatan Z) ophthalmic drops	
Therapeutic Classes (AHFS)	Prostaglandin analogs
Medications	Formulary, step therapy required Travoprost (Travatan Z) ophthalmic drops 0.004 %
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Reauthorization** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Travoprost (Travatan Z) ophthalmic drops step therapy criteria: • Documentation of a trial and failure or intolerance to latanoprost eye drops required.
	Travoprost (Travatan Z) ophthalmic drops are reserved for members who have used (or cannot/should not use) latanoprost eye drops.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Arikayce (amikacin)	
Therapeutic Classes (AHFS)	AMINOGLYCOSIDE ANTIBIOTICS
Medications	Formulary, PA required Arikayce (amikacin liposome) inhalation suspension
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a pulmonologist, or specialist in the treatment of infectious disease or cystic fibrosis
Coverage Duration	**Initial/ Re-Approval** 6 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Initial criteria for the use of Arikayce (amikacin liposome) inhalation suspension • Refractory MAC lung disease: defined as patients who did not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy AND • The medication is being prescribed at a dose that is within FDA approved guidelines
Criteria Statement	For the treatment of mycobacterium avium complex (MAC), Arikayce is reserved for members who do not have negative lung cultures after 6 months of using multiple treatments for this condition.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes, except update naming convention to reflect generic availability of Esbriet, pirfenidone

Antifibrotic Respiratory Tract Agents	
Therapeutic Classes (AHFS)	Antifibrotic Agents
Medications	Formulary, PA required Ofev (nintedanib) Pirfenidone (Esbriet) ~~(pirfenidone)~~
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber is a pulmonologist or lung transplant specialist
Coverage Duration	**Initial Approval** 6 months **Later Approval** 6 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**INITIAL CRITERIA FOR ALL DIAGNOSES:** • Patient is 18 years of age or older • Provider attests that they have reviewed the patient's other medications, and addressed all potential drug interactions • Documentation has been provided that the patient does not smoke **INITIAL CRITERIA FOR IDIOPATHIC PULMONARY FIBROSIS:** • Confirmed diagnosis of Idiopathic Pulmonary Fibrosis attested to by prescriber • Pulmonary function test indicate patient has Forced Vital Capacity (FVC) greater than or equal to 50% within 30 days of request **INITIAL CRITERIA FOR SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (ILD) (SSc-ILD):** • The request is for Ofev (nintedanib). • Confirmed diagnosis of SSc-ILD attested to by prescriber • FVC ≥ 40% within 30 days of request • Trial and failure of mycophenolate mofetil (MMF), cyclophosphamide or azathioprine. **INITIAL CRITERIA FOR CHRONIC FIBROSING INTERSTITIAL LUNG DISEASE (ILDS) WITH A PROGRESSIVE PHENOTYPE:** • The request is for Ofev (nintedanib). • Diagnosis of chronic fibrosing ILD (e.g. connective tissue disease [CTD]-associated ILD, chronic fibrosing hypersensitivity pneumonitis [HP], idiopathic non-specific interstitial pneumonia [iNSIP], unclassifiable idiopathic interstitial pneumonia [IIP], environmental/occupational lung disease or sarcoidosis) with a progressive phenotype attested to by prescriber • Recent (12 month) history of treatment with at least one medication to treat ILDs (e.g. a corticosteroid, azathioprine, mycophenolate mofetil (MMF), n-acetylcysteine (NAC), rituximab, cyclophosphamide, cyclosporine, or tacrolimus) • FVC ≥ 45% predicted within 30 days of request

	REAUTHORIZATION CRITERIA: • Documentation submitted indicates that the member has obtained clinical benefit from the medication • Documentation has been provided that the patient does not smoke
Criteria Statement	Ofev and ~~Esbriet~~ pirfenidone are reserved for members with a diagnosis of pulmonary fibrosis have pulmonary function tests with FVC over 50%, and have documentation of non-smoking status. Ofev is reserved for members with a diagnosis of systemic sclerosis-associated interstitial lung disease, pulmonary function tests with FVC greater than or equal to 40%, and who has used (or cannot/should not use) mycophenolate mofetil, cyclophosphamide, or azathioprine, and have documentation of non-smoking status. Ofev is reserved for members with a diagnosis of chronic fibrosing interstitial lung disease with a progressive phenotype, pulmonary function tests with FVC greater than or equal to 45% predicted, who has used (or cannot/should not use)) at least one medication to treat ILDs (e.g. a corticosteroid, azathioprine, mycophenolate mofetil, n-acetylcysteine (NAC), rituximab, cyclophosphamide, cyclosporine, or tacrolimus), and have documentation of non-smoking status.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: Update naming of referenced policies

Biologic Agents for Nasal Polyposis	
Therapeutic Classes (AHFS)	SKIN AND MUCOUS MEMBRANE AGENTS, MISC.; RESPIRATORY TRACT AGENTS, MISCELLANEOUS
Medications	Formulary, PA required Dupixent (dupilumab) Xolair (omalizumab) Nucala (mepolizumab)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Use of Dupixent, Nucala, or Xolair concomitantly or with another pulmonary biologic (e.g. Fasenra, Cinqair)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Patients must be 18 years age or older Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Must be prescribed by, or in consultation with an allergist/immunologist or otolaryngologist
Coverage Duration	**Initial Approval** If the criteria are met, the initial request may be approved for up to a 6-month duration. **Reauthorization** Reauthorization requests may be approved for 6 months. If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.

PA Review Criteria	****Xolair: For asthma, ~~and~~ urticaria, and food allergy, please refer to the "Xolair (omalizumab) for Asthma, ~~and~~ Urticaria, and IgE-Mediated Food Allergy" policy****
	
	****Dupixent: For atopic dermatitis, please refer to the "Agents for Atopic Dermatitis" policy; For asthma & COPD, please refer to the "Pulmonary Biologics for ~~Asthma~~Respiratory and Eosinophilic Conditions" policy****
	
	****Nucala: For asthma or other eosinophilic conditions, please refer to the "Pulmonary Biologics for ~~Asthma~~Respiratory and Eosinophilic Conditions" policy****
	
	Initial Authorization:
	• Diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP)
	• Medication is being prescribed at an FDA approved dosage
	• Patient is currently using an intranasal corticosteroid and will continue therapy, will be prescribed an intranasal corticosteroid with request, or has a medical reason for not using an intranasal corticosteroid
	• Documentation of ONE of the following:
	  ○ Trial and failure or intolerance or has a medical reason for not using ALL of the following therapies:
	  ▪ an intranasal corticosteroid
	  ▪ a systemic corticosteroid
	  ○ Prior surgery for nasal polyps
	
	Re-authorization:
	• Member will continue to use intranasal corticosteroid, or has a medical reason for not using an intranasal corticosteroid

	• Documentation has been provided that demonstrates a clinical benefit (e.g. improvements in symptom severity, nasal polyp score [NPS], sino-nasal outcome test-22 [SNOT-22], nasal congestion score [NCS]), nasal obstruction symptom visual analogue scale [VAS]) • Medication is being prescribed at an FDA-approved dosage
	When used for chronic rhinosinusitis with nasal polyps, Xolair, Nucala, or Dupixent are reserved for members who have used (or cannot/should not use) an intranasal steroid (and will continue using it) and additionally, who have used (or cannot/should not use) all of the following: intranasal corticosteroids and a systemic corticosteroid, OR has had prior surgery for nasal polyps.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Verquvo	
Therapeutic Classes (AHFS)	VASODILATING AGENTS, MISCELLANEOUS
Medications	Formulary, PA required Verquvo (vericiguat)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Patients must be 18 years age or older Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a cardiologist (or in consultation with cardiologist)
Coverage Duration	**Initial Approval** 12 months **Reauthorization** 12 months. If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.

PA Review Criteria	**Criteria For Authorization**
	• Medication is prescribed at an FDA approved dose
	• The medication is being used for the treatment of symptomatic chronic heart failure with reduced ejection fraction (less than 45%)
	• Documentation that the patient has had a previous hospitalization for heart failure or has required outpatient IV diuretics
	• Member is currently being prescribed, or will be prescribed, at least one of the following treatment regimens, or documentation has been provided that the member is not able to tolerate these agents:
	  ○ Angiotensin-converting enzyme (ACE) inhibitor OR angiotensin receptor blocker (ARB) OR angiotensin receptor/neprilysin inhibitor (ARNI)
	  ○ Mineralocorticoid receptor antagonist (e.g. spironolactone)
	  ○ Beta-blocker
	  ○ Sodium glucose cotransport 2 (SGLT-2) inhibitor (e.g. Steglatro)
	• Patient is not concomitantly using a long-acting nitrate (e.g. isosorbide mononitrate, transdermal nitroglycerin) or a phosphodiesterase-5 (PDE-5) enzyme inhibitor (e.g sildenafil)
	• Negative pregnancy test (for females of reproductive age; as indicated) within 30 days of request.
	• Prescriber attests to discussing with females of reproductive potential the need to use effective forms of contraception during treatment and for one month after stopping treatment.

	Verquvo is reserved for members with a diagnosis of symptomatic chronic heart failure with reduced ejection fraction (less than 45%) who have had a previous hospitalization for heart failure or have required outpatient IV diuretics, and is currently taking (or cannot/should not take) an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) or angiotensin receptor/neprilysin inhibitor, OR a mineralocorticoid receptor antagonist (e.g. spironolactone) OR a beta-blocker OR a sodium glucose cotransport 2 (SGLT-2) inhibitor (e.g. Steglatro); who is not using a long-acting nitrate and has a negative pregnancy test within the last 30 days (as appropriate).
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Siklos (hydroxyurea)	
Therapeutic Classes (AHFS)	BLOOD FORM.,COAG,THROMBOSIS AGENTS MISC.
Medications	Formulary, PA required Siklos (hydroxyurea) tablets
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a hematologist or other specialist with expertise in the diagnosis and management of sickle cell disease
Coverage Duration	**Initial Approval** If the criteria are met, the initial request may be approved for up to a 12-month duration. **Reauthorization** Reauthorization requests may be approved for 12 months. If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial authorization:** • Diagnosis of sickle cell disease • Request is for an FDA approved dose • Documented trial and failure or intolerance to hydroxyurea capsules at a maximum tolerated dose OR • Medical reason why patient is unable to use hydroxyurea capsules **Reauthorization:** • Prescriber attests member experienced a reduction in number of sickle cell crises or their condition is stable as a result of Siklos therapy • Request is for an FDA approved dose
Criteria Statement	Siklos is reserved for members with sickle cell disease who have used (or cannot/should not use) hydroxyurea capsules.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Presbyopia Agents	
Therapeutic Classes (AHFS)	Miotics
Medications	Vuity (pilocarpine HCl ophthalmic solution) Qlosi (pilocarpine HCl ophthalmic solution)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age Vuity: 40-55 years Qlosi: 45-64 years
Prescriber Restrictions	Prescribed by an optometrist or ophthalmologist
Coverage Duration	**Initial Approval** 6 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization:** • Diagnosis of presbyopia • Trial and failure or contraindication to corrective lenses (i.e., eye glasses, contact lenses) • Medication is prescribed at an FDA approved dose **Re-Authorization:** • Documentation or provider attestation of positive clinical response • Medication is prescribed at an FDA approved dose
Criteria Statement	Vuity and Qlosi are reserved for members who have used (or cannot/should not use) corrective lenses (i.e., eye glasses, contact lenses).
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Zurzuvae	
Therapeutic Classes (AHFS)	Antidepressants, Miscellaneous
Medications	Zurzuvae (zuranolone) capsule
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age According to package insert
Prescriber Restrictions	Prescriber must be a psychiatrist or an obstetrician-gynecologist.
Coverage Duration	If all of the criteria are met, the initial request will be approved for one 14-day course of Zurzuvae per postpartum period. Reauthorization will not be permitted.
PA Review Criteria	**Initial Authorization:** • Physician attestation of moderate to severe postpartum depression (PPD) diagnosis and submission of validated screening tool result(s) (e.g. Edinburgh Postnatal Depression Scale, Hamilton Depression Rating Scale) • Onset of a major depressive episode within 6 months of delivery • Medication is prescribed at an FDA approved dose
Criteria Statement	Zurzuvae is reserved for members who have a diagnosis of moderate to severe postpartum depression (PPD) and submission of validated screening tool result(s) (e.g. Edinburgh Postnatal Depression Scale, Hamilton Depression Rating Scale) with onset of a major depressive episode within 6 months of delivery.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Dificid	
Therapeutic Classes (AHFS)	Other Macrolides
Medications	Dificid (fidaxomicin)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by an infectious disease specialist or gastroenterologist
Coverage Duration	If the criteria are met, the request will be approved for up to a 10-day duration.
PA Review Criteria	**Authorization for initial Clostridium difficile infection:** 1. Documentation provided for intolerance or medical reason why patient is unable to use oral vancomycin 2. Dose requested follows FDA labeling **Authorization for recurrent Clostridium difficile infection:** 1. Documentation provided that patient has tried oral vancomycin for management of Clostridium difficile infection 2. Dose requested follows FDA labeling
Criteria Statement	Dificid is reserved for members who have either an initial or recurrent Clostridium difficile infection who have used (or cannot/should not use) oral vancomycin.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Emergency Use Authorization (EUA) Drugs/Products for COVID-19	
Medications	Any approved drug/product by EUA for COVID-19
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “other criteria”
Age Restrictions	As outlined within current FDA Emergency Use Authorization (EUA) guidelines
Prescriber Restrictions	N/A
Coverage Duration	As outlined within current FDA Emergency Use Authorization (EUA) guideline
Maximum Billable Units	Variable
Other Criteria	Emergency Use Authorization for COVID-19 related drugs/products (all must apply): • The requested drug/product has a currently active Emergency Use Authorization as issued by the U.S. Food and Drug Administration. • Use of the requested drug/product is consistent with the current terms and conditions of the emergency use authorization (such as appropriate age/weight, formulation, disease severity, concurrent use with other medications or medical interventions, etc.). • Attestation that the requested drug/product was purchased by the entity seeking payment (not provided at no charge/reimbursed by the U.S. government). If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.
Last Review Date	~~3/2024~~3/2025

Recommendation: No changes, minor formatting correction

Primary Hyperoxaluria Agents	
Medications	Oxlumo (lumasiran) Rivfloza (nedosiran)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber must be a nephrologist, urologist, hepatologist, or endocrinologist
Coverage Duration	A 6 month duration for initial approval and 12 months for renewal
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization**
	• Diagnosis of primary hyperoxaluria type 1 (PH1) confirmed by one of the following:
	  ○ Genetic testing confirming at least one mutation at the AGXT gene
	  ○ Liver biopsy showing decreased or absent alanine:glyoxylate aminotransferase (AGT) activity
	• Metabolic testing demonstrating one of the following:
	  ○ For Oxlumo (one of the following):
	  ▪ Increased urinary oxalate excretion (≥ 0.5 mmol/1.73 m2 per day[45 mg/1.73 m2 per day])
	  ▪ Increased urinary oxalate:creatinine ratio relative to normative values for age
	  ▪ Increased plasma oxalate level (≥ 20 µmol/L)
	  ○ For Rivfloza (one of the following):
	  ▪ Increased urinary oxalate excretion (≥ 0.5 mmol/1.73 m2 per day[45 mg/1.73 m2 per day])
	  ▪ Increased urinary oxalate:creatinine ratio relative to normative values for age
	• For Rivfloza: member has relatively preserved kidney function (e.g., EGFR ≥ 30 mL/min/1.73 m2)
	• Member is concurrently using pyridoxine or has tried and failed previous pyridoxine therapy for at least 3 months, or has a medical reason for not using pyridoxine
	• Member has no history of liver or kidney transplant
	• Medication is prescribed at an FDA approved dose
	• Patient is not using Oxlumo and Rivfloza concurrently
	Reauthorization
	• Members previously using pyridoxine will continue to use it, or have a medical reason for not using it
	• Documentation has been provided that demonstrates a clinical benefit (e.g. symptomatic improvement, reduction in urinary or plasma oxalate levels from baseline)
	• Medication is prescribed at an FDA approved dose
	• Patient is not using Oxlumo and Rivfloza concurrently
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review

Last Review Date	~~3/2024~~3/2025

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Recommendation: No changes

Tzield	
Medications	Tzield (teplizumab-mzwv)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for Healthcare Professional (USP DI), and the Drug Package Insert, and/or per the National Comprehensive Cancer Network (NCCN)
Exclusion Criteria	Type 2 diabetes (T2D)
Required Clinical Information	See "other criteria"
Age Restrictions	According to package insert
Prescriber Restrictions	Prescriber must be an endocrinologist
Coverage Duration	If all the criteria are met, the initial request will be approved for a one-time treatment
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	
	• Medication is prescribed at an FDA approved dose
	• Diagnosis of stage 2 type 1 diabetes (T1D) confirmed by presence of at least two of the following autoantibodies:
	  ○ Glutamic acid decarboxylase 65 (GAD) autoantibody
	  ○ Insulin autoantibody (IAA)
	  ○ Insulinoma-associated antigen 2 autoantibody (IA-2A)
	  ○ Zinc transporter 8 autoantibody (ZnT8A)
	  ○ Islet cell autoantibody (ICA)
	• Abnormal glucose on an oral glucose-tolerance test (or alternative glycemic test if an oral glucose-tolerance test is not available)
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review

Last Review Date	~~3/2024~~3/2025

Recommendation: No changes, minor formatting correction

Gene Therapy for Regular Red Blood Cell (RBC) Transfusion Dependent Beta-Thalassemia	
Medications	Zynteglo (betibeglogene autotemcel), Casgevy (exagamglogene autotemcel)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	Repeat use of same gene therapy agent Trial of a different gene therapy agent after another has been used
Required Clinical Information	See "other criteria"
Age Restrictions	Per FDA approved prescribing information
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	If all the criteria are met, the initial request will be approved for a one-time treatment for one gene therapy agent
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	• Medication is prescribed at an FDA approved dose
	• Member has a diagnosis of transfusion dependent beta-thalassemia
	• Member requires regular RBC transfusions defined as ONE of the following:
	  ○ History of ≥100 mL/kg/year of packed red blood cell (pRBCs) in the past 2 years
	  ○ History of ≥8 transfusions of pRBCs per year in the past 2 years
	• Patient has not had a prior HSCT or gene therapy treatment
	• Negative pregnancy test (if applicable)
	
	The safety and effectiveness of repeat administration of Zynteglo or Casgevy have not been evaluated and will not be approved.
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review

Last Review Date	~~3/2024~~3/2025

Recommendation: No changes

Pompe Disease Agents	
Medications	Lumizyme (alglucosidase alfa) Nexviazyme (avalglucosidase alfa-ngpt) injection Pombiliti (cipaglucosidase alfa-atga) + Opfolda (miglustat)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by a specialist in the treatment of Pompe disease, such as a genetic or metabolic specialist, neurologist, cardiologist, or pediatrician.
Coverage Duration	If all of the criteria are met, the request will be approved for 12 months.

Other Criteria	**Initial Authorization:**
	For infantile onset Pompe Disease (Lumizyme only):
	• Patient has a diagnosis of infantile-onset Pompe Disease, confirmed by one of the following:
	  ○ Enzyme assay showing a deficiency of acid alpha-glucosidase (GAA) activity in the blood, skin, or muscle
	  ○ Genetic testing showing a mutation in the GAA gene
	• Requested dose is appropriate per prescribing information (documentation of patient weight must be submitted with request)
	• Requested regimen will not be used in combination with other enzyme replacement therapies
	For late onset Pompe Disease (Lumizyme, Nexviazyme, or Pombiliti + Opfolda):
	• Patient has a diagnosis of late-onset (non-infantile) Pompe Disease, confirmed by one of the following:
	  ○ Enzyme assay showing a deficiency of acid alpha-glucosidase (GAA) activity in the blood, skin, or muscle
	  ○ Genetic testing showing a mutation in the GAA gene
	• Documentation patient has measurable signs or symptoms of Pompe disease
	• Results of a baseline 6-minute walk test (6MWT) and percent-predicted forced vital capacity (FVC) are provided (not required for patients who are not old enough to walk)
	• Requested dose is appropriate per prescribing information (documentation of patient weight must be submitted with request)
	• Requested regimen will not be used in combination with other enzyme replacement therapies (Exception: Pombiliti + Opfolda are to be used together)
	• For Pombiliti + Opfolda: Patient must have trial and failure of another enzyme therapy (Lumizyme or Nexviazyme)
	Re-Authorization:
	• Documentation or provider attestation of positive clinical response to therapy
	  ○ Infantile onset: provider attestation of member benefit
	  ○ Late onset: improvement, stabilization, or slowing of progression of percent-predicted FVC and/or 6MWT
	• Requested dose is appropriate per prescribing information (documentation of patient weight must be submitted with request)
	• Requested regimen will not be used in combination with other enzyme replacement therapies (Exception: Pombiliti + Opfolda are to be used together)

	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation: No changes

Adzynma	
Medications	Adzynma (ADAMTS13, recombinant-krhn)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a hematologist, oncologist, intensive care specialist, or specialist in the treatment of rare genetic hematologic diseases
Coverage Duration	On-demand therapy: If all criteria are met, the request will be approved for 1 month. Prophylactic therapy: If all criteria are met, the initial request will be approved for 6 months. Reauthorization requests will be approved for 12 months.

Other Criteria	**Initial Authorization**
	• Diagnosis of congenital thrombotic thrombocytopenic purpura (cTTP) as confirmed by BOTH of the following:
	  ○ Molecular genetic testing
	  ○ ADAMTS13 activity <10%
	• Prescriber attestation that member has not been diagnosed with any other TTP-like disorder (i.e., microangiopathic hemolytic anemia, immune-mediated thrombotic thrombocytopenic purpura [iTTP])
	• If request is for prophylactic therapy, member must also have a history of at least one documented TTP event
	• Member's weight
	• Request is for an FDA-approved dose
	
	Reauthorization
	• Documentation of positive clinical response to therapy (i.e., improvement in acute and subacute TTP events, platelet counts, microangiopathic hemolytic anemia episodes, or clinical symptoms)
	• Member's weight
	• Request is for an FDA-approved dose
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.

Last P&T Review Date	~~3/2024~~3/2025

Alameda Alliance for Health (IHSS)

Q1 2025 INTERIM FORMULARY UPDATES

These changes have been made to the Alliance's formulary recently. The changes were necessary to enhance the formulary.

Medication	Formulary Change
Carbamazepine Oral Tablet Chewable 200 MG	NF to F
Vivitrol Intramuscular Suspension Reconstituted 380 MG	NF to F
Sublocade Subcutaneous Solution Prefilled Syringe 100 MG/0.5ML	NF to F
Sublocade Subcutaneous Solution Prefilled Syringe 300 MG/1.5ML	NF to F
Buprenorphine HCl Sublingual Tablet Sublingual 8 MG	F-QL to F
Buprenorphine HCl Sublingual Tablet Sublingual 2 MG	F-QL to F
Lumakras Oral Tablet 240 MG	NF to F-PA
Lumakras Oral Tablet 320 MG	NF to F-PA
Differin External Gel 0.1 % OTC	F-PA to F
Labetalol HCl Oral Tablet 400 MG	NF to F
Simlandi (2 Syringe) Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	NF to F-QL (4 syringes per 28 days, Loading dose: 8 syringes)
Mesna Oral Tablet 400 MG	NF to F-AL (minimum age: 21 years)
Mesnex Oral Tablet 400 MG	F-AL to NF
Bismuth Subsalicylate Oral Tablet Chewable 262 MG	NF to F

Alameda Alliance for Health Q1 2025 PAD Updates

These changes have been made to the Alliance Physician Administered Drug (PAD) recently.
This list includes summary of changes and is not comprehensive.

HCPCS Code	HCPSC Description	Action
J0222	PATISIRAN (ONPATTRO)	Add PA Requirement
J0225	VUTRISIRAN (AMVUTTRA)	Add PA Requirement
J1411	ETRANACOGENE DEZAPARVOVEC (HEMGENIX)	Add PA Requirement
J1414	FIDANACOGENE ELEPARVOVEC (BEQVEZ)	Add PA Requirement
J3392	EXAGAMGLOGENE AUTOTEMCEL (CASGEVY)	Add PA Requirement
J3393	BETIBEGLOGENE AUTOTEMCEL (ZYNTEGLO)	Add PA Requirement
J3394	LOVOTIBEGLOGENE AUTOTEMCEL (LYFGENIA)	Add PA Requirement
J3398	VORETIGENE NEPARVOVEC-RZYL (LUXTURNA)	Add PA Requirement
J3401	BEREMEAGENE GEPERPAVEC-SVDT (VYJUVEK)	Add PA Requirement
Q2056	CILTACABTAGENE AUTOLEUCEL (CARVYKTI)	Add PA Requirement
Q2057	AFAMITRESGENE AUTOLEUCEL (TECELRA)	Add PA Requirement

ALAMEDA Alliance FOR HEALTH

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POLICY AND PROCEDURE

Policy Number	RX-001
Policy Name	Pharmaceutical Operating Processes Summary
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	04/01/2021
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

The purpose of this document is to outline the procedure for the structure, operation, functions, and scope of the Alameda Alliance for Health (the "Alliance") Pharmacy Department Operations.

PROCEDURE

To help assure continuing patient access to a quality-driven, cost-effective, rational, drug benefit through the Alliance Drug Formulary, the Alliance Pharmacy Department will complete the following activities and adhere to the following operating procedures. The elements of the pharmacy program (as specified below) will be reviewed and approved annually by the Pharmacy and Therapeutics (P&T) committee meeting.

I. Pharmacy and Therapeutics (P&T) Committee

A committee shall exist within the Alliance that will function as the policy-making body for all matters related to the therapeutic use of drugs and certain medical supplies. The P&T Committee is a subcommittee of the Alliance Board of Governors.

Details of P&T Committee operations and scope can be found in *RX 005 P&T Committee Roles and Scope.*

II. Formulary Management

The Alliance has an established process for maintaining, reviewing, and updating its drug formulary. The Alliance is committed to ensuring that all eligible Alliance members have access to high quality and cost-effective pharmaceutical care. The Alliance's formulary management process complies with the standards set by the Health & Safety Code, Sections

1367.20, 1367.21, 1367.24, 1367.25, and 1367.215.

Formulary management decisions are made by the P&T Committee and are based upon documented medical evidence. The formulary is updated and reviewed at least quarterly. Details of formulary management operations can be found in *RX-004 Formulary Management.*

III. Prior Authorization Process

The Alliance is committed to ensuring that all eligible Alliance members have timely access to covered pharmaceutical services that require authorization. The Alliance has an established process for reviewing and determining medical necessity of Prior Authorization (PA) requests. The Alliance's pharmaceutical authorization process complies with the standards set by the Health & Safety Code, Sections 1367.01, and CCR, Title 28, Section 1300.67.241, and the Welfare & Institutions Code, Section 14185. Prior authorization is not required for the provision of an emergency three (3) day supply of drugs. The Alliance considers the Prior Authorization process described in *RX-002 Prior Authorization Review Process* to be inclusive of all elements of the request process as defined by the National Committee for Quality Assurance (NCQA).

A request for a drug is only considered to be a PA request when there is an existing PA guideline (also known as criteria) for review. If a guideline does not exist, then it is treated as an exception request (see section IV below).

Providers are informed of the Alliance's prior authorization process for pharmaceutical services via the Alliance's Provider Manual, which can be found on the Alliance's website. Members are informed of the Alliance's prior authorization process for pharmaceutical services via the Alliance's Evidence of Coverage documents. The Alliance supplies all providers with the Medication Prior Authorization (PA) form and instructions for its use on the Alliance's website.

IV. Exception Process

The Alliance has an established process for reviewing and processing exception requests for pharmaceutical services that are not covered on the formulary and for which there exists no review guidelines, step therapy, or quantity limits. The Alliance is committed to ensuring that all eligible Alliance members have timely access to covered pharmaceutical services that require an exceptions review. The Alliance's pharmaceutical authorization process complies with the standards set by the Health & Safety Code, Sections 1367.01, and CCR, Title 28, Section 1300.67.241, and the Welfare & Institutions Code, Section 14185. Exceptions review is not required for the provision of an emergency three (3) day supply of drugs. The Alliance considers the Exception process described in *RX-003 Exception Review Process* to be inclusive of all elements of the NCQA-defined exceptions request process.

V. Generic Substitution

The Alliance requires that the generic version of a drug must be dispensed unless a medical reason prohibits the use of the generic version. If no generic drug exists, or if the

prescribing provider has provided medical documentation that no substitution should be made, a brand name drug may be dispensed**.** If a member needs a brand medication when the generic is available, the provider must submit a PA on the member's behalf for review. The PA must specify why the member would medically benefit from the branded version and cannot tolerate the generic version.

VI. Therapeutic Interchange

The Alliance promotes the use of the most cost-effective drug among all therapeutically comparable drugs within a particular therapeutic class. For covered drug classes, the most cost-effective drug(s) within that drug class is often selected as the drug of choice (upon approval from the P&T committee). When applicable, the PA guidelines may also steer the reviewer to recommend the most cost-effective drug within the requested drug class. Occasionally, the Alliance performs targeted provider outreach to switch patients from a less cost-effective drug to a more cost-effective one within the same class. If a member cannot use the most cost-effective drug within a class, the provider can submit a PA on the member's behalf for review. The PA must specify why the member would medically benefit from the less cost-effective drug and cannot use the most cost-effective drug.

VII. Step Therapy

The Alliance utilizes a step therapy program for certain medical conditions in which the most cost-effective and/or safest drug therapy has to be used first before other costly or risky drugs can be approved. The claims adjudication system of the contracted pharmacy benefit manager (PBM) scans for paid claims for the preferred drug before allowing the more costly or risky drug to pay at the time of claim submission. The history of paid claims would indicate that the member has a therapeutic failure to the preferred drug. In instances where there is no claims history for the claims adjudication system to review, the provider can submit an Exceptions Request on the member's behalf for review. The Exceptions Request must specify why the member would medically benefit from the more costly or risky therapy or why they cannot use the preferred therapy. These types of exceptions will be made following the procedures outlined in the policy and procedure document *RX-003 Exception Review Process* and found in the online Provider Manual Section 16 *Formulary and Pharmacy Services.*

VIII. Limits and Quotas

Certain drugs may be recommended to be limited to a determined number of doses (e.g., quantity limit) based on criteria including but not limited to: safety, potential overdose hazard, abuse potential, or approximation of usual doses per month. The P&T Committee will review all decisions regarding limits and quotas. If a member needs a medication beyond the specified quantity limit or quota, the provider can submit an Exceptions Request on the member's behalf for review. The Exceptions Request must specify why the member would medically benefit from a higher dose or treatment duration. These types of exceptions will be made following the procedures outlined in the policy and procedure document *RX-003 Exception Review Process* and found in the online Provider Manual Section 16 *Formulary and Pharmacy Services*.

Practitioners and members are educated and notified about limits and quotas and the exception request process through the practitioner and member notification mechanisms described in Sections IX and X below.

IX. Practitioner Notification of Pharmaceutical Management Procedures

Practitioners are notified of pharmaceutical management procedures and changes to lists and procedures through a number of mechanisms including the provider newsletter, fax bulletins, and the provider manual, which is provided to each practitioner both in writing and on the website. The information includes how to request authorizations or exceptions. The above information will be provided annually, at minimum, and after each modification.

X. Member Notification of Pharmaceutical Management Procedures

Members are notified at least once quarterly through member bulletins of the formulary rules and any formulary changes. In addition, the member bulletin will provide a link to the member section of the Alliance web site for detailed information on the formulary changes.

Information on practitioner and member notification is outlined in *RX-004 Formulary Management.*

XI. Override at the point of service

1. Contracted pharmacy staff can call the PBM's Provider Call Center to request an override for refill-too-soon rejections in certain situations.
   a. Pharmacy will call the PBM's provider call center for these overrides.
   b. PBM call center staff is allowed to enter the override according to the timeline set below:
      i. **Lost:** One (1) incident allowed per rolling 12 months (30-day supply only).
      ii. **Spilled:** One (1) incident allowed per rolling 12 months (30-day supply only).
      iii. **Stolen:** One (1) incident allowed per rolling 12 months (30-day supply only).
      iv. **Vacation:** One (1) incident allowed per rolling 12 months (up to 90-day supply only).
   c. Additional requests require a PA and the plan review (Outlined in *RX-003 Exception Review Process*)

XII. Member Eligibility

1. If a prescription claim is rejected at point-of-sale (POS) for "MEMBER WAS NOT ELIGIBLE ON DATE FILLED", the Alliance Member Services Department will verify member eligibility with the following steps before calling the Pharmacy Services department:
   a. ~~RXNova~~Darwin: Point-of-sale system used to verify claims history
   b. HealthSuite: Customer relation module where member demographics are stored, claims are processed, and calls are documented.
      i. If current eligibility is found, the Member Services Department will contact Pharmacy Services to update eligibility in RXNova. If Pharmacy Services is not available, please contact the Alliance IT Enrollment department to update eligibility.
      ii. If current eligibility is NOT found, the Alliance pharmacy personnel will forward case to Business Operation for eligibility update.

XIII. Regulatory Reporting

The Alliance will send required reports to regulatory agencies, including but not limited to the Department of Managed Health Care (DMHC) and the Centers for Medicare and Medicaid Services (CMS).

DEFINITIONS / ACRONYMS

Pharmacy and Therapeutics Committee (P&T) - The policy-making body for all matters related to the therapeutic use of drugs and certain medical supplies.

Department of Managed Health Care (DMHC) – State regulatory body governing health care plans.

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Department
Pharmacy Benefit Manager (Currently – *PerformRx*)
Member Services
Business Operation

RELATED POLICIES AND PROCEDURES

P&T Charter

RX-002 Prior Authorization Review Process
RX-003 Exception Review Process
RX-004 Formulary Management
RX-005 P&T Committee Roles and Scope

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None

REVISION HISTORY

4/1/2018, 3/25/2018, 12/11/2018, 11/13/2020, 3/16/2021, 6/21/2022, 3/28/2023, 4/10/2024, 3/18/2025

REFERENCES

- NCQA UM 12, Element B
- Alliance Provider Manual
- Health & Safety Code, Sections 1367.01
- CCR, Title 28, Section 1300.67.241
- Welfare & Institutions Code, Section 14185
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness.

POLICY AND PROCEDURE

Policy Number	RX-002
Policy Name	Pharmacy Benefit Prior Authorization Review Process
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	12/01/1997
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~9/24/2024~~
Compliance Committee Approval Date	TBD

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance") has an established process for reviewing and processing medical necessity-based authorization requests for pharmaceutical services that are on the formulary. The Alliance is committed to ensuring that all eligible Alliance members have timely and efficient access to covered pharmaceutical services that require authorization. The Alliance's pharmaceutical authorization process complies with the standards set by the California Health & Safety Code, Sections 1367.01; the California Code of Regulations (CCR) Title 28, Section 1300.67.241; and the California Welfare & Institutions Code, Section 14185. Prior authorization is not required for the provision of an emergency three (3) day supply of drugs. The Alliance covers medications for treating gender dysphoria or alleviating mental health or substance use.

This policy and the associated procedures pertain to general prior authorizations for medications.

PROCEDURE

I. Prior Authorization Process Guidelines

A. Prior authorization review and approval criteria (or Medication Review Guidelines) are required for the drugs or dosage forms included in the Alliance formulary that require prior authorization.

B. The Alliance's prior authorization requirements and review processes are available to practitioners and providers through the Alliance's Provider Manual, provider newsletters and on the Alliance's website. Likewise, they are available to members through the Alliance's Evidence of Coverage documents, member newsletters, and on the Alliance's website. The Alliance mails newsletters to members and providers annually, at minimum. Provider manuals are sent to providers when they join the Alliance and upon request thereafter. Evidence of Coverage documents are sent to members when they join the Alliance and upon request thereafter.

II. Submitting a Prior Authorization (PA) or Appeal

Prior authorizations and appeals may be filed either orally or in writing by the member/member's representative or the member's provider/provider's office authorized representative. Prior Authorizations are received by telephone via PerformRx help desk, PerformRx PA fax number or our direct pharmacy telephone number. Appeals are received by the Alliance grievance and appeals (G&A) department orally or in writing by the member/member's representative or member's provider/provider's office representative. The Alliance provides a prompt review of prior authorizations and appeal requests (24 hours for prior authorizations and up to 30 days for an appeal).

III. Prior Authorization Requirements and Processes

A. The Alliance supplies all providers with the Medication Prior Authorization (PA) form and instructions for its use. The member may initiate the PA review process by calling the Alliance customer service number and requesting a review. The Alliance will supply the member's provider with the PA form and instructions for use.

B. The Alliance does not accept PA forms completed by members or members' caretakers (although members and members' caretakers may initiate a request by phone, email, or any other communication method utilized by the Alliance Member Services Department).

C. The PA form shall be in compliance with Title 28, Division 1, Chapter 2, Article 7 § 1300.67.241. PA request can be made telephonically or through a web portal or a fax.

D. The Alliance shall not request the provider to submit more than "Minimum Amount of Material Information" in the prior authorization process to determine if the PA request should be approved or disapproved.

E. Providers are responsible for submitting a complete PA form to request authorization requests for medical necessity review. A PA form for an authorization request is only complete when all the information required to review the request and render a decision is provided.

F. Additional information that may be requested from the pharmacy, provider, member, or family member can include but are not limited to:
   1. Reason for the medication request
   2. Other medications tried and/or failed
   3. Other pertinent history
   4. Office and hospital records
   5. Drug allergies, resistance, or reactions
   6. Ability to reliably self-administer the medication
   7. Other medications the member is taking
   8. A history of present illness, with treatment plans and progress notes
   9. A clinical exam
   10. Laboratory testing results
   11. Patient psychosocial history
   12. Evaluations from other health care practitioners and providers
   13. Diagnostic images
   14. Operative and pathological reports
   15. Information regarding benefits for services or procedures
   16. Information regarding the local delivery system
   17. Patient characteristics and information

G. Outreach calls (up to 2 attempts within 24-hr TAT) may be made to the requesting provider to

request reasonably necessary clinical information when needed to make a PA decision for medication requests. For each outreach attempt, the reviewer is to document the following:

a) Name and title of person spoken to
b) Phone number called (if different from one already noted in the PA system)
c) What specific information was requested

H. The Alliance utilizes criteria that have been approved by the Alliance Pharmacy and Therapeutics (P&T) Committee. The criteria are objective in nature and utilize evidence-based guidelines, national guidelines, and current medical and pharmaceutical literature. The review guidelines are maintained in the Medication Request Guidelines (MRG) document.

I. The criteria in the MRG are reviewed quarterly by the P&T Committee, which is co-chaired by the Alliance's Chief Medical Officer and the Alliance's Senior Director of Pharmacy Services. The P&T Committee is made up of currently licensed pharmacists and physicians with expertise in developing, adopting, and reviewing criteria. This committee has the responsibility to apply relevant evidence-based guidelines and current medical evidence when recommending and approving revisions to the criteria. These criteria and process revisions are then applied to the MRG to be used by reviewers.

J. The criteria are applied with consideration to individual needs. This includes but is not limited to:
1. Allergy, intolerance, or resistance to a medication
2. Availability of a formulary alternative
3. The age of the member and comorbidities
4. Additional clinical complications
5. Home environment and transportation issues that may impact the member's ability to comply with the treatment plan
6. Clinical progress or lack of responsiveness to medications
7. Ability to safely self-administer drugs and whether specialized home care services may be required
8. Any psychosocial conditions which may impact medication administration

K. The local delivery system may also be factored into the criteria. Examples include:
1. Medications with limited distribution through specialty pharmacy vendors
2. Pharmacy does not have a formulary medication in stock
3. Member is not able to pick up medication from pharmacy and requires delivery

L. If a reviewer is not able to review a request using the MRG based on individual needs or delivery system considerations the request will be considered an Exception Request (***see RX-003 Exception Review Process***). The reviewer then adheres to the following process:
1. The reviewer documents the reason why the MRG cannot be used and refers the case to a pharmacist for review.
2. The pharmacist reviews the case and background materials. When appropriate, the pharmacist can approve the request, documenting the rationale for the authorization.
3. The pharmacist can modify or deny the request for the following reasons:
   a) Insufficient information was received to make a decision (as determined by the Alliance Medication Request Guidelines, national standard guidelines, prescribing information, or other sources of standard prescribing information).
   b) Not a covered benefit: The requested medication is not a covered benefit (<u>unless treating gender dysphoria or alleviating mental health or substance use</u>):
      (1) The product requested is a dietary supplement, Medical Food, or other products not approved by the FDA.
      (2) The product requested is being used for a cosmetic purpose.

(3) Appetite/weight suppressants being used for cosmetic purposes and with no medical necessity (as documented by clinic notes)
(4) The product requested is being used to aid/improve hair growth or impair/stop/reduce hair growth.
(5) The product requested is to be used by the member as part of a medical or clinical study protocol. Note that supporting medications that may be needed for the study (but are not directly a part of the study) are covered by Alameda Alliance.

c) Generic Substitution Required: The request is for a Brand Name Drug that has at least one Food and Drug Administration (FDA) A-B rated generic formulation available. Requests for "brand-name drug only" will be handled in accordance with the Alameda Alliance Medication Request Guideline for Brand Name Requests When Generic is Available.

d) Biosimilar Substitution Required: The request is for a Brand Name Drug that has at least one Food and Drug Administration (FDA) approved biologically similar product available. Requests for "brand-name drug only" will be handled in accordance with the Alameda Alliance Medication Request Guideline for Brand Name Requests when Biosimilar is Available.

e) **Non-Formulary:** The product requested is not on the formulary and the member has not met the non-formulary approval criteria as outlined by the Alameda Alliance Medication Request Guidelines for non-formulary medications.

f) **Criteria not met**: The product requested and accompanying information submitted does not meet the approval criteria (as reviewed and approved by the Alameda Alliance Pharmacy & Therapeutics Committee) and is outlined in the Alameda Alliance Medication Request Guidelines.

g) **Investigational:** The request is for off-label or investigational use that is not supported by drug compendia and its use is not supported by nationally recognized treatment guidelines or by two (2) peer reviewed articles.

h) **Medical Necessity**: Use of the requested product does not meet medical necessity. To meet medical necessity, the treatment must be ALL the following:
(1) Safe, effective, and within national standards of practice.
(2) Not experimental or part of a current clinical trial or study.
(3) Specific and treat the identified condition.
(4) Expected to improve health or prevent or delay progression of the condition from getting worse.
(5) Not primarily for convenience.
(6) Not being used to avoid legal consequences.
(7) Not to be contraindicated, dangerous to the patient, or have other reasons why the requested drug should not be used.

i) **Other Payor Responsibility**: There is documentation available showing that the medication should be covered by another payor (e.g., Medi-Cal, other commercial, Medicare, Fee-for-service, California Children's Services).

j) **Benefit Limit Exceeded**: The benefit limit for a drug or service (as reviewed and approved by the Alameda Alliance Pharmacy & Therapeutics Committee) and is outlined in the Alameda Alliance Medication Request Guidelines has been reached without documentation why further therapy is necessary.

k) Request for additional clinical information goes unanswered

l) **Retro Requests:** These requests will only be reviewed when received within 90 days of the given pharmacy product. Requests made on the 91st day and afterwards will be subject to denial.

M. Of the above listed denial reasons, the pharmacist will review the requests for medical necessity

(essentially becoming an ***Exception Request***, refer to ***RX-003 Exception Review Process***) if:

1. Clinical information provided does not meet criteria for use based on MRG.
2. The member has not tried and failed the initial treatment option for drugs that require step therapy.
3. Benefit rules cannot be applied AND there is no MRG.

N. The pharmacist will defer cases that cannot be denied based on the above listed denial reasons (and do not qualify as an ***Exception Request, see RX-003 Exception Review Process)***. These requests and any other highly complicated cases will be sent to an Alliance board-certified Medical Director for review.
   1. The Alliance Medical Director reviews the background of the case and, if needed, contacts the requesting provider for any additional information needed for the review.
   2. The Medical Director may render one of 3 decisions: approve, deny, or modify.
   3. The Medical Director finalizes the review and returns the case to the reviewing pharmacist with documentation of their decision and the rationale.

O. The reviewer documents the criteria and rationale for the decision in the pharmacy authorization system. If the decision is a denial, the specific reasons or missing information are clearly and concisely included.

P. The plan ensures that only licensed pharmacists, physicians, or other licensed health care professionals competent to evaluate the clinical issues can make decisions regarding medically necessary non-formulary drugs.

Q. Members receive a notice of action (NOA) letter with the outcome of the request, their rights, and the process to appeal the decision. The provider also receives a NOA via fax or regular mail. (see *RX-011 – Member and Provider Decision and Notification Requirements*)

IV. Authorization Processing Time Frames (***See RX-011 – Review and Notification Time Frames)***

For processing times of authorizations, the Alliance conforms to standards issued by the National Committee on Quality Assurance, and California state law. Please see Table 2 for detailed turnaround time requirements.

A. Prospective Standard Requests
   1. **Group Care (IHSS):** The plan makes decisions to approve, modify, or deny prescription drug authorization requests within 24 hours from time of receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases, and notifies the requesting provider by telephone or fax of the plan's determination within in 24 hours from time of receipt for urgent/emergent cases and for non-urgent cases in accordance with Title 28, Division 1, Chapter 2, Article 7 §1300.67.241
      a) The requested treatment shall be deemed authorized if the required information is provided and the Alliance fails to make a determination by the expiration of the applicable time frame.

V. Provision of Drugs during Emergency Circumstances

In emergency circumstances, prior authorization is not required for an emergency three (3) day supply of drugs that would otherwise require authorization. See *RX-009 Pharmaceutical Emergency Supply Provision*.

A. Alliance providers are informed of this policy via the Alliance's Provider Manual.
B. Alliance members are informed of this policy via member's Explanation of Coverage.
C. Alliance providers are responsible for following the prior authorization process for the remainder of the prescription.
D. The Alliance allows for payment of the three (3) day supply of the drugs even if the prior authorization request is subsequently denied.
E. The Alliance allows for payment of the three (3) day supply of the drugs even if the prior authorization request is subsequently denied.
F. Continuity of care requirements do not require the Alliance to continue coverage of drugs dispensed under this provision if they are not found to be medically necessary.

VI. Provision of Contraceptive Drugs

A. The Alliance covers all FDA approved contraceptive drugs, devices, and other products, including all FDA-approved contraceptive drugs, devices, and products available over the counter, as prescribed by the member's provider.
   1. The Alliance provides coverage of at least one FDA approved contraceptive drug, device, or product without cost sharing for the original, brand name contraceptive if there is no therapeutic equivalent generic substitute available in the market.
   2. The Alliance defers to the determination and judgment of the provider and provide coverage for the alternative prescribed contraceptive drug, device, product, or service without imposing any cost sharing requirements if the covered therapeutic equivalent of a drug, device, or product is deemed medically inadvisable by the member's provider.
   3. The Alliance does not infringe upon a member's choice of contraceptive drug, device, or product and shall not impose any restrictions or delays on the coverage required, including prior authorization, step therapy, or utilization control techniques.
   4. The Alliance clarifies that the exclusion from contraception coverage for religious employers does not apply to a contraceptive drug, device, procedure, or other product that is used for purposes other than contraception.
   5. The Alliance does not require a member to make any formal request (i.e., prior authorization requests, any utilization controls, or any other forms of medical management restrictions), other than a pharmacy claim, for coverage of receiving a 12-month supply of self-administered hormonal contraceptives at one time.

VII. Annual Review of Pharmacy Prior Authorization and UM Criteria

A. All pharmacy utilization management criteria undergo annual evaluation for appropriateness and effectiveness. Criteria are updated when necessary. The P&T committee reviews the pharmacy UM program, including delegated elements. The review encompasses scope, policies and procedures, and criteria as appropriate.

VIII. Monitoring of the PA process

A. The Alliance provides oversight of its PBM through an annual audit of the PA review process.
B. The Senior Director of Pharmacy Services reviews a monthly authorization report, which provides statistics on all approvals, denials, modifications to ensure that providers and members have been notified in accordance within the mandated turnaround times.
C. Inter-rater Reliability- the Alliance evaluates the consistency of decision making for those health care professionals involved in applying Pharmacy Criteria

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DEFINITIONS / ACRONYMS

Terminal Illness: An incurable or irreversible condition that has a high probability of causing death within one year or less (Health & Safety Code Section 1373.96 (c)(4)).

"Minimum Amount of Material Information": the information generated by or in the possession of the prescribing provider related to the patient's clinical condition that enables an individual with the appropriate training, experience, and competence in prescription drug prior authorization processing to determine if the prescription authorization request should be approved or disapproved. (Title 28, Division 1, Chapter 2, Article 7 § 1300.67.241)

Emergency Circumstances: When the enrollee's condition is such that the enrollee faces an imminent and serious threat to his or her health, including, but not limited to, the potential loss of life, limb, or other major bodily function, it is considered an emergency (Health and Safety Code § 1367.01 (h)(2)).

NCQA: National Committee on Quality Assurance

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Pharmacy Benefit Manager (Currently PerformRx)

RELATED POLICIES AND PROCEDURES

RX-003 Exception Review Process
RX-006 Pharmacy Services Staff Description
RX-008 PBM Delegated Audit Oversight
RX-009 Pharmaceutical Emergency Supply Provision

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

Table 1: Decision Types
Table 2: Turn-Around Times based on Regulatory Bodies
Table 3: Decision & Notification Time Frames for Alameda Alliance
Figure 1: Prior authorization and exception request workflow

REVISION HISTORY

12/01/1997, 3/25/2016, 10/12/2017, 12/11/2018, 11/13/2020, 3/16/2021, 6/21/2022, 9/20/2022, 6/20/2023, 9/26/2023, 4/10/2024, 9/24/2024

REFERENCES

- California Code of Regulations (CCR), Health & Safety Code, §§1367.01, 1367.21, 1367.22,1367.24, 1367.25 and 1373.96
- CCR Welfare & Institutions Code, §14185
- CCR Title 22, §§51003, 51014.1, 51014.2, 53854 and 53894
- CCR, Title 28, §1300.67.24
- MMCD Policy Letter 08-013
- NCQA, 2016 HP Standards & Guidelines, UM 5 (Timeliness of UM Decisions)
- NCQA, 2016 HP Standards & Guidelines, UM 7 (Denial Notices)
- NCQA, 2016 HP Standards & Guidelines, UM 13 (Procedures for Pharmaceutical Management)
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – MediCal Rx

MONITORING

This P&P is reviewed annually to ensure effectiveness.

APPENDIX

Table 1: Decision Types

a. IHSS

Reviewer Type	Approval	Denial	Modification	Deferral
PBM Clinicians	Yes	Yes	Yes	N/A
Plan Pharmacist	Yes	Yes	Yes	N/A
Plan Medical Director	Yes	Yes	Yes	N/A

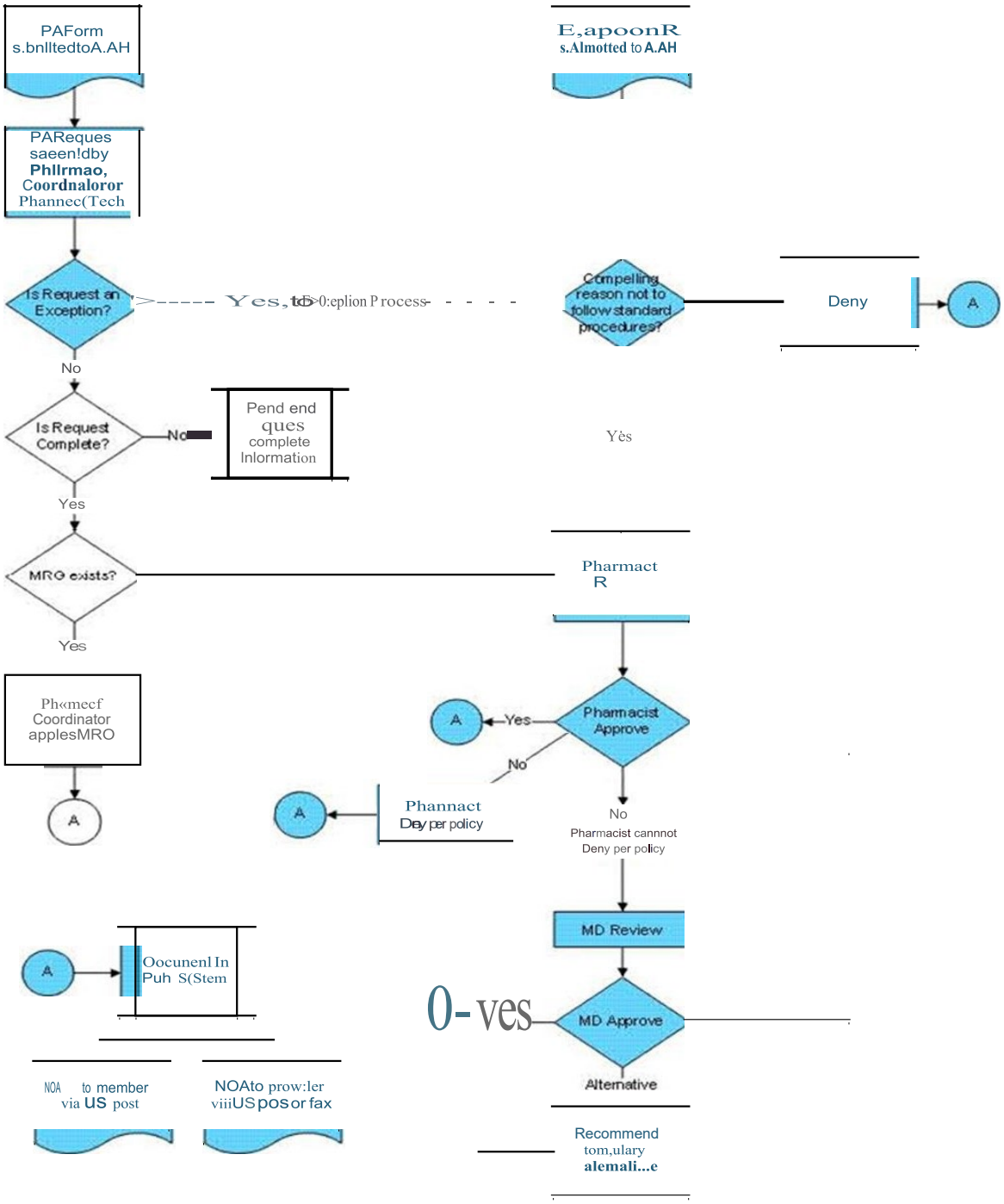
Table 2. Pharmacy Benefit Determination Turnaround Timetable of Different Regulatory Bodies

Type of Request	NCQA	DHCS	DMHC	**Alliance**
Prospective, Urgent	72 hours	72 hours	24 hours	**24 hours**
Prospective, Non-Urgent	15 calendar days	5 business days	72 hours	**72 hours**
Post-service	30 calendar days	30 calendar days	30 calendar days	**72 hours**

Table 3: Decision & Notification Time Frames

Type of Request	**Decision**	**Initial Notification**	**Written Notification**
Prospective, Urgent	Approval	A fax is sent to the requesting provider within 24 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		
Prospective, Non-Urgent	Approval	A fax is sent to the requesting provider within 72 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		
Post-service	Approval	A fax is sent to the requesting provider within 72 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		

Pharmaceutical Management Procedures
(Prior Authorization and Exception Process)



ALAMEDA Alliance FOR HEALTH

Health care you can count on.
Service you can trust.

POLICY AND PROCEDURE

Policy Number	RX-003
Policy Name	Exception Review Process
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	Group Care (IHSS)
Effective Date	6/16/2020
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance") has an established process for reviewing and processing medical necessity-based authorization requests for pharmaceutical services that are not on the formulary. The Alliance is committed to ensuring that all eligible Alliance members have timely and efficient access to covered pharmaceutical services that require authorization. The Alliance's pharmaceutical authorization process complies with the standards set by the California Health & Safety Code, Sections 1367.01; the California Code of Regulations (CCR) Title 28, Section 1300.67.241; and the California Welfare & Institutions Code, Section 14185. Prior authorization is not required for the provision of an emergency three (3) day supply of drugs (see RX-009, Pharmaceutical Emergency Supply Provision).

This policy and the associated procedures also pertain to the review process for exceptions to pharmaceutical management procedures, such as Step Therapy, Quantity Limits and Age Limits.

PROCEDURE

I. Exception Process Guidelines

A. Members and their providers are expected to follow pharmaceutical management procedures set forth by the Alliance. However, in some cases a member or provider may opt to seek an exception based on medical necessity. Examples of exception requests include (but are not limited to):

1. A request for coverage of a non-formulary item with no existing Medication Review Guidelines (MRG)
2. A request to bypass an implemented formulary management program, such as step therapy
3. A request to authorize a greater supply than standard quantity limits
4. Any request outside the existing pharmaceutical management procedure and authorization process

B. The Alliance's exception process instructions are available to practitioners and providers through the Alliance's Provider Manual, provider newsletters and on the Alliance's website. Likewise, it is available to members through the Alliance's Evidence of Coverage documents, member newsletters, and on the Alliance's web site. The Alliance mails newsletters to members and providers annually, at minimum. Provider manuals are sent to providers when they join the Alliance and upon request thereafter. Evidence of Coverage documents are sent to members when they join the Alliance, and upon request thereafter. Any change to the exception process will be communicated to providers through mail, e-mail, or fax.

C. The review is based on medical necessity. Specific attention is given to the medical necessity for the situation and whether there is sufficient reason to create an exception to the established procedures.

II. Exception Review Requirements and Process

A. An exception request may originate from a member or a provider. When requested by the member, an Alliance member services representative will contact the provider to initiate the request. Also, the Alliance pharmacy staff may advise a provider to redirect a Prior Authorization request to an exception request if the request falls outside the standard Prior Authorization rules.

B. Providers are responsible for submitting all required information for medical necessity review. A Pharmacy Technician reviews the requests to determine whether all required information has been provided. The Pharmacy Technician pends the request to obtain missing information from the requestor (via phone or fax). The following information may be requested from the pharmacy, provider, member, or family member can include but are not limited to:

1. Reason for the exception request
2. Other medications tried and/or failed
3. Other pertinent history
4. Office and hospital records
5. Drug allergies, resistance, or reactions
6. Ability to reliably self-administer the medication
7. Other medications the member is taking
8. A history of present illness, with treatment plans and progress notes
9. A clinical exam
10. Diagnostic testing results
11. Patient psychosocial history
12. Evaluations from other health care providers and providers
13. Photographs
14. Operative and pathological reports
15. Information regarding benefits for services or procedures
16. Information regarding the local delivery system

17. Patient characteristics and information

C. Types of Exception Requests – All Exception requests must be reviewed by an appropriate healthcare professional and decisions shall be made based on the available clinical evidence in the medical literature as well as any patient-specific factors. Types of Exceptions include (but are not limited to):

1. Quantity Limit (QL) Override

a) Quantity limits are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.

b) Providers must provide documentation for why the quantity limit is insufficient for the member and why formulary alternatives or alternate doses cannot be used. Potential QL override requests may involve:

i. Split dosing for tolerability

ii. One-time dose titration

iii. Requirement of a higher dose for efficacy (must be supported by clinical evidence)

2. Step Therapy (ST) Override

a) Step Therapy protocols are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.

b) Providers must submit necessary justification and supporting clinical documentation(through clinic notes documenting previous medication trials including dose/duration/time frame and/or pharmacy fill history) supporting the provider's determination that the required prescription drug is inconsistent with good professional practice for provision of medically necessary covered services to the member, taking into consideration the member's needs and medical history, along with the professional judgment of the member's provider. The basis of the provider's determination may include, but is not limited to, any of the following criteria:

i. The required prescription drug is contraindicated or is likely, or expected, to cause an adverse reaction or physical or mental harm to the member in comparison to the requested prescription drug, based on the known clinical characteristics of the member and the known characteristics and history of the member's prescription drug regimen.

ii. The required prescription drug is expected to be ineffective based on the known clinical characteristics of the member and the known characteristics and history of the member's prescription drug regimen.

iii. The member has tried the required prescription drug while covered by their current or previous health coverage or Medicaid, and that prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse reaction. The health care service plan may require the submission of documentation demonstrating that the member tried the required prescription drug before it was discontinued.

iv. The required prescription drug is not clinically appropriate for the member because the required drug is expected to do any of the following, as determined by the member's prescribing provider:

(1) Worsen a comorbid condition.

(2) Decrease the capacity to maintain a reasonable functional ability in performing daily activities.

(3) Pose a significant barrier to adherence to, or compliance with, the member's drug regimen or plan of care.

v. The member is stable on a prescription drug selected by the member's prescribing provider for the medical condition under consideration while covered by their current or previous health coverage or Medicaid.

(1) For non-transitioning members who are already established with Alliance, the Alliance does not consider use of medication samples provided through a physician office as a valid reason for approval/continuation of that medication, or as an acceptable step therapy to another medication.

(2) For non-transitioning members who are already established with Alliance, the Alliance shall allow provider attestation for OTC products that the member has been taking.

(3) For transitioning members until the Beneficiary can be seen by a Plan provider to establish a care plan, as required by Welfare & Institutions (W&I) Code, Section 14185(b), the Alliance will allow for continuation of single-source medications, including medication samples, if provided clinic notes showing all the following:

(a) Patient name

(b) Medication name, dose, and route of administration

(c) Quantity distributed

(d) Date medication was started and date last given/filled

c) The Alliance provides coverage for prescription drugs may require step therapy if there is more than one drug that is clinically appropriate for the treatment of a medical condition.

3. Age Limit (AL) Override

a) Age Limits are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.

b) For override of Age Limits, the provider must submit clinic notes, any relevant labs, and supporting clinical evidence (e.g., national guidelines, primary literature) that the drug being requested is safe and effective for the patient and why formulary alternatives cannot or should not be used.

4. Fill Limit (FL) Override

a) Fill limits (a maximum number of fills over a certain period of time) are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.

b) For override of Fill Limits, the provider must submit documentation for why the member requires additional medication beyond the limit in place, why formulary alternatives cannot or should not be used in the patient, and any relevant labs results and/or other clinical references,

national guidelines, or primary literature to support continued use of the drug requested.

5. Maximum Dose Exceeded Override

a) Maximum doses are set by the prescribing information/package insert for the medication upon FDA approval or by national guidelines for the condition being treated.

b) For use of doses beyond the maximum labeled dose, the provider must submit any relevant labs results, clinical references, national guidelines, and/or primary literature to support the use of a dose beyond the standard dose and justification for why a formulary alternative cannot be used in place of a higher dose of the requested medication.

6. Dose Consolidation Override

a) Quantity limits are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.

b) For approval of a doubling (or higher) of the number of tablets/capsules per prescription for a medication that has a higher strength tablet/capsule available, justification must be submitted for why that higher dose tablet/capsule cannot be used.

7. Partial Fill

a) The Alliance has availability of prescription partial fills of approved medically necessary medications.

8. Lost/Stolen Medication Override

a) Requests for non-controlled medications can be approved by Alliance pharmacy technicians upon request by the member, pharmacy, or provider.

b) For Lost/Stolen controlled medications, the member or provider must submit a police report to the plan that documents which medications were taken and the date the event occurred.

c) For more than one loss of controlled medications per 365 days, future approvals will be authorized only in consultation with the prescriber and your pharmacy.

9. Refill-Too-Soon Override

a) Refill-Too-Soon overrides will be handled on a case-by-case basis and by the medical necessity of the situation.

b) Lost/Stolen medication and vacation overrides will be handled by the corresponding exception policies.

10. Vacation Override

a) Vacation Overrides for up to 3 months (90 days) for travel outside California can be approved by the PBM or by the Alliance pharmacy technicians upon request by the member, pharmacy, or provider when documentation of the departure date, destination, and return date are provided for the following:

i. Non-specialty medications

ii. Non-single-source medications, and/or

iii. Non-controlled medications

b) <u>One vacation override per drug</u> per 365 days can be approved by the PBM and by the Alliance Pharmacy Technicians for medications described in section (C) 10a.

c) For ANY of the following scenarios, providers must submit a standard PA request for review by an Alliance clinical pharmacist with all required information described in section (C) 10a and medical necessity.
   i. Vacation overrides over 90 days outside California or over 30 days within California
   ii. More than one vacation override per drug per 365 days
   iii. Request for specialty, single-source, and/or controlled medications

11. Member Reimbursements
   a) The Alliance will allow member reimbursement of pharmaceutical drugs when required documents are received and appropriate criteria exclusions do not apply. G&A will submit the following required documents to distgrpPharmacy@alamedaalliance.org email:
      i. Member ID Number
      ii. Case Number
      iii. AAH member reimbursement form
      iv. Pharmacy receipt or Pharmacy report print out (must include price paid out of pocket, date, and Rx number)
      v. Pharmacy Leaflet (this includes medication details and member details as well as Rx number).

   b) Reimbursements are not valid and will not be approved when the following criteria exclusions apply:
      i. If the request is made before the 180 days accepted time frame per EOC requirement.
      ii. If the drug was not covered and required a Prior Authorization and Perform PA does not show any active approval for the date paid out of pocket.
      iii. If the required documents are not submitted (Note: re-review can be considered once all documents are received).
      iv. If the request is made for pharmaceutical services received outside of the United States.

   c) The Alliance Pharmacy Services Technician(s) will review each request to ensure that the required documents are available and criteria exclusions do not apply.

   d) Approved requests will be sent to Perform Rx for final review and appropriate reimbursement determination (e.g., check reimbursement mail-out dates, member eligibility and formulary product availability) that will take 7 – 10 business days.

12. Continuation of Therapy Override
   a) The Alliance shall allow continuation of therapy for members using medically necessary drugs when it can be shown through clinic notes/provider attestation for OTC products or prescription fill history

that the member has been taking the medication prior to enrollment.

b) For non-transitioning members who are already established with Alliance, the Alliance does not consider use of medication samples provided through a physician office as a valid reason for approval/continuation of that medication, or as an acceptable step therapy to another medication.

c) For non-transitioning members who are already established with Alliance, the Alliance shall allow provider attestation for OTC products that the member has been taking.

d) For transitioning members until the Beneficiary can be seen by a Plan provider to establish a care plan, as required by Welfare & Institutions (W&I) Code, Section 14185(b), the Alliance will allow for continuation of medically necessary medications, including medication samples, if provided clinic notes showing all the following:
   i. Patient name
   ii. Medication name, dose, and route of administration
   iii. Quantity distributed
   iv. Date medication was started and date last given/filled

e) For override of the formulary based on continuation of therapy the provider must submit clinical documentation showing the member has previously tried without success or cannot/should not take formulary alternatives, including any relevant labs.

13. Discharge Medication Override

a) Members being discharged on a medication will be approved given a one-time override for up to a 30-day supply. Future approvals will be based on the MRGs and the member's previous use of therapeutic alternatives.

14. Therapeutic Duplication Override

a) If the member is currently taking a medication that is therapeutically equivalent to the medication requested, the reviewing health care provider may deny the request.

b) For approval of a request of a medication that is therapeutically equivalent to a medication the member is already taking requires documentation from the provider that that the member is no longer taking the first medication, or the provider must submit any relevant labs results, clinical references, national guidelines, and/or primary literature to support the use of both medications together.

15. Day Supply Limit

a) The Alliance will cover up to 30 days' worth of medication per prescription, with the exception of the following:
   i. Certain maintenance medications: Up to 90 days per fill
   ii. Certain Specialty medications: Up to 14 days per fill
   iii. Contraceptives: Up to 365 days per fill

D. Exception Requests Based on Medical Necessity:

1. Since exception requests, by definition, do not have a MRG in place, the Pharmacy Technician will not be able to approve the request.
2. The reviewer documents the reason why the request qualifies as an Exception

request and refers the case to a pharmacist for review.

3. The pharmacist reviews the case and background materials. The pharmacist can approve Exception Requests when ALL the following criteria are met:
   a) History of failure, contraindication, or intolerance to all formulary alternatives, or no formulary alternatives exist (if applicable)
   b) The treatment plan is:
      i. Safe, effective, and within national standards of practice.
      ii. Not experimental or part of a current clinical trial or study.
      iii. Specific and treats the identified condition.
      iv. Expected to improve health or prevent or delay progression of the condition from getting worse.
      v. Not primarily for convenience.
      vi. Not being used to avoid legal consequences.
      vii. Not contraindicated or have other reasons why use of the drug should not be used.
   c) One of the following:
      i. Requested drug is FDA-approved for the condition being treated.
      ii. If requested for an off-label indication, the use is supported in compendia.
      iii. If the off-label use is supported by nationally recognized treatment guidelines or by two (2) peer reviewed articles.
3. The pharmacist will defer cases that cannot be denied based on the above listed denial reasons. These requests and any other highly complicated cases will be sent to an Alliance board-certified Medical Director for review.
   a) The Alliance Medical Director reviews the background of the case and, if needed, contacts the requesting provider for any additional information needed for the review.
   b) The Medical Director may render one of 3 decisions: approve, deny, or modify.
   c) The Medical Director finalizes the review and returns the case to the reviewing pharmacist with documentation of their decision and the rationale.
4. The reviewer documents the criteria and rationale for the decision in the pharmacy authorization system.
5. A pharmacist or a medical director can use nationally recognized treatment guidelines and other clinical information in support of making the decision.
6. Members receive a notice of action (NOA) letter with the outcome of the request and their rights and the process to appeal the decision. The provider also receives an identical copy of the NOA via fax or regular mail. All NOA letters sent to members and providers include their rights and the process to appeal the decision.

E. The qualifications and role of each reviewer in the medication exception review process is consistent with the reviewer roles documented in the *RX- 002 Prior Authorization Review Process*.

E. **External Review**

A request for an external review when the Alliance denies a prior authorization (PA) can be made for a drug that is not covered by the plan or for an investigational drug or

therapy. A request for an external review will not prevent the filing of a grievance or Independent Medical Review (IMR) with the California Department of Managed Health Care (DMHC). Requests for external review will be made in the Alliance Grievance and Appeals Department and then forwarded to Pharmacy Services to proceed with external review. ~~and completed in the Alliance Grievances and Appeals Department.~~

III. Pain Medication Requests for the Terminally Ill

A. Alameda Alliance shall define a Terminal Illness as an incurable or irreversible condition that has a high probability of causing death within one year or less (Health & Safety Code Section 1373.96 (c)(4)).
B. All prior authorization and exception requests submitted to Alameda Alliance shall be reviewed by clinical pharmacy staff to determine if the patient meets terminally ill status.
C. Terminally ill members shall identify as:
    1. Any member who is currently being treated by a hospice provider
    2. Members with terminal cancer
    3. Any physician directed end-of-life treatment plan that requires the use of the following medications:
        1) morphine 5mg/mL concentrated solution
        2) oxycodone 5mg/mL concentrated solution
        3) sublingual fentanyl formulations
D. Requests from providers for authorization of coverage for a member who has been determined to be terminally ill are approved or denied within 24 hours of the Alliance's receipt of the information requested to make the decision.
E. The requested treatment for a terminally ill member is deemed authorized if the applicable turn-around time has expired.
F. Any medications for pain for members deemed to be terminally ill shall be approved based on medical necessity.
G. The pharmacy department shall keep a log of any requests for pain medication that are deemed to be for a terminally ill member.
    1. The log shall be reviewed on a weekly basis for any denials.
    2. Pain medication requests for terminally ill members shall be tracked monthly and any trends shall be reported on to the Health Care Quality Committee (HCQC) on a quarterly basis.

A. All other medication requests for the terminally ill members

1. Requests from providers for authorization of coverage for a member who has been determined to be terminally ill are approved, modified, or denied **within 24 hours of the Alliance's receipt of the information requested to make the decision.** Only licensed physicians or health care professionals, competent to evaluate the clinical issues, make decisions to deny pain management for terminally ill patients.
2. The requested treatment for a terminally ill member is deemed authorized if the applicable time frame has expired when all the necessary medical information has been provided.
3. For terminally ill members, if a request is denied or more information is required, the Alliance contacts the requesting provider within 24 hours of the determination and provides an explanation of the determination and the

reason for the denial or need for more information.

IV. Provision of Drugs during Emergency Circumstances

In emergency circumstances, prior authorization is not required for an emergency three (3) day supply of drugs that would otherwise require authorization. See *RX-009 Pharmaceutical Emergency Supply Provision*

A. Alliance providers are informed of this policy via the Alliance's Provider Manual.
B. Alliance members are informed of this policy via member's Explanation of Coverage.
C. Alliance providers are responsible for following the prior authorization process for the remainder of the prescription.
D. The Alliance allows for payment of the three (3) day supply of the drugs even if the prior authorization request is subsequently denied.
E. Continuity of care requirements do not require the Alliance to continue coverage of drugs dispensed under this provision if they are not found to be medically necessary.

VI. **Non-Specialty Mental Health Services (NSMHS) has various services that will be provided when medically necessary, and is provided by PCPs or by licensed mental health Network Providers within their scope of practice (this includes, but is not limited to):**

A. Outpatient services for the purpose of monitoring drug therapy

VII. **Monitoring Process**

F. The Alliance provides oversight of its PBM through an annual audit of the PA review process.
G. The Senior Director of Pharmacy Services or designee reviews a monthly authorization report, which provides statistics on all approvals, denials, and modifications to ensure that providers and members have been notified in accordance within the mandated turnaround times.
H. Inter-rater Reliability Review (IRR)
    1. The **Senior Director of** Pharmacy Services **or designee** will conduct IRR annually for clinical pharmacists who review and make determinations for the exceptions requests.
    2. 8 cases will be pulled and reviewed. If 100% clinical pharmacist agreement is not found in all 8 cases then another 22 will be pulled and reviewed for a total of 30 cases.
    3. When a total of 30 cases are reviewed, at least 90% agreement between the clinical pharmacists will be attained. Otherwise, additional sessions will be held until the 90% agreement threshold is reached in a total of 30 cases.
    4. The Alliance will immediately supply remediation if the passing threshold is not met.
    5. New staff require testing prior to conducting utilization review without supervision.
    6. Results of the IRR will be reported to UM Committee.

DEFINITIONS / ACRONYMS

Pharmaceutical Management Procedures: Formulary drugs that have additional requirements or limits on coverage, such as Step Therapy (ST), Quantity Limits (QL) and Age Limits (AL).

Emergency Circumstances: When the enrollee's condition is such that the enrollee faces an imminent and serious threat to his or her health, including, but not limited to, the potential loss of life, limb, or other major bodily function, it is considered an emergency (Health and Safety Code § 1367.01 (h)(2)).

HCQC: Health Care Quality and Compliance Committee

NCQA: National Committee on Quality Assurance

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Pharmacy Benefit Manager (Currently PerformRx)

RELATED POLICIES AND PROCEDURES

RX-002 Prior Authorization Review Process
RX-006 Pharmacy Services Staff Description
RX-008 PBM Delegated Audit Oversight
RX-009 Pharmaceutical Emergency Supply Provision

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

Table 1 – Decision & Notification Time Frames
Attachment 1 – Exception Review Process Flow Chart

REVISION HISTORY

9/12/2012, 5/19/2016, 8/30/2018, 12/11/2018, 12/17/2019, 6/16/2020, 3/16/2021, 12/21/2021, 6/21/2022, 3/28/2023, 6/20/2023, 9/26/2023, 12/19/2023, 3/19/2024, 3/18/2025

REFERENCES

- California Code of Regulations (CCR), Health & Safety Code, §§1367.01, 1367.21, 1367.22, 1367.24, 1367.206 and 1373.96
- CCR, Welfare & Institutions Code, §14185
- CCR, Title 22, §§51003, 51014.1, 51014.2, 53854 and 53894
- CCR Title 28 §1300.67.24
- MMCD Policy Letter 08-013
- NCQA, 2016 HP Standards & Guidelines, UM 13 (Procedures for Pharmaceutical Management), Element E (Considering Exceptions)
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx
- DMHC APL 18-001 (OPL): Newly Enacted Statutes Impacting Health Plan License Filings
- DHCS Contract #23-30212, Exhibit A – Scope of Work

MONITORING

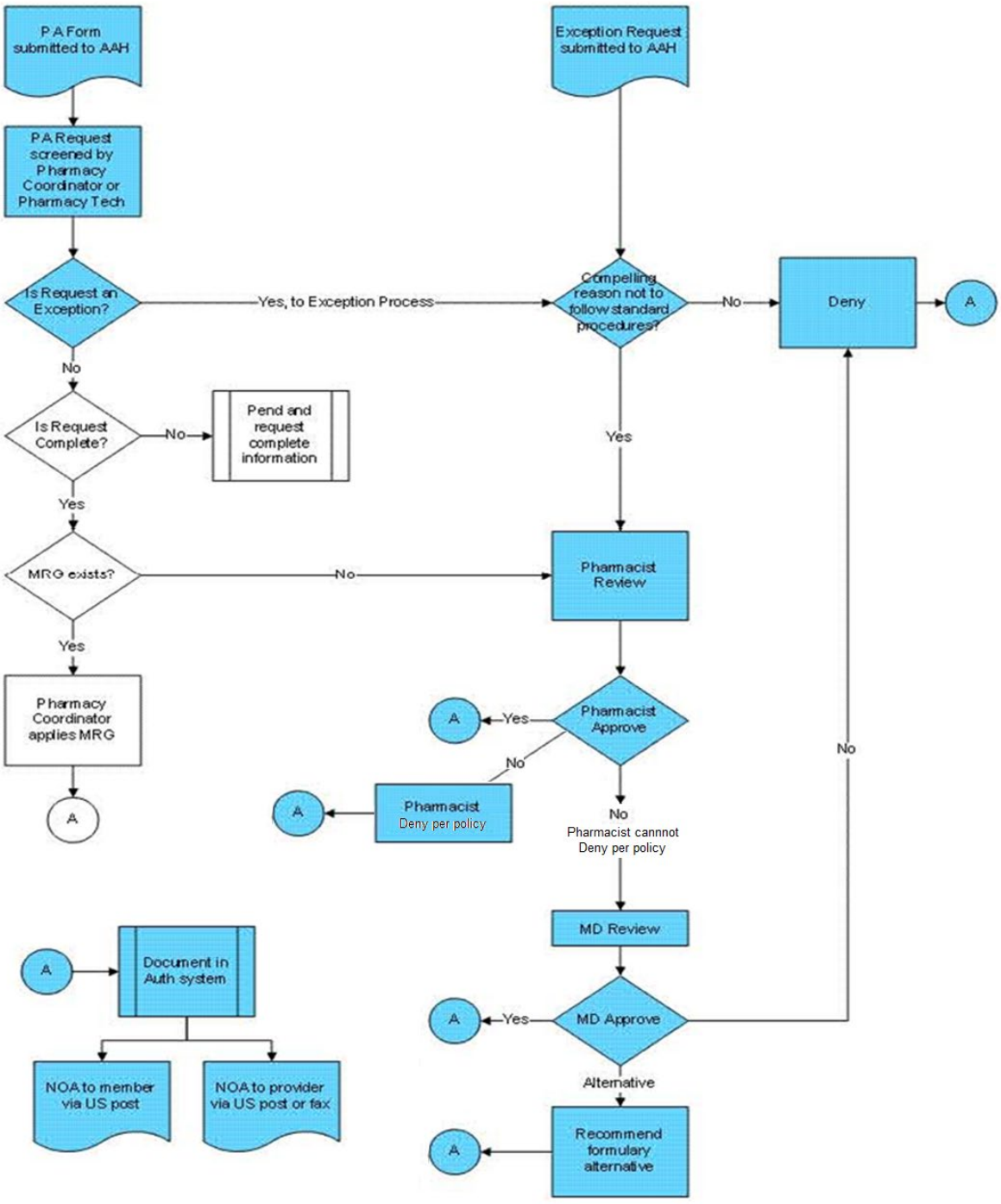
This P&P is reviewed annually to ensure effectiveness.

APPENDIX

Table 1: Decision & Notification Time Frames

Type of Request	Decision	Initial Notification	Written Notification
Prospective, Urgent	Approval	A fax is sent to the requesting provider within 24 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		
Prospective, Non-Urgent	Approval	A fax is sent to the requesting provider within 72 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		
Post-service	Approval	A fax is sent to the requesting provider within 72 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision

Pharmaceutical Management Procedures
(Prior Authorization and Exception Process)



POLICY AND PROCEDURE TEMPLATE

Policy Number	RX-004
Policy Name	Formulary Management
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	10/01/2007
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~12/17/2024~~
Compliance Committee Approval Date	TBD

POLICY STATEMENT

The Alameda Alliance for Health ("Alliance") has an established mechanism for maintaining, reviewing, and updating its drug formulary. The Alliance is committed to ensuring that all eligible Alliance members have access to high quality and cost-effective pharmaceutical care. The Alliance's formulary management process complies with the standards set by the Health and Safety Code, CCR, Section 1367.20, 1367.205, 1367.21, 1367.24, 1367.25, 1367.215.

PROCEDURE

A. Formulary

1. The Alliance's formulary is managed by the Pharmacy and Therapeutics (P&T) Committee.
2. The P&T Committee objectively appraises, evaluates, and selects pharmaceutical products for formulary inclusion or exclusion. Products are evaluated based on efficacy, safety, ease of use, and cost. This is an ongoing process to ensure the optimal use of therapeutic agents.
3. The Alliance's formulary is updated on a continuing basis after each meeting of the P&T Committee as well as between P&T Committee meetings when interim changes are implemented by Alliance pharmacy services. Alliance Providers are notified of all formulary changes in a timely manner, using provider bulletins on the Alliance's website.

4. Drugs newly approved by the Food and Drug Administration (FDA) are reviewed by the P&T Committee within six (6) months of FDA approval. The P&T Committee determines whether the newly approved drugs will require prior authorization from the Alliance or be included on the Alliance's formulary.
5. In accordance with Health & Safety Code, CCR, Section 1367.21, the Alliance allows for the coverage of any drug that is prescribed for use that is different from the FDA-approved use(s), provided that **all of the following conditions** are met:
   a. The drug is prescribed by a participating licensed health care professional for the treatment of:
      i. A life-threatening condition; or
      ii. A chronic and seriously debilitating condition, and the drug is medically necessary to treat that condition, and the drug is on the Alliance's formulary. If the drug is not on the Alliance's formulary, the prescriber's request is reviewed in accordance with Health & Safety Code, CCR, Section 1367.24 (see Policy #RX-0002a and RX-0002b, Prior Authorization and Exception Process).
   c. The drug has been recognized for the treatment of that condition by any of the following:
      i. The American Medical Association Drug Evaluations
      ii. The American Hospital Formulary Service Drug Information
      iii. The United States Pharmacopoeia Dispensing Information, Volume I, "Drug Information for Health Care Professionals"
      iv. Two articles from major peer reviewed medical journals that present data supporting the proposed off-label use(s) as generally safe and effective unless there is clear and convincing contradictory evidence presented in a major peer reviewed medical journal.
      v. It is the prescriber's responsibility to submit the supporting documentation.

6. The Alliance does not cover drugs within the following categories (unless treating gender dysphoria or alleviating mental health or substance use):
   a. Drugs for the treatment of cosmetic conditions
   b. Investigational or experimental drugs that are under clinical trial
   c. Over the Counter (OTC) drugs, with the following exceptions:
      (i) Certain OTCs are on the formulary based on plan review
7. The Alliance provides coverage for FDA-approved prescription contraceptive methods in accordance with Health & Safety Code, CCR, Section 1367.25.
8. The Alliance's formulary is located on the Alliance's website and is available to Alliance Providers, Pharmacies, and Members upon request.
9. The Alliance provides coverage of standard fertility preservation services when a covered treatment may directly or indirectly cause iatrogenic infertility, and are not within the scope of coverage for treatment infertility.
10. The Alliance provides copayments that will not be higher than the in-network pharmacy's retail price for a prescription drug.
11. The Alliance provides formulary prescription coverage for antiretroviral medications including PrEP without prior authorization/step therapy requirement.
~~11.~~ 12. The Alliance provides coverage for at least one medication approved by the FDA in each of the following categories without prior authorization, step therapy, or utilization review:
(1) Medication for the reversal of opioid overdose, including a naloxone product or

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another opioid antagonist.
(2) Medication for the detoxification or maintenance treatment of a substance use disorder, including a daily oral buprenorphine product.
(3) A long-acting buprenorphine product.
(4) A long-acting injectable naltrexone product.

B. Pharmacy and Therapeutics (P&T) Committee:

1. The P&T Committee's voting membership is as described in RX-005 P&T Committee Roles and Scope.
2. Per the P&T Charter, the P&T Committee is responsible for the following:
   a. Develop and implement effective drug utilization review treatment outcome systems to optimize the quality of the pharmacy services
   b. Review the formulary on a quarterly basis
   c. Ensuring that the formulary review considers all drugs approved by the Federal Drug Administration (FDA)
   d. Ensuring that deletions from the formulary are documented and justified.
3. The following are considered by the P&T Committee when reviewing the formulary:
   a. Alliance Provider recommendations for additions or deletion of drugs to the formulary
   b. Bioavailability data
   c. Cost comparisons against other drugs available to treat the same medical condition(s)
   d. Current therapeutic guidelines
   e. Dosage ranges by route and age
   f. Findings from the following agencies: governmental agencies, medical and pharmaceutical associations, the National Institute of Health, and regulatory body publications
   g. Medical literature and clinical trials
   h. Off-label uses
   i. Patient risk factors relative to contraindications, warnings, and precautions
   j. Patient utilization and experience
   k. Pharmacokinetic data
   l. Pharmacologic considerations (e.g. drug class, similarity to existing drugs, side effect profile, mechanism of action, therapeutic indication, drug-to-drug interaction potential, and clinical advantages over other products in the specific drug class)
   m. Risks versus benefits regarding clinical efficacy and safety of a particular drug relative to other drugs with the same indication
   n. Special monitoring or medication administration requirements

C. Notification of Formulary Changes to Providers and Members

1. The Alliance notifies its Providers about formulary additions, deletions, and modifications to policies and procedures - and after each quarterly P&T Committee meeting, or more frequently as needed. Providers are notified through the provider bulletin updates. Information will include, at a minimum:

a. Copayment and coinsurance requirements and the pharmaceuticals or pharmaceutical classes to which they apply
b. List of preferred pharmaceuticals or formularies
c. Prior authorization criteria
d. Procedures for generic substitution, therapeutic interchange, step therapy, or other management methods to which the practitioner's prescribing decisions are subject
e. Any other requirements, restrictions, limitations, or incentives that apply to the use of certain pharmaceuticals

2. The Alliance notifies its members about formulary additions, deletions, and modifications to policies and procedures after each quarterly P&T Committee meeting, or more frequently as needed. In addition, bulletins will provide a link to the Alliance web site for detailed information on the formulary changes. Information will include, at a minimum:
   a. Copayment and coinsurance requirements and the pharmaceuticals or pharmaceutical classes to which they apply
   b. List of preferred pharmaceuticals or formularies
   c. Prior authorization criteria
   d. Procedures for generic substitution, therapeutic interchange, step therapy, or other management methods to which the practitioner's prescribing decisions are subject
   e. Any other requirements, restrictions, limitations, or incentives that apply to the use of certain pharmaceuticals

3. Member Services Department is also notified of formulary changes. A copy of the Summary of Formulary Updates will be emailed to the Director of Member Services once available. The Director of Member Services will disseminate the information to Member Services Representatives as of the effective date of the change. In addition, any interim formulary or benefit changes will be communicated to the Director on an as-needed basis.

4. Providers may submit requests for formulary changes by using the Request for Formulary Review Form. (Attachment 1)
   a. The Request for Formulary Review Form is available on the Alliance's website and can be provided upon request.
   b. The P&T Committee reviews requests for change to the formulary on a quarterly basis.

D. Content Management of Formulary Changes

1. The Alliance regularly updates material available online to Providers and Members. The Alliance synchronizes the dates that different information resources are updated to ensure consistency. Upon completion, the following content is updated:

a. Alliance Provider website:
   i. Document of Summary of Formulary Updates document uploaded
   ii. Online Drug Formulary Search Tools: Current PBM updates the On-line Search tool to reflect the changes.
b. Printed version: PBM will prepare the printed version of the formulary after the changes have been implemented. This document will be posted on the website within 45 days of the P&T decisions. Alliance Member website:
   i. Online Drug Formulary Search Tools: Current PBM updates the On-line Search tool to reflect the changes.

Printed version: PBM will prepare the printed version of the formulary after the changes have been implemented. This document will be posted on the website within 45 days of the P&T decisions.

E. Non-Covered Drug Classes (unless treating gender dysphoria or alleviating mental health or substance use)

- Drugs used to treat hair loss or hair growth
- Drugs solely used for cosmetic purposes
- Over-the-counter medications (unless approved by the Alliance)
- Non-FDA approved medications (e.g. Medical Foods, herbal remedies, certain supplements, special foods or diet items)
- Nutrition products or household items used for convenience
- Investigational drugs (drugs being studied in clinical trials)
- Comfort or convenience items
- Items used for hygiene (unless criteria have been met. The Alliance will cover incontinence creams and washes when there is a medical need)
- Items used to test blood or other fluids (except blood glucose monitors)
- Drugs used to treat worker's compensation related injury

DEFINITIONS / ACRONYMS

- Formulary: list of drugs covered by the Alliance
- NCQA: National Committee on Quality Assurance

AFFECTED DEPARTMENTS/PARTIES

Utilization Management
Pharmacy Services
Member Services
Provider Relations

Communications and Outreach

RELATED POLICIES AND PROCEDURES

RX-002 Prior Authorization Review Process
RX-005 P&T Committee Roles and Scope
P&T Charter

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

Attachment 1: Request for Formulary Review

REVISION HISTORY

10/1/2007, 3/25/2016, 12/11/2018, 11/13/2020, 3/16/2021, 6/21/2022, 9/20/2022, 12/27/2022, 3/28/2023, 4/10/2024, 12/17/2024, 3/18/2025

REFERENCES

- NCQA UM 12, Element A**,** B, D

- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx
- DMHC APL 20-001 (OPL): Newly Enacted Statutes Impacting Health Plans
- DMHC APL 19-002 (OPL): Newly Enacted Statutes Impacting Health Plans
- DMHC APL 21-018 Guidance Regarding Preventative Health Services Coverage for HIV Preexposure Prophylaxis (PrEP)

This policy will be reviewed annually to ensure effectiveness.

ALAMEDA Alliance FOR HEALTH
Health care you can count on.
Service you can trust.

POLICY AND PROCEDURE

Policy Number	RX-005
Policy Name	P&T Committee Roles and Scope
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	02/01/2012
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~9/24/2024~~
Compliance Committee Approval Date	TBD

POLICY STATEMENT

The purpose of this document is to outline the procedure for the structure, operation, functions, and scope of the Alameda Alliance for Health ("the Alliance") Pharmacy and Therapeutics (P&T) Committee.

A committee shall exist within the Alliance that will function as the policy-making body for all matters related to the therapeutic use of drugs and certain medical supplies. The P&T Committee is a subcommittee of the Alliance Board of Governors.

PROCEDURE

To help assure continuing patient access to a quality-driven, cost-effective, rational, drug benefit through the Alliance Drug Formulary, the P&T Committee will complete the following activities and adhere to the following operating procedures.

All pharmacy criteria decisions made by the Committee will be based upon a thorough review of the relevant findings of government agencies, medical associations, national commissions, peer-reviewed journals, and authoritative compendia consulted in pharmaceutical determinations.

The Committee will apply the above findings in adopting the pharmaceutical management procedures, including those used in constructing the formulary or preferred status. Evidenced based guidelines and guidelines will be applied when determining the following:

A. For the non-covered pharmaceuticals, making available an exceptions process to obtain the drugs
B. Considerations regarding limiting access to drugs in certain classes
C. Considerations on whether a pharmaceutical class is covered, not covered, or covered with restrictions and within each class of pharmaceuticals the following considerations are made:
    a. Which pharmaceuticals are preferred or covered at any level
    b. The criteria for prior authorizations of any pharmaceutical not covered
    c. Exceptions process available to members
    d. Substitutions made automatically or with physician permission
    e. Evidence showing how preferred-status pharmaceuticals can produce similar or better results for a majority of the population than other pharmaceuticals in the same class

I. Organization and Operation

A. Membership

1. The Committee shall be comprised of the following members:
    a) Alliance Chief Medical Officer (Co-Chair) or designee
    b) Alliance Senior Director of Pharmacy Services (Co-Chair) or designee
    c) Practicing physician(s) representing Family Practice and/or Internal Medicine
    d) Practicing physician(s) representing Pediatrics
    e) Practicing physician(s) representing a medical specialty as needed in accordance with the agenda
    f) Practicing psychiatric specialist (e.g., psychiatric pharmacist/physician)
    g) Practicing community pharmacist(s) contracted with Alliance (not to exceed three)
2. Non-voting members:
    a) Alliance Pharmacy Benefit Management Company representative pharmacist(s)
    b) Alliance Director of Provider Relations or designee
    c) Designated personnel (physician, pharmacist, nurse, etc.) representing Quality Assurance.
3. Membership should represent health care providers who serve the Alliance's patient population.
4. All Committee members shall complete a conflict-of-interest form pertaining to any financial or other relationship with pharmaceutical manufacturers. All Committee members' affiliations with outside interests shall not impair the responsible exercise of his or her duties as a P&T Committee member. If they have financial interest with a particular pharmaceutical manufacturer, they will be excluded from discussing and voting on evaluations or policies regarding the manufacturer's product line. (Refer to Appendix 1)
5. Compensation: Voting P&T members who are not Alliance staff are eligible to receive a financial stipend for each attended meeting and e-voting completed

B. Quorum

A quorum, is defined as a simple majority of voting members, must be present to conduct the P&T Committee meeting. A consensus decision will be made on formulary additions, deletions, and drug use/benefit policies. If no consensus is established, the issue will be put to a vote with the decision determined by majority vote of the quorum.

C. Schedule

The P&T Committee shall meet quarterly, at least four times per year. If urgent matters (as determined by the Alliance Chief Medical Officer) pertaining to the selection or utilization of drugs arise between meetings, a telephone or electronic voting will be conducted with the members. All relevant matters discussed between meetings will be presented formally at the next meeting.

D. Materials

An agenda and supplementary materials, including minutes of the previous meeting, shall be prepared, and submitted to the Committee members at least 7 days prior to the meeting to ensure proper review of the material.

1. Minutes of the Committee proceedings shall be prepared and maintained in the permanent records of Alliance.

E. Formulary Change Requests

Alliance providers may request additions, deletions, and modifications to the Alliance Drug Formulary by completing Formulary Request Form found in the Alliance Provider Manual. All requests shall be communicated in writing or by fax to:

Alameda Alliance for Health
Pharmacy Services
1204 South Loop Road
Alameda, CA 94502
Fax: 877-748-4524

F. Pharmaceutical Management Procedures

1. The P&T Committee will review pharmaceutical management procedures including medication guidelines, criteria, and clinical evidence, at least once every 12-month period and update those procedures as necessary as a result of that review.

2. Newly approved and marketed drugs will not be a pharmacy benefit until reviewed for addition to the Drug Formulary. FDA AA or P rated drugs (drug indicated for treatment of AIDS and HIV related illness and drugs with important therapeutic gain over existing therapies) may be an exception to the rule.

3. Addition or deletion to the Drug Formulary will be conducted at least once a year. Exceptions will be a drug product with clinical evidence supporting a significant improvement or decline in reported efficacy,

safety, or cost as determined by the Committee.

4. All decisions by the Committee to add or delete a drug from the Drug Formulary will take effect the first calendar day of the second month after the meeting unless otherwise specified. This is to allow time to notify physicians and other providers and change systems if needed.

5. Appeals to the Committee decisions may be made in writing within one month of the decision notification to the Chair of the Committee. These will be addressed on a case-by-case basis at the discretion of the Committee Chair.

II. Functions and Scope

The functions and scope of this Committee are designed to meet the following goals: to provide quality health care, to manage and control drug costs, and to continue to grow while ensuring the necessary management of resources.

A. Drug Formulary (See RX-004, Formulary Management)

1. Maintain a list of routinely covered drugs acceptable for use in the ambulatory care setting and provide for its constant revision
2. The selection of items to be included in the Drug Formulary shall be based on objective pharmacoeconomic evaluation of their relative therapeutic efficacy, safety, and cost. Therapeutic efficacy, safety, and adverse effects will be considered as the primary reasons for formulary inclusion/exclusion. If those are deemed to be equivalent or similar, the committee will also consider the Pharmacoeconomics of formulary inclusion/exclusion of the drug.
3. The Committee will attempt to minimize duplication of the same basic drug type, drug entity or drug product.

B. Guidelines and Protocols

1. To review drug utilization patterns and establish guidelines, protocols, programs, and procedures that help ensure high quality, cost-effective drug therapy.

C. Drug Use Review (DUR)

1. To recommend, initiate or direct Drug Use Review (DUR) and quality assurance programs. This includes recommending target drug or disease states to review, approving criteria for use before review, reviewing results when completed, making recommendations to appropriate departments, providers, etc., to take corrective action when less than optimal therapy is discovered, and measure for change after corrective action is in place. When recommendations for corrective action involve an individual provider, particularly change in a provider's scope of practice, such recommendation will be reported to the Utilization Management Committee (UMC) ~~HCQC~~.

D. Scope of Decisions

1. The committee will make decisions on the following concerns:
2. Classes of pharmaceuticals

3. Classes preferred or covered at any level
4. An exceptions process available to members for obtaining non-covered pharmaceuticals
5. Considerations regarding limiting access to drugs in certain classes Within each class of pharmaceuticals

    (1) The pharmaceuticals preferred or covered at any level
    (2) The criteria for prior authorization of any pharmaceutical
    (3) An exceptions process available to members
    (4) Substitutions made automatically or with physician permission
    (5) This evidence can show how preferred-status pharmaceuticals can produce similar or better results for a majority of the population than other pharmaceuticals in the same class.

E. Evidence-Based Decision Making

These decisions are based on appropriate external evidence to support continued use of revisions of procedures or criteria set forth in section D.

The following are considered by the P&T Committee when reviewing the formulary:

1. The formulary will contain drugs which represent each mechanism of action sub-class within all major therapeutic categories of prescription drugs.. Drugs newly approved by the Federal Drug Administration (FDA) are reviewed by the P&T Committee within (6) months of FDA approval. The P&T Committee determines whether the newly approved drugs will require prior authorization from the Alliance or be included in the Alliance's formulary.
2. In accordance with the Health and Safety Code, CCR, Section 1367.21, the Alliance allows for the coverage of any drug that is prescribed for use that is different from the use which that drug had been approved for marketing by the FDA, provide that all the following conditions are met.
    a) The drug is prescribed by a participating licensed health care professional for the treatment of:
        (1) A life-threatening condition
        (2) A chronic and seriously debilitating condition, and the drug is medically necessary to treat that condition, and the drug is on the Alliance's formulary. If the drug is not on the Alliance's formulary, the prescriber'srequest is reviewed in accordance with Health & Safety Code, CCR, Section 1367.24.

    b) The drug has been recognized for the treatment of that condition by one of the following:
        (1) The American Medical Association Drug Evaluations
        (2) The American Hospital Formulary Service Drug Information.

(3) The United States Pharmacopoeia Dispensing Information, Volume 1, "Drug Information for the Health Care Professional."
(4) Two articles from major peer reviewed medical journals that present data supporting the proposed off-label use(s) as generally safe and effective unless there is clear and convincing contradictory evidence presented in a major peer reviewed medical journal.

3. Alliance Provider recommendations for addition or deletion of drugs to the formulary
4. Bioavailability data
5. Cost comparisons against other drugs available to treat the same medical condition(s)
6. Current therapeutic guidelines
7. Dosage ranges by route and age
8. Findings from the following agencies: governmental agencies, medical and pharmaceutical associations, the National Institutes of Health, and regulatory body publications
9. Off-label uses
10. Patient risk factors relative to contraindications, warnings, and precautions
11. Patient utilization and experience
12. Pharmacoeconomic data
13. Pharmacokinetic data
14. Pharmacologic considerations (e.g., drug class, similarity to existing drugs, side effect profile, mechanism of action, therapeutic indication, drug-to- drug interaction potential, and clinical advantages over other products in the specific drug class)
15. Risks versus benefits regarding clinical efficacy clinical efficacy and safety of a particular drug relative to other drugs with the same indication
16. Special monitoring or medication administration requirements

DEFINITIONS / ACRONYMS

Pharmacy and Therapeutics Committee (P&T) - The policy-making body for all matters related to the therapeutic use of drugs and certain medical supplies.

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services Department
Pharmacy Benefit Manager (Currently – *PerformRx*)

RELATED POLICIES AND PROCEDURES

P&T Charter
Alliance Bylaws – Section 6
RX-002 Prior Authorization Review Process
RX-004 Formulary Management

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENT

Appendix 1: Confidentiality & Conflict of Interest Form

REVISION HISTORY

11/13/2020, 3/16/2021, 6/21/2022, 3/28/2023, 6/20/2023, 4/10/2024, 9/24/2024, 3/18/2025

REFERENCES

- NCQA UM 12.A.1
- NCQA UM 12.D. 1 and 2
- H&SC 1367.24
- H&SC 1367.21
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness.

POLICY AND PROCEDURE

Policy Number	RX-006
Policy Name	Pharmacy Services Staff Description
Department Name	Pharmacy
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	07/15/2012
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance") has an established process for defining the roles for staff involved in the Prior Authorization (PA) and Exception review process. The Alliance is committed to ensuring that staff members involved in the Prior Authorization and Exception review process and are properly licensed and qualified.

This policy and the associated procedures pertain to role assignment for staff members involved in the review process for prior authorization and Exceptions requests.

PROCEDURE

The Alliance employs clinical pharmacists, physicians, pharmacy services specialists, pharmacy technicians, as key staff involved in the prior authorization and exception review process. The qualifications and role of each reviewer in the review process are as follows:

1. The Pharmacy Services Specialists and Pharmacy Technicians are certified clinical assistants. Both positions are tasked with receiving the PA request form, ensuring completeness, and contacting the provider for additional information. He orshe can approve a request only if it meets the criteria of the Medical Review Guideline (MRG). He or she must defer requests to the available supervisor (pharmacist or medical director) if the request cannot be approved. Currently, this role is delegated to the Alliance's Pharmacy Benefit Manager (PBM).
2. The PBM's pharmacists will review requests deferred by Pharmacy Services Specialists or Pharmacy Technicians and make determinations on the requests. The PBM's pharmacists can render one (1) decision: approval (with or without MRG).

Any requests that cannot be approved must be escalated to the Alliance Clinical Pharmacist.

3. The Clinical Pharmacist at the Alliance is a currently licensed pharmacist with the California Board of Pharmacy. He or she is tasked with overseeing the review process and daily operations and reviews requests that the PBM's Pharmacy Services Specialists and Coordinators, Pharmacy Technicians, and Clinical Pharmacists cannot approve. The Alliance pharmacist can render three (3) types of decisions: approval (with or without MRG), denial for requests based on Evidence of Coverage (EOC) limitations, and medical necessity denials based on the MRG criteria and/or RX-003 (Exception Review Process). Any requests that cannot be approved, denied based on EOC, or denied based on MRG or RX-003 must be escalated to the Medical Director. A currently licensed, board-certified physician Medical Director may also oversee medical necessity determinations when appropriate or when physician input is needed.

4. The Medical Director is a currently licensed, board-certified physician. He or she is tasked with overseeing the review process and daily operations on an as-needed basis when the pharmacist is not available. He or she is also responsible for reviewing all PA requests for which the pharmacist cannot render a decision.

DEFINITIONS / ACRONYMS

a) Medical Review Guideline: clinical criteria against which requests for prior authorization and exception requests are reviewed; approved by the Pharmacy and Therapeutics (P&T) Committee
b) NCQA: National Committee on Quality Assurance

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Pharmacy Benefit Manager (Currently PerformRx)

RELATED POLICIES AND PROCEDURES

RX-002 Prior Authorization Review Process
RX-003 Exception Review Process

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

Medical Review Guideline (Excerpt)

REVISION HISTORY

7/15/2012, 5/19/2016, 12/11/2018, 6/25/2019, 3/16/2021, 6/21/2022, 3/28/2023, 4/10/2024, 3/18/2025

REFERENCES

- NCQA 2016 HP Standards & Guidelines, UM 4 (Appropriate Professionals)
- NCQA 2016 HP Standards & Guidelines, UM 13 (Procedures for Pharmaceutical Management)
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal RX

DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out - Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness.

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POLICY AND PROCEDURE

Policy Number	RX-007
Policy Name	Pharmaceutical Patient Safety
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	05/01/2012
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

The purpose of this document is to outline the procedure for the functions and scope of the Alameda Alliance for Health (the "Alliance") Pharmacy Department Patient Safety activities.

The Alliance believes in providing appropriate and safe services to its members and works closely with its Pharmacy Benefit Manager (PBM) to ensure proper patient safety protocols are available and practiced to prevent patient safety issues related to pharmaceutical services.

The Alliance has adapted The National Coordinating Council for Medication Error Reporting and Prevention's (NCC MERP) definition of ''medication error," which is:

> ''Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice; healthcare products, procedures, and systems, including prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use."

PROCEDURE

I. Recalls and Withdrawals

A. The Food and Drug Administration (FDA) has three (3) different types of recalls, based on the potential severity of harm to the public.

1. Class I: recalls dangerous or defective products that may cause serious health problems or even death
2. Class II: recalls less dangerous products than Class I, that may cause only temporary health problems
3. Class III: recalls products for which use or exposure is not likely to cause adverse health consequences

B. Market withdrawal or voluntary recall is a removal or correction of a marketed product that FDA considers to be in violation of the laws it administers and against which it would initiate legal action (e.g., seizure)

C. The Alliance has a work process set up for Class I, II and voluntary recalls; unless deemed otherwise (e.g. lot level recalls), Class III recalls are not acted upon. In the case of notifications for drug recalls and/or withdrawals, the Alliance's PBM will provide lists of members and prescribers affected. The Alliance will then notify all affected members and/or providers by phone and/or mail of the recall. This notification will take place within 48 hours of notification from the PBM for Class I recalls and within 30 calendar days of FDA notification for Class II recalls and voluntary recalls.

D. The PBM is to generate drug specific reports from their claims data (updated daily) through a variety of data reporting tools. At a minimum, the reports contain the member and prescribing physician information. The Alliance will use these reports in the selection of which members to notify and any additional PBM tools in the notification process. The PBM's Clinical Services staff can assist the Alliance with constructing queries to support the notification process when requested.

E. The process for recalls, at a minimum, will include the following steps (in no specific order):

1. PBM provides the Alliance with a supplemental drug update, which is a specific communication regarding a change to the FDA status of a medication. This recall notice must be received within 48 business hours of initial notice from FDA.
2. All records in National Drug Data File (NDDF) are termed out by setting the recall/withdrawal flag.
3. Product is termed from the Alliance's formularies.
4. Product is termed from all applicable drug management programs.
5. Prior Authorizations for affected product are termed.

F. Drug withdrawal notifications may be provided to members and physicians. These notifications contain background information on the withdrawal, actions taken by the PBM, and recommendations for the Alliance. If the closest therapeutic alternative is a non-

formulary item a prior authorization will be entered in the interim. The PBM may notify the Alliance of the action taken regarding the drug that has been recalled/withdrawn within 48 hours for Class I and within 30 days for Class II recalls/withdrawals. The Alliance will not act on limited FDA withdrawal impacting specific lots of products. The PBM does not collect product lot numbers; therefore, it is not possible to identify utilization by members under these circumstances.

II. Medication Error Identification and Reduction (MEIR)

A. The Alliance may receive reports of medication errors from network pharmacies, prescribers, internal staff, and/or members.

B. The Alliance internal staff may include but are not limited to:
   1. Clinicians involved in review of prior authorization requests or appeals request
   2. Appeals and Grievances staff
   3. Member service representatives
   4. Quality Improvement Staff
   5. Pharmacy Staff

C. The Alliance staff will be trained to identify potential reportable medication errors and understand how to evaluate, resolve, document, and, if necessary, report to the appropriate authority.

D. A report of all received medication errors is presented quarterly to the UM Committee for the purpose of documenting medication errors, identifying trends and patterns, and to determine if further action is necessary (i.e. reporting the medication error to the FDA and/or relevant State Board(s) of Pharmacy).

E. When appropriate, reported medication errors are shared and discussed with downstream providers at the point of dispensing to ensure that corrective actions are implemented and future errors are prevented. These notifications shall be sent by mail with the option to discuss over the phone. This process shall comply with the medication error identification and reduction reporting requirements defined by Centers for Medicare and Medicaid Services (CMS), Utilization Review Accreditation Commission (URAC) and other regulatory and accreditation agencies.

III. Member Communication of Drug Recalls and Withdrawals

A. In addition to notifying members via letter or phone, as detailed above, the Alliance shall make public all drug recall and withdrawal information on the member portal of the plan website. The content can be located under “Safety Resources” within the “Pharmacy & Drug Benefits” section. Each recall and withdrawal shall be made published on the member portal within 5 business days of receipt of notification from the pharmacy benefit manager.

DEFINITIONS / ACRONYMS

a. FDA: Food and Drug Administration
b. NDDF: National Drug Data File
c. PBM: Pharmacy Benefit Manager (Currently, PerformRx)
d. URAC: Utilization Review Accreditation Commission
e. NCQA: National Committee on Quality Assurance
f. CMS: Centers for Medicare and Medicaid Services
g. NCC MERP: National Coordinating Council for Medication Error Reporting and Prevention.

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Department
Pharmacy Benefit Manager (PerformRx)
Provider Relations
Quality Improvement
Member Services

RELATED POLICIES AND PROCEDURES

P&T Charter

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None.

REVISION HISTORY

5/1/2012, 5/19/2016, 12/11/2018, 11/13/2020, 3/16/2021, 6/21/2022, 3/28/2023, 4/10/2024, 3/18/2025

- **REFERENCES**CMS Part D Manual, Chapter 7 – Prescription Drug Benefit Manual, section 20.5 – Medication Error Identification and Reduction (MEIR)
- PerformRx Policy, DRUM-1-02 - Internal Medication Error Identification and Reduction Systems
- NCQA, UM 12 Element C
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefit from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness by P&T Committee.

POLICY AND PROCEDURE

Policy Number	RX-008
Policy Name	PBM Delegated Audit Oversight
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	3/25/2016
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance) has a contract with its Pharmacy Benefit Manager (PBM) to administer many of the pharmacy services operations. The PBM contract shall indicate that they will comply with all applicable laws and regulations related to providing the Pharmacy Services to the Alliance members.

PROCEDURE

1. An annual audit shall be conducted by the Alliance staff or by a third-party vendor.
2. Audited areas shall be based on the current contract with the PBM. The areas of audit are as listed, but not limited to:
   a. Claims processing
   b. Formulary Management and Benefit Coding
   c. Prior Authorization Process
   d. Pharmacy Credentialing
   e. Pharmacy Encounter File Accuracy
   f. Compliance with the Health Insurance Portability and Accountability Act (HIPAA)
   g. Pharmacy Network Management
   h. Fraud, Waste, and Abuse (FWA) Training
   i. Drug Utilization Monitoring
3. Summary of audit and audit findings will be reviewed by the Pharmacy & Therapeutics (P&T) Committee and the Compliance Committee.

4. Ongoing audits will be conducted when closer and more frequent monitoring is warranted. They are, but not limited to:
   a. Maximum Allowable Cost (MAC) Pricing Management
   b. Turnaround Time for Outpatient Pharmacy Authorization Requests
5. On a quarterly basis, the current PBM will provide the summary of performance measurements as described in the contract.
6. The Alliance Senior Director, Pharmacy Services or designee will review the quarterly performance measures summary report and identify any problems with the completeness and effectiveness or other concerns about the PBM and present them to the P&T Committee.
7. The Alliance Senior Director, Pharmacy Services or designee will manage the audit findings from the annual audit, on-going monthly audits as well as the quarterly performance guarantee reports.
8. The Alliance adopts PerformRx policies for Pharmacy System User Access Review (CORE 1-08) and Utilization Management ("UM") System Controls (DRUM 1-05). These policies are adopted to ensure UM System Controls.
9. The Alliance will also have an NCQA crosswalk audit once a year that will be conducted by Alameda Alliance for Health Pharmacy Services staff.

If deficiencies are found during the audit, the Alliance will request a corrective action plan (CAP) and ensure implementation through a monitoring process as described in policy ADM-CMP-0042 Delegation Oversight.

DEFINITIONS / ACRONYMS

a. PBM: Pharmacy Benefit Manager (Currently, PerformRx)
b. HIPAA: Health Insurance Portability and Accountability Act
c. P&T Committee: Pharmacy and Therapeutics Committee

AFFECTED DEPARTMENTS/PARTIES

PBM

RELATED POLICIES AND PROCEDURES

- CMP-042 Delegation Oversight
- 

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RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None

REVISION HISTORY

12/11/2018, 06/25/2019, 3/16/2021, 5/26/2022 – IQIC ad hoc, 6/21/2022 – P&T, 3/28/2023, 4/10/2025~~5~~4, 3/18/2025

REFERENCES

- Title 22, CCR, Section 53854, 53214
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-cal RX
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out - Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness.

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POLICY AND PROCEDURE

Policy Number	RX-009
Policy Name	Pharmaceutical Emergency Supply Provision
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	4/1/2016
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance") shall arrange for pharmaceutical services to be available during regular business hours. In addition, the Alliance has an existing process to allow a three (3) day emergency fill at any contracted pharmacy to ensure the provision of drugs prescribed in emergency circumstances in amounts sufficient to last until the Member can reasonably be expected to have the full prescription filled California Code of Regulations, Title 22 §53854(1),(2) & (3)).

PROCEDURE

I. Contracted Pharmacies
   A. The Alliance delegates pharmacy contracting to its Pharmacy Benefit Manager (PBM). The PBM provides monthly reports of the pharmacy network in Alameda County. This report shall include the hours of operations of the contracted pharmacies.

II. Provision of Drugs During Emergency Circumstances
   A. "Emergency Circumstances" refer to any of the following situations:
      1. Emergency room (ER) discharge prescriptions
      2. Inpatient discharge prescriptions
      3. Any circumstance that involves an imminent and serious threat to the member, including, but not limited to, severe pain, potential loss of life, limb or major bodily function.

B. In emergency circumstances, as defined under Section A, prior authorization is not required for a three (3) day supply of drugs that would otherwise require authorization or exceptions.
C. Alliance providers are informed of this policy via the Alliance's Provider Manual.
D. Alliance providers are responsible for following the prior authorization process or exceptions process for the remainder of the prescription.
E. The Alliance allows for payment of the three (3) day supply of the drugs even in the event that the prior authorization or exceptions request is subsequently denied.
F. Continuity of care requirements do not require the Alliance to continue coverage of drugs dispensed under this provision if they are not found to be medically necessary.

III. Three (3) day Fill Procedure
A. The Alliance has a process in place to allow contracted pharmacies to process a 3-day supply under emergency situations.
B. The 3-day supply process is automated and does not require an authorization from the Alliance or the PBM's staff.
C. The dispensing pharmacist uses his or her clinical judgement to determine the level of emergency. An emergency situation is defined as a condition requiring expedited or urgent processing which includes any condition involving an imminent or serious threat to a member's health.
D. Emergency situations include but are not limited to: A discharge prescriptions from an inpatient stay or an Emergency Room visit, any other conditions that meet the criteria above (Section II. C.)

IV. Monitoring and Audit
A. The Alliance monitors a 3-day emergency override report on a monthly basis to ensure that members have access to a medication in emergency situations.
B. The findings of such monitoring will be reported to the - the P&T Committee.

DEFINITIONS / ACRONYMS

- PBM: Pharmacy Benefit Manager (currently, PerformRx)
- NCQA: National Committee for Quality Assurance

AFFECTED DEPARTMENTS/PARTIES

- Pharmacy Department

RELATED POLICIES AND PROCEDURES

- RX-001 Pharmaceutical Operating Processes Summary

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None

REVISION HISTORY

3/17/20, 03/16/21, 6/21/2022, 3/28/2023,
4/10/2024, 3/18/2025

REFERENCES

- CCR, Title 22§ 53854(1),(2) & (3)NCQA, 2016 HP Standards & Guidelines, UM 13 (Procedures for Pharmaceutical Management)
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal RX
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out - Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness.

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POLICY AND PROCEDURE

Policy Number	RX-010
Policy Name	Drug Utilization Management
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCAL, IHSS
Effective Date	10/01/2007
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

The Alameda Alliance for Health's (the "Alliance") Pharmacy Services unit has established Drug Utilization Review (DUR) procedures. The objective of DUR is to improve the quality of pharmaceutical care by ensuring that prescriptions are appropriate, medically necessary, and unlikely to result in adverse medical outcomes. The Alliance's DUR procedures comply with the Alliance's contract with the California Department of Health Care Services (DHCS). The Alliance will provide drug utilization encounter data to DHCS monthly.
Unless otherwise indicated, majority of DUR activities will be applicable to GroupCare only.

PROCEDURE

A. Drug Utilization Review (DUR) Overview:

1. DUR promotes patient safety by ensuring that prescriptions are appropriate, medically necessary, and unlikely to result in adverse medical outcomes.
2. All retail, specialty and mail service pharmacies are subject to Concurrent Reviews at point-of-sale and periodic Retrospective Reviews after adjudication.

B. Concurrent DUR:

1. This section does not apply to Medi-Cal line of business after the implementation of Medi-Cal Rx.
2. The Alliance's PBM ensures the safety of dispensed medications by notifying dispensing pharmacies of potential adverse events at the point-of-sale. The online messaging process classifies events at different levels of severity.
3. The PBM provides on-line, concurrent DUR messaging to pharmacies and takes appropriate action. Concurrent DUR includes but is not limited to the following

edits:

(a) Over- and under-utilization
(b) Duplication
(c) Drug-drug or drug-allergy interactions
(d) Drug-disease contraindications
(e) Drug dosage
(f) Drug-age precautions
(g) Drug-gender precaution
(h) Drug-pregnancy precautions

C. Retrospective DUR:

1. The Alliance's PBM will provide a list of on-demand retrospective DUR reports of various topics to monitor fraud, waste, or abuse. These reports are reviewed and may be used by the Alliance to support quality improvement programs (QIPs) and Disease Management programs.
2. The Alliance pharmacy staff or third-party vendor will run these reports as appropriate.
3. For Medi-Cal line of business, the Alliance will participate in Medi-Cal Global DUR Board and other DHCS organized pharmacy committee meetings.
4. For Medi-Cal line of business, the Alliance will receive comprehensive claims and PA history for their members and can use claims data for their own quality improvement, retrospective DUR activities, and coordination of care if needed including but not limited to identifying patterns of:
   (a) Therapeutic appropriateness
   (b) Adverse events
   (c) Incorrect duration of treatment
   (d) Over or under utilization
   (e) Inappropriate or medically unnecessary prescribing
   (f) Gross overprescribing and use
5. For Medi-Cal line of business, the Alliance will provide active and ongoing outreach to educate providers on common drug therapy problems (e.g., asthma medication ratio monitoring, opioid and naloxone co-prescribing, new prescribing guidelines, and advisories) with the goals of improving prescribing and dispensing practices, increasing medication compliance, and improvement of over-all beneficiary health.
6. For Medi-Cal line of business, the Alliance will be required to submit an annual DUR report to include any descriptions of any retro DUR activities and any innovative practices implemented by the plain in the prior federal fiscal year.
7.

For Medi-Cal line of business, the Alliance SIU (Special Investigations Unit) monitors and has a process for identifying and addressing fraud and abuse of controlled substances by the Alliance members and the health care Providers who are prescribing these drugs and pharmacies dispensing these drugs to the Alliance members. The Alliance SIU actively investigates any allegations of fraud, waste or abuse regarding the aforementioned substances.

D. Drug Utilization Data Submission

1. On a regular basis, no less than once monthly, the Alliance's PBM sends the

encounter data in the mutually agreed-upon format to the Alliance.

2. The Alliance's IT team will prepare the data for monthly submission. (See Policy IT Monthly Encounter Data)

E. Monitoring of DUR Process

1. Concurrent DUR reports and/or ~~-~~Retrospective DUR reports are reviewed by the Alliance pharmacy staff or third-party vendor ~~a~~and Senior Director, Pharmacy Services or designee and reported to the UM Committee and Board of Governors (BOG).~~Quality Improvement Health Equity Committee (QIHEC).~~

2. Pursuant to 42 CFR 438.3(s)(4) and (5), the Alliance is to operate a drug utilization review (DUR) program that complies with the requirements described in Section 1927 (g)of the Social Security Act (the Act) and submit an annual report on the operation of its DUR program activities to DHCS.

F. Preventing Opioid Overutilization

1. This section only applies to Group Care line of business after the implementation of Medi-Cal RX. The Alliance will ensure safe and effective use of opioids which include but are not limited to the following:

(a) Any long-acting opioid will require a prior authorization (PA)

(b) Short acting opioids will have quantity and day supply limits

(c) Members who are receiving above 500 MME (morphine milligram equivalent) will require a PA

(d) Concurrent use of any opioids and benzodiazepines or opioids and antipsychotics

(e) The Alliance will ensure that the DUR program meets or exceeds applicable provisions of Section 1004 requirements of the SUPPORT for Patient and Communities Act: A retrospective claims review process that monitors when an individual is concurrently prescribed opioids and benzodiazepines or opioids and antipsychotics.

G. Monitoring Anti-psychotics, Mood stabilizers and Anti-depressants

1. The Alliance will monitor appropriate use of anti-psychotics, mood stabilizers, and anti-depressant medications for all children 18 years of age and under including foster care children enrolled under the California Medicaid State Plan. The Alliance will ensure the following processes:

(a) Quarterly monitoring of children using anti-psychotics, mood stabilizers and anti-depressants.

(b) Quarterly monitoring of providers with children using anti-psychotics, mood stabilizers and anti-depressants.

DEFINITIONS / ACRONYMS

- PBM: Pharmacy Benefit Manager (Currently, PerformRx)
- IT: Information Technology Department
- MME: ~~-~~Morphine Milligram Equivalent
- PA: Prior Authorization

AFFECTED DEPARTMENTS/PARTIES

- PBM
- IT

RELATED POLICIES AND PROCEDURES

- PerformRx P&P: DRUM-3-01 Concurrent Drug Utilization Management Program
- Policy IT Monthly Encounter Data

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None.

REVISION HISTORY

10/7/2007, 8/24/2017, 12/11/2018, 6/25/2019, 3/17/2020, 3/16/2021, 6/15/2021, 6/21/2022, 3/28/2023, 12/19/2023, 4/10/2024, 3/18/2025

REFERENCES

- DHCS All Plan Letter 19-012 Federal Drug Utilization Review Requirements Designed to Reduce Opioid Related Fraud, Misuse and Abuse
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal RX
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx
- DMHC APL 23-026 Federal Drug Utilization Review Requirements Designed to Reduce Opioid Related Fraud, Misuse and Abuse
- DHCS Contract #23-30212, Exhibit A – Scope of Work

MONITORING

This P&P will be reviewed annually to ensure effectiveness and compliance with regulatory and contractual requirements.

Utilization data is reviewed for trends and analysis, and any identified potential fraud and abuse concerns are reported to the Compliance department. This includes potential fraud and abuse related to controlled substances by members, health care providers prescribing to the member, and pharmacy dispensing the drugs to members.

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POLICY AND PROCEDURE

Policy Number	RX-011
Policy Name	Decision and Notification Requirements
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	10/12/2017
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance") has an established process and timeframes for reviewing requests and sending out notification to the members and providers (Notice of Action). The Alliance is committed to ensuring that all requests for prior authorization or exception requests are reviewed in a timely manner. The Alliance's process for sending notifications to the member and provider regarding approved, modified, or denied authorization requests (also known as the "Pharmacy NOA Policy") complies with the standards set by the California Health & Safety Code, Sections 1367.01; the California Code of Regulations (CCR) Title 28, Section 1300.67.241; and the California Welfare & Institutions Code, Section 14185. Prior authorization is not required for the provision of an emergency three (3) day supply of drugs (see RX-009, Pharmaceutical Emergency Supply Provision).

This policy and the associated procedures also pertain to the review process for exceptions to pharmaceutical management procedures, such as Step Therapy, Quantity Limits and Age Limits.

PROCEDURE

I. Decision Review Time Frames (Turn-around times)

A. For all covered outpatient drug Prior Authorization requests, a decision will be rendered (Approved/Modified/Denied) within 24 hours from time of the receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases.

B. In all cases and for all decisions, notice of the decision rendered will be sent to the

requesting provider either by telephone, fax, mail, or other electronic communication within 24 hours from time of receipt for urgent/emergent cases and 72 hours from time of the receipt of non-urgent cases.

II. Decision Notification Time Frames - The Alliance provides notification of the decision within the following time frames:

A. Approvals

1. Notification of approval of Prior Authorization or Exception requests are made via facsimile or phone to the requesting provider and dispensing pharmacy (if the pharmacy is known) within 24 hours from time of the receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases.
2. The Alliance Pharmacy Services Department is responsible for ensuring all notifications are sent within 24 hours from time of the receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases. If the act of sending of the notifications is delegated to a vendor, The Alliance Pharmacy Services Department shall monitor notification times monthly to ensure compliance with the notification time frame.
3. Approval Notifications shall include at a minimum:
    1) The name of the medication requested
    2) The quantity and duration of treatment being approved.

B. Denials and Modifications

1. Notifications of denial or modification of Prior Authorization or Exception requests are made via facsimile or phone to the requesting provider and dispensing pharmacy (if the pharmacy is known) within 24 hours from time of the receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases after decision has been made. The Alliance notifies MEMBERS of a decision to Deny, or Modify requests for exceptions or prior authorization by sending WRITTEN notification to the member within 24 hours from time of the receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases after the decision has been made.
2. The Alliance notifies PROVIDERS of a decision to Deny, or Modify requests for exceptions or prior authorization by sending WRITTEN notification to the requesting provider within 24 hours from time of the receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases after the decision has been made.
3. Notifications of denied or modified requests shall include:
    1) Clear and concise explanations of the reasons for the denial and clinical reasons as applicable
    2) The name of the medication requested
    3) The quantity and duration of treatment being denied
    4) The name of the Medical criteria, benefit provision, Pharmacy or UM policy, or Medication Review Guideline used to make the decision
4. The notification includes the medication names, the amount requested, and the requested duration of treatment denied.
5. Providers are notified by telephone or fax within 24 hours from time of the receipt for urgent/emergent cases and within 72 hours from time of receipt for non-urgent cases after the decision has been made. The written notification includes the medication names, the amount requested, and the

duration of treatment denied. Written notifications to the physician or other health care provider of a denial, , or modification of a request will include the name and telephone number of the health care professional responsible for the denial, or modification. The telephone number provided is the direct number or an extension, to allow the physician or health care provider easily to contact the professional responsible for the denial, or modification

6. A standardized form is used, and the following information is included:
    1) The name and address of the Alliance and the state toll-free telephone number for obtaining information for legal service organizations for representation.
    2) Requesting providers are notified by telephone or fax within 24 (for urgent requests) or 72 hours (for non-urgent requests) of the final decision of the exception request in accordance with California Health and Safety Code Section 1367.01. The name and phone number of the person responsible for making the decision is included in the written notification. The notification includes the medication names, the amount requested, and the duration of treatment denied.

VI. Monitoring Process

A. The Senior Director of Pharmacy Services or designee reviews a monthly authorization report, which provides statistics on all approvals, denials, and modifications to ensure that providers and members have been notified in accordance within the mandated turnaround times.

B. The Senior Director of Pharmacy Services or designee shall audit at random up to twelve NOA letters per month. This audit shall include the following:
    1. Evaluation of whether the correct determination was made
    2. Evaluation of whether the correct rationale was used
    3. Whether all acronyms and medical terms were defined
    4. If the letter contains a specific reason for denial
    5. If the letter is easy to understand (clear and concise)
    6. If the criteria used to make the decision has been cited

C. If errors are found, they will be immediately addressed (e.g. new PA entered with correct decision, contact PBM, or discussion with the staff member who made the error).

V. Provider Access to the Decision maker

A. All letters shall contain the name of the clinician who made the decision and the phone number where they can be reached.

B. A log of physician calls and subsequent callbacks shall be kept and reviewed monthly for any barriers. Any barriers found will be immediately addressed.

Table 1: Decision & Notification Time Frames

Type of Request	Decision	Initial Notification	Written Notification
Prospective, Urgent	Approval	A fax is sent to the requesting provider within 24 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		
Prospective, Non-Urgent	Approval	A fax is sent to the requesting provider within 72 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		
Post-service	Approval	A fax is sent to the requesting provider within 72 hours of receipt of the request	NONE
	Modification		Written notification to the member and provider is generated and deposited with the United States Postal Service in time for pick-up within one business day after the decision
	Denial		

Table 2: Determination Turnaround Timetable of Different Regulatory Bodies

Type of Request	NCQA	DHCS	DMHC	**Alliance**
Prospective, Urgent	72 hours	72 hours	24 hours	**24 hours**
Prospective, Non-Urgent	15 calendar days	5 business days	72 hours	**72 hours**
Post-service	30 calendar days	30 calendar days	30 calendar days	**30 calendar days**

DEFINITIONS / ACRONYMS

- Pharmaceutical Management Procedures: Formulary drugs that have additional requirements or limits on coverage, such as Step Therapy (ST), Quantity Limits (QL) and Age Limits (AL).

- Terminal Illness: An incurable or irreversible condition that has a high probability of causing death within one year or less (Health & Safety Code Section 1373.96 (c)(4)).

- Emergency Circumstances: When the enrollee's condition is such that the enrollee faces an imminent and serious threat to his or her health, including, but not limited to, the potential loss of life, limb, or other major bodily function, it is considered an emergency (Health and Safety Code
- § 1367.01 (h)(2)).

HCQC: Health Care Quality and Compliance

Committee NCQA: National Committee on Quality

Assurance

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Pharmacy Benefit Manager (Currently PerformRx)

RELATED POLICIES AND PROCEDURES

RX-002 Prior Authorization Review Process
RX-006 Pharmacy Services Staff Description
RX-008 PBM Delegated Audit Oversight
RX-009 Pharmaceutical Emergency Supply Provision

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

Attachment 1 – Prescription Drug Prior Authorization Request Form
Attachment 2 – Exception Review Process Flow Chart

REVISION HISTORY

10/12/2017, 12/11/2018, 3/16/2021, 3/15/2022, 3/28/2023, 4/10/2024, 3/18/2025

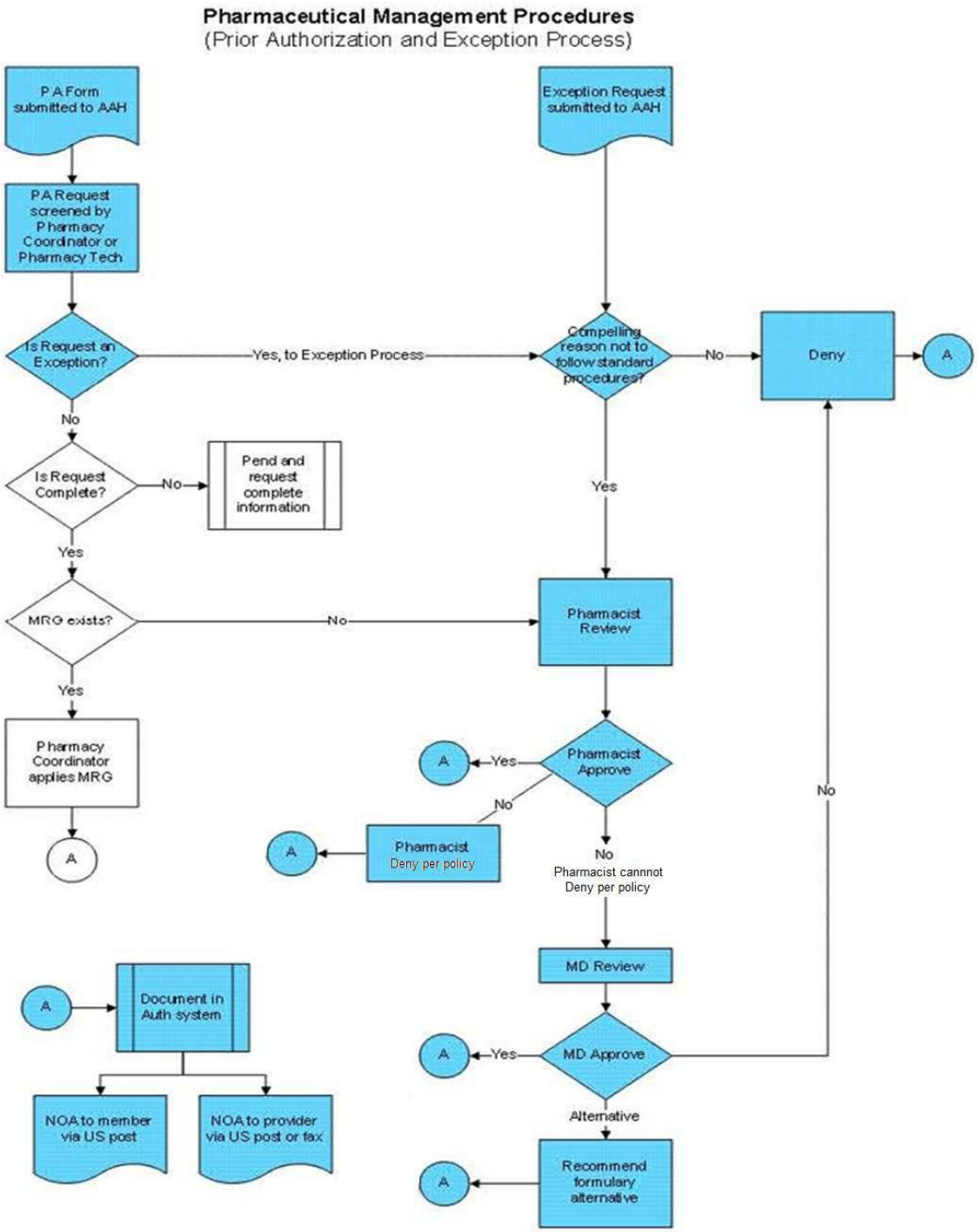
REFERENCES

- California Code of Regulations (CCR), Health & Safety Code, §§1367.01,1367.21, 1367.22, 1367.24 and 1373.96
- CCR, Welfare & Institutions Code, §14185
- CCR, Title 22, §§51003, 51014.1, 51014.2, 53854 and 53894
- CCR Title 28 §1300.67.24
- MMCD Policy Letter 08-013
- NCQA, 2016 HP Standards & Guidelines, UM 13 (Procedures for Pharmaceutical Management), Element E (Considering Exceptions)
- Welfare and Institutions Code, Section 14185**, 42 CFR 438.3(s)(6), and Section 1927(d)(5)(A) of the Social Security Act**
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – MediCal Rx

MONITORING

This P&P is reviewed annually to ensure effectiveness.

APPENDIX


Pharmaceutical Management Procedures
(Prior Authorization and Exception Process)
PA Form submitted to AAH
Exception Request submitted to AAH
PA Request screened by Pharmacy Coordinator or Pharmacy Tech
Is Request an Exception?
Yes, to Exception Process
Compelling reason not to follow standard procedures?
No
Deny
A
No
Is Request Complete?
No
Pend and request complete information
Yes
Yes
MRG exists?
No
Pharmacist Review
Yes
Pharmacy Coordinator applies MRG
A
A
Yes
Pharmacist Approve
No
A
Pharmacist Deny per policy
No
Pharmacist cannnot Deny per policy
No
MD Review
A
Document in Auth system
A
Yes
MD Approve
NOA to member via US post
NOA to provider via US post or fax
Alternative
A
Recommend formulary alternative

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POLICY AND PROCEDURE

Policy Number	RX-012
Policy Name	DU Policies - Pharmacy Portal & DU Access
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCAL
Effective Date	04/01/2021
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~6/11/2024~~
Administrative Oversight Committee Approval Date	TBD~~8/21/2024~~

POLICY STATEMENT

The purpose of this document is to outline the procedure on how to identify Designated Users (DU) to the Medi-Cal Rx secure Managed Care Plan (MCP) Pharmacy Portal and DU Access Request and for utilization of Medi-Cal Rx secure MCP Pharmacy Portal by the Alameda Alliance for Health (the "Alliance") Pharmacy Department activities.

The Pharmacy Department will work with the state's designated Pharmacy Benefit Manager (PBM) to maintain and track a list of DUs and utilization of Medi-Cal Rx secure MCP Pharmacy Portal through collaboration with Case Management (CM), Utilization Management (UM), Quality Improvement (QI), Grievance and Appeal (G &A), Member Services (MSR) and delegated partners monthly to identify a new user or remove the user who is no longer with the organization.

The Pharmacy Department will communicate to internal stakeholders in case if Medi-Cal Rx secure MCP Pharmacy Portal is down.

PROCEDURE

I. Identification of Designated Users (DU) to the Medi-Cal Rxsecure MCP Pharmacy Portal

A. For a new internal DU request, the requestee, or someone on behalf of the requestee within AAH will email the Pharmacy Department

(distgrpPharmacy@alamedaalliance.org) with the new DU requests containing the following information: name, title, phone number, and email of the new DU requestee. For internal stakeholder AAH requests, the pharmacy technician will be sure that the approved DU requestees meet the appropriate criteria. Approved operational roles for our internal DU access are: Pharmacy, Care Management, Behavioral Health, and Grievances.

B. For a new Delegate Partner DU request, the pharmacy technician and/or Designated User Access Request Coordinator (DUARC) will send out an email to the Senior Director of Pharmacy Benefits or Pharmacy Leaders/Directors for Delegate Partners once monthly.

II. Submission of DU Access Request

A. Pharmacy Technician and/or DUARC will fill out the DHCS-6520-Medi-Cal MCP Designated User System Access Request Form, both for internal AAH stakeholders as well as for Delegate Partners.

B. Once the lists are updated with the new DU access requests for the week, designated pharmacy technician and/or DUARC will send MediCalRxProvisioning@PrimeTherapeutics.com for approval from DHCS and Prime Therapeutics.

III. Maintenance of Designated Users List and Utilization of Medi-Cal Rx Okta Portal

The Alliance will receive User Access Audit Reports from Prime Therapeutics via a secure file transfer protocol or other secure method. These Alliance specific User Access Audit Reports will be created in an Excel file format for consumption and utilization by the Alliance to audit and verify DU lists and appropriate DU access. The Alliance will take action regarding access privileges for any DU, and must provide that request in accordance with the Medi-Cal Rx Designated User Policy and Procedure Manual.

A. Pharmacy Technician and/or DUARC will screen the Internal Alliance DU list monthly and as needed at the discretion of the pharmacy team.
   1. Expired users (i.e. employees who are no longer with the Alliance or no longer require access) will be removed from the list and report to DHCS and Prime Therapeutics via forwarding an updated DHCS-6520-Medi-Cal MCP Designated User System Access Request Form requesting termination of the respective user within 24 hours of the notification to pharmacy department so that the DU's access can be terminated.
   2. Removed expired users will be added to our internal Expired User List (Term List)

B. Pharmacy Technician and/or DUARC will screen the External Delegate Partner DU list monthly and as needed at the discretion of the pharmacy team.
   1. Email the Delegated Partners for their updated active DU requestee lists
   2. Save as an excel in the appropriate drive

IV. How To Use the MCP Pharmacy Portal

A. MCP Pharmacy Portal Access:
   1. Users may access the Medi-Cal Rx secure MCP Pharmacy Portal at: https://medi-calrx.dhcs.ca.gov/home/
   2. Users may also choose to access the Okta SSO Prime Therapeutics Tool directly at: https://ciam.primetherapeutics.com/

B. Use and Navigation of the MCP Pharmacy Portal:
   1. Access to the Health Plan Portal is available only to approved users. If access has been granted, an individual can enter the secured area of the Health Plan Portal.
   2. Clicking on the Health Plan Portal button on the Medi-Cal Rx Web Portal Home page will prompt a HIPAA notification which users must click AGREE to continue.
   3. Users with credentials will be able to log into the secured area of the Health Plan Portal using the Okta℠ SSO tool via Prime Therapeutics. From here, users may click on the appropriate tile for the application they wish to access: FirstTrax Client Interface(FirstCI), or MRx Explore.

V. MCP Pharmacy Portal system down communication

A. If the MCP Pharmacy Portal system is down (i.e. if claims are no longer being received from Prime Therapeutics or if there are any other related technical issues) then:
   1. Identify technical issues.
   2. Write email containing detailed information on the technical issue including time of occurrence, effected users, and any other pertinent information.
   3. Email to: MediCalRxMCPinterfaceSupport@PrimeTherapeutics.com and Carbon Copy internal stakeholders so that they are informed when Medi-Cal Rx secure MCP Pharmacy Portal is down.

DEFINITIONS / ACRONYMS

a. PBM: Pharmacy Benefit Manager (Currently, Prime Therapeutics)
b. DU: Designated Users
c. MCP: Managed Care Pan
d. CM: Case Management
e. UM: Utilization Management
f. QI: Quality Improvement
g. G &A: Grievance and Appeal
h. MSR: Member Services
i. P & T: Pharmacy & Therapeutic Committee

AFFECTED DEPARTMENTS/PARTIES

a. Pharmacy Department
b. Pharmacy Benefit Manager (Prime Therapeutics)
c. Case Management
d. Utilization Management
e. Quality Improvement
f. Grievance and Appeal
g. Member Services
h. Provider Relations

RELATED POLICIES AND PROCEDURES

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS


FirstCI User Guide (002).pdf


FirstCI Patient Search Job Aid.pdf


Medi-Cal Rx Managed Care Plan MeetandGreet


MCP CL Preseal


DHCS-6520-Medi-C MCP Designated

REVISION HISTORY

4/13/2021, 6/15/2021, 6/21/2022, 3/28/2023, **8/21/2024,** 3/18/2025

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Red = Substantive Updates

REFERENCES

- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-cal RX
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out - Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness by P&T Committee.

POLICY AND PROCEDURE

Policy Number	RX-013
Policy Name	Medical Benefit Physician/Facility-Administered Drugs (PAD) Prior Authorization Review Process
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCAL, IHSS
Effective Date	7/17/2023
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~6/11/2024~~
Administrative Oversight Committee Approval Date	TBD~~8/21/2024~~

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance") has an established process for reviewing and processing medical necessity-based physician/facility-administered drugs (PAD) authorization requests for pharmaceutical services that are on the formulary. The Alliance is committed to ensuring that all eligible Alliance members have timely and efficient access to covered pharmaceutical services that require authorization. The Alliance's pharmaceutical authorization process complies with the standards set by the California Health & Safety Code, Sections 1367.01, 1373.96; the California Code of Regulations (CCR) Title 28, Sections 1363.5, 1367.01, . The Alliance covers medications for treating gender dysphoria or alleviating mental health or substance use. The Alliance ensures parity in coverage of pharmaceuticals used to treat medical/surgical, mental health, and substance abuse disorders.

PROCEDURE

I. Prior Authorization Process Guidelines

A. Prior authorization review and approval hierarchal criteria are utilized and required as outlined in UM-001 (or with PAD Medication Review Guidelines) for the appropriate pharmacy authorizations.

B. The Alliance utilizes evidence-based prior authorization criteria approved by the P&T Committee. Prior authorization criteria are developed and reviewed annually and are based established by organizations such as Medi-Cal guidelines (if for Medi-Cal line of business), Milliman Care Guidelines, Food and Drug Administration (FDA), National Comprehensive Cancer Network (NCCN), UpToDate, and National Institutes of Health (NIH). The Alliance

covers pharmaceuticals in accordance with 42 CFR section 438.900 et seq, to ensure parity in medical/surgical, mental health, and substance abuse benefits and treatment.

II. Prior Authorization Procedures

A. All providers are required to submit prior authorization for Healthcare Common Procedure Coding System (HCPCS) / National Drug Code (NDC) codes that are listed and in alignment with P&T committee approved PA criteria as appropriate.

B. Required information provided on all requests should include:

a) Member demographic information
b) Practitioner demographic information
c) Requested service/procedure to include specific Current Procedural Terminology (CPT)/Healthcare Common Procedure Coding System (HCPCS) code(s)
d) Member diagnosis (Specific International Classification of Disease (ICD) Code/Description)
e) Clinical indications necessitating service
f) Pertinent medical history, treatment, or clinical data
g) Location of service to be provided
h) Requested/anticipated duration of therapy
i) Proposed date(s) of services

C. Prior authorization requests must be submitted electronically or by fax to the Alliance UM Department.

a) Pharmacy department will manage the end-to-end process when providers send a PAD PA for the Alliance members. This entails some of the following duties below:
   i. Verify eligibility, coverage, and network
   ii. Check if there are benefit restrictions
   iii. Generate letter of notifications for approval, partial approval, and denial

A. Retro Requests: The Alliance does not accept post-service or retrospective authorization requests for nonemergent or non-urgent services that would require prior authorization more than 90 days past the date of service.

The exception criteria under which a post service / retrospective request greater than 90 days after the date of service may be considered are:

1. Member eligibility issues, i.e., unable to validate eligibility at time of service, incorrect eligibility information at time of service.
2. In-patient services where the facility is unable to confirm enrollment with the Alliance.

B. Pre-Service/Post-Service Review for Pharmacy Technician (PT)

A. Upon receipt of the authorization request, the PT will review the request for:
   (1) Member eligibility
   (2) Completeness of the request
      (a) Presence of medical codes,
      (b) Presence of medical records

B. Once the authorization request review is complete, the PT enters the authorization request into the clinical information system and routes it to the appropriate UM PT processing queue.

C. Upon selecting authorization request from the queue, the assigned PT reviews the pre-service/post-service authorization request that includes:

(1) The UM PT reviewer performs a review of the pre-service/post-service/ associated with PAD authorization request and clinical information presented using the appropriate UM criteria, according to UM-001 Utilization Management Policy or UM Program.

(a) The PT Reviewer documents the decision-making process in the clinical information system.

(b) The PT Reviewer workflow includes:

(i) For authorization requests meeting criteria under the scope of the PT, the PT Reviewer approves the request and generates the Member and Provider approval notification.

(ii) For authorization requests not consistent with the request (i.e., conflicting CPT Codes to diagnosis, conflicting HCPCs to documentation, etc.), or otherwise are outside of PT scope, where there is a potential for delay, denial, modification, or termination, and for cases involving benefit exhaustion or benefit termination, the PT Reviewer forwards the request to the Pharmacist Reviewer.

C. Pre-Service/Post-Service Review Pharmacist Reviewer (PR)

A. Pharmacist Reviewer performs a medical necessity review of the authorization request and clinical information presented using the appropriate UM criteria, according to UM-001 Utilization Management Policy or UM Program.

(1) The PR utilizes evidence-based criteria and hierarchical criteria process for approving, modifying, deferring, requested services (as applicable).

(a) The hierarchal criteria process:

(i) Regulatory and contractual requirements

(ii) Evidence based guidelines

(iii) Alliance specific guidelines

(iv) National medical association consensus

(v) Medical necessity/medical judgement

(2) The PR Reviewer documents the clinical decision-making process in the clinical information. The documentation must include a review of the clinical information and application of the appropriate criteria used in the determination.

III. The Alliance's Pharmacy Department processes pharmacy authorization requests in accordance with the procedures described in UM Policy # 001 – Utilization Management and UM Policy #057 (as it may relate to pharmacy services).

a. Outreach calls (up to 3 attempts) may be made to the requesting provider to request reasonably necessary clinical information when needed to make a PA decision or enter missing required clinical information for medication requests. For each outreach attempt, the reviewer is to document the following:

i. Name and title of person spoken to

ii. Phone number called (if different from one already noted in the PA system)

iii. What specific information was requested

IV. Continuity of Care for Covered Services for Newly Enrolled Medi-Cal and GroupCare Beneficiaries

A. PAD CoC requests are managed using the same mechanisms and processes as UM Policy #036 Continuity of Care for Terminated and Non-Participating Providers, UM Policy #058, Continuity of Care for New Enrollees Transitioned to Managed Care After Receiving A Medical Exemption, and UM Policy#059 Continuity of Care for Medi-Cal Beneficiaries Who Transition into MediCal Managed Care.

V. Continuation of Therapy

A. The Alliance shall allow continuation of therapy for members using medically necessary drugs when it can be shown through clinic notes or medication fill history that the member has been taking the medication prior to enrollment.

B. For transitioning members until the Beneficiary can be seen by a Plan provider to establish a care plan, as required by Welfare & Institutions (W&I) Code, Section 14185(b), the Alliance will allow for continuation of medically necessary medications if provided clinic notes showing all of the following:

1. Patient name
2. Medication name, dose, and route of administration
3. Quantity distributed
4. Date medication was started and date last given/filled

VI. Annual Review of PAD Prior Authorization and UM Criteria

a. All PAD utilization management criteria undergo annual evaluation for appropriateness and effectiveness. Criteria are updated when necessary. The P&T committee reviews the pharmacy UM program, including delegated elements. The review encompasses scope, policies and procedures, and criteria as appropriate.

VII. Monitoring of the PA process

a. Inter-rater Reliability- the Alliance evaluates the consistency of decision making for those health care professionals involved in applying PAD Criteria.

VIII. Pharmacy Department will communicate with Utilization Management (UM), Communications & Outreach, Medical Directors, Provider Services (PR), Member Services (MSR), Claims and Benefit Configuration Departments to implement prior authorization restriction requirements in Heath Suite and outreach to providers and members.

IX. Pharmacy Services will comply with appropriate UM policies as they relate to pharmacy supported authorizations, NOA letters and regulatory requirements (see related policies section for reference).

DEFINITIONS / ACRONYMS

- PAD: Physician/Facility-Administered Drugs
- NCQA: National Committee on Quality Assurance
- UM: Utilization Management

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Utilization Management
Claims

Benefit Configuration
Member Services
Provider Relations
Communications and Outreach

RELATED POLICIES AND PROCEDURES

UM-001 Utilization Management
UM-036 Continuity of Care for Terminated and Non-Participating Providers
UM-051 Timeliness of UM Decision Making and Notification
UM-051 Attachment A UM Timeliness Standards for Medi-Cal and Group Care
UM-054 Notice of Action
UM-057 Authorization Service Request
UM-058 Continuity of Care for New Enrollees Transitioned to Managed Care After Receiving A Medical Exemption
UM-059 Continuity of Care for Medi-Cal Beneficiaries Who Transition into MediCal Managed Care

REVISION HISTORY

6/20/2023, 12/19/2023,-
8/21/2024, 3/18/2025

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Red = Substantive Updates

REFERENCES

- NCQA UM 12, Element A**,** B, D
- Alliance Provider Manual

- Health & Safety Code, Sections 1363.5, 1367.01, 1367.21, 1367.215, 1373.96
- Senate Bill 855 – Mental Health as a Medical Necessity
- DHCS All Plan Letter 22-012 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx
- DHCS All Plan Letter 22-032 Continuity of Care for Medi-Cal Beneficiaries Who Newly Enroll in Medi-Cal Managed Care from Medi-Cal FFS, and for Medi-Cal Members who Transition into a New Medi-Cal Managed Care Health Plan on or after January 1, 2023
- DHCS APL 23-004 Skilled Nursing Facilities -- Long Term Care Benefit Standardization And Transition Of Members To Managed Care
- DHCS APL 23-027, Subacute Care Facilities -- Long Term Care Benefit Standardization and Transition of Members to Managed Care
- DHCS APL 23-023 – Intermediate Care Facilities for Individuals with Developments Disabilities – Long Term Care Benefit Standardization and Transition of Members to Managed Care
- DHCS Contract #23-30212, Exhibit A – Scope of Work
- 2024 Medi-Cal Managed Care Plan Transition Policy Guide

MONITORING

This policy will be reviewed annually to ensure effectiveness.

APPENDIX

Table 1: Medical Benefit Determination Turnaround Timetable of Different Regulatory Bodies

Type of Request	NCQA	DHCS	DMHC	**Alliance**

Prospective, Urgent	72 hours	72 hours	72 hours	**72 hours**

Prospective, Non-Urgent	Medi-Cal: 14 calendar days Group Care: 15 calendar days	5 business days	5 business days	**5 business days**
Post-service	30 calendar days	30 calendar days	30 calendar days	**30 calendar days**

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POLICY AND PROCEDURE TEMPLATE

Policy Number	RX-014
Policy Name	Physician/Facility-Administered Drugs (PAD) Prior Authorization List Management
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCAL, IHSS
Effective Date	12/19/2023
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~3/19/2024~~
Administrative Oversight Committee Approval Date	TBD~~8/21/2024~~

POLICY STATEMENT

The Alameda Alliance for Health ("Alliance") has an established mechanism for maintaining, reviewing, and updating its physician/facility-administered drug prior authorization list. The Alliance is committed to ensuring that all eligible Alliance members have access to high quality and cost-effective pharmaceutical care. The Alliance's Physician/Facility-Administered Drugs (PAD) Prior Authorization List Management process complies with the standards set by the Health and Safety Code, CCR, Section 1363.5, 1367.01, 1367.21, 1367.215. The Alliance covers medications for treating gender dysphoria or alleviating mental health or substance use.

PROCEDURE

A. Physician/Facility-Administered Drugs Prior Authorization List Management

1. The Alliance's PAD PA List Management is managed by the Pharmacy and Therapeutics (P&T) Committee with consultation support from PBM and third-party vendor.
2. The P&T Committee objectively appraises, evaluates, and selects physician administered drugspharmaceutical products for prior authorization requirements inclusion or exclusion. Products are evaluated based on efficacy, safety, ease of use, and cost. This is an ongoing process to ensure the optimal use of therapeutic agents.

3. The Alliance's PAD PA List Management is updated on a continuing basis after each meeting of the P&T Committee as well as between P&T Committee meetings when interim changes are implemented by Alliance pharmacy services. Alliance Providers are notified of all prior authorization changes in a timely manner, using Alliance's website and fax.
4. Drugs newly approved by the Food and Drug Administration (FDA) are reviewed by the P&T Committee within six (6) months of FDA approval. The P&T Committee determines whether the newly approved drugs will require prior authorization from the Alliance to be included on the Alliance's PAD PA List for review of medical necessity.
5. In accordance with Health & Safety Code, CCR, Section 1367.21, the Alliance allows for the coverage of any drug that is prescribed for use that is different from the FDA-approved use(s), provided that **all of the following conditions** are met to show medical necessity:
    a. The drug is prescribed by a participating licensed health care professional for the treatment of:
        i. A life-threatening condition; or
        ii. A chronic and seriously debilitating condition, and the drug is medically necessary to treat that condition, and the drug is on the Alliance's PAD PA List.
    c. The drug has been recognized for the treatment of that condition by any of the following:
        i. The American Medical Association Drug Evaluations
        ii. The American Hospital Formulary Service Drug Information
        iii. The United States Pharmacopoeia Dispensing Information, Volume I, "Drug Information for Health Care Professionals"
        iv. Two articles from major peer reviewed medical journals that present data supporting the proposed off-label use(s) as generally safe and effective unless there is clear and convincing contradictory evidence presented in a major peer reviewed medical journal.
        v. It is the prescriber's responsibility to submit the supporting documentation.

6. The Alliance covers pharmaceuticals in accordance with 42 CFR section 438.900 et seq, to ensure parity in medical/surgical, mental health, and substance abuse benefits and treatment.

B. Pharmacy and Therapeutics (P&T) Committee:

1. The P&T Committee's voting membership consists of the Alliance's Chief Medical Officer or designee, the Alliance Senior Director of Pharmacy Services or designee, (4) four licensed practicing physicians and practicing community pharmacists contracted with Alliance (not to exceed 1/3 of the voting membership of the committee or three pharmacists, whichever is greater). The non-voting membership may include a clinical pharmacist from the Alliance's Pharmacy Benefit Manager (PBM), a representative from the Alliance's Quality Improvement Unit, Alliance Operations Unit, and practicing physicians representing a medical specialty as needed in accordance with the agenda and the specific medications or subjects being reviewed.
2. Per the P&T Charter, the P&T Committee is responsible for the following:

a. Develop and implement effective drug utilization review treatment outcome systems to optimize the quality of the pharmacy services
b. Review the list on a quarterly basis
c. Ensuring that the PAD PA List review considers all drugs approved by the Federal Drug Administration (FDA)
d. Ensuring that deletions from the PAD PA List are documented and justified.

3. The following are considered by the P&T Committee when reviewing the PAD PA List:
   a. Alliance Provider recommendations for additions or deletion of drugs to the PAD PA List
   b. Bioavailability data
   c. Cost comparisons against other drugs available to treat the same medical condition(s)
   d. Current therapeutic guidelines
   e. Dosage ranges by route and age
   f. Findings from the following agencies: governmental agencies, medical and pharmaceutical associations, the National Institute of Health, and regulatory body publications
   g. Medical literature and clinical trials
   h. Off-label uses
   i. Patient risk factors relative to contraindications, warnings, and precautions
   j. Patient utilization and experience
   k. Pharmacokinetic data
   l. Pharmacologic considerations (e.g., drug class, similarity to existing drugs, side effect profile, mechanism of action, therapeutic indication, drug-to-drug interaction potential, and clinical advantages over other products in the specific drug class)
   m. Risks versus benefits regarding clinical efficacy and safety of a particular drug relative to other drugs with the same indication
   n. Special monitoring or medication administration requirements

C. Notification of PAD PA List Changes

1. The Alliance notifies its Providers about PAD PA List additions, deletions, and modifications and after each quarterly P&T Committee meeting, or more frequently as needed. Providers are notified through the Alliance website update and provider fax.
2. Utilization Management (UM), Community Outreach Medical Director, Provider Services (PR), Member Services (MSR), Claims and Benefit Configuration Departments are also notified of PAD PA List changes. A copy of the Summary of Prior Authorization Updates will be emailed to the Director of UM, PR, MSR, C &O once available. The Director of UM, PR, and MSR will disseminate the information to UM Medical Director, UM Managers, UM coordinator, Provider Services Representatives, and Member Services Representatives as of the effective date of the change. In addition, any interim changes will be communicated to the Director on an as-needed basis.

DEFINITIONS / ACRONYMS

- PAD: Physician/Facility-Administered Drugs
- Formulary: list of drugs covered by the Alliance
- NCQA: National Committee on Quality Assurance
- UM: Utilization Management
- PR: Provider Relations
- MSR: Member Services
- C&O: Communications and Outreach

AFFECTED DEPARTMENTS/PARTIES

Utilization Management
Pharmacy Services
Member Services
Provider Relations
Communications and Outreach

RELATED POLICIES AND PROCEDURES

RX-002 Prior Authorization Review Process
RX-005 P&T Committee Roles and Scope P&T Charter
UM-001 Utilization Management
UM-036 Continuity of Care for Terminated and Non-Participating Providers
UM-051 Timeliness of UM Decision Making and Notification
UM-051 Attachment A UM Timeliness Standards for Medi-Cal and Group Care
UM-054 Notice of Action
UM-057 Authorization Service Request
UM-058 Continuity of Care for New Enrollees Transitioned to Managed Care After Receiving A Medical Exemption
UM-059 Continuity of Care for Medi-Cal Beneficiaries Who Transition into MediCal Managed Care

REVISION HISTORY

New Policy: 8/21/2024, 3/18/2025

REFERENCES

- NCQA UM 12, Element A, B, D
- Alliance Provider Manual
- Health & Safety Code, Sections 1363.5, 1367.01, 1367.21, 1367.215
- Senate Bill 855 – Mental Health as a Medical Necessity
- DHCS All Plan Letter 22-012 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness.

POLICY AND PROCEDURE

Policy Number	RX-015
Policy Name	Pharmaceutical Safe Use Monitoring of Physician Administered Drugs
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	Medi-Cal, IHSS
Effective Date	12/17/2024
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/18/2025~~12/17/2024~~
Compliance Committee Approval Date	TBD

POLICY STATEMENT

The purpose of this document is to outline the procedure for the functions and scope of the Alameda Alliance for Health (the "Alliance") Pharmacy Department for notifying providers and patients of any potential harm as discovered by drug recalls and any other drug safety alerts in relation to physician administered drugs.

PROCEDURE

A. Pharmacy Technicians will check Pharmacy Department email inbox for FDA Recall Alerts that are not lot specific.
   1. The Food and Drug Administration (FDA) classifies recalls based on the degree of health hazard.
      a. Class I: a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death.
      b. Class II: a situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.
      c. Class III: a situation in which use of, or exposure to, a violativeproduct is not likely to cause adverse healthconsequences.

B. The Pharmacy Department will work with Analytics Department to identify members and prescribing providers impacted for recalls classified as Class I, Class II and Market Withdrawals recall.
    i. Impacted members are those who have a medical claim for the recalled physician administered drug within 180 days prior to the recall.
    ii. Impacted prescribing providers are those who prescribed the recalled physician administered drug within 180 days prior to the recall on a medical claim.

C. The Pharmacy Department will work with Provider Services and Communications to ensure impacted members and providers will be notified by letter.
    a. When a Class I Recall is issued, AAH will notify impacted members and prescribing providers by letter within 15 calendar days of the FDA notice or whichever is more expeditious.
    b. When a Class II Recall or Market Withdrawal is issued, the Pharmacy Department identifies members and prescribing providers impacted by the recall and notifies them by letter within 30 calendar days of the FDA notice.
        i. The letter will contain the specific details of the recall, including, but not limited to, drug name, strength and specific safety concerns.

D. The Pharmacy Department will forward recall notice and impact report to impacted internal AAH departments such as but not limited to Provider Services, Member Services, Utilization Management and Claims Department.

DEFINITIONS / ACRONYMS

a. FDA: Food and Drug Administration
b. NCQA: National Committee on Quality Assurance
c. CMS: Centers for Medicare and Medicaid Services

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Department
Provider Services
Analytics
Communication and Operations
Member Services
Utilization Management
Claims
Configuration and IT

RELATED POLICIES AND PROCEDURES

P&T Charter
RX-007-Pharmaceutical Patient Safety

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None.

REVISION HISTORY
3/18/2025

- **REFERENCES**
- NCQA, UM 11 Element C
- US Department of Food and Drug Administration (FDA) Recalls, Corrections and Removals
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefit from Managed Care to Medi-CalRx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx

MONITORING

This policy will be reviewed annually to ensure effectiveness by P&T Committee.

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Policy Number	RX-016
Policy Name	Self-Administered Drugs Requested Under Medical Benefit
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	All Line of Businesses
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

The purpose of this document is to outline the procedure for when self-administered drugs requested under Alameda Alliance for Health medical benefit.

Drugs approved by FDA for self-adminstration by the patient do not require direct supervision by a qualified provider or licensed/certified health professional may not be covered under the Alameda Alliance for Health medical benefit.

PROCEDURE

1 Self-administered drugs requested on the medical benefit will be reviewed on a case by case basis for medical necessity.

1.1 Drugs that are considered self-administered drugs are based on the following

1.1.1 FDA has approved for self-administration at home and does not require administration in a healthcare setting by a medical provider.

1.1.2 Drug is not typically administered or directly supervised by a healthcare provider in an outpatient setting
1.1.3 Route of administration (e.g., oral, inhaled, intranasal, topical, rectal, subcutaneous, or self-injectable intramuscular injections)
1.1.4 Dosage Form (e.g., prefilled syringe, auto-injector, tablet, capsule, suppository, nasal spray, metered dose inhaler, nebulized solution)
1.1.5 Standards of medical practice allowing for self-administration (e.g., self-infused hemophilia factor)
1.1.6 Evaluation of any established medical literature or compendia including but not limited to:
1.1.6.1 FDA approved prescribing information
1.1.6.2 Manufacturer provided medical literature
1.1.6.3 Peer reviewed medical literature
1.1.6.4 Evidence-based practice guidelines
1.1.6.5 Self-administration utilization statistics
1.1.6.6 Compendia (e.g., IBM Micromedex® DRUGDEX®, Clinical Pharmacology)

2 Drugs that are carved out of Alliance Medical Benefit will not be covered (any drug when used for the treatment of infertility, erectile dysfunction, or cosmetic use), Medi-Cal Fee-for-Service (HIV/AIDS, hemophilia, opiate & alcohol detoxification, antipsychotics and some antidepressants).
3 Medical necessity reviewed as case-by-case basis is defined as reviewing the member's medical records and relevant documents provided by provider.
4 Requests from providers to review medical necessity must include but not limited to:
4.1 Diagnosis (indication for use)
4.2 Pertinent labs, clinic notes, specialist consultations which document medical necessity of the drug
4.3 Clinical documentation to support medical necessity of the need to administer the medication in a medical setting by healthcare professional instead of home setting
4.4 Reasons why a covered injectable therapeutic alternative is not being used, if a suitable indicated alternative drug exists.
4.5 Reasons why the member must receive the dose(s) from a medical provider instead of receiving from a pharmacy for administration at home, such as:
4.5.1 Teaching self-administration
4.5.2 Adjusting or titrating the dose
4.5.3 Monitoring for immediate side effects
4.5.4 Emergency
4.5.5 Underlying medical condition that prevents self-administration of drug
4.6 Medical necessity is met when
4.6.1 Documentation of medical necessity for provider administration of a typically self-administered drug, such as:
4.6.2 the drug is administered as part of a procedure or may be needed during or immediately after a procedure or infusion (such as a pre-medication or medication given to treat an infusion reaction)

OR the drug provides an immediate clinical benefit from an in-office dose, and it is not medically appropriate to delay administration until the member obtains drug at pharmacy.

DEFINITIONS / ACRONYMS

FDA- Food Drug Administration

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Department
Provider Services
Analytics
Communication and Operations
Member Services
Utilization Management
Claims
Configuration and IT
Grievance and Appeals

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

[List revision dates starting with original effective date – this is the date that revisions were approved at AOC, and is a running list of approval dates from AOC]

REFERENCES

[List references such as regulatory citations]

MONITORING

[Describe the supervising activities in progress to ensure they are on-course and on-schedule in meeting the objectives and performance targets of this policy.]

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POLICY AND PROCEDURE TEMPLATE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Continuity of Care
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	Medicare D-SNP
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the name of the committee here, otherwise put N/A
Subcommittee Approval Date	Pharmacy and Therapeutics Committee If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

The Continuity of Care Policy (CCP) ensures that Alameda Health Alliance (Alliance) Medicare beneficiaries are provided the opportunity to continue a medication on which they are stabilized, including non-formulary (NF) or formulary medications with utilization management (UM) that may require them to try prerequisite drugs or meet specific criteria. The intent is to allow the beneficiary to continue on the requested medication as to not compromise the beneficiaries' health and well-being. The CCP assures that Sponsor is in compliance with applicable regulations governing the Medicare Part D requirement that Sponsors treat all beneficiaries enrolled in the health plan equally.

PROCEDURE

1. Alliance includes the following therapeutic classes/pharmacological classes in the Continuity of Care Program:
    a. Anticonvulsants
    b. Antidepressants
    c. Antineoplastics
    d. Antipsychotics
    e. Anti-HIV retrovirals
    f. Immunosuppressants
    g. Insulin
    h. Oral diabetic agents
    i. Antiarrhythmics
    j. Anticoagulants
    k. Antiparkinson Agents
    l. Angiotensin Receptor Blockers
    m. Multiple Sclerosis Agents
    n. Ophthalmic Agents
    o. Thyroid hormones
    p. Pulmonary Antihypertensives
    q. Urinary Antispasmodic
    r. Additional drug classes may be included upon review

2. When the information contained within a Coverage Determination Request submitted or the physician's supporting statement indicates the beneficiary is "stabilized" on or has been receiving the requested medication for ninety (90) days or greater, the Continuity of Care policy applies.
    2.1 If the requested drug is not a Part D coverable drug and/ or a statutory exclusion, the request is denied.
    2.2 If there are beneficiary concerns, Alliance or its contracted PBM contacts the prescribing physician to resolve within the required coverage determination timeframes.
    2.3 If the requested drug is a narcotic, stimulant, or high-risk medication (HRM) this CCP does not apply.

3. Upon determination that the beneficiary qualifies for continuation of the medication under the Continuity of Care policy, the Coverage Determination will be approved for as long as the member is prescribed the medication and enrolled in the plan. A note reflecting the approval was through the CCP is entered in the Coverage Determination system. All CMS requirements for the coverage determination are followed.

4. The entry of the authorization in the Alliance contracted PBM's adjudication system will be tested in the system for an immediate fill, 3 months out and 1 year out to ensure the claim processes for the beneficiary.
    a. Test claims are stored in the system for documentation purposes.

5. Disruption analysis prior to each coverage year

5.1 During the last quarter of each plan year, a disruption analysis will be created by the Alliance or its contracted PBM. This disruption analysis will include all the beneficiaries affected by a year over year formulary change.

5.2 Beneficiaries affected by formulary changes will be assessed to determine if the medications are subject to the Continuity of Care policy. If beneficiaries have a brand to generic change, it will be communicated to them before year end. Other medication changes (formulary to non-formulary) should be reviewed and information about the coverage determination process should be provided to the member/prescriber.

6. Extension of a Coverage Determination for the following year:

6.1 The Alliance Pharmacy Operations team will review prior authorizations in the last quarter of the year to decide if an extension is appropriate. If so, the extension (override) will be put in for an additional year with an expiration date of December 31 of the following year.

6.2 In addition, exceptions for non-formulary drugs and quantity limits will also be reviewed for extension. If the Pharmacy Operations team feels the extension is appropriate according to the formulary for the next year, the coverage determination team will enter the overrides.

6.3 Members who receive a coverage determination extension will be notified by letter at least 60 days prior to the date the coverage ends.

DEFINITIONS / ACRONYMS

Appointed Representative - An individual either named by an enrollee including his/her prescribing physician or authorized under State or other applicable law to act on behalf of the enrollee. The Appointed Representative form is found on the Alliance website.

Centers for Medicare & Medicaid Services (CMS) - refers to the federal agency within the Department of Health and Human Services that administers the Medicare program and oversees all Medicare Advantage Organizations.

Coverage Determination - refers to any decision (i.e., an approval or denial for a prescription drug) made by The Alliance or its Pharmacy Benefit Manager (PBM), regarding payment or benefits to which a member believes he or she is entitled. Presentation of a prescription at the pharmacy counter is not a coverage determination.

Dismissal - A decision not to review a request for an initial determination because it is considered invalid or does not otherwise meet Medicare Part D requirements.

Effectuation - refers to payment of a claim, authorization or provision of a benefit The Alliance has approved. For the purpose of this policy, effectuate is intended to include oral and written notification to the member, written notification to the prescriber and override entry in PBM claims payment system so that a claim is paid.

Exceptions - refer to requests for a non-formulary Part D covered drug, changing the tier copay ("tiering exception") or waiver of Prior Authorization requirements.

Formulary - refers to the list of Part D drugs covered by The Alliance for members enrolled in its plans/ The Formulary is a continually updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis and/or treatment of disease and promotion of health.

Independent Review Entity (IRE) - An independent entity contracted by CMS to review adverse level 1 (redetermination) appeal decisions made by the plan. The current contractor is C2C Innovative Solutions Inc. (C2C).

Low Income Cost-share Subsidy (LICS) - refers to the Medicare subsidy specific to Part D for qualified beneficiaries in the form of reduced co-payments.

Pharmacy Benefits Manager (PBM) - Perform Rx is The Alliance's PBM and provides the POS claims processing system for pharmacy claims.

Part D drug - A drug that may be dispensed only upon a prescription, is being used for medically-accepted indication as defined by section 1927(k)(6) of the Social Security Act, and is one of the following:

- A drug that is described in sections 1927(k)(2)(A)(i) through (iii) of the Act;
- A biological product described in sections 1927(k)(2)(B)(i) through (iii) of the Act;
- Insulin described in section 1927(k)(2)(C) of the Act;
- Medical supplies associated with the delivery of insulin;
- A vaccine licensed under section 351 of the Public Health Service Act and its administration.

Prior Authorization (PA) - An evaluation of the drug's prescribed use against a predetermined set of CMS approved criteria in order to determine whether the drug/drug class will be covered by the beneficiary's insurance plan.

Provider Supporting Statement - refers to the reasons provided by the prescriber when a drug being requested is not on the Formulary or the prescriber requests a waiver of the UM requirements. The statement has to indicate reasons why the member cannot use a Formulary drug, a Formulary drug with no UM edits or a lower-cost sharing drug.

Quantity Limits (QL) - refers to a dose restriction, including the number and/or dosage form, that causes a particular Part D drug not to be covered for the number of doses and/or dosage form prescribed

Step Therapy (ST) - refers to a particular Part D drug not to be covered until the requirements of the plan's coverage policy are met, which requirements are approved by CMS

Redetermination - Level 1 Part D appeal which reviews an adverse coverage determination, including the findings upon which the decision was based and any other submitted evidence.

Reopening - A remedial action taken to change a binding determination or decision even though the determination or decision may have been correct at the time it was made.

Tolling - The start of the timeframe for a standard or expedited exception request if the sponsor is waiting to receive the prescriber's supporting statement. A plan may toll a request for up to 14 (fourteen) days. Reimbursement requests are not eligible for tolling.

Utilization Management (UM) edits - refer to the requirements for the approval of a drug which can be one of the following: prior authorization (PA), step therapy (ST), or a quantity limit (QL).

Withdrawal - A verbal or written request to rescind or cancel an initial determination.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

Part D Formulary Development and Management
Pharmacy and Therapeutics Committee
Part D Coverage Determinations

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

[List revision dates starting with original effective date – this is the date that revisions were approved at AOC, and is a running list of approval dates from AOC]

REFERENCES

42 CFR 423.578(b), 42 CFR 423.566(a)(b).

MONITORING

[Describe the supervising activities in progress to ensure they are on-course and on-schedule in meeting the objectives and performance targets of this policy.]

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POLICY AND PROCEDURE TEMPLATE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Medicare Part D Hospice
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	Medicare Advantage
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

It is the policy of Alameda Alliance for Health (Alliance) to ensure drugs for Medicare beneficiaries in a hospice setting are being billed to the appropriate part of Medicare. Hospice is covered for beneficiaries under Medicare Part A. Hospice providers are responsible for providing medications necessary for palliative care and management of the beneficiary's terminal illness and related conditions.

PROCEDURE

Alliance does not pay for drugs that should be covered under the Part A Hospice benefit for beneficiaries in a hospice setting. Drugs prescribed for beneficiaries that are unrelated to the terminal illness or related conditions are subject to standard Part D formulary management practices.

Four categories of drugs are considered hospice "always" drugs and are handled via prior authorization (PA) and list on PBM Pre-Processing Drug List:

- Analgesics
- Antinauseants
- Laxatives
- Antianxiety

For the PBM's claim adjudication system to reject the claim at the point of sale for a Part A vs Part D PA related to hospice coverage, the member must have an active hospice attribute associated with their eligibility profile and the claim's date of service must fall within the attribute's start and end date values.

The Hospice approved form is used to:

- Document that a drug is unrelated to a beneficiary's terminal illness, and
- To convey a change in hospice status.

The Centers for Medicare & Medicaid Services (CMS) expects plan sponsors to use the documentation presented by the Hospice provider or prescriber and to update the beneficiary's hospice information until the notice is received from CMS on the daily transaction reply report (DTRR).

1. The Pharmacy Benefit Manager (PBM), on behalf of Alliance MAPD, has established procedures for:

    a. Rejections coded for Hospice members - If a 4C (Hospice) code is submitted on a claim, the claim will be rejected for A3 (this product may be covered under Hospice). Any subsequent claims not containing this code should be paid per plan benefits until the plan is notified by CMS.
        i. For the PBM's adjudication system to reject the claim at the point of sale for a Part A vs Part D PA related to hospice coverage, when a 4C is submitted by the pharmacy, the member must have no active hospice attribute associated with their profile.

2. To prevent duplicate payments under Part D for drugs covered under the Part A hospice benefit, upon being notified by CMS via the DTRR that the beneficiary is receiving hospice care, Part D plan sponsors must utilize segment 08 within PBM Type 24 (Member Attribute Load file) to create a hospice member attribute. This is required for the PBM's adjudication system to reject hospice related claims at the point of sale.

    - Upon receiving a hospice Transaction Reply Code (TRC) for the beneficiary via the DTRR, plan sponsors may then utilize segment 08 within the Type 24 file to indicate that the member has Hospice.

3. Alliance's contracted PBM maintains a Pre-Processing Drug List of drugs that require PA for Part D members with an active hospice attribute.

- If the NDC submitted on the claim is not on the PBM's hospice PPDL **OR** if the drug is a compound, normal processing rules apply. Each compound represents a unique drug entity and normally the PBM is unable to determine at the point of sale the medical condition for which the compound was prescribed.

4. Any written documentation supporting the beneficiary's hospice status must be managed by the Alliance. If the documentation is given to the Alliance's contracted PBM, the PBM will advise the individual/entity to send the written documentation directly to the plan sponsor for action.

5. Upon receipt and review of the written documentation, plan sponsors can perform one of the following actions:
    - Enter a PA override within the PBM's claims adjudication system (see the relevant PBM procedure for details).
    - Plan authorized personnel can contact the PBM's Call Center to request an operational hospice override for the beneficiary.
    - Update the member's eligibility record to reflect the beneficiary's hospice status (admission or discharge) via Segment Code 08 of the PBM's Type 24 file.

DEFINITIONS / ACRONYMS

Beneficiary: An individual enrolled in a Alliance Medicare Advantage Part D Plan, also known as an Enrollee or Member.
Coverage Determination: A decision made by or on behalf of a Part D plan sponsor regarding payment or benefits to which an enrollee believes he or she is entitled.
HPMS – Health Plan Management System
PBM: Pharmacy Benefit Manager
PDE: Prescription Drug Event is a summary record submitted to CMS. The PDE data are not the same as individual drug claim transactions but are summary extracts using CMS defined standard fields.
Point of Sale (POS): A capability of retail pharmacies to electronically access plan design and eligibility information to process and transmit drug claims data at the time of purchase.
PPDL – Pre-Processing Drug List which is the list of drugs that require PA for Part D members with an active hospice attribute.
PPS: A Prospective Payment System (PPS) is a method of reimbursement in which Medicare payment is made based on a predetermined, fixed amount.
Prior Authorization (PA) – A process whereby certain designated preferred drugs must meet established before the prescription can be covered.
Transaction Reply Report (TRR): A report that CMS provides to Part D sponsors containing details of the rejected and accepted enrollment transactions that CMS has processed for a Part D sponsor's contract(s) over a specified time period.
TRC: Transaction Reply Code

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

[List revision dates starting with original effective date – this is the date that revisions were approved at AOC, and is a running list of approval dates from AOC]

REFERENCES

HPMS Memo – Part D Payment for Drugs for Beneficiaries Enrolled in Medicare Hospice – Final 2014 Revised Guidance, July 18, 2014

HPMS Memo – Hospice Approved Form – Clarification on Hospice Form Usage, March 24, 2015

2019 Final Call Letter, published April 2, 2018 – CARA guidance, Hospice beneficiaries exempt from opioid management programs

NCPDP WG9 Hospice Task Group – October 4, 2018

MONITORING

1. **Retrospective Review**

   Alliance will perform a retrospective review of claims for Hospice members to determine proper coverage under the bundled payment and coordinate with the Hospice provider.

   - Daily reject reviews
   - Monthly retrospective reviews
     a. Alliance's contracted PBM produces a Hospice Claims Report once a month that Part D plan sponsors may use to identify claims that may have paid inappropriately under the Part D benefit. This may occur when:
        - The plan sponsor adds the hospice attribute to the member's profile after the PBM has already processed the claim(s); or
        - The drug is not in one of the four categories identified by CMS but is related to the beneficiary's terminal illness or related conditions. While CMS does not expect plan sponsors to review paid claims retrospectively for drugs outside of the four categories, all Part D retrospective review requirements continue to apply to these claims.

2. Payment Recovery

Upon determining that a claim paid inappropriately under the Part D benefit, Alliance will work directly with the hospice facility to coordinate repayment.

- This is consistent with CMS guidance which states that plan sponsors should work directly with the hospice provider *instead of* requiring the pharmacy to reverse and rebill the original claim.
- An exception may apply if the network pharmacy involved is also the hospice pharmacy, in which case the reverse and rebill process may be the most appropriate approach.
- To assist with the payment recovery process, CMS publishes hospice contact information in HPMS. To access the hospice, contact list in HPMS, click on "Data Extract Facility", then select "Contact Information". The Hospice Contact Information file is listed in the first dropdown box on that page.

3. PDE Exclude Process

Alliance will work with the PBM to exclude the PDE record when the drug should have been covered under Part A. The PBM is able to support this via the PDE Exclude process, which will remove the 'D' status and the TrOOP and TDS accumulators from the claim without reversing it.

To initiate the PDE exclusion process, the PBM requires plan sponsors to provide authorization and the applicable claim data. The plan assigned PDE Analyst will complete the PDE claim exclusion process.

POLICY AND PROCEDURE TEMPLATE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Medicare Part D Medication Therapy Management (MTM)
Department Name	[e.g., "Compliance"]
Department Officer	[e.g., "Compliance Officer"]
Policy Owner	[Title of Owner]
Line(s) of Business	Medicare Advantage
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the name of the committee here, otherwise put N/A
Subcommittee Approval Date	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

To define the process for identifying, enrolling, and managing Part D members who qualify for Alameda Alliance for Health (Alliance) Medication Therapy Management (MTM) program.

PROCEDURE

Alliance's MTM program is designed to ensure covered Part D drugs prescribed to targeted beneficiaries are appropriately used to optimize therapeutic outcomes through improved medications use, and to reduce the risk of adverse events.

1.0 Alliance's MTM program adheres to the following requirements:

1.1 Is furnished by a pharmacist or other qualified provider;

1.2 Distinguishes between services in ambulatory and institutional settings;

1.3 Must be developed in cooperation with licensed and practicing pharmacists and physicians;

1.4 Enrolls targeted beneficiaries using an opt-out method of enrollment;

1.5 Targets beneficiaries for enrollment in MTM at least quarterly during the plan year;

2.0 MTM Program Parameters

2.1 Targeted beneficiaries have multiple chronic diseases, with three (3) chronic diseases being the maximum number a Part D sponsor may require for targeted enrollment; and

2.2 Are taking multiple Part D drugs with eight (8) drugs being the maximum number of drugs a Part D plan sponsor may require as the minimum number of Part D drugs that a beneficiary must be taking for targeted enrollment. The minimum threshold may be any number equal to or between two (2) and eight (8); and

2.3 Are likely to incur annual Part D drug costs of at least $1,623 in 2025; **OR**

2.4 Is an At-risk beneficiary (ARB) as defined at 42 CFR §423.100

- ARBs are beneficiaries with an active coverage limitation under Alliance's Drug Management Program (DMP) .
- Sponsors are encouraged, but not required, to offer MTM services or other interventions to beneficiaries who fill at least one prescription for an anti-hypertensive medication to support the Millions Hearts™ initiative to control high blood pressure and improve access and adherence to these medications. Also, equitable access to cancer screening and targeting the right treatments for cancer patients are top priorities under the goals of the Cancer Moonshot.

3.0 Alliance offers the following MTM services for each beneficiary enrolled in the program:

3.1 Interventions for both beneficiaries and prescribers

3.2 Comprehensive Medication Reviews (CMRs) – annually

- Includes an interactive, person-to-person, or telehealth consultation performed by a pharmacist or other qualified provider; and

- May result in a recommended medication action plan (MAP);
- If a beneficiary is offered the annual CMR and is unable to accept the offer to participate due to cognitive impairment, the pharmacist or other qualified provider may perform the CMR with the beneficiary's prescriber, caregiver, or other authorized individual.
- Standardized action plans and summaries that comply with CMS requirements for the standardized format. This includes medication action plans (MAPs) and personalized medication lists (PMLs).

3.3 Targeted Medication Reviews (TMRs) – at least quarterly and as needed

- May address specific or potential medication-related problems
- Assess the findings of these reviews to determine if a follow-up intervention is necessary for the beneficiary and/or their prescriber
- May offer follow-up interventions to beneficiaries' prescribers to resolve medication-related problems or provide other opportunities to optimize the targeted beneficiaries' medication use. These prescriber consultations may be faxed or mailed or interactive.
- The TMR is distinct from a CMR because it is focused on specific actual or potential medication-related problems.

3.4 Information about safe disposal of prescription drugs that are controlled substances, drug take back programs, in-home disposal and cost-effective means to safely dispose of such drugs per 42 CFR § 423.153(d)(1)(vii)(E).

- Provide the information at least annually as part of the CMR, TMR or other MTM correspondence;

4.0 Enrollment and Targeting:

4.1 Alliance enrolls targeted beneficiaries using an op-out method of enrollment.

- Every year Alliance auto-enrolls targeted beneficiaries who meet the eligibility criteria unless the beneficiary declines enrollment. Alliance identifies targeted beneficiaries for enrollment at least quarterly during each year.

4.2 Targeted beneficiaries have three (3) multiple chronic diseases. Alliance's utilizes the following chronic diseases as qualifying for MTM:

- Alzheimer's disease

- Bone disease-arthritis (including osteoporosis, osteoarthritis and rheumatoid arthritis)
- Chronic Health Failure (CHF)
- Diabetes
- Dyslipidemia
- End-Stage Renal Disease (ESRD)
- Respiratory disease (including asthma, chronic obstructive pulmonary disease (COPD), and chronic lung disorders)
- Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)
- Hypertension
- Mental health (including depression, schizophrenia, bipolar disorder, and chronic/disabling mental health conditions) **AND**

4.3 Are taking at least eight (8) Part D drugs;

- In identifying the number of Part D drugs, sponsors must include all Part D maintenance drugs and may include all Part D drugs **AND**

4.4 Are likely to incur annual Part D drug costs of at least $1623 in 2025; **OR**

4.5 Is an At-risk beneficiary (ARB) as defined in 42 CFR §423.100

4.6 Enrolled beneficiaries may refuse or decline individual services without having to disenroll from the MTM program.

- Rarely, a beneficiary may request to be permanently opted out of the MTM program in the current and future years. Alliance will honor the request and not re-target the beneficiary in future contract years.

- In all cases, Alliance will maintain documentation of beneficiary requests to opt out of the MTM program.

4.7 Once enrolled, Alliance will not disenroll a beneficiary from the MTM program if they no longer meet eligibility criteria. Enrolled beneficiaries will remain in Alliance's MTM program for the remainder of the calendar year.

4.8 Alliance will promote continuity of care by performing an analysis at the end of the year to identify current MTM participants who will again meet eligibility criteria for the next program year. Alliance will use claims from the previous year for projections.

5.0 Required MTM Services

Per 42 CFR §423.2267(d)(2)(ii), Part D sponsors may provide any required material or content electronically with prior consent from the enrollee. This includes the CMR offer letter, TMRs, the CMR Summary in CMS' standardized format, and information about safe disposal of controlled substances. Documents delivered electronically will be considered

to be received by the enrollee as of the date the plan sends it; not when the enrollee opens/accesses it.

5.1 Interventions for both beneficiaries and prescribers;

5.2 Comprehensive Medication Reviews (CMRs) – Alliance will offer a CMR to all beneficiaries enrolled in the MTM program at least annually (within one year of the last CMR). Alliance or Delegate will actively engage beneficiaries to increase the number of CMRs.

- Alliance will offer a CMR as soon as possible after enrollment in the MTM program, but no later than sixty (60) days after being enrolled in the MTM program.
- A CMR offer is not successful if a mailed letter is returned, or the beneficiary phone number is invalid.
- Alliance will maintain document of offers (date and who the offer was delivered or communicated to).
- Includes an interactive, person-to-person, or telehealth consultation performed by a pharmacist or other qualified provider.
- Alliance will use more than one approach whenever possible to reach all eligible targeted beneficiaries and will not rely on passive outreach offers.
- The CMR will happen in real-time and include prescriptions, over-the-counter (OTC) medications, herbal therapies, and any dietary supplements.
- A CMR may result in a recommended medication action plan (MAP)
    - Examples of medication therapy problem recommendations made as a result of MTM services include, but are not limited to:
        - Needs additional therapy
        - Unnecessary drug therapy
        - Dosage too high
        - Dosage too low
        - More effective drug available
        - Adverse drug reaction
        - Medication non-compliance/non-adherence
        - Vaccine administration
    - Examples of medication therapy problem resolutions made as a result of MTM recommendations include, but are not limited to:
        - Initiate medication
        - Change medication (product in different therapeutic class, dose, dosage form, quantity, or interval
        - Discontinue or substitute medication (discontinue drug, generic substitution, therapeutic substitution, or formulary substitution)

- Medication compliance/adherence

- Alliance will provide a summary of the results of the CMR to the beneficiary in CMS' Standardized Format.
    - An individualized, written summary in CMS' Standardized Format is provided following each CMR within fourteen (14) calendar days.
- Alliance will document who delivered the CMR, who received the CMR, when the CMR was delivered, including a copy of the CMR and the delivery of the member letter date.
- If an enrolled beneficiary declines the annual CMR, Alliance will continue to offer interventions to the prescriber, perform TMRs at least quarterly to assess medication use, and will provide the required safe disposal information.

5.3 Targeted Medication Reviews (TMRs) – Alliance will perform TMRs for all beneficiaries enrolled in the MTM program at least quarterly, with follow-up interventions as necessary.

- Alliance will offer follow-up interventions with beneficiaries' prescribers to resolve medication-related problems or optimize medication use. These consultations may be passive (e.g., faxed or mailed) or interactive when determined necessary.
- TMRs may address specific or potential medication-related problems;
- TMRs may be performed to assess medication use;
- May monitor whether any unresolved issues need attention;
- May be used to determine if new drug therapy problems have arisen; and/or
- Assess if the beneficiary has experienced a transition in care.

5.4 Safe disposal of prescription drugs that are controlled substances

- Is provided at least annually as part of the CMR, TMR or other MTM correspondence. Alliance provides this information in the MTM welcome letter.
- Includes information on at least two (2) drug take-back programs near the enrollee as identified by their zip code;
- Includes information on in-home disposal; and
- Includes information on cost-effective means to safely dispose of such drugs

6.0 Cognitively Impaired Beneficiaries (in any care setting)

6.1 If the beneficiary is unable to accept the offer to participate in the CMR, Alliance will perform the CMR with the beneficiary's prescriber, caregiver, or other authorized individual, such as a health care proxy or legal guardian.

- The beneficiary must be cognitively impaired and unable to make decisions regarding his/her medical needs;

- This flexibility to perform the CMR with an individual other than the beneficiary does not apply to situations where Alliance is unable to reach the beneficiary, there is no evidence of cognitive impairment, or when the beneficiary declines a CMR offer.

- If the beneficiary is unable to accept the offer to participate in a CMR, but cannot identify another individual to participate, a CMR cannot be performed. Alliance will offer the other required MTM services.

- Alliance will maintain documentation or rationale for any determination regarding a beneficiary's cognitive impairment.

7.0 Optimizing MTM in the Long-Term Care (LTC) setting

7.1 MTM and CMRs for beneficiaries in LTC provide opportunities to serve this vulnerable population and improve their medication use and quality of care. offering and delivering CMRs are effective in reaching beneficiaries and take into consideration how to reach the beneficiaries according to their setting and needs. In the LTC setting, a greater risk of both physical and cognitive issues may impact the beneficiary's ability to conduct a phone interview.

7.2 In LTC, adherence is less of an issue, and MTM can be used to identify overuse, medications without a clear indication, suboptimal dosing and polypharmacy.

7.3 MTM can be used as an opportunity to align medication use with the beneficiary's goals in addition to the care teams.

7.4 Alliance will consider using qualified provider to perform the CMR, such as the involvement of a pharmacist who has a relationship with the LTC facility.

7.5 Alliance will work with the beneficiary's treating physician, facility healthcare team, their caregiver or authorized representative, and/ or consultant pharmacist to avoid conflicting recommendations when recommending medication therapy changes.

7.5 Regardless of cognitive status, many LTC residents may prefer to involve their authorized representative or caregiver in the CMR, and this will be considered for this population.

- One tool that could be used in nursing homes to identify if a beneficiary is cognitively impaired and unable to accept the offer to participate in the CMR is the Brief Interview of Mental Status (BIMS) in the Minimum Data Set 3.0. The nursing staff, including but not limited to the Director of Nursing, also may be a valuable asset to ascertain information about a beneficiary's functional status, cognitive status, and medications, as well as caregiver(s) or authorized representative(s).
- Perceived barriers due to a beneficiary's social determinants of health (SDOH) do not mean that the beneficiary is unable to participate in a CMR. MTM providers are expected to engage the targeted population in a manner that these beneficiaries can understand and use, regardless of any language or other barriers that exist.
- Failure to provide services to beneficiaries disadvantaged by poverty, language, or other SDOH factors suggests discriminatory practices, which may be in violation of the Social Security Act or other federal requirements regarding access to services and subject to CMS non-compliance.

8.0 Website

8.1 Alliance has a separate section or page on their website at: <URL for Alameda Alliance for Health MTM website>, which includes the following:

- Description of the MTM program including the purpose and benefit of MTM and the eligibility requirements;
- Information on how to obtain MTM service documents, including the medication list;
- The service is offered at no charge to members eligible for the MTM program;
- Summary of MTM services offered;
- Information describing how a beneficiary will know if they are eligible and enrolled into the MTM program; and
- Information about the CMR and TMRs, including how the reviews are conducted and delivered, time commitments, and materials the beneficiary will receive;
- Alliance contact for questions regarding the MTM program; and
- A clarifying statement that MTM services are not considered a benefit.

9.0 Administration and Annual MTM Program Submission

9.1 MTM program services provided to targeted beneficiaries is an administrative cost (included in the plan bid), incident to appropriate drug therapy and not an additional benefit.

9.2 MTM programs are based on the contract year. MTM program submissions are due annually usually the last week of May through first week of June.

9.3 Alliance will have a process in place to measure, analyze, and report the outcomes of the MTM programs; determine whether or not goals of therapy have been reached; capture medication therapy recommendations and resolutions made as a result of the MTM recommendations; and capture beneficiary satisfaction with MTM services, providers, and outcomes

9.4 In addition to the MTM program description, an attestation of Alliances' compliance with Part D MTM program requirements must be submitted through HPMS and must be completed by the CEO, COO, or the CFO

DEFINITIONS / ACRONYMS

At-Risk Beneficiary (ARB): An ARB is a beneficiary is identified to be at-risk by the health plan under its drug management program (DMP), or by the sponsor of the beneficiary's immediately prior Part D plan under its DMP and such identification has not been terminated before disenrollment.

Comprehensive Medication Review (CMR): A CMR is a systematic process of collecting patient-specific information, assessing medication therapies to identify medication-related problems, developing a prioritized list of medication-related problems, and creating a plan to resolve them with the patient, caregiver and/or prescriber.

A CMR is an interactive in person or synchronous telehealth consultation conducted in real-time between the patient and/or other authorized individual, such as prescriber or caregiver, and the pharmacist or other qualified provider and is designed to improve patients' knowledge of their prescriptions, over-the-counter (OTC) medications, herbal therapies and dietary supplements, identify and address problems or concerns that patients may have, and empower patients to self-manage their medications and their health condition(s).

Drug Management Program (DMP): A DMP is a program established by Part D sponsors for beneficiaries at-risk for misuse or abuse of frequently abused drugs (FADs). DMPs address overutilization of FADs while maintaining access to such drugs as medically necessary.

Frequently abused drugs (FADs): Opioids (except buprenorphine for medication-

assisted treatment {MAT} and injectables) and benzodiazepines are FADs for the purposes of the Part D DMP.

Medication Action Plan (MAP): A personalized plan to assist the targeted MTM beneficiary in getting the best results from their medications.

Medication Therapy Management (MTM): MTM is a patient-centric and comprehensive approach to improve medication use, reduce the risk of adverse events, and improve medication adherence. MTM programs include high-touch interventions to engage the beneficiary and their prescribers.

Personal Medication List (PML): A medication list provided for the MTM beneficiary after the pharmacist-patient discussion to include prescription medications, over-the-counter drugs, herbals, vitamins, and minerals. It addresses why and how the patient used the medication, the date started, prescriber, and if applicable, the reasons why and when a medication was stopped.

Targeted Medication Review (TMR): A TMR is performed at least quarterly to assess medication use, monitor whether any unresolved issues need attention, new drug therapy problems have arisen, or if the beneficiary has experienced a transition in care. This assessment can be person-to-person and/or system generated.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

[List revision dates starting with original effective date – this is the date that revisions were approved at AOC, and is a running list of approval dates from AOC]

REFERENCES

Prescription Drug Benefit Manual, Ch. 7 – Medication Therapy Management and Quality Improvement Program (Rev. 11, 02-19-10)

HPMS Memo – Contract Year 2022 Part D Medication Therapy Management Program Guidance and Submission Instructions – May 6, 2024

HPMS Memo – Contract Year 2022 Part D Medication Therapy Management Program Guidance and Submission Instructions - April 30, 2021

§423.153(d) Medication Therapy Management Program requirements

HPMS Memo-Contract Year 2025 Part D Medication Therapy Management Program Guidance and Submission Instructions-May 06, 2024

Relevant federal regulations for MTM programs may include Federal Communications Commission requirements for accessibility, as defined in 47 CFR Part 64 Subpart F; Americans with Disabilities Act (ADA): Nondiscrimination on the Basis of Disability by Public Accommodations and in Commercial Facilities, 28 CFR Part 36; Nondiscrimination on the Basis of Race, Color, National Origin, Sex, Age, or Disability in Health Programs or Activities Receiving Federal Financial Assistance and Programs or Activities Administered by the Department of Health and Human Services Under Title I of the Patient Protection and Affordable Care Act or by Entities Established Under Such Title, 45 CFR Part. 92; Section 504 of the Rehabilitation Act, Nondiscrimination on the Basis of Handicap in Programs or Activities Receiving Federal Financial Assistance, 45 CFR Part 84; and 21st Century Communications and Video Accessibility Act (CVAA). Part D sponsors should also refer to the standards for communications and marketing found at 42 CFR § 423.2267(a).

MONITORING

I. Outcomes Measured

A. Alliance has a process in place to measure, analyze and report the outcomes of its MTM program.

1. Were goals of therapy reached?
2. What were the medication therapy recommendations made as a result of the MTM recommendations?
3. How was beneficiary satisfaction with MTM services, providers, and outcomes rated for Alliance?

a. The following specific outcomes were submitted for Alliance's 20XX MTM program submission:

i. Part D Reporting Requirements;
ii. Medication adherence measure (proportion of days covered);
iii. Emergency department visits;
iv. Hospital admissions;
v. Length of hospital stay; and
vi. Statin Use in Persons with Diabetes measure

II. CMRs

A. Monitor CMR completion rates and member outreach attempts weekly

POLICY AND PROCEDURE TEMPLATE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Part D Delegation Oversight and Monitoring
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	Medicare Advantage
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the name of the committee here, otherwise put N/A
Subcommittee Approval Date	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

Alameda Health Plan Alliance (the Alliance) delegates certain Medicare Part D activities solely or in combination. At all times, the Alliance maintains accountability for the provision of services for its Medicare membership and the ultimate responsibility for fulfilling the terms and conditions as set out in the contract with The Centers for Medicaid and Medicare Services (CMS). Through the Oversight Program as described in this document, the Organization ensures that delegated services meet the Alliances' standards for care and service and all applicable state, CMS, and accreditation requirements. First tier, downstream and related entities may be subject to any applicable civil and criminal laws for fraud perpetrated in the delivery of the Part D benefit, such as the False Claims Act or the Anti-Kickback statute.

Prior to executing a contract or delegation agreement the Alliance determines the capacity of the potential first tier, downstream or related entity (FDR) to assume responsibility for delegated activities and maintain the Alliance standards, and applicable state, CMS, and accreditation requirements. The initial assessment process for each type of delegated function is outlined in the Pre-Delegation Audit Program.

The Agreement for Delegation of Responsibilities is a mutually agreed upon document between the Alliance and first tier, downstream or related entity which specifies the delegated activities, responsibilities of the Alliance and the FDRs, the frequency of reporting to the Alliance (at least semi-annual), the process by which the delegation will be evaluated, the remedies, including revocation of the delegation, available to the Alliance if the FDR does not fulfill its obligations, and provisions for the use of protected health information (PHI) by the first tier, downstream or related entity. Any sub-delegation by the first tier entity must be approved by the Alliance. The sub-delegation agreement between the first tier entity and the downstream or related entity must meet the aforementioned specifications. The Alliance determines whether they or the first tier entity will directly monitor the downstream or related entity's compliance with delegation requirements.

For potential FDRs that are not accredited/certified by the Utilization Review Accreditation Commission (URAC) an onsite-initial assessment visit is conducted before the contractual relationship is finalized. If the FDR is not in full compliance with delegated standards, the FDR's action plan and timeline to achieve full compliance is reviewed. The oversight process may be modified for accredited/certified organizations as applicable. If the FDR is in full compliance for all delegated standards, the Alliance will assess compliance with applicable State, CMS, and the Alliance-specific requirements. The need for an onsite visit and/or file audit is at the sole discretion of the Alliance. The Alliance determines the frequency and format of contact with the FDR to ensure compliance with established, revised, or new state, CMS, and accreditation requirements. The FDR is required to comply with the Alliance reporting requirements. The FDR must provide any reporting to be provided to any regulatory oversight entity to the Alliance prior to submission.

PROCEDURE

1. CONFIDENTIALITY

The Alliance deems it of utmost importance to protect the confidentiality of member information and records. This information is maintained and/or disclosed in compliance with the requirements of corporate policy and all applicable state, CMS, and accreditation requirements, including but not limited to the Health Insurance Portability and Accountability Act (HIPAA). All protected health information (PHI) specific to individually identifiable members and/or others is confidential and subject to the terms of corporate policy. A HIPAA Business Associates Agreement is signed by the FDR and the Organization prior to the effective date of the agreement. Additionally, the FDR signs an attestation that HIPAA training has been completed for all business associates and downstream entities.
The FDR is responsible to provide immediate notice to the organization of any suspected violations related to HIPAA, Privacy, standards of conduct, code of ethics and fraud/waste/abuse and provide immediate notice when suspected violations are confirmed.

2. RESPONSIBILITY:

The Alliance's Board of Directors has ultimate responsibility for the Oversight of Medicare Part D Delegation. They delegate oversight of the Policy to the Compliance Committee of the Board.

The Chief Compliance Officer is responsible for obtaining approval from the Medicare Compliance Committee (MCC) and ultimately from the Board of Directors. The Compliance Committee is responsible for communicating the policy and procedures to appropriate staff within the Alliance and to our partners in the FDR(s).

The Compliance Committee ensures that the oversight of delegated functions process meets all regulatory requirements, that desk procedures are current, and that associates adhere to policies and procedures. The Chief Financial Officer or designee ensures claims payment oversight processes meet all regulatory requirements, that desk procedures are current, and that associates adhere to policies and procedures. Vendors which are delegated for claims payment provide an audit report (i.e. SAS 70 or comparable report) which is reviewed by the contract owner and the Compliance and Program Integrity Department. The SAS 70 report or comparable are reported to the Medicare Compliance Committee for review and evaluation. The Compliance Committee will recommend corrective actions and follow up should deficiencies or compliance trends be identified. In addition, for Medicare Advantage membership a certification regarding the accuracy, completeness, and truthfulness of the data and acknowledgement that the data will be used for the purpose of obtaining federal reimbursement will be required.

The XXXX accept approvals for delegated and sub-delegated activities based on the review and approval of initial oversight assessments by its sub-committee(s), reviews delegation reports and results of quarterly evaluations and annual assessments, monitors the effectiveness of corrective action plans, reviews and accepts meeting minutes from its sub-committee(s), and recommends changes to this policy. The Compliance Officer also periodically (routinely and ad hoc) reviews and audits FDR operational processes against approved procedures, and ensures that all applicable regulations are complied with.

3. PRE-DELEGATION

1. 3.1 When delegation is requested, designated Alliance staff initiates the oversight process with the approval of senior management. An acknowledgment letter is mailed with a request for documents specific to the delegation functions requested. Designated staff assembles the initial assessment team and coordinates all assessment activity and documents and presents results to the applicable delegation oversight committee(s). To accommodate business needs, ad hoc meetings and electronic review and approval may substitute for routine scheduled meetings. At a minimum, the team will assess and review the following:

    3.1.1 The entities' ability to perform the required tasks. The Alliance will ensure the delegate meets both contractual and regulatory requirements (specifically, CMS requirements).
    3.1.2 Policies and procedures specific to the delegated functions.

3.1.3 Operational capacity to perform the delegated functions.
3.1.4 Resources (administration and financial) sufficient and qualified to perform required functions.
3.1.5 Is entity excluded from participating in the federal health program (excluded parties lists):
3.1.6 General Services Administration – Excluded Parties List System (EPLS)
3.1.7 Office of Inspector General – List of Excluded Individuals/Entities (LEIE)

4.0 DELEGATION OVERSIGHT PROCEDURES

4.1.1 Once delegation has been approved and a contract executed, FDRs submit reports on a monthly and/or quarterly basis (unless otherwise specified) to the Director of Pharmacy, as directed. The scope, content and metrics of the reports, as well as audit measures, as applicable, for each specific Medicare Part D delegated function are defined in ***the contract, and include the ability of*** **the Alliance** ***to request and receive ad hoc reports within a reasonable timeframe, as needed to conduct business and compliance operations.***.

4.1.2 In addition to the monthly oversight reports, special focus may be placed upon observed trends, the results of actions initiated by the FDR, and the results of corrective actions taken. The FDR may be required to submit a quarterly report summarizing the quality activities completed during the quarter, identifying barriers to improvement in care and service and the effectiveness of any improvement plans. The reports summarizing the quality activities completed during the quarter will be reported to the Medicare Compliance Committee.

4.1.3 At least annually, there is a comprehensive review of the FDR's ability to provide the delegated services according to the standards of the Alliance and applicable state, CMS, and accreditation requirements. (If utilization management and/or Medication Therapy Management Program (MTMP) are delegated, then at least annually the Director of Pharmacy reviews and approves the FDR's Utilization Management and/or MTM Program Description.) If utilization management is delegated, then at least annually, the committee reviews and approves the FDR's relevant utilization program documents. The results of the comprehensive review of FDR's ability to provide delegated services according to the standards of the Alliance and applicable State, CMS and accreditation requirements will also be reported to the Chief Compliance Office and will be reviewed at the MCC.

4.1.4 If monitoring and/or audits identify non-compliance with standards, a plan of corrective action must be developed and approved by the delegation committee. If Medicare membership is impacted this information will also be shared with the Medicare Compliance Committee. Follow up audits may be scheduled until compliance with the Alliance standards is reached. The initial assessment tool is used during the annual evaluation.

4.1.5 Discretionary visits/audits for delegated services may be performed on a routine basis, and whenever the Alliance has reason to believe that the FDR's ability or willingness to perform the delegated function(s) may be compromised. The results of these discretionary visits/audits for delegated services will be conducted by the Director of Pharmacy and provided to the Chief Compliance Officer and/or Medicare Compliance Officer and to the MCC as appropriate. The Compliance Officer and/or the MCC may recommend follow-up discretionary visits/audits for delegated services upon review of compliance trends or reported incidents.

4.1.6 Criteria include, but are not limited to:

a. Failure to fully comply with a corrective action plan.
b. Substantial policy changes that deviate from the Alliance or state, CMS, or accreditation requirements.
c. Suspected or reported financial constraints such as bankruptcy or impending bankruptcy which may impact the delivery of services to members.
d. Reported/alleged fraud, waste and abuse, privacy or HIPAA violations.
e. Sale/merger/acquisition involving the first tier, downstream or related entity.
f. Major changes in the leadership of the first tier, downstream or related entity.
g. Staffing changes which impact operations.
h. Failure to comply with CMS requirements as mandated under the Alliance's contract.

4.1.7 The Alliance reserves the right to, at any time; require remediation by an FDR for failure to fulfill contractual obligations including development and implementation of a corrective action plan. Failure to cooperate with remediation or failure to implement an agreed upon corrective action plan in the specified time frame may result in termination of the agreement (revocation) and return of delegated activities to the Alliance.

5.0 RECORD RETENTION

5.1 The Alliance and its FDRs will maintain all books, documents, papers and/or records relating to Medicare members for **up to ten (10) years from the final date of the contract period** or ten (10) years from the date of any audit if later. The Alliance and its FDRs agree to permit CMS, the U.S. Department of Health and Human Services, and the Comptroller General, or their designees the right to inspect any pertinent information related to the contract during the contract term, for **up to ten (10) years from the final date of the contract period**, and in certain instances described in the Medicare Advantage regulation(s), periods in excess of ten (10) years, as appropriate, (ten (10) years from the date of any audit, if later.)

DEFINITIONS / ACRONYMS

Audit ('Auditing'): An audit refers to a formal review of compliance with a particular set of internal (e.g., policies and procedures) or external (e.g., laws and regulations) standards used as base measures.

Corrective Action Organization (CAP): A formal document outlining Organization or provider compliance deficiencies and establishing an Organization to institute changes aimed at correcting the deficiencies.

Centers for Medicare and Medicaid Services ('CMS'): Is a federal agency within the United States Department of Health and Human Services (DHHS) that administers the Medicare program and works in partnership with state governments to administer Medicaid. In addition to these programs, CMS has other responsibilities, including the administrative simplification standards from the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Delegation ('Delegated'): The legal assignment to others of the authority for particular functions, tasks and decisions on the original party's behalf. The original party remains liable for compliance with any and all rules and requirements pertaining to the delegated functions.

Downstream Entity: Refers to any party that enters into a written arrangement, acceptable to CMS, below the level of the arrangement between a Sponsor and a First Tier Entity.

First Tier Entity: Refers to a party that enters into a written arrangement acceptable to CMS with a Sponsor to provide *administrative services or health care services* for Medicare beneficiaries under Medicare Advantage (MA) or Part D (PDP) Organizations.

Monitoring Activities ('Monitoring'): Reviews that are repeated regularly during the normal course of operations. Monitoring activities may occur to ensure corrective actions are undertaken or when no specific problems have been identified to confirm ongoing compliance.

Related Entity: Is any entity that is related to the Sponsor by common ownership or control and either:

- Performs some of the Sponsor's management functions under contract or delegation
- Furnishes services to Medicare enrollees
- Leases real property or sells materials to the Sponsor at a cost of more than $2,500 per contract period (usually one year)

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

[List revision dates starting with original effective date – this is the date that revisions were approved at AOC, and is a running list of approval dates from AOC]

REFERENCES

[List references such as regulatory citations]

MONITORING- REPORTS AND AUDITS

1.0 Member Call Center

42 CFR 423.128;Medicare Managed Care Manual, Chapter 3

1.1 Monthly review call center statistics report to verify compliance with CMS requirements, including:

a. Average speed to answer
   - 80% of calls answered within 30 seconds

b. Abandonment rate
   - Less than 5%

c. Average hold time
   - Not to exceed 2 minutes (Five star threshold=≤ 11 sec)

d. Volume

e. Inquiry type

f. Peak call times

1.2 Quarterly review training documentation including:

a. Training program

b. Attendees

c. Who conducted the training

1.3 Quarterly perform 'secret shopper' calls to ensure compliance with CMS requirements.

1.4 Annually review scripts to ensure compliance with CMS requirements.

1.5 Periodic review of call content to determine answer accuracy rate and the need for additional training.

2.0 Toll-Free Technical Call Center

42 CFR 423.128;Medicare Managed Care Manual, Chapter 3

2.1 Monthly review call center statistics report to verify compliance with CMS requirements, including:

a. Average speed to answer
   - 80% of calls answered within 30 seconds

b. Abandonment rate
   - Less than 5%

c. Average hold time
   - Not to exceed 2 minutes

d. Volume

e. Inquiry type
f. Peak call times
- Must operate a 24-hour call center if pharmacies in the network maintain such hours.

2.2 Quarterly review training documentation including:
a. Training program
b. Attendees
c. Who conducted the training

2.3 Quarterly perform 'secret shopper' calls to ensure compliance with CMS requirements.

2.4 Annually review scripts to ensure compliance with CMS requirements.

3.0 Performs Negotiations with Prescription Drug Manufacturers and Others for Rebates, Discounts, or Other Price Concessions on Prescription Drugs

42 FR § 423.514(a)

3.1 Quarterly review report detail, including:
a. Manufacturer/company name
b. Drug name
c. Rebates received
d. Pending rebates
e. Prior rebates
f. Description
g. Value
h. Justification

3.2 Ensure DIR attestation provided

4.0 Manages, Produces and Provides Beneficiary Explanation of Benefits (EOBs)

42 CFR 423.2267;Medicare Managed Care Manual, Chapter 3

4.1Monthly audit a random sample per contract and Organization benefit package.
a. Verify timeliness of mailing.
b. Verify inclusion/accuracy of:
- TrOOP.
- Deductible, if applicable.
- Annual out-of-pocket threshold.
- Appeals rights.

c. Ensure use of CMS approved EOB.

5.0 Operates a Drug Utilization Management (DUR) (Concurrent Edits) Program

42 CFR 423.153;Prescription Drug Benefit Manual, Chapter 7

5.1 Quarterly review system logs which list, at a minimum, the following:
a. Number of concurrent DUR messages
b. Point of sale edits
c. Denials
d. Reversals and theoretical cost implications of edits.

- Concurrent/point of sale edits should include: therapeutic duplication, age/gender related contraindications, over/under utilization, drug-drug interactions, incorrect drug dosage or duration of drug therapy, drug-allergy contraindications, and clinical abuse/misuse. If edits are "hard", i.e. pharmacist cannot fill prescription until criteria is met, review override statistics and evidence for overrides.

5.2 Annually review/revise Utilization Management Program for compliance with CMS requirements.
5.3 Annual summary report including, but not limited to:
a. Review that the prescribed drug therapy is performed before each prescription is dispensed at the point of sale or distribution.
b. Operational systems are in place designed to ensure ongoing periodic examination of claims data and other records in order to identify patterns of inappropriate or medically unnecessary care associated with specific drugs.
5.4 Include statistics and evidence of overrides by the pharmacy at point of service and text comments in conformity with NCPDP standards.

6.0 Operates a Drug Utilization Management (Retrospective DUR) Program
42 CFR 423.153 (c)(3);Prescription Drug Benefit Manual, Chapter 7

6.1 Annually review Utilization Management Program for compliance with CMS requirements.
6.2 Annually ensure receipt of summary report including, but not limited to:
a. Medication errors and identification programs and outcomes (how many were received and resolved).
b. Review that the prescribed drug therapy is performed before each prescription is dispensed at the point of sale or distribution.
c. Operational systems are in place designed to ensure ongoing periodic examination of claims data and other records in order to identify patterns of inappropriate or medically unnecessary care associated with specific drugs.
d. Include statistics and evidence of overrides by the pharmacy at point of service and text comments in conformity with NCPDP standards.

7.0 Develops a Retail Pharmacy Network, and Maintains Access
42 CFR 423.120;Prescription Drug Benefit Manual, Chapter 5

7.1 Monthly receive electronic file reflecting any changes in the network.
a. Any changes impacting access or availability must be reported immediately.
7.2 At least annually, review GeoAccess reports to ensure compliance with CMS convenient access standards.
7.3 Annually review all retail network pharmacy contract templates to ensure compliance with CMS requirements including, but not limited to:
a. 'Extended day supplies' language if extended day supplies of medications are offered through mail order.*
b. Record keeping requirements (prescription records in their original format for 3 years and electronic format for the remaining 7 years of the 10 year requirement).

c. Record keeping requirements (books, records, documents and other evidence of accounting procedures and practices for 10 years).

d. Access to facilities.

e. 'Any willing provider' language stating that standard contracting terms and conditions will be offered to any pharmacy willing to meet those standard contracting terms and conditions.

f. Post or distribute notices instructing members to contact the Organization to obtain a coverage determination or exception.

g. Comply with minimum pharmacy practice standards established by the state(s).

7.4 Annually 'secret shop' random network pharmacies to ensure notices regarding coverage determinations and exceptions are posted.

7.5 Annual Part D CMS reporting due May 31.*

g. Due to Health Plan no later than April 21.

8.0 Develops and Maintains a Home Infusion Pharmacy Network, and Maintains Access
42 CFR 423.120 (a)(4);Prescription Drug Benefit Manual, Chapter 5

8.1 Monthly receive electronic file reflecting any changes in the network.

a. Any changes impacting access or availability must be reported immediately.

8.2 At least annually review GeoAccess reports to ensure compliance with CMS convenient access standards.

8.3 Annually review all home infusion pharmacy network contract templates to ensure compliance with CMS requirements including, but not limited to:

a. Inclusion of the provision for delivery of home infusion drugs in a form that can be administered in a clinically appropriate fashion in the member's place of residence.

b. Home infusion drugs are delivered within 24 hours of discharge from an acute care setting if prescribed.

c. Professional services and ancillary supplies necessary for home infusion drugs are in place before they are dispensed to the member in their place of residence, and provide both short term acute care (IV antibiotics) and LTC chronic care therapies.

d. Record keeping requirements (books, records, documents and other evidence of accounting procedures and practices for 10 years).

e. Access to facilities.

f. Comply with minimum pharmacy practice standards established by the state(s).

8.4 Annual CMS Part D reporting due May 31.

a. Due to Health Plan no later than April 21.

9.0 Develops and Maintains a Long Term Care (LTC) Pharmacy Network, and Maintains Access
42 CFR 423.120(a)(5);Prescription Drug Benefit Manual, Chapter 5

9.1Monthly receive electronic file reflecting any changes in the network.

a. Any changes impacting access or availability must be reported immediately.

9.2 At least annually, review GeoAccess reports to ensure compliance with CMS convenient access standards.
9.3 Annually review all LTC pharmacy network contract templates to ensure compliance with CMS requirements including, but not limited to:

a. The inclusion of the provision for offering standard contracting terms and conditions, including performance and service criteria for LTC pharmacies in its service area that request a contract.

b. Provision to ensure that every Alliance enrollee residing in a LTC facility has access to covered Part D drugs through one or more network LTC pharmacy.

c. Record keeping requirements (books, records, documents and other evidence of accounting procedures and practices for 10 years).

d. Access to facilities.

e. Comply with minimum pharmacy practice standards established by the state(s).

9.4 Annual CMS Part D reporting due May 31.

a. Due to Health Plan no later than April 21.

10.0 Develops and Maintains an Indian/Tribal/Urban Pharmacy Network
42 CFR 423.120(a)(6);Prescription Drug Benefit Manual, Chapter 5

10.1 Monthly provide electronic file reflecting any changes in the network, if applicable.

a. Any changes impacting access or availability must be reported immediately.

10.2 At least annually, review GeoAccess reports to ensure compliance with CMS convenient access standards, if applicable.
10.3 Annually review all I/T/U network pharmacy contract templates to ensure compliance with CMS requirements, if applicable.

a. Ensure I/T/U pharmacies are offered standard contracting terms and conditions and that members have convenient access.

b. Record keeping requirements (books, records, documents and other evidence of accounting procedures and practices for 10 years).

c. Access to facilities.

11.0 Out of Network Pharmacy Access
42 CFR 423.124;Prescription Drug Benefit Manual, Chapter 5

11.1 Quarterly review out of network utilization statistics including, but not limited to:

a. Geographic location.

b. Reason.

- Member is out of service area (travel).
  - Becomes ill.
  - Loses medication.
  - Requires refill.
- Prescription not typically stocked at network pharmacy within reasonable driving distance.
- Prescription dispensed by out of network institution.

c. Ensure appropriate limitation applied as per policy.

12.0 Access to Vaccines
42 CFR 423.104;Prescription Drug Benefit Manual, Chapter 5

12.1 Quarterly review report detailing statistics for vaccines:

a. Number dispensed in network pharmacy.

b. Number dispensed by a provider in provider's office (via network pharmacy distribution of vaccine).

c. Number dispensed using out of network approach.

13.0 Provides Notice of Formulary Changes
42 CFR 423.120(f);Medicare Managed Care Manual, Chapter 3; Prescription Drug Benefit Manual, Chapter 6

13.1 Quarterly audit a random sample of all formulary changes, including all contracts and Organization benefit packages. The sample should include, but not be limited to, the following:

a. CMS approval of change.

b. Type of formulary change (drug addition, tier structure, utilization management).

c. Timely notification to affected members.

d. Timely notification to other entities (pharmacies, etc.).

e. Appropriate information contained in notification.

f. Formulary change pushed to:

- Website.
- Print (errata sheet).
- EOB

14.0 Maintains a Pharmacy and Therapeutics (P&T) Committee
42 CFR 423.120(b)(1);Prescription Drug Benefit Manual, Chapter 6

14.1 Quarterly, review P&T Committee Minutes and processes for compliance with CMS requirements including, but not limited to, the following:

a. Meetings held no less than quarterly.

b. Review of formulary management activities (annual approval of formulary; step therapies, etc.).

c. Documentation of committee decisions (what information was provided to ensure an informed decision, i.e. clinical review, peer-reviewed medical literature, etc.).

d. New FDA approved drug product review and decision making process within required timeframes.

e. Inclusion of a Part D drug has advantages in terms of safety and efficacy.

f. Utilization Management Program review and approval.

g. Review of policies that guide exceptions and utilization management processes.

h. Medication Therapy Management Program review and approval.

h. Committee comprised of a majority of practicing physicians and pharmacists; including at least one of each who are independent and free of conflict of interest.

14.2 Annual Part D CMS reporting due February 28.

a. Notify Health Plan by January 31.

14.3 CMS notified within 30 days of any changes to the composition of the P&T Committee, if applicable. (Quarterly CMS required reporting)

a. Health Plan notified within 15 days of any such changes.

15.0 Develops or Manages the Formulary

42 CFR 423.100;Prescription Drug Benefit Manual, Chapter 6

15.1 Quarterly perform a random audit of prescription drug event (PDE) data to ensure:

a. Copayments applied correctly
b. LICs level applied (if applicable)
c. Non-formulary drug adjudicated at appropriate tier

15.2 Monthly compare CMS approved formulary with updated abridged and/or comprehensive to ensure that they are identical.

15.3 Monthly ensure the website has updated formulary, formulary changes, current utilization management information including prior authorization criteria, step therapy and quantity limits.

16.0 Participates In or Manages the Transition Process

42 CFR 423.120(b)(3;Prescription Drug Benefit Manual, Chapter 6

16.1 Monthly review summary of transition fill claims for transition eligible members, to include:

a. Number of paid claims reviewed
    - Number of issues identified
    - Number of affected members
b. Number of rejected claims reviewed
    - Number of issues identified
    - Number of affected members

16.2 Monthly review summary of member and prescriber notification mailing, to include:

a. Number of member notifications distributed
    - Number accurate
    - Verification of timely delivery
b. Number of provider notifications distributed
    - Number accurate

16.3 CMS required annual monitoring in January (if selected)

16.4 Quarterly perform an audit on a random sample of transition notices, including screen shots, documenting the adjudication of transition supplies. Include retail and LTC from all contracts and all Alliance benefit packages.

16.5 Quarterly perform an audit on a random sample of transition letters per contract and Alliance benefit package. Verify the inclusion of appropriate formulary alternatives, prior authorization or formulary exception requirements.

17.0 Creates or Manages the Medication Therapy Management (MTM) Program
42 CFR 423.153(d)(2);Prescription Drug Benefit Manual, Chapter 7

17.1 Annually review MTM program to ensure compliance with CMS requirements, including but not limited to:
    a. Developed in cooperation with licensed physicians and pharmacists.
    b. Targets enrollees with specific, multiple chronic conditions.
17.2 Semi-annually review number of members enrolled in the MTM program.
17.3 Semi-annually review number of members who have opted-out of the MTM program and reasoning (voluntary; deceased; etc.).
17.4 Ensure opt-out members are permanently removed from future program correspondence, unless member specifically requests program information.
17.5 Quarterly review members with completed comprehensive medication reviews.
17.6 Quarterly review members receiving targeted monitoring.
17.7 Quarterly cross walk members in MTM program with members being case managed.
17.8 Quarterly review utilization and outcome measures reported for all MTM program enrollees.
17.9 Ensure receipt of annual survey results.
17.10 Annual CMS Part D report due February 28.
    a. Due to Alliance no later than February 1.

18.0 Ability to Support Electronic Prescribing (E-Prescribing)
42 CFR 423.160;Prescription Drug Benefit Manual, Chapter 7

18.1 Quarterly review e-prescribing from in network pharmacies. Review should include, but not be limited to, the following:
    a. Pharmacy type (retail, home infusion, LTC).
    b. Volume.
    c. High number of errors or other anomalies.
    d. Compliance with CMS requirements.
18.2 Quarterly report to reflect in network pharmacies enabled to receive e-prescribing versus utilization:
    a. Pharmacy type (retail, home infusion, LTC).
    b. Number enabled to receive e-prescribing.
    c. Number utilizing e-prescribing.
18.3 Annual CMS Part D reporting due May 31 (Q1 data).
    a. Due to Alliance no later than April 21.

19.0 Performs Administration and Tracking of Enrollees' Drug Benefits in Real Time (TrOOP and Total Drug Costs)
42 CFR 423.128;Prescription Drug Benefit Manual, Chapter 14

19.1 Quarterly audit a random sample of member claims history and movement through their benefit. Ensure samples include in network and out of network claims and take into account any adjustments due to COB, retro LICS reversal, etc.

19.2 Quarterly audit a random sample of PDE records to match against live claims and ensure accurate calculations in line with CMS instructions.

19.3 Quarterly verify that inbound/outbound TrOOP is coordinated with the FIR contractor per required timelines.

a. Are the transactions processing appropriately?
b. Are TrOOP amounts reported accurately?

20.0 Creates or Manages a Fraud, Waste and Abuse (FWA) Program

42 CFR 423.504(b)(4)(vi);Prescription Drug Benefit Manual, Chapter 9

20.1Ensure all employees upon hire, and annually thereafter all employees, Board members, Officers, first tier and downstream entities are reviewed (data scrubbed) against the following exclusion lists:

a. General Services Administration – Excluded Parties List System (EPLS)
b. Office of Inspector General – List of Excluded Individuals/Entities (LEIE)

20.2 Should any employee, Board member, Officer, first tier and downstream entity appear on the list ensure they are immediately removed from work related to any federal health program (including Part D) and appropriate corrective action is taken.

20.3 Monthly review the following:

a. Number of reported incidents
b. Type of reported incident
c. Action taken
d. Required reporting, if applicable (state, federal)
e. Outcome
f. Report to appropriate committee (Compliance, Quality, etc.)

20.4 Annually review FWA program and related policies and procedures to ensure compliance with CMS requirements.

20.5 Annually review the following to ensure compliance with CMS requirements, including but not limited to:

20.6 Ensure all new employees receive:

a. Code of Conduct (new employees must sign attestation)
b. Applicable policies and procedures
c. Appropriate training
d. Method of communicating compliance related questions/concerns

20.7 Annually, ensure the Code of Conduct and appropriate policies and procedures have been distributed to all employees. If revised prior to annual distribution, ensure these updates were distributed.

20.8 Notify Health Plan of any reported incidents within 5 days.

20.9Annual CMS Part D reporting due February 28.

a. Due to Alliance no later than January 14.

21.0 Performs Adjudication and Processing of Pharmacy Claims at the Point of Sale

42 FR § 423.120(b); § 423.104; § 423.782

21.1 Monitor and perform quality assurance on eligibility files

a. Daily review eligibility file load reports to ensure an appropriate number of records of loaded and monitor and verify members who terminate

b. Monthly verify that LIS changes have loaded appropriately into claims system

21.2 Monthly review (monitor) claims report to ensure compliance with CMS requirements.

a. Number of paid claims.

b. Number of rejected claims.

c. Number of issues identified.

d. Number of affected members.

e. Timeliness (percent paid timely)

22.0 Overpayment and under payment timeliness.

42 CFR 423.466

22.1 Semi-annual CMS Part D reporting due August 31 (Jan-Jun) and February 28 (Jul-Dec).

a. Due to Health Plan no later than July 21 (Jan-Jun) and January 21 (Jul-Dec).

23.0 Develop and Operate Online Claims Processing System

42 CFR 423.120

23.1 Monthly ensure a real-time, online claims processing system is operating according to CMS standards:

a. 98% response within 4 seconds.

b. 99% of claims paid with no errors.

c. 99% system availability.

d. Overpayments and underpayments are resolved within 45 days.

24.0 Performs Coordination with Other Drug Benefit Programs-COB (Including, for example, Medicaid, Medigap, etc.)

42 CFR 423.464;Prescription Drug Benefit Manual, Chapter 14

24.1 Quarterly audit random sample of claims for a selection of members with COB on record.

a. Pull corresponding EOBs

b. Verify COB appropriately applied.

24.2 Quarterly audit random sample of claims with N1 transactions to ensure:

a.Appropriate adjustments, including status of TrOOP or non-TrOOP eligible.

24.3 Annually review policies and procedures, including:

a. Method of surveying members with CMS supplied COB.

b. Method of reporting inconsistencies and updates to CMS.

24.4 Annually audit random sample of COB files received from CMS to ensure data was appropriately loaded in system.

24.5 Annually monitor to ensure that COB indicator from enrollment/eligibility is appropriately entered in claims adjudication process.

25.0 Operates a Coverage Determination Process

42 CFR 423.566-572;Prescription Drug Benefit Manual, Chapter 18

25.1 Quarterly audit random sample of initial coverage determinations, including all contracts and Organization benefit packages, to ensure compliance with the following:

a. CMS required time frames.

b. CMS approved model notice (including appeals rights, if applicable) utilized

c. Timely notification to member.

d. Approved criteria utilized.

e. Health Plan defined quality assurance criteria utilized.

25.2 Quarterly audit random sample of expedited coverage determinations, including all contracts and Organization benefit packages, to ensure compliance with:

a. CMS required time frames.

b. CMS approved model notice (including appeals rights, if applicable) utilized.

c. Timely notification to member.

d. Approved criteria utilized.

25.3 IRE case referrals to ensure compliance with:

a. Number of forwarded cases.

b. Type of cases.

c. Timely notification to member.

d. Required time frames.

e. Documentation requests.

f. Delivery method.

g. The Plan should be notified of cases sent to the IRE prior to sending the case whenever possible

25.4 Quarterly CMS Part D reporting due May 15 (Q1); August 15 (Q2); November 15 (Q3); February 15 (Q4)

a. Due to Health Plan no later than April 21 (Q1); July 21 (Q2); August 21 (Q3); January 21 (Q4)

26.0 Operates an Exception Process

42 CFR 423.578;Prescription Drug Benefit Manual, Chapter 18

26.1 Quarterly audit random samples (including all contracts and Organization benefit packages) of tiering exception requests and non-formulary exception requests to ensure compliance with the following:

a. Required time frames.

b. Model notice(s).

c. Physician supporting statement (if applicable).

26.2 Quarterly CMS Part D reporting due May 15 (Q1); August 15 (Q2); November 15 (Q3); February 15 (Q4)

a.Due to Health Plan no later than April 21 (Q1); July 21 (Q2); August 21 (Q3); January 21 (Q4)

27.0 Creation and Submission of Data Files to CMS

CFR § 423.336(c)(1); § 423.343(c)(1); § 423.343(d)(1)

27.1Annually ensure pharmacy network and NDC pricing files are:

a. Created according to CMS guidelines.

b. Submitted timely.

c. Accepted.

27.2 Annually ensure PDE and DIR data is:

a. Created according to CMS guidelines.

b. Submitted timely (May 31 and June 30, respectively).

27.3 Monthly ensure submission of PDE files.

a. Monitor PDE acceptance rate.

ALAMEDA Alliance FOR HEALTH

Health care you can count on.
Service you can trust.

POLICY AND PROCEDURE TEMPLATE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Vaccine Benefit
Department Name	Pharmacy Department
Department Officer	Chief Medical Officer
Policy Owner	Director of Pharmacy
Line(s) of Business	[Line(s) of business impacted by this policy. E.g., MCAL, MCARE, and/or IHSS]
Effective Date	[Original date policy was approved by committee – MM/DD/YYYY – TBD for new policies]
Subcommittee Name	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the name of the committee here, otherwise put N/A
Subcommittee Approval Date	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee – MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

Medicare provides coverage under Part B for Flu, Pneumonia, Hepatitis B (for people at high and intermediate risk), COVID-19, and certain reasonable and necessary vaccines to treat an injury or exposure to a disease (If a patient gets a tetanus vaccination because of an accidental puncture wound, it's a Part B-covered vaccine. However, if the patient gets a tetanus booster shot, unrelated to injury or illness, it's a Part D covered vaccine).

Part D plans cover all commercially available vaccines when they're reasonable and necessary to prevent illness, except those covered by Part B. Per CMS requirements, coverage for Part B and Part D vaccines and related administration costs is provided by AAH without any member cost-sharing, deductible or co-insurance.

PROCEDURE

1. Part B Vaccine Administration
    1.1 Influenza OR Pneumonia OR Hepatitis B OR COVID-19
    1.2 Included vaccination administration elements:
        a. the immunizing professional's time in physically delivering the vaccine to a beneficiary
        b. the resources encompassing the supplies (syringe, gauze, band-aid, alcohol prep pad, etc.
        c. the indirect costs of the office
        d. professional liability
2. Part D Vaccine Administration
    2.1 All commercially available adult vaccines recommended by the Advisory Committee on Immunization Practices (ACIP)
    2.2 Included vaccine administration elements:
        a. Dispensing fee (if applicable)
        b. Vaccine administration fee
        c. Vaccine ingredient cost
    2.3 Network pharmacies should bill for Part D vaccines, including associated administration costs, on 1 claim when the same provider is both dispensing and administering the vaccine
    2.4 Members are not subject to any out-of-pocket costs for Part D vaccines and administration
    2.5 If members are required to pay for a vaccine administration fee at an out-of-network pharmacy they may submit a request for 100% reimbursement via the Direct Member Reimbursement policy

DEFINITIONS / ACRONYMS

CMS Compendia: Section 1860D-2(e)(1)(B) of the Act limits "medically-accepted indication," by reference to section 1927(k)(6) of the Act, to any use of a covered Part D drug which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in section 1927(g)(1)(B)(i) of the Act. The compendia are:

- American Hospital Formulary Service Drug Information (AHFS-DI)
- National Comprehensive Cancer Network (NCCN) Drug and Biologics Compendia
- Micromedex Drug Dex
- Clinical Pharmacology
- Lexi-Drugs

Part D sponsors are responsible for ensuring that covered Part D drugs are prescribed for "medically accepted indications." Part D sponsors may rely on utilization management policies and procedures to make such determinations, but pharmacists are not required to contact each prescriber to verify whether a prescription is being used for other than a medically accepted indication.

Designee: Another company or vendor that Alliance retains to perform certain PBM-related functions on behalf of Alliance (currently Vendor Name is its external vendor for P&T activities related to Alliance formularies and utilization management.)

Excluded Part D Drug Categories: Part D drugs do not include drugs or classes of drugs, or their medical uses, which may be excluded from coverage or otherwise restricted under Section 1927(d)(2) of the Act, except for smoking cessation agents.
Excluded:
- Agents when used for anorexia, weight loss, or weight gain (even if used for a non-cosmetic purpose (i.e., morbid obesity)).
- Agents when used to promote fertility.
- Agents when used for cosmetic purposes or hair growth.
- Agents when used for the symptomatic relief of cough and colds.
- Prescription vitamins and mineral products, except prenatal vitamins and fluoride preparations.
- Nonprescription drugs.
- Covered outpatient drugs which the manufacturer seeks to require as a condition of sale that associated tests or monitoring services be purchased exclusively from the manufacturer or its designee.
- Agents when used for the treatment of sexual or erectile dysfunction (ED). ED drugs will meet the definition of a Part D drug when prescribed for medically accepted indications approved by the FDA other than sexual or erectile dysfunction (such as pulmonary hypertension). However, ED drugs will not meet the definition of a Part D drug when used off-label, even when the off-label use is listed in one of the compendia found in section 1927(g)(1)(B)(i) of the Act: American Hospital Formulary Service Drug Information, United States Pharmacopeia-Drug Information (or its successor publications), and DRUGDEX Information System.

Food and Drug Administration (FDA): The federal agency that reviews drug products for safety and efficacy. A drug may not be marketed in the United States unless it has received approval from the FDA.

Part D Drug: A Part D drug means a drug that may be dispensed only upon a prescription, is being used for a medically accepted indication as defined by section 1927(k)(6) of the Act, and is one of the following:
- A drug that is described in sections 1927(k)(2)(A)(i) through (iii) of the Act.
- A biological product described in sections 1927(k)(2)(B)(i) through (iii) of the Act.
- Insulin described in section 1927(k)(2)(C) of the Act.
- Medical supplies associated with the delivery of insulin.
- A vaccine licensed under section 351 of the Public Health Service Act and its administration.

A covered Part D drug is a Part D drug that is included in a Part D sponsor's formulary, or treated as being included in a Part D plan's formulary as a result of a coverage determination or appeal under 42 CFR 423.566, 423.580, and 423.600, 423.610, 423.620 and 423.630, and obtained at a network pharmacy or an out-of-network pharmacy in accordance with 42 CFR 423.124.

Pharmacy & Therapeutics (P&T) Committee: An external advisory committee comprised of healthcare professionals (physicians, pharmacists, nurses, etc.) that is responsible for managing and administering the drug formulary system, including utilization management strategies.

Prior Authorization (PA): A utilization management strategy used for drugs that have:

- A high potential for misuse or inappropriate use.
- Severe adverse effects associated with use.
- Special monitoring required; and/or
- High cost, especially if other agents are available.
- Ensures coverage of drugs for FDA-approved uses, or for unapproved, or off-label, uses that are supported by adequate medical evidence.

Protected Classes: Part D sponsor formularies must include all or substantially all drugs in the immunosuppressant (for prophylaxis of organ transplant rejection), antidepressant, antipsychotic, anticonvulsant, antiretroviral, and antineoplastic classes.
Formularies must include substantially all drugs in these six categories that are FDA approved by the last CMS specified Health Plan Management System (HPMS) formulary upload date for the upcoming contract year. New drugs or newly approved uses for drugs within the six classes that come onto the market after the CMS specified formulary upload date will be subject to an expedited P&T committee review.

The expedited review process requires P&T committees to decide within 90 days, rather than the normal 180-day requirement. At the end of the 90-day period, these drugs must be added to Part D plan formularies. Part D sponsors may not implement prior authorization or step therapy requirements that are intended to steer beneficiaries to preferred alternatives within these classes for enrollees who are currently taking a drug.

Non-Formulary Drug: Means both Part D drugs that are not on the Sponsor's formulary and that are on the Sponsor's formulary but require prior authorization or step therapy under a plan's utilization management rules. [Definitions / acronyms used by the Alliance (please note, Alameda Alliance for Health should be shortened to Alliance, not AAH, for continuity across policies)

When available the definitions in the DHCS contract should be used]

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

[List revision dates starting with original effective date – this is the date that revisions were approved at AOC, and is a running list of approval dates from AOC]

REFERENCES

Chapter 6 – Part D Drugs and Formulary Requirements Sec. 10.14
Chapter 5: Benefits and Beneficiary Protections Sec. 60.2-60.3.4

MONITORING

As part of Part D paid claim report review, assure that members are not assessed cost-sharing for covered vaccines.

Alameda Alliance for Health
1240 South Loop Road
Alameda, CA 94502
Phone Number: **1.510.747.4567**
Toll-Free: **1.877.932.2738**
People with hearing and speaking impairments (CRS/TTY): **711/1.800.735.2929**

www.alamedaalliance.org

90-Day Supply on Maintenance Medications

Medications are available for Alliance Group Care Members through choice in-network retail pharmacies or Walgreens Mail Service pharmacy. Prescriptions are filled with generic versions, when available and medically necessary. Certain medications are subject to prior authorization (PA) review by Alameda Alliance for Health (Alliance).

This list may not include all 90-day maintenance medications as product updates are being made periodically. Questions about drugs not included on this list should be directed to the Alliance Pharmacy Services Department at **1.510.747.4541**. Products in red are new additions to the list.

Asthma & COPD

Arnuity Ellipta
Atrovent HFA
Combivent
Flovent Diskus
Flovent HFA
Fluticasone/Salmeterol blister w/device
Fluticasone/Salmeterol Respiclick
Montelukast
Qvar Redihaler
Spiriva HandiHaler
Spiriva Respimat
Stiolto Respimat
Theophylline
Tudorza Pressair

Blood Pressure & Heart Health

Acetazolamide
Aliskiren
Aliskiren/Amlodipine
Amiloride
Amiodarone
Amlodipine/Benazepril
Aspirin/Dipyridamole
Atenolol
Atenolol/Chlorthalidone
Azilsartan
Benazepril
Benazepril/HCTZ
Bisoprolol Bisoprolol/HCTZ
Bumetanide

Blood Pressure & Heart Health (cont.)

Candesartan
Captopril
Carvedilol
Chlorthalidone
Cilostazol
Clonidine
Clopidogrel
Digoxin
Diltiazem
Dipyridamole
Dronedarone
Enalapril
Enalapril/HCTZ
Eprosartan

Blood Pressure & Heart Health (cont.)

Eprosartan/HCTZ
Felodipine
Flecainide
Fosinopril
Furosemide
Guanfacine
Hydralazine
Hydrochlorothiazide
Indapamide
Irbesartan
Irbesartan/HCTZ
Isoproterenol
Isosorbide Dinitrate
Isosorbide Mononitrate
Labetalol
Lisinopril
Lisinopril/HCTZ
Methyldopa
Methyldopa/HCTZ
Metolazone
Metoprolol Succinate
Metoprolol Tartrate
Mexiletine
Midodrine
Minodixidil
Nadolol
Niacin
Nicardipine
Nifedipine
Nitroglycerin
Olmesartan

Blood Pressure & Heart Health (cont.)

Pentoxifyline
Pindolol
Prazosin
Propafenone
Propranolol
Propranolol/HCTZ
Quinidine gluconate
Quinidine sulfate
Ramipril
Reserpine
Sotalol
Spironolactone
Spironolactone/HCTZ
Telmisartan
Telmisartan/HCTZ
Terazosin
Triamterene/HCTZ
Valsartan/HCTZ
Verapamil
Warfarin

Diabetes

Chlorpropamide
Glimepiride
Glipizide
Glyburide
Glyburide, micronized
Glyburide/Metformin
Metformin
Nateglinide
Pioglitazole/Metformin

Diabetes (cont.)

Pioglitazone
Rosiglitazone
Rosiglitazone/Metformin
Tolazamide
Tolbutamide

Gastrointestinal Health

Balsalazide
Sulfasalazide
Ursodiol

Gout

Allopurinol
Probenecid

High Cholesterol

Atorvastatin
Cholestyramine/Aspartame
Colestipol
Docosahexanoic Acid/EPA
Ezetimibe/Simvastatin
Fenofibrate
Fenofibrate, nanocrystalized
Fluvastatin
Gemfibrozil
Lovastatin
Omega-3 Fatty Acids/Fish Oil
Omega-3 Fatty Acids/Vitamin E
Simvastatin

Liver Disease
Adefovir
Baraclude solution
Entecavir
Lamividine
Tenofovir 300mg tablets
Vemlidy
Viread

Men's Health
Alfuzosin
Doxazosin
Finasteride
Tamsulosin
Terazosin

Mental Health
Bupropion
Duloxetine
Escitalopram
Fluoxetine
Mirtazapine
Paroxetine
Sertraline
Trazodone

Miscellaneous
Cabergoline
Fludrocortisone
Hydroxychloroquine
Hydroxyurea
Leflunomide
Methazolamide

Miscellaneous
Methotrexate
Methylsulfate
Neostigmine

Myasthenia Gravis
Edrophonium Chloride
Physostigmine Salicylate
Pyridostigmine Bromide

Osteoporosis & Paget's Disease
Alendronate
Calcitonin (Salmon)
Raloxifene

Parkinson's & Alzheimer's
Bromocriptine
Carbidopa/Levodopa
Donepezil
Entacapone
Pramipexole
Ropinirole

Seizures & Epilepsy
Carbamazepine
Clobazam
Clonazepam
Divalproex sodium
Ethosuximide
Ezogabine
Gabapentin
Levetiracetam
Levetiracetam NaCl

Seizures & Epilepsy
Phenobarbital
Phenytoin
Primidone
Rufinamide
Tiagabine
Topiramate
Valproic Acid
Zonisamide

Thyroid Conditions
Armour Thyroid
Levothyroxine
Liothyronine
Methimazole
Propylthiouracil

Transplant
Azathioprine
Mycophenolate Mofetil
Mycophenolate Sodium
Tacrolimus

Urinary Incontinence & Retention
Bethanechol
Desmopressin
Oxybutinin

Vitamins & Nutritional Health
B Complex with Vitamin C
Calcitriol
Calcium Acetate 667 mg
Calcium Carbonate

Vitamins & Nutritional Health

Calcium Carbonate/Vitamin D2
Calcium Carbonate/Vitamin D3
Calcium Citrate/Vitamin D2
Calcium Citrate/Vitamin D3
Calcium Glubionate
Calcium Gluconate
Calcium Lactate
Calcium Phosphate/Vitamin D3
Cholecalciferol (Vitamin D3)
Cyanocobalamin (Vitamin B-12)
Ferrous Sulfate
Folic Acid
Folic Acid with Multivitamins
Magnesium Oxide
Multivitamins
Potassium Bicarbonate
Potassium Chloride
Pyridoxine
Thiamine

Women's Health

Estradiol
Estrogens, Conjugated
Estrogens, Conjugated/Medroxyprogesterone Acetate
Estrogens, Esterified
Estrogens, Esterified/Methyltestosterone
Norethindrone Acetate/Ethinyl Estradiol

ALAMEDA Alliance FOR HEALTH

Up to 365-Day Supply on Contraceptives

Generic products are listed under **LABEL NAME** by their ingredient components.

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
ALYACEN 1/35	NORETHINDRONE & ETHINYL ESTRADIOL	1 MG-35MCG	TABLET
ALYACEN 7/7/7	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/0.75MG/1MG- 35MCG	TABLET
AMETHIA	LEVONORGESTREL & ETHINYL ESTRADIOL & ETHINYL STRADIOL	0.15MG-30MCG/10MCG 3 MONTH DOSE PACK	TABLET
AMETHIA LO	LEVONORGESTREL/ETHINYL ESTRADIOL & ETHINYL ESTRADIOL	0.10MG-20MCG/10MCG 3 MONTH DOSE PACK	TABLET
AMETHYST	ETHINYL ESTRADIOL & LEVONORGESTREL	90MCG-20MCG	TABLET
APRI	ETHINYL ESTRADIOL & DESOGESTREL	0.15MG-0.03MG	TABLET
BALZIVA	ETHINYL ESTRADIOL & NORETHINDRONE	0.4MG-35MCG	TABLET
BEYAZ	DROSPIRENONE/ ETHINYL ESTRADIOL/ LEVOMEFOLATE CALCIUM	3MG-0.02MG-0.45MG	TABLET
BRIELLYN	ETHINYL ESTRADIOL & NORETHINDRONE	0.4MG-35MCG	TABLET
CAMRESE	LEVONORGESTREL/ETHINYL ESTRADIOL & ETHINYL ESTRADIOL	0.15MG-30MCG 3 MONTH DOSE PACK	TABLET
CAMRESE LO	ETHINYL ESTRADIOL & LEVONORGESTREL	0.10MG-20MCG 3 MONTH DOSE PACK	TABLET
CONCEPTROL	NONOXYNOL 9	4%	VAGINAL GEL
CONDOMS	CONDOMS, LATEX, LUBRICATED	N/A	TOPICAL
DROSPIRENONE-ETHINYL ESTRADIOL	DROSPIRENONE-ETHINYL ESTRADIOL	3MG-0.03MG	TABLET
ELLA	ULIPRISTAL	30MG	TABLET
ENSKYCE	DESOGESTREL & ETHINYL ESTRADIOL	0.15MG-0.03MG	TABLET
GENERESS FE	NORETHINDRONE & ETHINYL ESTRADIOL & FERROUS FUMARATE	0.8MG-25MCG/75MG	TABLET
GIANVI	DROSPIRENONE & ETHINYL ESTRADIOL	3MG-20MCG	TABLET

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
GILDESS 1.5/30	NORETHINDRONE & ETHINYL ESTRADIOL	1.5MG-30MCG	TABLET
GILDESS 1/20	NORETHINDRONE & ETHINYL ESTRADIOL	1MG-20MCG	TABLET
GILDESS FE 1/20	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1MG-20MCG/75MG	TABLET
GILDESS FE 1.5/30	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1.5MG-30MCG/ 75MG	TABLET
GYNOL II	NONOXYNOL 9	3%	VAGINAL GEL
INTROVALE	LEVONORGESTREL & ETHINYL ESTRADIOL	0.15MG-30MCG	TABLET
JOLESSA	LEVONORGESTREL & ETHINYL ESTRADIOL	0.15MG-30MCG	TABLET
JUNEL 1.5/30	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL	1.5-0.03MG	TABLET
JUNEL 1/20	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL	1MG-20MCG	TABLET
JUNEL FE 1.5/30	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1.5-0.03MG	TABLET
JUNEL FE 1/20	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1MG-20MCG	TABLET
KARIVA	DESOGESTREL-ETHINYL ESTRADIOL	0.15MG/0.02MG-0.01MG	TABLET
LEVONORGESTREL-ETHINYL ESTRADIOL	LEVONORGESTREL-ETHINYL ESTRADIOL	0.1MG-20MCG (84)/10MCG (7) 3 MONTH PACK	TABLET
LEVONORGESTREL-ETHINYL ESTRADIOL	LEVONORGESTREL-ETHINYL ESTRADIOL	0.1MG-20MCG	TABLET
LEVONORGESTREL-ETHINYL ESTRADIOL	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-30MCG 3 MONTH PACK	TABLET
LEVONORGESTREL	LEVONORGESTREL	0.75 MG	TABLET
LEVONORGESTREL	LEVONORGESTREL	1.5 MG	TABLET
LO LOESTRIN FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-10MCG/75MG	TABLET
LOMEDIA 24 FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-20MCG/75MG	TABLET
LORYNA	DROSPIRENONE & ETHINYL ESTRADIOL	3MG-20MCG	TABLET
LOW-OGESTREL	NORGESTREL & ETHINYL ESTRADIOL	0.3MG-30MCG	TABLET
LUTERA	LEVONORGESTREL & ETHINYL ESTRADIOL	0.1MG-20MCG	TABLET
MARLISSA	LEVONORGESTREL & ETHINYL ESTRADIOL	0.15MG-30MCG	TABLET

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
MICROGESTIN 1.5/30	NORETHINDRONE & ETHINYL ESTRADIOL	1.5MG-30MCG	TABLET
MICROGESTIN 1/20	NORETHINDRONE & ETHINYL ESTRADIOL	1MG-20MCG	TABLET
MICROGESTIN FE 1.5/30	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1.5MG-30MCG/ 75MG	TABLET
MICROGESTIN FE 1/20	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-20MCG/75MG	TABLET
MINASTRIN 24 FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-20MCG/75MG	TABLET
NATAZIA	DIENOGEST & ESTRADIOL VALERATE	3MG/2MG-2MG/ 2MG-3MG-1MG	TABLET
NECON 0.5/35	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG-35MCG	TABLET
NECON 1/35	NORETHINDRONE & ETHINYL ESTRADIOL	1MG-35MCG	TABLET
NECON 1/50	NORETHINDRONE-MESTRANOL	1MG-50MCG	TABLET
NECON 10/11	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG-35MCG/ 1MG-35MCG	TABLET
NECON 7/7/7	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/0.75MG/1MG-35MCG	TABLET
NEXPLANON	ETONOGESTREL	68MG	SUBDERMAL
NORETHINDRONE	NORETHINDRONE	0.35MG	TABLET
NORGESTIMATE-ETHINYL ESTRADIOL	NORGESTIMATE-ETHINYL ESTRADIOL	0.25MG-35MCG	TABLET
NORGESTIMATE-ETHINYL ESTRADIOL	NORGESTIMATE-ETHINYL ESTRADIOL	0.18MG/0.215MG/ 0.25MG-25MCG	TABLET
NORGESTIMATE-ETHINYL ESTRADIOL	NORGESTIMATE-ETHINYL ESTRADIOL	0.18MG/0.215MG/ 0.25MG-35MCG	TABLET
NORINYL 1+50	NORETHINDRONE-MESTRANOL	1MG-50MCG	TABLET
NORTREL 1/35	NORETHINDRONE & ETHINYL ESTRADIOL	1 MG-35MCG	TABLET
NORTREL 7/7/7	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/0.75MG/ 1MG-35MCG	TABLET
NUVARING	ETONOGESTREL/ETHINYL ESTRADIOL	0.12MG-0.015MG	VAGINAL RING
OGESTREL	NORGESTREL & ETHINYL ESTRADIOL	0.5MG-50MCG	TABLET
PORTIA	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-0.03MG	TABLET
QUARTETTE	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-20MCG/ 0.15MG-25MCG 3 MONTH DOSE PACK	TABLET
QUASENSE	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-30MCG 3 MONTH DOSE PACK	TABLET
RECLIPSEN	DESOGESTREL-ETHINYL ESTRADIOL	0.15MG-0.03MG	TABLET

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
SAFYRAL	DROSPIRENONE-ETHINYL ESTRADIOL-LEVOMEFOLATE	3MG-0.03MG-0.451MG	TABLET
TILIA FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG/20MCG-30MCG-35MCG (75MG)	TABLET
TODAY CONTRACEPTIVE SPONGE	NONOXYNOL 9	1000MG	VAGINAL SPONGE
TRI-LEGEST FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG/20MCG-30MCG-35MCG (75MG)	TABLET
TRI-NORINYL	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/1MG/0.5MG-35MCG	TABLET
TRI-LO-SPRINTEC	NORGESTIMATE-ETHINYL ESTRADIOL	0.18MG/0.215MG/ 0.25MG-25MCG	TABLET
TRIVORA	LEVONORGESTREL/ETHINYL ESTRADIOL	0.05MG-0.075MG-0.125MG/ 0.03MG-0.04MG-0.03MG	TABLET
VAGINAL CONTRACEPTIVE FILM	NONOXYNOL 9	28%	VAGINAL FILM
VAGINAL CONTRACEPTIVE FOAM	NONOXYNOL 9	12.5%	VAGINAL FOAM
VELIVET TRIPHASIC REGIMEN	DESOGESTREL/ETHINYL ESTRADIOL	0.1MG-0.125MG-0.15MG/25MCG	TABLET
VESTURA	DROSPIRENONE-ETHINYL ESTRADIOL	3MG-20MCG	TABLET
XULANE	NORELGESTROMIN-ETHINYL ESTRADIOL	4.86MG-0.53MG	TRANSDERMAL PATCH
ZENCHENT FE	NORGESTIMATE-ETHINYL ESTRADIOL (FERROUS FUMARATE)	0.4MG-35MCG/75MG	TABLET
ZOVIA 1/35E	ETHYNODIOL DIACETATE-ETHINYL ESTRADIOL	1MG-35MCG	TABLET
ZOVIA 1/50E	ETHYNODIOL DIACETATE-ETHINYL ESTRADIOL	1 MG-50MCG	TABLET

If you need help reading this document or would like a different format, please call the Alliance Member Services Department at **1.510.747.4567**.

Si necesita ayuda para leer este documento, o le gustaría tenerlo en un formato diferente, llame al Departamento de Servicios al Miembro de Alliance al **1.510.747.4567**.

如果您需要幫助閱讀此文檔或需要不同的格式，請致電Aliiance計畫成員服務處，電話：**1.510.747.4567**。

Nếu quý vị cần giúp đỡ đọc tài liệu này hoặc muốn một định dạng khác, vui lòng gọi cho Ban Dịch vụ Hội viên Alliance theo số **1.510.747.4567**.

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Alameda Alliance for Health
1240 South Loop Road
Alameda, CA 94502

PHARMACY & THERAPEUTICS COMMITTEE

Record of Committee Meeting Minutes

Tuesday, December 17, 2024 | 5:00pm – 7:00pm

Status	Voting Committee Members	Organization	Initials	Officer / Notes
P	Donna Carey, MD	Chief Medical Officer-Alliance	DC	Chairman
P	Nora Tomassian, Pharm D	Interim Director of Pharmacy Services	NT	Co-Chair
P	Rahel Negash, Pharm D	Pharmacy Services Supervisor – Alliance	RN	
P	Aaron Basrai, PharmD	Haller's Pharmacy	AB	BOG
P	Paul Bayard, MD	La Clinica de la Raza (CHCN)	PB	
P	Ivan Lee, MD	Private Practice	IL	
P	Bao Dao, MD	Epic Care	BD	
P	Charles Raynor, PharmD	Alameda County Behavioral Health Dept.	CR	

P=Present; PH=Call-in; A=Absent; CMO = Chief Medical Officer; DOPS=Director of Pharmacy Services; BOG = Board of Governors Representative

Status	Regular Guests	Organization	Initials	Role / Department
P	Iryna Makukh	PerformRx	IM	Pharmacy Formulary Management.
P	Liza Rosendale	PerformRx	LR	Clinical Program Manager
P	Pat DeHoratius	PerformRx	PD	Manager Formulary/DUR
P	Barrie Cheung	PerformRx	BC	Regional Pharmacy Director
A	Ramon Tran Tang, PharmD	Alameda Alliance	RT	Clinical Pharmacist
P	Jefferey Bencini, Pharm D	Alameda Alliance	JB	Clinical Pharmacist
P	Timothy Tong, Pharm D	Alameda Alliance	TT	Clinical Pharmacist
A	Beverly Juan, MD	Alameda Alliance	BJ	Medical Director
A	Darryl Crowder	Alameda Alliance	DC	Provider Relations
P	Bibek Sandhu, PharmD, MBA	PillarRX	SB	Consulting Pharmacist

Other Guests	

Follow-up Items:

Clerk of the Committee: Benita Ochoa

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
I) Call to Order	D. Carey	• Agenda Overview	Call to order at: 6:03PM	
II) Informational Updates	D. Carey N. Tomassian	Informational Update • New P&T member: Dr. Charles Raynor – Alameda Behavioral Health, Director of Pharmacy Services DC: First, we have a new P&T member and so our new member was just voted in on Friday, first meeting today. So, Doctor Charles Raynor, who is the Alameda Behavioral Health Director of Pharmacy, is he on? CR: I've been with the county for 18 years. So glad to be here. Thank you for having me. • BOG vote – stipend. DC:. Moving on to our BOGI wanted to talk about our stipend. And we have decided that we're going to do a stipend that is going to be the same across the board. And so, we will be sending out an e-mail to all of the voting members about the stipend and the change of stipend and the date that it's effective. Just wanted to give you a heads up that you'll be getting some additional information about the stipend and the change in an e-mail from us very shortly. I want to verify exactly the date of effect, so that it will come into the e-mail. OK, any questions about that? All right, feel free to reach out if you do have a question. • D-SNP P&P updates DC: We are going to move into being a dual special needs population plan in just in January of 2026. We are making plans and moving forward. And so, as a result, we have a number of P&PS that are designated and for our decent population. So those updates were in the packet and there were some questions from the committee members that we can kind of talk about either here or in the E voting section. So, let's postpone questions, I guess in the E voting section. • Recruitment for permanent director of pharmacy services DC: We also have been really blessed to have Doctor Tomassian with us as our temporary director of pharmacy services for the alliance. So, we are recruiting for a permanent Director of Pharmacy Services, hopeful that that job description will be out within the next week or so and then we will be recruiting. So, if you have any knowledge of people who have health plan experience and are looking for a director role, we will have a role and position available.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		NT: OK, so I'm Nora Tomassian, for those of you who don't know me yet, I am the interim pharmacy director and I'm here for this P&T committee and probably for the next one. And then after that, you'll have your permanent pharmacy director. • Optum Pharmacy network inclusion starting 1/1/2025. NT: So, I was going to talk to you about the Optum pharmacy network inclusion. Starting 1/1/2025, we will use our PBM Perform RX's pharmacy network and they in turn partner with companies who manage pharmacy network. The new network will be Optum's network So, there's going to be more pharmacies that are going to be included and Optum has does a good job with contracting independent pharmacies, chain pharmacies and negotiating optimum prices for everyone. And so, there's going to be some optimization of the payments to the pharmacies and one of them being you know the flu shots are going to the payment back to the pharmacies are going to improve for the pharmacist. They will because it will allow them to account for the administration fee etcetera. There is one other thing I wanted to talk to you about, that's the electronic prescriptions on the provider portal. So, we've always allowed E prescribing. So Electronic Prescription submissions. We can receive prescriptions from providers in one of the three ways either fax PA or verbal PA like a telephonic PA or an electronic PA. Up until recently that electronic PA function wasn't really used that much by the network providers. So on 12/1, we change our system, our PA review system, to something called MHK, which is a more common in the industry. And with that we will change our Electronic Prescription system to the way we intake electronic prescriptions. So, we're going to be aligning a little bit more with Medical RX that uses a company called Covermymeds. So, there's going to be a link on the provider site where they can click on it, sign up or create an account and submit through Covermymeds electronic prior authorization. So, we only started rolling this out two weeks ago, 17 days ago and we already have many more. And now we're getting a lot more electronic prescriptions. It looks like providers like it and we're going to continue to monitor. I think it's probably easier for them to use it. They create an account, somebody from the office can enter the information and we'll be also monitoring providers who are not able to access the service. But I think so far so good. Does anyone have any questions about:. The pharmacy network and the electronic prior prescription prior authorization. PB: So, then whether it's Optum pharmacy or whatever the PPM is their network is we're still going to use Covermymeds as possible. NT: Yes,. So that has that's separate from the pharmacy network. The pharmacy network is a separate thing, but the electronic PA is something else. We used to have an electronic PA form on our website which required the physician to fill it out and submit it. It wasn't liked or used and now it is a link to another website. It's called Covermymeds and as you know, it's pretty user friendly. • Electronic prescriptions on provider portal update		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		NT: And, and I think our providers think the same way too, because we've gotten many, many more electronic prior authorizations than we had in the last six months. We had only one in the last six months, and we had, I don't know, about 50 or 60 in the last two weeks. PB: Yeah, no, I think we're very familiar with Covermymeds just because of medical RX. I mean that's pretty much the way even medical RX told you don't use us to use Medicare for my meds. So, it's certainly, I think that the communication about the need for the PA is variable. So, whether the pharmacy tells you APA is required or they electronically or whether they fax it to you, that's the big difference. And whether they are even willing to start APA for you varies from pharmacy to pharmacies. Some pharmacies won't do it. They just say it's not covered, you need to get a PA and let us know when you're done. So that behavior is quite variable amongst between the pharmacy chains and individual pharmacies. But regardless, you know, I'm going to appreciate the change to Covermymeds. So, it's more it's more unified approach. NT: I have a question derived from your comment. So, so if a pharmacy starts a prior authorization on cover my meds, how is the physician to know and provide the information? PB: So sometimes they've called us and sometimes they've faxed us to say that they've started it, and they give us the six use a six-letter key. I believe it's a 5 or 6 letter key and you use that to find the patient, although you also have, and you also get, I'll get an e-mail sometimes that will ping me. It'll give me the six letters. Unfortunately, it doesn't give me the name and date of birth, which you actually have to have to find it in, in your, in your system. So that piece sometimes doesn't work out. But the, the better pharmacies let us know that they, they start the PA and they let us know that they started it. So, then we can just use the key to get in. So, to get in and complete the request. Yes, yeah, cause they've done their part, which is great. And they, they include the, all the ID numbers, all that stuff. That's really something they can do. And then all I have to do is just the clinical piece. Oh yeah, that's the ideal state. AB: One other good thing. Covermymeds is like pretty much industry standard. Our pharmacies, like most pharmacies, the system automatically will generate the form and automatically fill out all the member ID information and stuff like that. And like what Doctor Bayard was saying is after we're done, we can go back and look at it and send, send a message to the provider through Covermymeds. So, they'll send it fax, it'll send an e-mail or whatever just like he gets. So we can do that too. But I have a question about like the PBM is, is Optum RX now going to be the PBM or is it going to be they're just the network that we're going to use the network? NT: Yeah, it is just the pharmacy network for Optum. Yeah, the PBM is still going to be perform RX. But if you're wondering if a physician is wondering what happened to the authorization before we have a chance to send a letter or before they receive the letter, they're able to go in and kind of find out whether		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		it's been approved or denied or it's if it's still processing or somebody's working on it. The only thing I'm not sure of, and maybe you can help with that, Can the pharmacy also check it? AB: It's not so clear. It really doesn't give us the status usually no. It's just kind of more like a hand off and we pass it off. Well, we, I'm in the LTC space, so we actually fill out the entire PA and we just submit it on the doctor's behalf. Cause in Medical we can't, but the other plans don't allow us. I'm not sure. Is that allowed for the alliance because I know the Alliance of pharmacies allowed to submit full PA as well, but those are options that you guys have to choose if it's available or not. Can the pharmacy submit, or can it have to be the provider if some plans allow it? NT: It has to be the provider. The pharmacy can start the prior authorization like Doctor Bayard was saying that the doctor has to complete it. The pharmacy cannot provide the whole thing. AB: But we can double check on this one with medical rules, check on the medical rules if we're allowed to. NT: Yeah, yeah. So I think we, we can clarify a couple of things here. One is that can we allow the pharmacies from A-Z to submit the authorization to Covermymeds based on the rules, DHCS rules #2 another answer we can bring back to the P&T is that once if the doctor submits it, the pharmacy starts, the doctor submits it, who then is authorized to go in there and kind of check the status. That could be a good, a good thing to know. PB: Yeah, I think I agree. The closing loop cannot. It doesn't always go quite like it should I, I should be getting a ping from covering my meds that our PA was approved, and I haven't been getting it. And I've told them I brought it to their attention and that's not, I'm not saying. So, I have to remember to check to see if it was approved. And then I don't know what happens at the pharmacy level. I tell the patient, look, the medicine's approved, go get it. You should be able to get it. Sometimes I've called the pharmacy and said, you know, it's approved, can you run it? But I don't know what the pharmacy That's something I never see is what's what, how the pharmacy finds out it was approved. Usually, it seems like they run it and it goes through and yeah, but someone has to tell them to run it and it's either me or the patient. AB: So, yeah, that's how it is. We have no idea sometimes. Nobody tells us. We just try it. We run a claim. BD: Now for the electronic PA that's sent to provider, is that only within for the provider who within Alameda network or does it for all providers? NT: So, the provider has to have a portal. So, it is on the provider portal in Alameda. So, the provider has to create Yeah. And so it is not on the public side, it is on the provider portal. **Questions:**		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		CR: Wondering with the change of pharmacy networks if you're losing any current pharmacies that are utilized NT: Yeah, my understanding is that we are gaining pharmacy, not losing pharmacies we can bring back this answer because we want to double check with the PBM.		
III) **Pharmacy Utilization Reports (Quarter 3, 2024)**	N. Tomassian	(All matters listed on the Consent Calendar are to be approved with one motion unless a member of the P&T Committee removes an item for separate action. Any consent calendar item for which separate action is requested shall be heard as the next Agenda item in closed session.)		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Top 50 Drugs by Cost (IHSS) NT: So, I am going to go over the top 50 drugs by cost for the third quarter 2024 and is it for IHSS or is it I was going to, I thought I was going to go over Medi-Cal, but. It's OK, I can do this. So yep, I think that's what's the area. Yeah. So, for the IHSS top 50 drugs, the first drug is going to be Biktarvy, which is a medication for HIV. And it is at #1, it was number one last quarter as well. There are 4. There are the claims have gone up by 4, but there's one less member. Ozempic is at #2, #7 and #8. These are the different strengths of Ozempic, 268 total claims for 117 members. There was an increase of 59 claims and 14 members for the fourth quarter. This is a trend that we're going to see increasing as more and more providers are ordering or comfortable ordering GLP-1 agonist. Zejula is down to #3 with three claims for one member. This is managed via Oral Injectable Oncology Medications [MRG]. Rezurock is up to #4 with three claims for one member and Paxlovid is up at #5 with 65 claims for 65 members. I have heard today the PBM say that that this is going to be picked up again by the state, I think, and so we may see a different number next time we're going to talk about Paxlovid. So the government used to pay for Paxlovid before they stopped paying for it. They wanted the plan to pay for it and now they changed their minds, they want it back. And that is the summary for the first several drugs, 10 drugs. PB: Can I ask a question? I think like this. I brought this up last time too, because the oral Rybelsus, the cost of it, if I'm reading it right is $1000 for a claim. And then on the Ozempic, which is the injectable version, looks like it's, I guess it's about the same $1000 for yeah, it's $1000 for. Is that $1000 for a month's supply? NT: It's, it's about on average GLP one receptor agonists are about $1000 per month's supply. The net net cost for the drug may be a little less for the injectables because we do have some, you know, some rebates. But the oral drug we do not have, even though it's an oral drug, it is, we're getting more utilization on it, but it's, it's still not as popular as Ozempic. And don't forget the Ozempic's once a week injections. Once the patients get the hang of the get over the, the fear of injecting themselves, I think they prefer having one shot once a week rather than daily dose. Next, next slide, please. - Top 50 Drugs by Cost (Medi-Cal) NT: OK. So now these are the medical top 50 drugs by cost for the third quarter 2024. So, we there they have been an increase in the cost of the drugs and it's a $3,000,000 increase. But it's, there's many more claims. Biktarvy again, it's a #1 spot. Ozempic also remains at #2 spot. Jardiance is picking up. It has more and more indications. So it is, it is at #3 and #4 each one is a different strength and each one, each strength is for a different indication.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		And Skyrizi, it's at #5 spot from is at #5 spot down from I think there's a typo in there, but there is a there's three more claims from since the last quarter. But as you can see, that there's some similarities with Biktarvy, Ozempic, Ozempic, Ozempic everywhere. Next slide please. Any questions about this slide? OK, OK. **<u>Questions:</u>** - Top 50 PA Reviewed Drugs by Volume (IHSS) - NT: Am I going over this slide as well? RN: Yes. NT: OK. So, the 50 prior authorization requests, now the number of the PA request is not that high, 179 for the top 50 requests. That's because the membership is also very low compared to Medi-Cal membership. Wegovy is #1 and #9 with 31 total requests and 10 approvals. The approval rate for Wegovy is low. Now as a reminder, Wegovy is a GLP-1 receptor agonist that is indicated for weight loss. It is not indicated for diabetes. Jardiance is at #2 and #8 with 19 requests and 14 approvals. So, for Jardiance we have 73% approval rate. Lidocaine patches are #3 with 14 requests and 3 approvals, the 21% approval rate because lidocaine can be requested for off label use that are not in the compendia. And we have Ozempic at #4 with 10 requests and 3 approvals and Vemlidy at #5 with 9 requests and 3 approvals. And those are the criteria for approval, trial and failure of entecavir for Hepatitis B. All right. - Top 50 PA Reviewed Drugs by Volume (Medi-Cal) NT: Now we're back to Medi-Cal with volume wise. Now instead of the cost, we're looking at what are being utilized in the Medi-Cal line of business. And for the top 50 drugs, there is a decrease in the number of claims. I looked at this a little bit in detail to find out why there is a decrease, and I realized this is for the third quarter of 2024. So it's summer months. Certain medications didn't show up in the summer months and I'm thinking more of inhaler drugs, etcetera don't show up in the summer months. That's why there is some decrease in the number of claims, but albuterol still at number one spot with 10,967 claims for 8957 members. Ibuprofen is at #2, aspirin was at #3 and now it's at #4 and fluticasone has dropped to #4 from the #2. There was a decrease from the last quarter and again it is not flu season in the summer. So, chances are asthma and flu probably not exacerbated as much in the summer months. There is some increase in the diclofenac gel. It has risen from the #7 spot to #5 spot. So, an increase of 612		

<table>
<tr><th>Agenda Item</th><th>Discussion Leader</th><th>Discussion Summary</th><th>Action</th><th>Notes</th></tr>
<tr><td></td><td></td><td>claims compared to last quarter. And of course, diclofenac gel is available over the counter as well. Think I am done. Any questions for what you saw? Right, thank you. Page 1.</td><td></td><td></td></tr>
<tr><td>IV) E-Voting Material/Consent Agenda</td><td>N. Tomassian
B. Ochoa</td><td>E-Voting Material/Consent Agenda
The following items have been sent to the voting committee for review via E-voting
TBD, PharmD, Senior Pharmacy Director – Alameda Alliance
Benita Ochoa, CPhT, Lead Pharmacy Technician – Alameda Alliance
(All matters listed on the Consent Calendar are to be approved with one motion unless a member of the P&T Committee removes an item for separate action. Any consent calendar item for which separate action is requested shall be heard as the next Agenda item in closed session.)
<table>
<tr><th>Monographs/Class Reviews</th><th>Changes</th></tr>
<tr><td>Blood Glucose Test Strips class review</td><td>• No changes</td></tr>
<tr><td>Calcium and Vitamin D class review</td><td>• No changes</td></tr>
<tr><td>Osteoporosis Agents class review</td><td>• No changes</td></tr>
<tr><td>Pulmonary Arterial Hypertension Agents class review</td><td>• No changes</td></tr>
<tr><td>Urinary Tract Antispasmodics class review</td><td>• No changes</td></tr>
<tr><th>Medication Request Guidelines</th><th>Changes</th></tr>
<tr><td>Oral and Injectable Oncology Medications</td><td>• No changes</td></tr>
<tr><td>Non-Formulary/Prior Authorization Required Medications</td><td>• No changes</td></tr>
<tr><td>Step Therapy Exception</td><td>• No changes</td></tr>
<tr><td>Prior Authorization Exception</td><td>• No changes</td></tr>
<tr><td>Urinary Incontinence Agents</td><td>• Naming change to reflect generic availability of Myrbetriq as mirabegron</td></tr>
<tr><td>Blood Glucose Testing Supplies</td><td>• No changes</td></tr>
<tr><td>Butorphanol (Stadol NS)</td><td>• No changes</td></tr>
<tr><td>Corticotropin</td><td>• Remove duplicate specialist prescriber restriction</td></tr>
</table></td><td>Approved via e-voting:
Yes: 6
No: 0
Abstained: 1</td><td></td></tr>
</table>

Agenda Item	Discussion Leader	Discussion Summary		Action	Notes
		Endari	• No changes		
		Diclofenac sodium (Solaraze) 3% gel	• No changes		
		Growth Hormone	• Remove discontinued drug SaizenPrep		
		Rapid-Acting Insulin	• No changes		
		Long-Acting Basal Insulin	• No changes		
		Isotretinoin capsules	• Remove discontinued drug Myorisan		
		Gonadotropin Releasing Hormone (GNRH) Agonists	• No changes		
		Self-administered Disease Modifying Therapies (DMTs) for Multiple Sclerosis	• No changes		
		dalfampridine (Ampyra)	• No changes		
		Ophthalmic Anti-Inflammatory Agents	• No changes		
		Fentanyl Citrate	• No changes		
		Proton Pump Inhibitors (PPIs)	• No changes		
		Ranolazine (Ranexa, Aspruzyo)	• No changes		
		Temazepam (Restoril)	• No changes		
		Testosterone Agents	• No changes		
		Thalomid (thalidomide)	• No changes		
		Topical Diclofenac	• No changes		
		Oral Anti-Fungals	• Change naming convention of Noxafil to reflect its generic availability		
		Gattex (teduglutide)	• No changes		
		Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors	• No changes		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes

Otezla (apremilast) for Behcet Disease	• No changes
Rayaldee (calcifediol ER)	• No changes
Korlym (mifepristone)	• No changes
Tetracycline Antibiotics	• No changes
Agents for graft versus host disease	• No changes
Janus Kinase Inhibitors for Nonsegmental Vitiligo	• No changes
Budesonide Nebulization Solution (Pulmicort Respules)	• No changes
Lodoco	• No changes
Sohonos	• No changes
Physician Administered Drug (PAD) Guidelines	**Changes**
Injectable/Specialty Medications	• No changes
Oral and Injectable Oncology Medications	• No changes
Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	• No changes
Viltepso	• No changes
Veopoz	• No changes
Lantidra	• No changes
Bleeding Disorder Products	• No changes
Interim Formulary Updates	
See p. 188 in packet	
Summary of Physician Administered Drug (PAD) Updates	
• None	
Pharmacy Policy & Procedure Updates	
• RX-004 Formulary Management	
D-SNP P&Ps (11, clean versions)	

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		• Medicare Medication Coverage under Part A, Part B or Part D • Claim Adjudication • Part D Coverage Determinations • Drug Utilization Management • Medicare Part D Daily Rejected Claims Review • Medicare Part D End Stage Renal Disease (ESRD) • Part D Appeals (Redeterminations) • Part D Formulary Development and Management • Pharmacy and Therapeutics (P&T) Committee Delegation Oversight and Monitoring • Prescription Drugs Event (PDE) Submission, Rejection, Monitoring and Resolution - Part D Transition Process **ED Oversight** • **None** **90 Day Maintenance List updates** • **NA** **P&T Meeting Minutes** • P&T Meeting Minutes Q3 September 24, 2024		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes

Interim Formulary Changes

These changes have been made to the Alliance's formulary recently. The changes were necessary to enhance the formulary.

Medication	Formulary Change
Zepbound Subcutaneous Solution 2.5 MG/0.5ML	NF to F-PA
Zepbound Subcutaneous Solution 5 MG/0.5ML	NF to F-PA
Otezla Oral Tablet 20 MG	NF to F-PA
Otezla Oral Tablet Therapy Pack 4 x 10 & 51 x20 MG	NF to F-PA
Novavax COVID-19 Vaccine Intramuscular Suspension Prefilled Syringe 5 MCG/0.5ML	NF to F
Comirnaty Intramuscular Suspension 30 MCG/0.3ML	F to NF
Comirnaty Intramuscular Suspension Prefilled Syringe 30 MCG/0.3ML	F to NF
Novavax COVID-19 Vaccine Intramuscular Suspension 5 MCG/0.5ML	F to NF
Spikevax Intramuscular Suspension 50 MCG/0.5ML	F to NF
Spikevax Intramuscular Suspension Prefilled Syringe 50 MCG/0.5ML	NF to F
Comirnaty Intramuscular Suspension Prefilled Syringe 30 MCG/0.3ML	NF to F

Agenda Item	Discussion Leader	Discussion Summary		Action	Notes
		Potassium Chloride ER Oral Tablet Extended Release 15 MEQ	NF to F		
		Dasatinib Oral Tablet 20 MG	NF to F-PA		
		Dasatinib Oral Tablet 50 MG	NF to F-PA		
		Dasatinib Oral Tablet 70 MG	NF to F-PA		
		Dasatinib Oral Tablet 100 MG	NF to F-PA		
		Dasatinib Oral Tablet 80 MG	NF to F-PA		
		Dasatinib Oral Tablet 140 MG	NF to F-PA		
		OXcarbazepine ER Oral Tablet Extended Release 24 Hour 300 MG	NF to F		
		OXcarbazepine ER Oral Tablet Extended Release 24 Hour 600 MG	NF to F		
		Sprycel Oral Tablet 20 mg	F-PA to NF		
		Sprycel Oral Tablet 50 mg	F-PA to NF		
		Sprycel Oral Tablet 70 mg	F-PA to NF		
		Sprycel Oral Tablet 100 mg	F-PA to NF		
		Sprycel Oral Tablet 80 mg	F-PA to NF		
		Sprycel Oral Tablet 140 mg	F-PA to NF		
		Oxtellar XR Oral Tablet Extended Release 24 Hour 300 MG	F to NF		
		Oxtellar XR Oral Tablet Extended Release 24 Hour 600 MG	F to NF		

<table>
<tr><th>Agenda Item</th><th>Discussion Leader</th><th>Discussion Summary</th><th>Action</th><th>Notes</th></tr>
<tr><td></td><td></td><td>The following changes have been made to the Alliance ‘s PAD PA list recently. These changes were necessary to evaluate medical necessity based on medical guidelines, utilization, and other information.
<u>Physician Administered Drug (PAD) Prior authorization (PA) list Updates</u>

<table><tr><th>HCPCS Code</th><th>HCPCS Description</th><th>Action</th></tr><tr><td><u>NA</u></td><td><u>NA</u></td><td><u>NA</u></td></tr></table></td><td></td><td></td></tr>
<tr><td>V) New Business</td><td>Iryna Makukh</td><td><u>New MRG</u>

<u>IM</u>- Good evening, everybody

- So, our first new policy is for Ohtuvayre, and it was recently approved.

<u>Ohtuvayre</u>

- It's the first phosphodiesterase 3 and phosphodiesterase 4 inhibitor indicated for the maintenance treatment of COPD in adult patients
- Inhibition of PD3 and PD4 results in accumulation of intracellular levels of cyclic AMP and cyclic GMP and this leads to various downstream signaling effects and results in bronchodilation and reduction of inflammation in the Airways.
- Inhibition of PD3 and PD4 results in accumulation of intracellular levels of cyclic AMP and cyclic GMP and this leads to various downstream signaling effects and results in bronchodilation and reduction of inflammation in the Airways.
- Ohtuvayre is an inhaled drug is inhaled through a standard jet nebulizer twice daily
- Guidelines have not been updated since the approval of Ohtuvayre
- Mainstream treatment options include short acting beta agonists, short acting acting muscarinic antagonists, long-acting beta agonists and long-acting anti muscarinic antagonists.
- Inhaled corticosteroids products are also part of therapy, but standard of care maintenance therapy for COPD is typically dual long-acting anti muscarinic antagonists with long-acting beta agonists
- So, LAMA/ LABA or triple therapy with LAMA/ LABA and inhaled corticosteroids
- So Ohtuvayre will likely be used as add on therapy in patients who are not adequately controlled with one or more guideline directed COPD maintenance therapies.
- Ohtuvayre was approved based on phase three enhanced trials where patients were randomized to Ohtuvayre twice daily or placebo over 24 weeks.
- And these trials demonstrated Ohtuvayre’ s clinical benefits both as standalone treatment and when used alongside other maintenance drugs for COPD.
- Patients receiving treatment with Ohtuvayre demonstrated a significant increase in the primary endpoint of change from baseline in average FEV 1 area under the curb post dose at 12 weeks compared with placebo.
- The price is $2949 per month based on WAC.</td><td>Move to approve:
1st: DB
2nd:PB</td><td></td></tr>
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Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- And moving on to the criteria, patients with primary diagnosis of asthma will be excluded for prescribing information and as they were and as they were excluded from clinical trials, and it's not indicated for asthma. - And another exclusion is concomitant use of oral PD4 inhibitors like roflumilast, which is also APD 4 inhibitor approved for COPD, since this will be a duplication of therapy - For age restriction, Ohtuvayre was approved in adults. - So, we boarded it as according to packet insert and the for coverage duration, the initial request will be approved for six months and this matches enhanced clinical trials which were of 24 weeks duration and reauthorization requests for up to a 12-month duration. - For the initial authorization, we are asking for the diagnosis of COPD along with documentation of pre and post albuterol FEV1/ FVC ratio of less than 0.7, which is a standard to confirm the diagnosis of COPD. - We're asking for documentation of a score of at least 2 on the MMRC dysplasia scale or a score of at least 10 on the COPD assessment test. - And both these assessment tests are used in practice to assess severity, disease severity and help guide treatment recommendation. - MMRC score matches the exclusion criteria in the trials, and the CAT score matches the guideline for the indication of maintenance therapy - Additionally, we are asking of maintenance triple therapy consisting of acting muscarinic antagonist LAMA and long acting beta2 agonist LABA, and inhaled corticosteroid, or documented medical reason why the member is unable to use these therapies - And again, this is per standard of care therapy for COPD maintenance per guidelines - Also, we require that the drug is being prescribed at an FDA approved dose - And for the authorization we're looking for clinical benefit from the medication and that the drug is being prescribed at an FDA approved dose - And that's all for this criteria. - Any questions? **<u>Nemluvio</u>** - We can move on to the next page, Page 325. - And this is the new policy for Nemluvio - Nemluvio is an interluking 31 receptor antagonist indicated for the treatment of adults with prurigo nodularis. - Prurigo nodularis is considered a rare skin condition. - Estimates suggest that it may affect 72 to 87 people per 100,000 worldwide and higher rates observed in older adults and those with underlying conditions like atopic dermatitis or chronic kidney disease - It is estimated that there are up to 181,000 patients with PM in the US. - The exact cause is unknown, but neural, neuropsychological, and immunologic processes are thought to play a role in its pathophysiology.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Prurigo nodularis is characterized by intensely itchy, symmetrically distributed nodules on the arms, legs, and trunk, and they can have significant negative impact on sleep, mental health, and quality of life. - Prior to Nemluvio, only Dupixent was FDA approved for Perigo nodularis and that was back in September 2022. - Most therapies commonly used are off label and include topical and oral portable steroids, topical carcinogen inhibitors and vitamin D analogs - Nemluvio is the first FDA approved drug that targets interleukin 31 and the second FDA approved drug for the treatment of Prurigo nodularis behind Dupixent - And dosing is based on weight. - The price is $4240 per month for maintenance dose for a 70-kilogram adult and that's based on that. - The approval for Nemluvio was supported by results from Phase 3, Olympia One and Olympia 2 trials. - The core primary endpoints were met in both trials - In Olympia One and Olympia, 256% and 49% of Nemluvio treated patients, respectively, achieved at least a four-point reduction in each intensity as measured by the Peak Pruritus Numeric Rating Scale by week 16 and as compared to only 16% of patients who received placebo. - Investigators global assessment success, defined as clear or almost clear skin, was reached by 26% and 38% of Nemluvio treated patients in Olympia One and Olympia 2 respectively, also by week 16 and there was versus 7% and 11% of patients in the placebo groups - As for the criteria, patient must be 18 years of age or older per indication. - Prescriber must be an allergist, immunologist or dermatologist, since PN is a rare condition that needs to be managed by a specialist - The primary endpoint was measured at 16 weeks, but since it's a chronic condition and not to be too restrictive, 6 months for initial approval should be feasible and reauthorization request for a 12-month duration. - For initial authorization we require, diagnosis of PM is based on clinical examination and core findings include pruritus lasting at least six weeks and this was also in trials inclusion criteria. Also, member has to have at least 20 lesions, 20 PM lesions. - Presence of firm nodular lesions is part of core symptoms for diagnosis - In trials, patients had at least 20 lesions on the entire body - Also, we asked for documentation of patient’s weight since dosing is based on weight and that the member has at least two-week trial of one of the following moderate potency or higher topical corticosteroid or topical carcinoid inhibitor. - Patients with a diagnosis of severe PN should already have used a topical steroid or TCI which aligns with both guidelines and clinical practice - For re-authorization, we ask for documentation or provider at the station of positive clinical response documentation of patients wait and that medication is prescribed at an FDA approved dose and this criteria is pretty straightforward. - Any questions on this one?		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- OK **<u>Yorvipath</u>** - We can move on to our third criteria - We have criteria for Yoryipath, and it was recently approved. - It's a parathyroid hormone analogue - It's indicated for the treatment of hypoparathyroidism in adults or HP. - HP is a rare endocrine disorder characterized by insufficient levels of PTH resulting in low calcium and elevated phosphate levels in the blood and can cause a range of symptoms depending on the extent of the deficiency. - From potentially life-threatening complications such as arrhythmias and laryngospasms to manifestations such as cataracts, dental abnormalities, and dermatologic manifestations, many of these symptoms can be resolved through treatment of the hypocalcemia. - There are numerous etiologists of age of HP including post-surgical, autoimmune and generic disorders. - Diagnosis is made through laboratory testing of calcium and PTH levels, which for patients with HP will show hypocalcemia, low PTH, hyperphosphatemia, and normal magnesium. - Damage to the parathyroid gland during surgery most common cause of HP and accounts for over 80 percent of cases, however, the surgical HP does not always translate to chronic HP and is often only acute, lasting 4 days two months. - While there is no Standard Time frame after which HP is considered chronic, guidelines generally give a range of at least 6 to 12 months, and the incidence of chronic HP in the United States is approximately 70 to 90,000 individuals, so pretty rare. - Treatment of HP typically involves oral calcium and vitamin D supplementation - PTH replacements therapy is often added for patients who are unable to maintain stable serum and urinary calcium levels with calcium and vitamin D supplementation alone. - The only other PTH analog approved for HP was net Para - However, it was recalled in 2019, and manufacturing will be discontinued completely by the end of 2024. - Yoryipath is a prodrug of PTH, and it's self-administered once daily via subcutaneous injection. - The price is $21,924.00 per month based on. - Going into criteria, patient must be 18 years of age or older per indication - It's only for adults - Prescriber must be an endocrinologist or in consultation with an endocrinologist. - So, this condition should be managed by or in consultation with a specialist. - Since this is a rare disease, members with acute post-surgical HP or those who are at increased risk of osteosarcoma would be excluded and this is per labeled limitations of use - A drug was not studied in the acute post-surgical HP and per Pi warnings and precautions of increased risk of osteosarcoma. - For coverage duration, the initial request will be approved for a six-month duration.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Pivotal trial endpoints for safety and efficacy we're at 26 weeks and reauthorization request is for 12-month duration. - Since this is a chronic condition, for initial authorization we asked for confirmed diagnosis of chronic HP or put surgical, autoimmune, genetic or idiopathic origins for at least six months. - And here we are trying to ensure that the patient is truly in the realm of chronic HP and not in an acute setting - There is no really consensus on the definition of chronic HP, but most recent guidelines provide a range of 6 to 12 months and also trials were 26 weeks long. - So, six months seems appropriate for confirmation that the HP has been in chronic and not acute - Also, we ask for provider at the station that patient is currently receiving conventional therapy including active vitamin D and elemental calcium and that patient's disease cannot be adequately controlled on this conventional therapy alone. - Also, we ask for provider at the station that patient is currently receiving conventional therapy including active vitamin D and elemental calcium and that patient's disease cannot be adequately controlled on this conventional therapy alone. - In trials, your report was only evaluated in adults with inadequately controlled disease or on conventional therapy as defined by elemental calcium and vitamin D. - Additionally, we require current labs for the following albumin corrected. - Serum calcium must be at or above 7.8mg per deciliter - To start therapy and serum vitamin D level must be at or about 20 nanograms per milliliter to start therapy - Since your path is dosed and titrated based on lab values, this specific lab values are coming from Pi limitations of use for your V path. - And lastly for initial authorization medication should be prescribed at an FDA approved dose. - And for reauthorization, we want to ensure that there is documentation of a recent albumin corrected serum calcium in the lower half of the normal reference range or just below the normal reference range. - This is from labeling as well. - And albumin corrected calcium was in the primary endpoint of pivotal trial and it's indicative of positive clinical benefit. - And the second bullet point in the reauthorization is having one of the following patient no longer requires active vitamin D or therapeutic doses of calcium. - Ideally, they will be able to use just your repath and don't have to continue the conventional therapy chronically or patient has had a significant reduction in required dosages of active vitamin D or therapeutic doses of calcium and is still actively titrating doses of Yoryipath. - This would also show clinical benefit - And lastly, medication should be prescribed at an FDA approved dose and that's all for this criteria for Yoryipath. - Any questions?		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		<u>Ileal bile acid transporter inhibitors (IBATs)</u> - OK, Next, we have a policy for filial bile acid transporter inhibitors page 327. - So, this is the new policy for Bylvay and Livmarli. - Bylvay is an ILIO bile acid transporter inhibitor indicated for the treatment of pruritus in patients three months of age and older with progressive familial intrahepatic Cholestasis or PFIC, and it's also indicated for the treatment of cholestatic pruritus in patients 12 months of age and older with allergy L syndrome. - Livmarli is also an IOL bile acid transport inhibitor, also indicated for the treatment of cholestatic pruritus, but in patients three months of age and older with allergy L syndrome and for treatment of cholestatic pruritus in patients 12 months of age and older with PFIC. - Both drugs have limitation of use that they are not recommended in a subgroup of PFIC type 2 patients with specific ABCB 11 variants resulting in non-functional or complete absence of the bile salt export pump protein. - Both Bylvay and with Livmarli are reversible inhibitors and they decrease the reabsorption of bile acids, primarily the salt forms from the terminal ilium. - Just a little background on the on these rare disease states - PFIC is a rare pediatric generic disorder which is characterized by defective secretion of bile acids or other components of bile from the liver. - Exact prevalence is unknown, but estimated between one in 50,000 and one in 100,000 individuals - These young patients in cure growth failure, fast soluble vitamins, malabsorption, progressive liver disease and have increased risk for hepatocellular carcinoma. - The condition is progressive and ultimately leads to the need for liver transplant in most patients - One of the hallmark features of the disease affecting patients' quality of life is severe intractable pruritus. - Prior to the approval of these new therapies, there were no existing drugs for this disease state. - Initial therapy for patients with all forms of PFIC is Ursodiol, which may improve liver function and pruritus in some patients - Other treatments, such as surgical intervention to divert bile flow, may improve pruritus and slow disease progression, and a liver transplant is the only known curative treatment. - Alagille syndrome is also a rare inherited disorder - It can affect multiple organ systems but most often leads to fewer interlobular bile ducts and that results in reduced bile flow or Cholestasis and subsequent liver damage. - ALGS or ALGL syndrome occurs in approximately 1 in 30,000 to one in 45,000 individuals and conventional treatments for ALGS may include also ursodiol to increase bile flow and other drugs that may reduce itching like cholestyramine, diphenhedronine or sertral. - So, pruritus is a common symptom in patients with both PFIC and Alagille syndrome. - Liymarli is available as an oral solution and price of Livmarli for PFIC is $226,380.00 per month and that's based on a maximum dose of 38 milligrams per day. - And for Alagille, price is around $170,000 per month and the Max dose for that indication is 28.5 milligrams per day.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Bylvay is available as oral pallets and capsules and - Price of Bylvay is $217,197.00 per month at Max dose of 6 milligrams per day and that's for PFIC and for Alagille it would be around $130,000 per month for like a 30-kilogram child. - So now let's look into criteria. - We have age restrictions that are according to package insert since different indications of different aging. - Also, agents should be prescribed by or in consultation with a specialist since there are these are rare diseases and for coverage duration initial approval for six months. - Bylvay efficacy was evaluated in trials for both conditions at 24 weeks and Liymarli efficacy was evaluated at 22 weeks for eligible and 26 weeks for PFIC and for continuation of therapy. - We have 12 months duration for approval - For initial authorization, we're asking for PFIC diagnosis with specific PFIC subtypes that were studied for efficacy in trials - We're asking for documentation that patient does not have that ABCB 11 variant that results in non-functional or complete absence of bile salt export pump protein, and this is per limitations of use in the Pi for both agents. - We're looking for history of moderate too very severe pruritus based on a patient population in trials as well as documentation of patients weight since dosing is based on weight. - Also asking for prescriber at the station to monitor liver, liver function tests and fat-soluble vitamin levels during treatment and this is per warnings and precautions in the prescribing information per Pi. - For persistent or current liver test abnormalities relative to baseline, treatment should be discontinued. - Also, for fat soluble vitamin deficiencies, if deficiency persists or worsens despite supplementation, treatment should be discontinued as well. - Next, we asking for baseline theorem, bile acid level and documentation of trial and failure or contraindication to at least one of the following or Orsodial or cholestyramine or Clozabila - Orsodial is usually used as first line standards of care treatment just call erratic stimulates bile flow from the liver, alleviates pruritus symptoms and replaces toxic bile acids call Zalim or cholestyramine bile acid sequestrants and they are another treatment option. - And lastly, the dose should be within FDA approved guidelines. - And for the second indication for initial authorization for Alagille syndrome, we require diagnosis of Alagille syndrome. - Documented history of moderate to varicerar pruritus - This is based on patient population and trials. - Again, documentation of trial and failure or medical reason why the member is unable to use all of the following Orsodial, cholestyramine or Kozela as in the previous indication and rifampin. - Rifampin is usually added as an adjunct to Orsodial in patients with Alagille syndrome, that's if the pruritus still remains problematic - And we also asked for prescriber at the station that the member has colostasis since approximately 10 to 15% of patients with Alagille do not have colostasis and therefore would not benefit from treatment		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- And that's for the same reasons Pi warnings of hepatotoxicity and bile acid depletion leading to deficiency of fat-soluble vitamins. - Lastly, the prescribed dose should be within FDA approved dosing guidelines - And for reauthorization we are required documentation of clinical benefit indicating each of the following and improvement in pruritus and reduction in serum bile acid level from baseline. - Both of these were primary and secondary endpoints in trials - Also, we asked for documentation of patients weight and prescriber attestation to monitor living function tests and FSV levels or fat soluble vitamin levels again because of hepatotoxicity risk and deficiency of that soluble vitamins. - Additionally, a prescriber attestation is required that patients has had no evidence of hepatic decompensation as per Pi drugs should be permanently discontinued if hepatic decompensation occurs. - It's a counter indication with Pi. - And lastly, we require FDA approved dosing, - And this is it for this criteria. - Any questions? **IML-**I have a question **IML-**I was wondering why the requirement for PFIC says use of one of them or and the other one says use of all of them. **IM-**We decided to go a little more restrictive on Alagille syndrome since it's more prevalent like a lot more prevalent than the PFIC and also there are more options here for Alagille syndrome. Rifampin is often added. That's why we decided just to be more a little more restrictive with this indication and require all three. **IML**-I'm not just wondering if just to be consistent you know like the other one that require the two or something. **IM**-Yeah, the PFIC requires 1, **IML**- Just the one, yeah, yeah and this require all three decision for one versus 2. **IM-**I'm just wondering, yeah, just I, think the reason was just because Alagille syndrome is, is has more prevalence than the PFIC. But we could we can modify this and like to be consistent or so Orsodial would definitely be the first line, and for PFIC we can also say to use two of the following, and then for Alagille, we can also say to use two of these three, if that would make more sense to you. **IML-**Yeah, that would yeah, that would make more sense. **IM-**OK, OK, then we can we can modify that,we'll do that Any other questions on this one? OK.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		New PAD - So, the next policy, the next we're moving on to the PAD criteria, new PAD criteria's and that's on page 329. **Kisunla** - So, this is the first new PAD policy we have here for Kisunla and it's a recently approved treatment for Alzheimer's disease. - Treatment with Kisunla should be initiated in patients with mild cognitive impairment or mild dementia stage of the disease. - And this is the population in which treatment was initiated in clinical trials - The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. - Alzheimer's disease is the most common form of dementia in older adults, accounting for 60 to 80% of cases in the US. - In 2011, there were approximately 4.5 million prevalent cases of clinical AD in persons over 65 years old and the prevalence is expected to more than triple by the year 2050 to 13.8 million cases in the USAD is hypothesized to be caused in part by amyloid beta deposition in the brain leading to synaptic dysfunction and neurodegeneration - Kisunla is an amyloid beta directed antibody indicated for the treatment of adults with early symptomatic AD. - The approved indication includes patients with AD who have mild cognitive impairment or mild dimension stages of AD with confirmed amyloid pathology. - Kisunla is administered every four weeks as an IV infusion and what's different about this new therapy is that healthcare provider can consider stopping dosing with Kisunla based on reduction of amyloid plaques to minimal levels on amyloid PT imaging. - So this is the first and only approved amyloid plaque targeting therapy that uses a limited duration treatment option based on amyloid plaque removal. - Kisunla was approved based on results from phase three placebo-controlled, double-blind Trail Trailblazer ALZ 2 study, where patients were randomized to receive Kisunla every four weeks or placebo for a total of up to 72 weeks. - The treatment was switched to placebo based on amyloid PT levels measured at week 24, week 52, and week 76. - Patients treated with Kisunla who were less advanced in their disease showed a significant slowing of decline of 35% compared with placebo on the Integrated Alzheimer's Disease Rating Scale. - In particular, their preclinical AD price is $2780 per month for maintenance dosing. - Going into criteria, patients should be 60 to 85 years old and this is for clinical trials exclusion criteria. - Inclusion criteria prescriber must be a neurologist. - This condition should be managed by a specialist as per exclusion criteria.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- As per exclusion criteria, patients with moderate to severe AD would be excluded since Kisunla is only indicated for mild stage of the disease. - Additionally, patients with neurodegenerative disease caused by a condition other than AD would be excluded since the drugs was only studied in patients with mild AD. - For initial authorization, the request will be approved for six months. - Efficacy was assessed after 18 months - However, patients amyloid plaque levels were assessed at 24 weeks in the study and six months initial authorization is consistent with what we have with other amyloid beta directed treatments for AD to assess clinical benefit - For reauthorization, the request will be approved for six months also, patients in the study were evaluated for discontinuation at six and then 12 months - So, it's a good benchmark to evaluate patients and determine if they need to continue therapy. - For initial authorization, we asked for diagnosis of mild cognitive impairment caused by AD or mild AD dementia consistent with stage 3 or 4 Alzheimer's disease as evidenced by at least one of the following scales. - Stage 3 or 4 is part of the indication, and the trial had MMSE score requirement between 20 and 28 and the other two scales are also routinely used in practice, so that's why we included them. - Next, the request is for FDA approved dose - Additionally, we ask for documentation of both of the following recent positive results for the presence of beta amyloid plaques on PT scan - Here we are requiring confirmation of beta amyloid plaques since this drug works by removing them and we also require recent baseline MRI scan. - This is per package insert that requires a baseline MRI scan prior to starting the treatment and this is due to the risk of amyloid related imaging abnormalities or area which is a black box warning for the drug. - Next, we want to ensure that physician has assessed baseline disease severity utilizing an objective measuring tool and these scales were in endpoints used in clinical trials. - Some of these are newer, but CDSB has been used for a really long time and the other measures are also routinely used in clinical practice. - We also require that the patient has no recent history of stroke, seizures or TIA or findings on neuroimaging that indicate an increased risk for intracerebral hemorrhage - These patients were excluded from the trials due to the risk or amyloid relating imaging abnormalities that can lead to stroke, seizure or TIA - For reauthorization, we ask that the require the request is for the FDA approved dose that patient continues to have a diagnosis of mild commutative impairment caused by AD or mild AD dementia consistent with stage 3 or 4 as evidenced by at least one of the following scales - Here we are just confirming that the patient is still in the FDA approved stage of Alzheimer's disease and have not progressed to a moderate or severe stage where the drug is not indicated - Also, we're requiring a provider at the station of safety monitoring and management of amyloid related imaging abnormalities area and intracerebral hemorrhage as this is recommended for prescribing information - Here we just want to ensure that provider is following a safety monitoring protocols.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Additionally, we're asking for documentation that the member has experienced clinical benefit from the medication such as stabilization or decreased rate of decline in symptoms from baseline and that the patient has no recent history of stroke, seizures or TIA - And again, this is because patients were excluded from trial due to the risk of area and that can lead to stroke, seizures or TIA. - And that's that's all I have for Kisunla - Any questions on this criteria? **<u>Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) Agents</u>** - OK, we can move on to the next page and we have a second new PAD criteria on page 331. - And this new criteria was this is for chronic inflammatory demyelinated demyelinating polyneuropathy agents or CIDP agents - This new criteria was prompted by the recent approval of Medgar Hytrulo for CIDP. - It's the first targeted treatment for CIDP - Just some background on the disease state. - CIDP is a rare neurologic disorder that includes inflammation of nerve roots, peripheral nerves and the myelin sheath. - They start to get destroyed and that damage to myelin sheath blocks nerve signals to the loss of nerve fibers, this result in weakness, paralysis, more dysfunction and sensory disturbances, so it's a fairly significant and debilitating disease - It can affect any age group, the onset can begin at any decade of life but is most common at the age of 50 and males are twice more likely to get it than females. - It is rare, the prevalence is around 5 cases per 100,000 individuals worldwide - Guidelines recommend treatment for CIDP include corticosteroids, IVIG or subcutaneous immune globulin as first line. - They can also recommend a plasma exchange, but that would be after trial and failure of IVIG or corticosteroids. - We've got high Trulla is the first targeted treatment for CIDP - It is administered as a 30 to 92nd subcutaneous injection once weekly. - For the policy, the prescriber restriction includes that prescriber must be a neurologist or neuromuscular specialist and this is due to a very specific nature of this rare disease. - As far as coverage duration, the initial request will be approved for three months and that was the primary endpoint at pivotal trial to show efficacy and safety for this drug. - For continuation, it will be for 12 months since this is a chronic disease. - For the initial authorization, we required diagnosis of CIDP confirmed by electrodiagnostic test results. - And this is important since CIDP may present very similarly to other numerous disorders and it's pretty challenging to diagnose. - So, electrodiagnostic tests should be performed in all patients with suspected CIDP as this is a critical component of the evaluation. - Next condition is that the patient has progressive or lapsing remitting disease course for at least two months and this is per key trial inclusion criteria		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Additionally, patient has an inadequate response, significant intolerance or contraindication to IVIG or subcutaneous immunoglobulin. - Since these are first line therapies - Corticosteroids and plasma exchange can also be tried as first line therapy. - However, it is important to note that over 25% of patients failed first line treatment for CIDP. - And as we've got Hydrola is significantly more costly, three times more costly than IVIG or SCIG, we thought it is appropriate to manage it in terms of trial and failure of immunoglobulin response. - And lastly, medication is prescribed at an FDA approved dose and under reauthorization we have the usual documentation or provider at a station of significant clinical improvement in neurologic symptoms or stabilization of the disease and that the medication is prescribed at an FDA approved dose. - And this is all for the CIDP agents' policy. - Any questions on this one? **IM-** OK, so these were all new policies, new MRG and new PAD policies. I don't know if you want to vote or should we go to the class review.		
VI) Class Reviews, Monographs, and Recommendations-	Iryna Makukh	1. **Topical Agents for Actinic Keratosis Class Review** - We can do the review of topical agents for actinic keratosis class review - And actinic keratosis is a chronic skin condition in which keratinocyte neoplasm or actinic keratosis as they call them a case their cure on skin and due to a long-term exposure to ultraviolet radiation. - A case most often present as red inflamed scaly macules, papules or plaques and are generally diagnosed based on appearance alone. - In case routinely treated due to the risk for progression to keratinocyte carcinomas, including squamous cell carcinomas. - And let's look at utilization on page 345 - Here we had seven claims for six members for total cost of $249.42 and an average cost per claim of $35.63. - The most highly utilized medication was Imicrimov 5% topical cream packet with six claims followed by Diclofenac 3% gel with one claim. - There were no prior authorization requests and according to published guidelines for patients with cure or as isolated a case lesion directed treatment with cryosurgery is recommended - But for patients with multiple AK\ still directed treatment with topical medications approved and also photodynamic therapy may be used for AK. - So topical medications improved for AK include the antineoplastics for uracil and turbinebulin, the immunomodulator and meclomod and the non steroidal anti-inflammatory diclofenac.	Move to approve: 1st: BD 2nd: AB	

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Our current guidelines support the use of flour, uracil, imaquimod or terdenebilin for first line topical therapy and diclofenac is recommended as a second line option and that's based on lower quality of evidence. - Alameda has flour uracil cream topical solution and imacromod 5% on formulary. - They are generic, most cost effective first line products. - Most of the utilization was with imacromod 5% topical cream. - Alameda has also diclofenac 3% topical gel on formulary and there was one claim in the last quarter. - So here we recommend changing diclofenac to FPA status to formulary with prior authorization status since diclofenac is second line treatment option and it's more costly and we do have A PA criteria for it on the next page 346. - So, the PA criteria requires trial and failure of either Florauracil or imigramod which are first line therapies and are more cost effective. - And these were all recommendations and all changes for this drug class - Any questions?		
		Cobenfy Monograph **New MRG: Cobenfy** - We have a monograph for Cobenfy on page 348. - Cobenfy was recently approved for the treatment of schizophrenia in adults. - Schizophrenia is the most common psychotic disease with an estimated prevalence ranging from 0.6 to 1.9% in the US and 0.3 to 0.7% globally - About 100,000 people in the US are diagnosed with schizophrenia yearly and it is estimated there are around 2.6 million patients in the US. - Standard of care as you know are antipsychotics targeting dopamine receptors and modulating serotonin levels. - Antipsychotics are available in two main classes, first generation typical and 2nd generation at typicals. - While current treatments can be effective in managing symptoms for some patients, approximately 30% of people do not respond to therapy, with an additional 50% experiencing only a partial improvement in symptoms or unacceptable side effects. - So Kubuntu represents the first new mechanism of action to treat schizophrenia in more than 30 years. - It's a combination of zanomolin, which is the normal mechanism of action agent - It is a mascarinic agonist, and trospium chloride is a mascarinic antagonist. - So the mechanism of action of the novel's anomaly is due to its activity agonist activity at M1 and M4 mascarinic acetylcholine receptors in the central nervous system, while trospium antagonizes		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		the mascarinic receptors primarily in the peripheral tissues and offsets the peripheral cholinergic effects of zenomaly. - And through this new mechanism of action side effects that are usually seen with current antipsychotics, such as metabolic side effects and movement disorders, they were not observed with Cobenfy. - It did not cause weight gain or extrapyramidal symptoms in the clinical trial program and does not carry the same black box warning. - So, most side effects were mild to moderate and transient GI side effects. - Also, what's different about this medication is it's one of the 1st that treating both positive and negative symptoms of schizophrenia. - The approval of Cobenfy was based on evidence from 2 pivotal trials, Emergent 2 and Emergent 3. - They included 470 patients aged 18 to 65 with diagnosed schizophrenia. - Both trials assess the change from baseline in Positive and Negative Syndrome scale, or Penn's total score at week five. - Of the patients who participated in Emergent 2 and Emergent 3, participants in the Cobenfy group experienced a 9.6 point and an 8.4 point greater reduction respectively in Penn's total score at week 5 compared to placebo. - So, this data on efficacy and side effect profile of the agent are from 5 weeks of in hospital treatment of patients having an acute exacerbation of schizophrenia - So there is still a lack of long term data. - Additionally, Cobenfy was compared to placebo rather than being compared to the current standards of care treatment options. - There are several ongoing trials to assess the long term safety and efficacy of Cobenfy - The price is $1850 per month based on black and it's a parity with some other branded antipsychotics. - The recommended starting dose is 150 per 20 milligram capsule - It's used twice orally twice daily for at least two days and then it can be titrated up to a maximum of 125 per 30 milligrams orally twice daily. - Oral Cobenfy stands out due to its efficacy on positive and negative symptoms of schizophrenia and lack of undesirable side effects such as weight gain and movement disorders. - However, there is a need for additional information on the long-term efficacy and safety and that should become available in the near future. - As for the criteria, let's go to page 357, - So here our member must be 18 years of age and older and that's per indication - Prescriber must be a psychiatrist or in consultation with a psychiatrist since we are requiring trial and failure below with two or more other antipsychotics first.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Specialist extraction makes sense here for patient safety and for coverage duration. - The initial request will be approved for six months since it's a new product with limited efficacy data, so we're requiring 6-month initial check in and for continuation of therapy, the request will be approved for 12 months. - For initial authorization, we are requiring diagnosis of schizophrenia consistent with DSM 5 criteria, documented trial and failure with two alternative formulary preferred antipsychotic agents or a medical reason is provided for not using any typical or atypical antipsychotic agents. - And due to wide availability of multiple generic cost-effective antipsychotics, we are requiring a few prior trials or a reason why the patient can't do that. - And since APA guidelines indicate treatment choice is highly individualized, we did not recommend specific agents or classes here. - But because the typicals are very commonly used first line, this is what we expect to see a lot of. - And also medications should be prescribed at an FDA approved dose. - And we require provider at the station that patient does not have any of the following moderate or severe hepatic impairment and treated narrow angle glaucoma, urinary retention and gastric retention since these are all contraindications in the labeling for reauthorization, we require documentation or provided at the station of positive clinical response such as improvement in positive and or negative symptoms of schizophrenia and that the medication is prescribed at an FDA approved dose. - Also, we have we set this criteria for review to practicing psychiatrist who is also a pharmacist, and you know they agreed with this policy. - Any questions on Cobenfy? - OK.		
		Tecelra Monograph **New PAD: Tecelra** - The next we have monograph with the Tecelra page 359. - Tecelra was recently approved for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are positive for HLA antigen serotypes HLA A 0201, 0202, 0203 or 0206 and whose tumor expresses the Melanoma associated antigen A4 or MAGE A4 as determined by FDA approved or cleared companion diagnostic devices. - So, this indication is approved under accelerated approval based on overall response rate and durability of response. - Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. - Just a little background on the disease. - Sarcoma is a broad term of a group of cancers that begin in bones and soft tissues.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- There are many different types of sarcoma and treatments varies based on location and type of sarcoma - Soft tissue sarcoma forms in the tissues that connect and surround other body structures. - Approximately 13,000 patients are diagnosed with soft tissue sarcoma in the US each year, and of these 13,000 patients, 5 to 10% would have synovial sarcoma. - Synomial sarcomas are a type of rare solid tumor cancers that typically form in areas around joints, and this can include bones and soft tissue such as fat, nerves, muscles, and blood vessels. - The 5-year survival rate of Synomial sarcomas is about 20 percent with most patients undergoing through multiple lines of chemotherapy treatment - Treatment options for soft tissue sarcoma include surgery as the main treatment to remove the tumor, radiation therapy, chemotherapy for certain types or advanced cases, and immunotherapy to stimulate the immune system to attack cancer cells. - So Tecelra is a T-cell immunotherapy. - It makes use of patient's own immune cells and modifies them to target cancer cells. - Antigen specific activation of Tecelra via T-cell receptor peptide HLA 802 complex results in T-cell proliferation of cytokine secretion and killing of Melanoma associated antigen A4 that's expressed in synovial sarcoma cells. - The cellular was approved based on Phase 2 Spare Head One trial results - It demonstrated a 43.2 overall response overall response rate, a 4.5% complete response rate and a median response duration of six months. - A confirmatory trial is currently undergoing to verify our clinical benefits. - The Cellar represents the first T cell receptor gene therapy for solid tumor and the first treatment option for synovial sarcoma in more than a decade. - It's estimated that 400 patients per year in the US will qualify for Tecelra treatment. - The price is $727,000 for a one-time IV infusion treatment. - And moving on to the criteria on page 365 - For age restriction we have according to packet insert next prescriber must be an oncologist or covers duration, it will be approved for one time treatment since safety and effectiveness of repeat administration has not been evaluated. - For exclusion criteria, patients will be excluded if they are positive for the HLA a 0205 serotype, and this is listed as a contraindication in the prescribing information and also is in the exclusion criteria in Spare Head One trial - For the initial authorization, we asked for diagnosis of unresectable or metastatic synovial sarcoma per indication. - Documentation that patients are positive for the HLA stereotypes that the drug was approved for. - This is also per indication - Additionally, documentation that the tumor expresses the MAGE A4 antigen. - This is also part of the indication in the Pi. - We also asked for documentation of treatment with prior chemotherapy. - This is per indication in the Pi and trial inclusion criteria. - All patients received prior chemotherapy in trials		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Also, member must have an Eastern Cooperative Oncology Group performance status of 0 or one and this requirement matches trials inclusion criteria and that medication is being prescribed at an FDA approved dose. - Again, there is no reauthorization since this drug hasn't been evaluated for repeat administration. - And that's all I have for Tecelra. - Any questions? - OK. - So now we will review emerging criteria. - **RN**-Thank you, Irena. Before we continue to the pharmacy benefit updates for MRGS, did we want to vote for new business and class review or did we want to wait till the end? **DC**-Let's go ahead and do vote for the class review, OK, And new business and the new business, OK. And we have a motion to approve class review and new business **DC**-I didn't see who made the motion. Paul Bayard, Doctor Bayard and Doctor Basari for a second. **DC**-Great. Thank you. So, we had a motion and a second all in favor of approving the new business and the class review reviews say aye, please. **ALL**-Aye, aye, aye aye. **DC**-Great Any no's anyone abstain? Great, Fantastic. Thank you. **RN**-Awesome.		
VII) Medication Request Guidelines	R. Negash	The committee has reviewed and discussed the following updates and additions to the Medication Review Guidelines (MRG) Guideline (Changes): **1. Injectable Methotrexate** - OK, so we can move on to our medication request guidelines. - These are specific to the pharmacy benefit, and we already see the first policy up there, the injectable methotrexate. - So here there's a simple change. - We're just removing the Reditrex since it's no longer on the market, it's been discontinued. - And so now we have Rasuvo in its place as the preferred product. - There's no other changes to this policy. - Are there any questions on this? - OK, we can move to the next one. - And for the sake of time, I will continue through the policies. - And please let me know if I'm going too fast or if there's a question. **Comments:**	Move to approve: 1st: AB 2nd: PB	

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		Guideline (Changes): **2. Immunizations** - The next one is on page 369. - This is for immunizations. - And so here you can see that we're adding two new products. - The first is Capvaxive, and MResvia. - And so, since they're now available, we're putting it on formulary. - And then if we scroll down to the next page, you can also see that we're adding a non-formulary agent just for alignment and that is the Ixchiq product. - And so, we have review criteria for that. - And then there's no other changes to this policy. **Comments:** Guideline (Changes): **3. Botulinum Toxins A&B** - OK, if there's no questions, we can move to Page 371. - And here we have our botulinum toxins A&B policy. - And here we do have a small change. - We're adding Candesartan to the preferred list of agents for chronic migraine since it's now recommended per guidelines with the AHS American Headache Society. - And then there's no other changes to this policy. - And if there's no questions, we can move to the next policy. **Comments:** Guideline (Changes): **4. Jesduvroq** - It's for Jesduvroq. - And so, as you can see, we're changing the name since we're adding another agent, Vafseo oral tablets. - You can also see in the medication section, we're striking Jesduvroq oral tablets since they have been removed from the market. - It's a manufacturer voluntary recall based on business decisions not related to safety or efficacy. - And then in the exclusion criteria, we're removing that concomitant use of strong CYP2C8 inhibitor like gemfibrozil since this relates to just Jesduvroq. - And then if we move to the PA review criteria section, we can see in that first bullet point that we're updating the language around the length of dialysis and CKD requirement to just relate to the FDA approved labeling. - And this is because the new added agent Vafseo needs to be a three-month duration dialysis and CKD requirement instead of four with Jesduvroq.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- On the second bullet point, we're also updating the hemoglobin baseline requirement to reflect the package insert of 8 to 11 g/dL. - And this is with the pivotal, the pivotal trials. - And then with the 4th bullet point, we're removing Jesduvroq current ESA product requirements since it relates to the removed from market agent. - And then there are no other changes to the policy for this. - I can pause for questions if there are any. - OK. **Comments:** Guideline (Changes): **5. Ocaliva** - The next one is on page 375, Ocaliva. - So, we can see here there's another policy name change and it's because we're adding two agents. - The first one is Iquirvo and the next is Livdelzi. - And you can see throughout the policy that these agents are being added. - And then we're also removing the Ocaliva specific dosing language and leaving in the coverage duration section since it's specific to just that agent. - And this policy will be expanded to more than just one agent in the PA review criteria. - On the second bullet point, we're expanding the required use or preferred use of the UDCA product and monotherapy requirement to all agents, not just Ocaliva. - And then the 4th bullet point here, we're updating the provider attestation so that it's specific to Ocaliva. - So we're looking for requests to state that there's no compensated cirrhosis with portal vein hypertension. - And this update can also be found in the reauthorization criteria. - Additionally, in the reauthorization criteria, you can see that we're allowing for an approval of a 10-milligram dosing if a 5-milligram dose was initially given, and this will be allowed for up to three months. - And this is just to maximize clinical benefit without the need of any laboratory findings and approved results. - There's no other changes on this policy. **Comments:** Guideline (Changes): **6. Vigabatrin (Sabril)** - And if there's no questions, we can move to Page 377. - This is for our Vigabatrin or Sabril criteria. - And here we're adding a new agent for infantile spasms. - It's an oral solution.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- So, you can see here that it's added in the infantile spasm area as an additional option. - And this is for our pediatric patients. - There's no other changes on this particular policy. **Comments:** Guideline (Changes): **7. Oxbryta (voxelotor)** - And then the last policy here is Oxbryta. - So, this one is actually being removed from market. - So, we're going to retire this policy since it no longer applies to any active agents that are available. - And it's being removed from market because there were findings that the benefits no longer outweighed the risks due to imbalance of vaso-occlusive crisis and fatal events. - Alternatives to this therapy include hydroxyurea like Siklos or Droxia, and also Endari. - And that actually concludes the medication request guidelines. - Thank you. **Comments:** DC: Do we need to vote on those guidelines? RN: Yes. DC: Can I get a motion to approve our guideline changes? AB: I'll make a motion. DC: Is there a second? DB: Second, I second. DC: OK. Thank you. DC: All in favor of approval of our changes say aye. PB, CR, AB, DB, IM: aye. DC: OK. Thank you. DC: Any no'ss and anyone abstain? DC: Fantastic. Motion carries. Thank you. **Comments:** No changes recommended at this time. No further discussion.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
VIII) Physician Administered Drug (PAD) Policies	Iryna Makukh	Guideline (Changes): **1. Complement Inhibitors** - So here we recommend adding PiaSky to the policy. This is a new complement C5 inhibitor indicated for the treatment of adult and pediatric patients 13 years and older with PNH and body weight of at least 40 kg. PiaSky is a monoclonal antibody that binds to complement protein C5 like Soliris, inhibiting its cleavage into C5A and C5B and therefore preventing the formation of the membrane attack complex. - What makes PiaSky a little different is it binds to a different C5 binding site than current treatments, which provides effective treatment for patients with specific gene mutations that don't respond to current therapies. There are several changes that are needed to add PiaSky to the policy. - We added coverage duration of 6 months for initial requests since the efficacy was assessed at 24 weeks in clinical trial for PiaSky. - Reauthorization requests will be approved for 12 months as this is a chronic condition. - In the initial authorization section, the request is for a dose that is FDA approved or a nationally recognized compendia in accordance with the patient's diagnosis, age, body weight, and concomitant medical conditions. - We just added body weight language here to ensure appropriate dosing since PiaSky is only indicated for patients with weight of at least 40 kg. - The other change to this section is we are adding PiaSky and updating the language on the documentation of vaccination against meningococcal disease. - So, per prescribing information, all these agents have black box warning of serious meningococcal infections. - We recommend rewording this requirement to documentation that patients comply with the most current advisory committee on immunization practices recommendations for vaccinations against encapsulated bacteria. This is to better align with the prescribing information. - The last change that's needed here is to rewrite diagnosis requirement for PNH so that it encompasses all agents and to specify that the specific hemoglobin requirement only applies to Empaveli. So, that's per treatment population in the trial for Empaveli. - RBC clone of more than 10% was the threshold from a trial with Soliris and it varies per trial for the different agents approved for this disorder or is not listed at all in the information - Also, per guidelines, there is no hard cut off for this variable or that clone size always indicates disease severity. - So, we suggested modifications to documentation of diagnosis by high sensitivity flow cytometry which would serve the purpose of confirming that patients have PNH since this is a gold standard test for PNH that shows the presence of clonal cells. Also, PiaSky does not hold any specific hemoglobin requirements like Empaveli. - In trials, patients were required to have diagnosis of PNH confirmed by flow cytometry which is already included in the criteria. - Everything else stays the same in the criteria, these are the only changes.	Move to approve: 1st: BD 2nd: PB	

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		Comments: PB: Are you saying encapsulated bacteria because they found other issues besides meningococcus? IM: We just decided to go with a broader statement just to make sure that we are compliant in case ASCP makes any changes to the guideline. We just looked in the Pi and tried to stay closer to the Pi prescribing information and that's why. PB: Ok, yeah, I'm not sure offhand if I'm a provider. I know what you mean by encapsulated bacteria, but I assume you will point that out to the prescribing provider or whoever is handling that? IM: Yeah, I think that's how they word it in the Pi as well as in the prescribing information. BD: So, it's a complimentary inhibitor pathway, so that's why they need vaccination prior for heme for all the encapsulated mostly meningococcus. It's part of the requirement for most of the heme who provide this. PB: No, I'm definitely familiar with the medication and the meningococcal risk, I just wasn't aware that there were other bacteria that were involved. So, that was my main question. BD: I agree with you, I don't think the other one was mentioned before. IM: We just wanted to be consistent with the Pi, do you want us to change it to just say meningococcal material? PB: No, that's fine, if it's in the Pi it's fine. I was just curious how that came about. Guideline (Changes): **2. Neuromyelitis Optica Spectrum Disorder (NMOSD) Agents** - - Pg. 383 Here Ultomiris was recently approved for the treatment of adults with neuromyelitis optical spectrum disorder who are anti aquaporin for antibody positive. - We recommend adding Ultomiris to the criteria since it has the same mechanism of action and box warning as Soliris and is similarly priced. The same exact exclusion criteria apply to Ultomiris.as the other agents since it was not approved AQP 4 antibody negative NMOSD. - The criteria for initial authorization for Soliris are pretty appropriate for Ultomiris and is mainly based on prescribing information. - Also, I wanted to mention that international guidelines were recently updated to include the newer agents for NMOSD. The consensus from these guidelines is that patients who show efficacy on less expensive off label therapies can stay on these therapies and do not need to initiate a biologic or a completement inhibitor. - So, the stuff that we have in this policy is still appropriate and the reauthorization section is also appropriate as is. - So, there are no other changes to this criteria. **Comments:** N/A Guideline (Changes): **3. Botulinum Toxins A&B** - Pg. 385 Similarly to the MRG criteria, our recommendation here is to just add candesartan as an option for trial and failure for the diagnosis of chronic migraines.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- As per newest guidelines from AHS, candesartan is considered as one of the first line of therapies for migraine prevention based on clinical trial evidence and real-world experience with this therapy. - So, that's the only change to this criteria. **Comments:** N/A Guideline (Changes): **4. Myasthenia Gravis Agents** - Here, just a small change to update again to the language on the documentation of vaccination against meningococcal disease for Soliris and Ultomiris. - So, here we are going with a general statement just to align with the prescribing information and to stay current if there are any updates. - No other changes to this criteria. **Comments:** PB: Could we please go back to the previous criteria, the one before this, for the myasthenia gravis? PB: What's your provision for zero negative myasthenia patients? IM: All these agents are approved only for antibody positive for anti-acetylcholine receptor antibodies positive, and also for anti-muscle specific tyrosine kinase positive. They're not approved for a zero negative disease. PB: Well, they're still used whether you know, it's FT approval or not in it. I'm not sure you have all the tests. I think there are, is that all the serological test that you are going to have for myasthenia? I feel like there's one that sometimes comes up, I'm not recalling the name. IM: We included the ones that are in the indications, not sure if there is another one, we're missing. PB: It's fine, I'm sure somebody's trying to get it though, they will get it clarified. I'm pretty sure there's another antibody test that's not on this that's going to be positive. It's not on the list and I'm sorry, it's not coming to my mind. Ok, that's fine. IM: Yes, I'm sorry, I think these are the only two I saw in the Pi information, but I'll check on that if I see anything else. I'll get back to you. PB: Ok. Guideline (Changes): **5. Gene therapy for sickle cell disease** - Pg. 389 Here we recommend to update trial and failure in the policy and that comes as a result of Oxbryta being removed from the market. - So, here we are just changing trial and failure to one agent to remove Oxbryta due to its discontinuation. - No other changes to this policy. **Comments:** N/A		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
IX) Informational Updates on New Developments in Pharmacy	Iryna Makukh	<u>New Product Review</u> • New Products were discussed.		

BRAND NAME	GENERIC NAME/DOSAGE FORM	RECOMMENDATION
Piasky	Crovalimab-akkz injection solution 340 mg/2ml	Non-formulary (see updated PAD policy)
Vafseo	Vadadustat oral tablet 150mg, 300mg	Non-formulary (see updated MRG policy)
Adalimumab-ryvk	Adalimumab-ryvk (2 Syringe) Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	Non-formulary
Taltz	Ixekizumab 20mg/0.25ml, 40mg/0.5ml prefilled syringe	Non-formulary
Otezla	Apremilast 20 mg oral tablet Apremilast oral tablet Therapy Pack 4 x 10 & 51 x20 MG	F-PA (already added via CRF)
Livmarli	Maralixibat 19mg/ml oral solution	Non-formulary (see new MRG policy)
Pantoprazole Sodium-NaCl	Pantoprazole Sodium-NaCl Intravenous Solution 40-0.9 MG/100ML-%, 80-0.9 MG/100ML-%	Non-formulary
Vancomycin	Vancomycin HCl intravenous solution reconstituted 1.75 gm, 2 gm	Non-formulary

			Cyclophosphamide	cyclophosphamide intravenous solution 1 gm/2ml, 2 gm/4ml	Non-formulary			
			Zepbound	Tirzepatide subcutaneous solution 2.5mg/0.5ml, 5mg/0.5ml	F-PA (already added via CRF)			
			Retevmo	Selpercatinib 40mg, 80mg, 120mg, 160mg oral tablet	Non-formulary			
			Vigafyde	Vigabatrin 100mg/ml oral solution	Add to F-PA (see updated MRG policy)			
			MydCombi	Tropicamide-phenylephrine ophthalmic solution cartridge 1-2.5%	Non-formulary			
			Tecelra	Afamitresgene Autoleucel intravaneous suspension 10000000000 cells	Non-formulary (see new PAD policy)			
			Nemluvio	nemolizumab Subcutaneous Auto-injector 30 MG	Non-formulary (see new MRG policy)			
			Crexont	Carbidopa and levodopa 35-140mg, 52.5-210mg, 70-280mg, 87.5-350mg oral capsule extended release	Non-formulary			
			Voranigo	Vorasidenib 10mg, 40mg, oral tablet	Non-formulary			

			Neffy	Epinephrine nasal solution 2mg/0.1ml	Non-formulary			
			Livdelzi	Seladelpar oral capsule 10mg	Non-formulary (see updated MRG policy)			
			Lazcluze	Lazertinib mesylate 80mg, 240mg oral tablet	Non-formulary			
			Tevimbra	Tislelizumab-jsgr intravenous solution 100mg/10mL	Non-formulary			
			Vabysmo	Faricimab-svoa intravitreal solution prefilled syringe 6 mg/0.05mL	Non-formulary			
			Onyda XR	clonidine hydrochloride Oral Suspension Extended Release 0.1 MG/ML	Non-formulary			
			Yorvipath	Palopegteriparatide subcutaneous solution pen-injector 168 mcg/0.56ml, 294 mcg/0.98ml, 420 mcg/1.4ml	Non-formulary (see new MRG policy)			
			Tryvio	Aprocitentan oral tablet 12.5mg	Non-formulary			
			Rytelo	Imetelstat 47 mg, 188 mg intravenous vial	Non-formulary (new PAD policy was added in Q3 2024)			
			Veltassa	Patiromer 1 gram packet	Add to F-ST-QL (ST—requires trial and failure of Lokelma; QL—60/30 days)			

			Freestyle Libre	Freestyle Libre 3 Plus Sensor	Non-formulary			
			Ebglyss	lebrikizumab subcutaneous solution auto-injector 250 mg/2ml	Non-formulary			
			Femlyv	norethindrone acetate and ethinyl estradiol orally disintegrating tablets 1-0.02 mg	Add to formulary			
			Tremfya	guselkumab 200 mg/2ml subcutaneous prefilled syringe, 200mg/2ml subcutaneous pen-injector, 200 mg/2ml via	Non-formulary			
			Tecentriq Hybreza	atezolizumab and hyaluronidase-tqjs subcutaneous solution 1875-30000 mg-ut/15ml	Non-formulary			
			Ocrevus Zunovo	ocrelizumab & hyaluronidase-ocsq subcutaneous solution 920-23000 mg-ut/23ml	Non-formulary			
			Miplyffa	Arimoclomol oral capsule 47mg, 62mg, 93mg, 124mg	Non-formulary			
			Dolobid	Diflunisal oral tablet 250mg	Non-formulary			
			Cobenfy	xanomeline and trospium chloride 50-20mg, 100-20mg,	Non-formulary (see new MRG policy)			

Agenda Item	Discussion Leader	Discussion Summary			Action	Notes
			125-30mg oral capsule xanomeline and trospium chloride oral capsule therapy pack 50-20 & 100-20 mg			
		Truqap	Capivasertib oral tablet therapy pack 160mg, 200mg	Non-formulary		
		Lumryz	Sodium oxybate starter pack oral therapy pack 4.5 & 6 & 7.5 gm	Non-formulary		
		Aqneursa	Levacetylleucine 1 g oral packet	Non-formulary		
		Zituvimet XR	sitagliptin and metformin hydrochloride extended release 24 hour oral tablet 50-500mg, 50-1000mg, 100-1000mg	Non-formulary		
		FreeStyle Libre 2 Plus sensor	FreeStyle Libre 2 Plus sensor	Non-formulary		
X) Old Business		• **Tadalafil (Cialis) for BPH MRG** - N/A • **Febuxostat (Uloric) MRG** - N/A **Comments:** RN: So, this last item relates to old business from our last P&T meeting. We discussed Naloxone and having that available at pharmacies to dispense with pharmacists prescribing. So, there are 2 recommendations we wanted to make to the committee to see if we wanted to move forward with this logic. The first one is to allow pharmacists to prescribe the Naloxone therapies at dispensing pharmacies. If so,				

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		then the second recommendation would be to potentially recoup payment for those pharmacies who are not following the regulatory recommendations and guidelines for dispensing Naloxone. It's outlined above in those bullet points and in the FAQ on pg. 404 and 405. Feel free to let me know if there's anything I may have missed on this. Nora? NT: I'm not sure if we've got a lot of discussion about this, but if so, we can defer that to the next meeting, so that we can have a discussion. DC: I recognize again that we are beyond 7PM, so if there's not any objections, we'll defer this to our first quarter P&T 2025.		
XI) Public Comment	D. Carey	• No comment		
Adjournment	D. Carey	• P&T Committee Member Forms **Meeting adjourned at 7:17PM**	None	

Signed by:
Nora Tomassian
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Nora Tomassian, PharmD
Interim Pharmacy Director,
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01/31/2025 | 2:07 PM PST
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Rahel Negash, PharmD
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02/19/2025 | 12:53 PM PST
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Donna Carey, MD
Chief Medical Officer
Alameda Alliance for Health

02/03/2025 | 9:58 AM PST
Date

New

Niemann-Pick Disease Type C	
Therapeutic Classes (AHFS)	Other Miscellaneous Therapeutic Agents
Medications	Miplyffa (arimoclomol), Aqneursa (levacetylleucine)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Concomitant use of Miplyffa and Aqneursa
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	According to package insert Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a neurologist, geneticist, or specialist in the treatment of Niemann-Pick disease type C (NPC)
Coverage Duration	If all of the criteria are met, the request will be approved for 6 months If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review

PA Review Criteria	**Initial Authorization:**
	• Diagnosis of NPC as confirmed by genetic testing demonstrating one of the following:
	  ○ Mutations in both alleles of NPC1 gene or NPC2 gene
	  ○ Mutation in one allele of NPC1 or NPC2 AND either a positive filipin-staining or elevated cholestane triol/oxysterols (>2x the upper limit of normal)
	• Documentation that member has at least one neurological sign of NPC (i.e., cognitive decline, vertical supranuclear gaze palsy, ataxia, seizures, etc.)
	• Documentation that member is ambulatory
	• For Miplyffa, prescriber must also attest that member will use in combination with miglustat
	• Member's weight
	• Request is for an FDA-approved dose
	
	Re-Authorization:
	• Documentation of positive clinical response to therapy (i.e. improvement or stabilization in ambulation, fine motor skills, swallowing, or speech)
	• Member's weight
	• Request is for an FDA-approved dose

Criteria Statement	Miplyffa and Aqneursa are reserved for members who have a diagnosis of NPC, are ambulatory, and have at least one neurological sign of NPC. Additionally, Miplyffa is reserved for members who will take it in combination with miglustat.
Last P&T Review Date	3/2025

Vyalev	
Therapeutic Classes (AHFS)	Dopamine Precursors
Medications	Vyalev (foscarbidopa and foslevodopa)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Concurrent use with a nonselective monoamine oxidase (MAO) inhibitor (such as phenelzine or tranylcypromine)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	According to package insert
Prescriber Restrictions	Prescriber must be a neurologist or in consultation with a neurologist
Coverage Duration	If all of the criteria are met, the initial and reauthorization requests will be approved for 12 months. If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review

PA Review Criteria	**Initial Authorization:**
	• Diagnosis of advanced Parkinson's Disease
	• Medication is prescribed at an FDA approved dose
	• Prescriber attestation or documentation that the patient is experiencing persistent motor fluctuations despite optimized carbidopa/levodopa therapy (including a minimum of 2.5 hours of "off" time per day)
	• Patient is taking ≥400 mg of levodopa/day
	• Documented trial and failure (or contraindication) to **at least two** of the following adjunctive medication classes:
	  ○ COMT-inhibitors (e.g., entacapone)
	  ○ Dopamine agonists (e.g., ropinirole, pramipexole)
	  ○ MAO-B inhibitors (e.g., rasagiline, selegiline)
	
	Re-Authorization:
	• Documentation or provider attestation of positive clinical response (i.e. increase in "on" time without troublesome dyskinesia, decreased "off" time)
	• Medication is prescribed at an FDA approved dose

Criteria Statement	Vyalev is reserved for members who have a diagnosis of advanced Parkinson's disease, who experience persistent motor fluctuations despite optimized carbidopa/levodopa therapy, are taking at least 400 mg of levodopa per day, and who have used (or cannot/should not use) at least two of the following medication classes: COMT-inhibitors, dopamine agonists, and MAO-B inhibitors.
Last P&T Review Date	3/2025

Zepbound for Moderate to Severe Obstructive Sleep Apnea	
Therapeutic Classes (AHFS)	Incretin Mimetics
Medications	Zepbound (tirzepatide)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	• Requests for Zepbound solely for a diagnosis of weight reduction and maintenance for overweight or obesity • Concurrent use of any glucagon-like-peptide-1 receptor agonist • Personal history of Type 1 or Type 2 diabetes • Personal or family history of medullary thyroid carcinoma • Multiple Endocrine Neoplasia syndrome type 2
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	According to package insert
Prescriber Restrictions	Provider must be a specialist in the treatment of sleep disorders, or in consultation with a specialist in the treatment of sleep disorders
Coverage Duration	If all of the criteria are met, the request will be approved for up to 6 months for initial requests, and 12 months for renewal requests If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review

PA Review Criteria	**Initial Authorization (all of the following must be met):**
	• Requested dose is appropriate per labeling
	• Patient's body mass index (BMI) is provided and is ≥30 kg/m^2
	• Documentation of current diagnosis of moderate to severe obstructive sleep apnea
	• Documentation of trial and failure regarding lifestyle changes and behavioral modification (e.g., healthy diet and increased physical activity) to reach a BMI < 30 kg/m^2
	• One of the following:
	  ○ Results of sleep testing showing patient's apnea hypopnea index (AHI) ≥ 15 while currently on PAP therapy
	  ○ Results of sleep testing showing patient's apnea hypopnea index (AHI) ≥ 15 and patient had a previous trial and failure of PAP therapy or a medical reason is provided why the patient is not able to use PAP therapy
	• Patient is not pregnant
	
	Re-Authorization:
	• Requested dose is appropriate per labeling
	• Documentation of positive clinical response to therapy (i.e., improvement patient's AHI, improvement in daytime sleepiness, sleep arousals, snoring)
	• Patient is adherent to therapy, as evidenced by claims records demonstrating ≥80% fill rate

Criteria Statement	Zepbound is reserved for members who have a diagnosis of moderate to severe obstructive sleep apnea, are not pregnant, and have a BMI ≥30 kg/m^2 , and who have results of sleep testing showing AHI ≥15 while currently on PAP therapy or AHI ≥15 and had a previous trial and failure of PAP therapy or are unable to use PAP therapy, and who had trial and failure regarding lifestyle changes and behavioral modification.
Last P&T Review Date	3/2025

New

Vyalev	
Medications	Vyalev (foscarbidopa and foslevodopa)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Concurrent use with a nonselective monoamine oxidase (MAO) inhibitor (such as phenelzine or tranylcypromine)
Required Clinical Information	See "Other Criteria" below
Age Restrictions	According to package insert
Prescriber Restrictions	Prescriber must be a neurologist or in consultation with a neurologist
Coverage Duration	If all of the criteria are met, the initial and reauthorization requests will be approved for 12 months.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization**
	• Diagnosis of advanced Parkinson's Disease
	• Medication is prescribed at an FDA approved dose
	• Prescriber attestation or documentation that the patient is experiencing persistent motor fluctuations despite optimized carbidopa/levodopa therapy (including a minimum of 2.5 hours of "off" time per day)
	• Patient is taking ≥400 mg of levodopa/day
	• Documented trial and failure (or contraindication) to **at least two** of the following adjunctive medication classes:
	  ○ COMT-inhibitors (e.g., entacapone)
	  ○ Dopamine agonists (e.g., ropinirole, pramipexole)
	  ○ MAO-B inhibitors (e.g., rasagiline, selegiline)
	
	Reauthorization
	• Documentation or provider attestation of positive clinical response (i.e. increase in "on" time without troublesome dyskinesia, decreased "off" time)
	• Medication is prescribed at an FDA approved dose
	
	If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review

Last Review Date	3/2025

Alameda Benchmark Analysis and Recommendation: Q1 2025 P&T

USP Category: Antiparasitics

USP Class: Antiprotozoals

The recommendation is to add Tinidazole Oral Tablet 250 MG and 500 MG (DDIDs: 87863 and 31342) to formulary in order to meet the benchmark of 10 formulary medications in this drug class.

Benchmark Count	Formulary Count	Recommended Formulary Additions	Tier	Rationale
10	9	Tinidazole Oral Tablet 250 MG (DDID: 87863) Tinidazole Oral Tablet 500 MG (DDID: 31342)	F, Tier 1	Other antiprotozoals that are not on formulary include benznidazole, impavido, lampit, alinia, nitazoxanide, humatin, paromomycin, arakoda, and krintafel. Tinidazole is cost effective commercially available formulation with several approved indications (amebic liver abscess - infection caused by Entamoeba histolytica; bacterial vaginosis; infection by Giardia lamblia; Infection caused by Entamoeba histolytica - Intestinal infectious disease; Trichomoniasis). Tinidazole will be added to formulary in order to meet the benchmark.

USP Category: Hormonal Agents, Stimulant/ Replacement/ Modifying (Sex Hormones/ Modifiers)

USP Class: Anabolic Steroids

The recommendation is to add Bijuva Oral Capsule 0.5-100 MG and 1-100 MG (DDIDs: 225399 and 205688) to formulary in order to meet the benchmark of one formulary medication in this drug class. Another agent in this category is Oxandrolone, however, it is no longer on the market in an active formulation.

Benchmark Count	Formulary Count	Recommended Formulary Additions	Tier	Rationale
1	0	Bijuva Oral Capsule 0.5-100 MG (DDID: 225399) Bijuva Oral Capsule 1-100 MG (DDID: 205688)	F, Tier 2	There are only 2 members of this class: Bijuva and Oxandrolone. Oxandrolone is now unavailable commercially. Bijuva will be added to the formulary to meet the benchmark.

USP Category: Ophthalmic Agents

USP Class: Ophthalmic Intraocular Pressure Lowering Agents, Other

During Q3 2024 P&T it was recommended to remove Apraclonidine HCl Ophthalmic Solution 0.5 % due to no utilization and adequate alternatives. However, we recommend adding it back to formulary to meet the benchmark for this drug class.

Benchmark Count	Formulary Count	Recommended Formulary Additions	Tier	Rationale
7	6	Apraclonidine HCl Ophthalmic Solution 0.5 % (DDID: 24856)	F, Tier 1	Other Ophthalmic Intraocular Pressure Lowering Agents that are not on formulary include brinzolamide, phospholine Iodide reconstituted solution, Rhopressa, and brimonidine-timolol solution. Adding apraclonidine is the most cost-effective solution to meet the benchmark.

Multiple Sclerosis

Executive Summary

Class Overview

Multiple sclerosis (MS) is a chronic central nervous system disease, causing inflammation and demyelination in multifocal areas. This damage leads to progressive central nervous system dysfunction and disability, which can include sensory disturbances in limbs, visual loss, disturbances in balance and motor control, vertigo, bladder and bowel problems and pain. It is the most frequent cause of permanent disability in young adults among central nervous system disorders, aside from trauma.

There are several phenotypes of MS. Clinically isolated syndrome (CIS) is the first clinical episode that is suggestive of MS. The episode, which by definition must last for at least 24 hours, is characteristic of MS but does not yet meet the criteria for a diagnosis of MS because patients who experience a CIS may or may not go on to develop the develop the chronic disease. Relapsing remitting MS (RRMS) is the most common type of MS at disease onset and is characterized by episodes of disease exacerbation (relapses) followed by periods of partial or complete recovery called remission. Within the first decade of disease, approximately 50% of RRMS patients will develop secondary progressive MS (SPMS), which is characterized by a progressive worsening of disease between relapses. Primary progressive MS (PPMS) is when the disease progresses from onset with no remissions. Disease severity in terms of neurologic disability is highly variable, dependent on multiple factors such as frequency of relapses, how quickly they worsen, and the degree of residual disability between relapses. Disability tends to increase over time, and complications related to MS can lead to death.

Treatment of PPMS is more difficult than relapsing forms with only two approved disease modifying therapies (DMTs) (Ocrevus® [ocrelizumab] and Ocrevus Zunovo™ [ocrelizumab and hyaluronidase-ocs]) available in the US. Conversely, many DMTs are available for relapsing forms of MS. Current guidelines recommend that everyone with a diagnosis of clinically definite RRMS should begin DMT as considerable evidence has shown that earlier treatment is associated with better long-term outcomes. DMTs include:

- Injectable monoclonal antibodies such as natalizumab, ocrelizumab, rituximab, ofatumumab, and alemtuzumab, which may be preferred for patients with more active disease, who highly value efficacy, and who can be considered risk-tolerant
- Oral therapies such as fumarates, sphingosine 1-phosphate (S1P) receptor modulators, teriflunomide, and cladribine, which may be preferred for those who desire self-administration oral medication over injections
- Platform injection therapies (the first DMTs approved for MS) such as interferon beta-1 and glatiramer acetate, which may be preferred for their safety profiles

While these treatments do not cure RRMS, they have shown benefit for patients by decreasing relapse rate and slowing the accumulation of brain lesions, therefore hopefully slowing disease (and presumably disability) progression. Various organizations exist whose purpose is to advocate for advances in the treatment of MS – Accelerated Cure Project for MS, The Consortium of Multiple Sclerosis Centers (CMSC), National Multiple Sclerosis Society. Many are members of the larger group the MS Coalition. Advocacy organizations may publish consensus statements or guidelines, however, these publications must be closely evaluated for source of funding, foundation in evidence-based medicine, and intended audience. Guidelines published by professional clinical organizations, such as the American Academy of Neurology (AAN),

are founded in evidence-based medicine, demonstrated by grading of evidence. Guidelines published by the AAN have been included within.

Utilization Findings

There were 7 claims for 3 members, for a total cost of $22,865.91 and an average cost per claim of $3,266.56. The most highly utilized medications were Glatiramer and Teriflunomide, with 3 claims each, followed by Vumerity with 1 claim. There were 2 prior authorization requests with 1 approval (50%).

Recommendations

- Change Avonex (interferon beta 1a) 30 mcg/0.5 mL intramuscular pen kit and syringe kit from F to F-PA to match the criteria status
- Change teriflunomide from F-PA to F and add to preferred agents in the criteria since it's cost effective and there was utilization
- Update naming conventions to reflect generic availability of Gilenya and Aubagio in the criteria

Clinical Summary

MS is a chronic central nervous system disease, causing inflammation and demyelination in multifocal areas. This damage leads to progressive central nervous system dysfunction and disability, which can include sensory disturbances in limbs, visual loss, disturbances in balance and motor control, vertigo, bladder and bowel problems and pain. It is the most frequent cause of permanent disability in young adults among central nervous system disorders, aside from trauma.

The most widely accepted theory is that MS begins as an inflammatory autoimmune disorder mediated by autoreactive lymphocytes. Alternate theories include an (but not autoimmune) etiology due to a chronic viral infection or a nonimmune noninflammatory etiology due to a genetically determined neuroglial degenerative process. The estimated female-to-male ratio of MS incidence is approximately 2:1, with some data suggesting the ratio is even higher. Incidence and prevalence can vary geographically, but the mean age of MS onset ranges from 28 to 31 in various studies with clinical disease usually becoming apparent between the ages of 15 to 45. Possible risk factors for MS include genetics (especially variation involving the HLA-DRB1 locus), the Epstein-Barr virus, geographic factors, sun/UV exposure/serum vitamin D levels, tobacco smoking, and child/adolescent obesity.

For initial diagnosis, typically patients will present with one or more episodes of:

- Unilateral optic neuritis
- Painless binocular diplopia
- Focal brainstem or cerebellar syndrome
- Partial transverse myelitis with sensory and/or motor symptoms.

Patients with these episodes that are additionally experiencing relapses and remissions and/or have an onset of ages 11 and 50 years old are further evaluated by the number of clinical attacks and then lesions through examination and brain MRI. Patients with one attack and at least two lesions may not have a diagnosis of MS confirmed but are considered high risk and should start disease modifying therapy. Patients with two or more clinical attacks and clinical evidence of at last one lesion with reasonable historical evidence of a prior attack involving in a distinct central nervous system location have confirmed MS and should start disease modifying therapy.

There are several phenotypes of MS: CIS, RRMS, SPMS, and PPMS.

CIS is the first clinical episode that is suggestive of MS. The episode, which by definition must last for at least 24 hours, is characteristic of MS but does not yet meet the criteria for a diagnosis of MS because patients who experience a CIS may or may not go on to develop the develop the chronic disease. Patients may experience a monofocal episode, in which they experience one single neurological sign or symptom, or a multifocal episode, in which they may experience multiple signs or symptoms, and more than 85% of those diagnosed with CIS progress to MS. RRMS is the most common type of MS at disease onset, and is characterized by episodes of disease exacerbation (relapses) followed by periods of partial or complete recovery called remission. Within the first decade of disease, approximately 50% of RRMS patients will develop SPMS, which is characterized by a progressive worsening of disease between relapses. As of note, SPMS is a diagnosis that can only be made in hindsight with no labs or other clinical indicators evidencing the transition. PPMS is when the disease progresses from onset with no remissions. Disease severity in terms of neurologic disability is highly variable, dependent on multiple factors such as frequency of relapses, how quickly they worsen, and the degree of

residual disability between relapses. Disability tends to increase over time, and complications related to MS can lead to death.

The average life span of 25 to 35 years after the diagnosis of MS is made is often stated, though is very difficult to estimate and varies widely from patient to patient. Some of the most common causes of death in MS patients are secondary complications resulting from immobility, chronic urinary tract infections, compromised swallowing and breathing. Other complications include bowel and bladder dysfunction, cognitive impairment, fatigue, gait disturbance and balance problems, heat sensitivity, motor symptoms, pain, paroxysmal symptoms, sensory symptoms, sexual dysfunction, vertigo, and visual disturbances.

Treatment of PPMS is more difficult than relapsing forms with only one approved DMT (Ocrevus® [ocrelizumab]) available in the US. Conversely, many DMTs are available for relapsing forms of MS. Current guidelines recommend that everyone with a diagnosis of clinically definite RRMS should begin DMT as considerable evidence has shown that earlier treatment is associated with better long-term outcomes. DMTs include:

- Injectable monoclonal antibodies such as natalizumab, ocrelizumab, rituximab, ofatumumab, and alemtuzumab, which may be preferred for patients with more active disease, who highly value efficacy, and who can be considered risk-tolerant
- Oral therapies such as fumarates, sphingosine 1-phosphate (S1P) receptor modulators, teriflunomide, and cladribine, which may be preferred for those who desire self-administration oral medication over injections
- Platform injection therapies (the first DMTs approved for MS) such as interferon beta-1 and glatiramer acetate, which may be preferred for their safety profiles

While these treatments do not cure RRMS, they have shown benefit for patients by decreasing relapse rate and slowing the accumulation of brain lesions, therefore hopefully slowing disease (and presumably disability) progression. One product, dalfampridine (Ampyra®), is a symptomatic agent indicated to improve walking speed for MS patients and Acthar® (corticotropin) is used for treatment of MS exacerbations. As the MS treatment landscape continues to expand, first generation DMTs could fall out of favor. Drugs like glatiramer (Copaxone®) and interferons, once preferred for their safety profiles, are being replaced with drugs that are both safe as well as more effective.

For oral therapy, Tecfidera® is a market-leading, twice-daily oral therapy of choice for patients with RRMS, especially in initial treatment, due to its clean safety profile and clinical efficacy. Tecfidera® is currently generically available, however, its gastrointestinal (GI) side effects can be an obstacle to its use. Although they diminish over time, the GI side effects of Tecfidera® can affect adherence.

Gilenya® (fingolimod) had been the only approved sphingosine-1-phosphate (S1P) modulator until recently and competes directly with Tecfidera® in the oral MS category. Over the last 5 years, Mayzent® (siponimod), Zeposia®, and Ponvory® (fingolimod) have all joined the S1P modulator class. The key differentiator of these S1P competitors is the first-dose bradycardia safety concern and monitoring required for Gilenya®. Monitoring for Mayzent® and Ponvory® is required only on some patients, and Zeposia® does not require first-dose monitoring for any patients. Additionally, in clinical trials, Ponvory® reduced annual relapses by 30% compared with Aubagio®. Although the head-to-head data are impressive, it is unclear if Ponvory® is superior to the other three S1P products without additional data. While there is strong data for these class of drugs, the anti-CD20 class of drugs are believed to be more potent than S1Ps at controlling MS. For instance, the anti-CD20 Kesimpta® (ofatumumab) has its own head-to-head data versus Aubagio®, and the Kesimpta® data look even better than Ponvory®, with a greater than 50% reduction in relapses.

In 2021, the FDA approved Tascenso ODT® (fingolimod) 0.25 mg orally disintegrating tablet, for the treatment of relapsing forms of MS, in pediatric patients 10 years of age and older and weighing less than or equal to 40 kg. It has the same active ingredient as Gilenya®, which comes as 0.25 mg and 0.50 mg hard capsules and does not have any weight restrictions in its indication.

Anti-CD20 monoclonal antibodies have gained traction over the last few years due to their high efficacy and favorable safety profile. Anti-CD20 monoclonal antibodies that are indicated for MS include Ocrevus® (ocrelizumab), Kesimpta® (ofatumumab), and Briumvi® (ublituximab-xiiy). More and more neurologists have selected anti-CD20s, particularly Ocrevus®, as initial DMT and as a treatment to switch to when other types of DMTs do not work. All three have similar efficacy, however, Ocrevus® is the market leader because it was first to market and has both favorability and familiarity for neurologists. Kesimpta® has a subcutaneous (SQ) route of administration that is given once monthly, while both Ocrevus® and Briumvi® are administered as an intravenous(IV) infusion every 6 months. Anti-CD20s are being promoted as both a more efficacious and safer DMT compared to currently available products. This appears to be true when compared to most DMTs, especially one with high efficacy like Lemtrada® (alemtuzumab) and Tysabri® (natalizumab) which are associated with several potentially severe side effects and subject to Risk Evaluation and Mitigation Strategy (REMS) programs. On September 13, 2024, the FDA approved Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq), a SQ formulation that is administered by a healthcare provider. While both Ocrevus® and Ocrevus Zunovo™ are given every 6 months, the SQ administration of Ocrevus Zunovo™ is notably faster, taking approximately 10 minutes, compared to the 2 hours or more required for IV infusion of Ocrevus®.

Copaxone® (glatiramer) remains a self-injectable therapy of choice for initial treatment in RRMS due to favorable safety and tolerability as well as being seen as an option for women considering pregnancy and breastfeeding. Currently, Sandoz and Mylan have FDA-approved 20 mg and 40 mg competing generic glatiramer products, with several additional generics in the pipeline. The presence of these products and the resulting market price reduction has lead payers to place a glatiramer step requirement prior to approving other significantly more expensive multiple sclerosis treatments. The addition of other generics in the MS category , specifically among oral therapies, has also heavily influenced formulary management. In the past 4 years, generics for Tecfidera®, Aubagio®, and Gilenya® have launched, and as a result, more payers have moved to a “generic first” requirement.

Several other drugs are in the pipeline for MS. Fenebrutinib, toleburtinib, remibrutinib, and masitinib are all oral Bruton's tyrosine kinase (BTK) inhibitors that would represent a new class of therapies for MS. All four are in Phase 3 trials, with potential approval coming in 2026–2027. The BTK inhibitors will likely be used following one or more generic products in the MS category. Anti-CD 20 molecules in the pipeline include a high dose formulation of Ocrevus® as well as an ocrelizumab biosimilar. GA Depot® (glatiramer) is a once-monthly formulation of glatiramer that patients would most likely prefer over Copaxone® due to convenience. It was expected to be approved in 2024, however, the FDA issued a complete response letter (CRL) and it’s unclear when or if this product will hit the market.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
Glatiramer (Copaxone®, Glatopa®)	Treatment of patients with relapsing forms (RRMS, CIS, active SPMS) of MS	20 mg/mL: once daily SQ 40 mg/mL: three times per week SQ
Extavia®, Betaseron® (interferon beta-1B)	Treatment of relapsing forms (RRMS, CIS, active SPMS) of MS to reduce the frequency of clinical exacerbations	Initially 0.0625 mg (0.25 mL) SQ every other day, increase by 0.0625 mg every 2 weeks over a 6 week period to 0.25 mg (1 mL) every other day
Rebif®, Rebif® Rebidose® (interferon beta-1A)	Treatment of patients with relapsing forms (RRMS, CIS, active SPMS) of MS to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability	Initially, 20% of the prescribed dose SQ three times per week; titrate over a 4 week period to 22 mcg or 44 mcg SQ three times per week
Avonex® (interferon beta-1A)		Recommended dose: 30 µgrams IM once a week, can be titrated to reduce flu-like symptoms.
Plegridy® (peginterferon beta-1A)	Treatment of patients with relapsing forms (RRMS, CIS, active SPMS) of MS	Recommended dose: 125 µgrams every 14 days. Dose should be titrated, starting with 63 µgrams on day 1, 94 µgrams on day 15, and 125 µgrams (full dose) on day 29.
Ocrevus® (ocrelizumab)	Treatment of adult patients with relapsing (RRMS, CIS, active SPMS) or primary progressive forms of MS	Start dose: 300 mg IV infusion, followed two weeks later by a second 300 mg IV infusion; subsequent doses: 600 mg IV infusion every 6 months
Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocs)		920 mg-23,000 units SQ in the abdomen over approximately 10 minutes every 6 months
Lemtrada® (alemtuzumab)	Treatment of patients with relapsing forms (RRMS, active SPMS) of MS. Because of its safety profile: • Use should generally be reserved for patients who have had an inadequate response to ≥ two drugs indicated for the treatment of MS • Not recommended for use in patients with CIS	Administer by IV infusion over 4 hours for 2 treatment courses: • First course: 12 mg/day on 5 consecutive days. • Second course: 12 mg/day on 3 consecutive days 12 months after first treatment course. Following the second treatment course, subsequent treatment courses of 12 mg per day on 3 consecutive days may be administered, as needed, at least 12 months after the last dose
Tysabri® (natalizumab)	Monotherapy for the treatment of patients with relapsing forms (RRMS, CIS, active SPMS) of MS	300 mg infused IV over one hour, every four weeks; do not give as an IV push or bolus
Briumvi® (ublituximab-xiiy)	Relapsing forms of MS (RRMS, CIS, active SPMS) in adults	Administer by IV infusion: • First infusion: 150 mg • Second infusion: 450 mg given two weeks after the first infusion

Medication	Indications	Dosing/Administration
		• Subsequent infusions: 450 mg given 24 weeks after the first infusion and every 24 weeks thereafter
Kesimpta® (ofatumumab)	Relapsing forms of MS (RRMS, CIS, active SPMS) in adults	Initially 20 mg SQ at weeks 0, 1 and 2 followed by 20 mg SQ once monthly starting at week 4
Teriflunomide (Aubagio®)	Treatment of patients with relapsing forms (RRMS, CIS, active SPMS) of MS	7 to 14 mg orally once daily, with or without food
Fingolimod (Gilenya®)	Treatment of relapsing forms (RRMS, CIS, active SPMS) of MS in patients 10 years of age and older	Adults and pediatric patients (≥ 10 years of age) weighing > 40 kg: 0.5 mg orally once daily, with or without food Pediatric patients (≥ 10 years of age) weighing ≤ 40 kg: 0.25 mg orally once daily, with or without food Requires first dose monitoring (including re-initiation after discontinuation > 14 days and dose increases)
Tascenso ODT® (fingolimod)	Treatment of pediatric patients with relapsing forms of MS (RRMS, CIS, active SPMS) 10 years of age and older and weighing less than or equal to 40 kg.	0.25 mg orally once daily, with or without food. Requires first dose monitoring (including re-initiation after discontinuation > 14 days and dose increases)
Dimethyl fumarate (Tecfidera®)	Treatment of patients with relapsing forms (RRMS, CIS, active SPMS) of MS in adults	Starting dose: 120 mg twice a day (BID), orally, for 7 days; maintenance dose after 7 days: 240 mg BID
Bafiertam™ (monomethyl fumarate)		Starting dose: 95 mg BID orally for 7 days; maintenance dose after 7 days: 190 mg (2 x 95 mg capsules) BID
Vumerity® (diroximel fumarate)		Starting dose: 231 mg BID for 7 days; maintenance dose after 7 days: 462 mg BID
Mayzent® (siponimod)	Treatment of relapsing forms (RRMS, CIS, active SPMS) of MS in adults	CYP2C9 Genotypes *1/*1, *1/*2, or *2/*2: • Titration: 0.25 mg day 1, 0.25 mg day 2, 0.5 mg day 3, 0.75 mg day 4, 1.25 mg day 5 • Maintenance: 2 mg PO daily CYP 2C9 Genotypes *1/*3 or *2/*3 • Titration: 0.25 mg day 1, 0.25 mg day 2, 0.5 mg day 3, 0.75 mg day 4 • Maintenance: 1 mg PO daily If titration dose is missed for > 24 hours or maintenance dose is missed for ≥ 4 consecutive daily doses, reinitiate treatment with day 1 of the titration regimen
Ponvory® (ponesimod)	Treatment of relapsing forms of MS (RRMS, CIS, active SPMS) in adults.	• Titration: 2 mg orally on days 1 & 2, 3 mg on days 3 & 4, 4 mg on days 5 & 6, 5 mg on day 7, 6 mg on day 8, 7 mg on day 9, 8 mg on day 10, 9 mg on day 11, and 10 mg on days 12, 13, & 14

Medication	Indications	Dosing/Administration
		Start maintenance dosing of 20 mg orally daily on day 15
Zeposia® (ozanimod)	For the treatment of relapsing forms (RRMS, CIS, active SPMS) of MS in adults	• 0.23 mg once daily days 1-4; 0.46 mg once daily days 5-7; 0.92 mg once daily starting on day 8
Mavenclad® (cladribine)	Treatment of relapsing forms (RRMS, CIS, active SPMS) of MS in adults. Because of its safety profile, use is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS	3.5 mg/kg body weight administered orally and divided into 2 yearly treatment courses (1.75 mg per kg per treatment course). Each treatment course is divided into 2 treatment cycles: Administration of First Treatment Course • First Course/First Cycle: start any time. • First Course/Second Cycle: administer 23 to 27 days after the last dose of First Course/First Cycle. Administration of Second Treatment Course • Second Course/First Cycle: administer at least 43 weeks after the last dose of First Course/Second Cycle. • Second Course/Second Cycle: administer 23 to 27 days after the last dose of Second Course/First Cycle. Administer the cycle dosage as 1 or 2 tablets once daily over 4 or 5 consecutive days. • Following the administration of 2 treatment courses, do not administer additional cladribine treatment during the next 2 years. Treatment during these 2 years may further increase the risk of malignancy. The safety and efficacy of reinitiating cladribine more than 2 years after completing 2 treatment courses has not been studied.
Mitoxantrone	Reducing neurologic disability and/or the frequency of clinical relapses in patients with secondary (chronic) progressive, progressive relapsing, or worsening RRMS (i.e., patients whose neurologic status is significantly abnormal between relapses).	12 mg/m2 given as a short (approximately 5 to 15 minutes) IV infusion every 3 months. Left ventricular ejection fraction, CBC (including platelets), liver function tests, and pregnancy testing should be evaluated prior to each dose.
Dalfampridine (Ampyra®)	Improve walking in adult patients with multiple sclerosis.	Maximum recommended dosage is 10 mg BID (approximately 12 hours apart), with or without food. In patients with mild renal impairment (CrCl 51–80 mL/min), Ampyra may reach plasma levels associated with a greater risk of seizures, and the potential benefits should be carefully

Medication	Indications	Dosing/Administration
		considered against the risk of seizures in these patients.
Acthar® (corticotropin)	Treatment of exacerbations of MS in adults	Daily intramuscular or SQ doses of 80-120 units for 2-3 weeks may be administered. It may be necessary to taper the dose.

PERFORMRx℠

Boxed Warnings and Contraindications

Medication	Boxed Warnings	Contraindications
Glatiramer (Copaxone®, Glatopa®)	None	Known hypersensitivity to glatiramer acetate or mannitol
Extavia®; Betaseron® (interferon beta-1B)		History of hypersensitivity to natural or recombinant interferon beta, albumin or mannitol
Rebif®, Rebif® Rebidose®; Avonex® (interferon beta-1A)		History of hypersensitivity to natural or recombinant interferon beta, albumin, or any other component of the formulation
Plegridy® (peginterferon beta-1A)		History of hypersensitivity to natural or recombinant interferon beta or peginterferon, or any other component of the formulation
Ocrevus® (ocrelizumab)		History of life-threatening infusion reaction to Ocrevus®, active hepatitis B virus infection
Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocs)		History of life-threatening infusion reaction to Ocrevus® or Ocrevus Zunovo™, active hepatitis B virus infection
Lemtrada® (alemtuzumab)	Autoimmune effects, infusion reactions, malignancies, and stroke	Infection with Human Immunodeficiency Virus
Tysabri® (natalizumab)	Progressive multifocal leukoencephalopathy (PML)	Patients who have or have had PML, hypersensitivity reaction to Tysabri®
Briumvi® (ublituximab-xiiy)	None	Active hepatitis B virus (HBV) infection
Kesimpta® (ofatumumab)		
Teriflunomide (Aubagio®)	Hepatotoxicity and risk of teratogenicity	Severe hepatic impairment, pregnancy/females of reproductive potential not using contraception, hypersensitivity, current leflunomide treatment
Fingolimod (Gilenya®)	None	Recent myocardial infarction (MI), unstable angina, stroke, transient ischemic attack, decompensated heart failure (HF) with hospitalization, Class III/IV HF, history of Mobitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome (unless patient has a pacemaker), baseline QTc interval ≥ 500 msec., cardiac arrhythmias requiring treatment with Class Ia or Class III anti-arrhythmic drugs, hypersensitivity to fingolimod or its excipients
Tascenso ODT® (fingolimod)		
Dimethyl fumarate (Tecfidera®)		Known hypersensitivity to dimethyl fumarate or any inactive ingredients
Bafiertam® (monomethyl fumarate)		Known hypersensitivity to monomethyl fumarate, dimethyl fumarate or diroximel fumarate or any excipients Concurrent therapy with dimethyl fumarate or diroximel fumarate
Vumerity® (diroximel fumarate)		Hypersensitivity (e.g., anaphylaxis, angioedema) to diroximel fumarate, dimethyl

Medication	Boxed Warnings	Contraindications
		fumarate, or to any component of the formulation; concomitant use of dimethyl fumarate
Mayzent® (siponimod)	None	CYP2C9*3/*3 genotype; MI, unstable angina, stroke, TIA, decompensated HF requiring hospitalization, or Class III or IV HF in the past 6 months; Mobitz type II second- or third-degree AV block, or sick sinus syndrome, unless patient has a functioning pacemaker
Ponvory® (ponesimod)		In the last 6 months, experienced MI, unstable angina, stroke, transient ischemic attack (TIA), decompensated heart failure requiring hospitalization, or Class III/IV heart failure; presence of Mobitz type II second-degree, third-degree AV block, sick sinus syndrome, or sino-atrial block, unless the patient has a functioning pacemaker
Zeposia® (ozanimod)		MI, unstable angina, stroke, TIA, decompensated HF requiring hospitalization, or class III or IV HF in the last 6 months; Mobitz type II second- or third-degree AV block, sick sinus syndrome, or sinoatrial block, unless the patient has a functioning pacemaker; severe untreated sleep apnea; concomitant use of a monoamine oxidase inhibitor
Mavenclad® (cladribine)	May increase risk of malignancy, risk of teratogenicity	Current malignancy; pregnancy; men or women of reproductive potential who do not plan to use effective contraception during therapy and for 6 months after the last dose in each treatment course; HIV infection; active chronic infections (e.g., hepatitis or tuberculosis [TB]); breastfeeding (during treatment or for 10 days after last dose)
Mitoxantrone	Experienced physician, bone marrow suppression, cardiotoxicity, secondary leukemia, appropriate administration	Hypersensitivity to mitoxantrone products
Dalfampridine (Ampyra®)	None	History of seizure, moderate or severe renal impairment (CrCl ≤50 mL/min), History of hypersensitivity to Ampyra® or 4-aminopyridine
Acthar® (corticotropin)		Never to be given IV, administration of live or live attenuated vaccinations, children < 2 years of age with suspected congenital infections, treatment of approved indications when accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction,

Medication	Boxed Warnings	Contraindications
		patients with scleroderma, osteoporosis, systemic fungal infections, ocular herpes simplex, recent surgery, history of or the presence of a peptic ulcer, congestive HF, uncontrolled hypertension, or sensitivity to proteins of porcine origin

PERFORMRx℠

Warnings/Precautions

Medication	Warnings/Precautions
Glatiramer (Copaxone®, Glatopa®)	• Post-injection reaction • Chest pain • Lipoatrophy and skin necrosis • Modified immune response
Extavia®, Betaseron® (interferon beta-1B)	• Hepatic injury • Anaphylaxis and other allergic reactions • Depression and suicide • Congestive HF • Injection site necrosis and reactions • Leukopenia • Thrombotic microangiopathy • Flu like symptom complex • Drug induced lupus erythematosus
Rebif®, Rebif® Rebidose®, Avonex® (interferon beta-1A)	• Neuropsychiatric disorders • Hepatic injury • Anaphylaxis and other allergic reactions • Injection site reactions including necrosis • Caution in cardiovascular disease • Decreased peripheral blood counts • Thrombotic microangiopathy • Autoimmune disorders • Seizures
Plegridy® (peginterferon beta-1A)	• Hepatic injury • Depression and suicide • Seizure • Anaphylaxis and other allergic reactions • Injection site reactions • Congestive HF • Decreased peripheral blood counts • Thrombotic microangiopathy • Autoimmune disorders
Ocrevus® (ocrelizumab) Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocs)	• Infusion reactions • Infections • PML • Reduced immunoglobulins • Malignancies • Immune-mediated colitis
Lemtrada® (alemtuzumab)	• Cholecystitis • GI toxicity • Hepatitis • Pneumonitis • PML • Thyroid disorders

Medication	Warnings/Precautions
	• Hemophagocytic lymphohistiocytosis (HLH) • Has not been studied in patients with HBV or HCV; use with caution due to risk for reactivation • Not recommended for patients with inactive disease or who are stable on other treatment • Do not administer live vaccines
Tysabri® (natalizumab)	• Herpes infections • Hepatotoxicity • Hypersensitivity reactions • Immunosuppression/infections • Thrombocytopenia
Briumvi® (ublituximab-xiiy)	• Infusion reactions • Infections • Reduced immunoglobulins • Fetal risk

Kesimpta® (ofatumumab)	• Infection
	• Risk for HBV reactivation
	• PML
	• Reduced immunoglobulins
	• Injection site reactions
	• Drug interactions
	  ○ Additive immunosuppression with other immunosuppressants
	  ○ Immunizations – do not give live vaccines in patients who recently received ofatumumab; the efficacy of vaccine (immune response to vaccines) in patients using ofatumumab is unknown

Teriflunomide (Aubagio®)	• White blood cell count reduction-risk of infection • Anaphylaxis, angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis • Peripheral neuropathy • Increased blood pressure • Embryofetal toxicity
Fingolimod (Gilenya®)	• Infections • PML • Macular edema • Posterior reversible encephalopathy syndrome (PRES) • Respiratory effects • Liver injury • Fetal risk • Increased blood pressure • Cutaneous malignancies • Fetal risk • Tumefaceative MS
Tascenso ODT® (fingolimod)	• Bradyarrhythmia and atrioventricular block • Infections • PML • Macular edema

Medication	Warnings/Precautions
	• Liver injury • Posterior reversible encephalopathy syndrome (PRES) • Fetal risk • Severe increase in disability after stopping Tascenso ODT • Tumefaceative MS • Increased blood pressure • Malignancies
Dimethyl fumarate (Tecfidera®)	• Anaphylaxis and angioedema • PML • Lymphopenia • Liver injury • Herpes zoster and other serious opportunistic infections
Bafiertam™ (monomethyl fumarate)	• Anaphylaxis and angioedema • PML • Infections • Lymphopenia • Hepatotoxicity • Flushing
Vumerity® (diroximel fumarate)	• PML • Lymphopenia • Infections • Flushing • Dermatitis/irritation • GI events • Hepatotoxicity • Proteinuria
Mayzent® (siponimod)	• Infections • Macular edema • Bradyarrhythmia and atrioventricular conduction delays • Respiratory effects (dose depending reduction in absolute FEV1) • Liver injury • Increased blood pressure • Fetal risk • Posterior reversible encephalopathy syndrome • Unintended additive immunosuppressive effects • Severe increased disability upon discontinuation • Immune system effects upon discontinuation
Ponvory® (ponesimod)	• Infections • Bradyarrhythmia and atrioventricular conduction delays • Respiratory effects • Liver injury • Increased blood pressure • Cutaneous malignancies • Fetal risk • Macular edema

Medication	Warnings/Precautions
Zeposia® (ozanimod)	• AV block, bradycardia • Hepatotoxicity • Hypertension • Infections (pre-assessment test for VZV immunity or vaccinate for VZV) • Lymphopenia • Macular edema • Neurotoxicity • PML • Respiratory effects • Cardiovascular • Hepatic impairment • Fetal harm
Mavenclad® (cladribine)	• Malignancies • Risk of teratogenicity • Lymphopenia • Infection • Hematologic toxicity • Graft-versus-host-disease with blood transfusion • Liver injury • Hypersensitivity • Cardiac failure
Mitoxantrone	• Myelosuppression • IV administration only • Secondary acute myeloid leukemia • Cardiac effects • Fetal harm • Secondary infections
Dalfampridine (Ampyra®)	• Seizures • Anaphylaxis • Avoid concomitant use with other forms of 4-aminopyridine (4-AP, fampridine)
Acthar® (corticotropin)	• Infections • Adrenal insufficiency after prolonged therapy • Cushing's syndrome • Elevated Blood Pressure, Salt and Water Retention and Hypokalemia • Vaccination • Masking of Symptoms of Other Underlying Disease/Disorders • Gastrointestinal Perforation and Bleeding • Behavioral and Mood Disturbances • Comorbid Diseases • Ophthalmic Effects • Immunogenicity Potential • Use in Patients with Hypothyroidism or Liver Cirrhosis • Negative Effects on Growth and Physical Development • Decrease in Bone Density • Use in Pregnancy: Embryocidal effect

Practice Guidelines

Rae-Grant A, Day GS, Marrie RA, et al. Practice Guideline Recommendations Summary: Disease-modifying Therapies for Adults with Multiple Sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018;90(17):777-788.

- Starting DMT: Recommendations
  - Clinicians must ascertain and incorporate/review preferences in terms of safety, route of administration, lifestyle, cost, efficacy, common adverse effects (AEs), and tolerability in the choice of DMT in people with MS being considered for DMT. (Level A)
  - Clinicians must engage in an ongoing dialogue regarding treatment decisions throughout the disease course with people with MS. (Level A)
  - Clinicians should discuss the benefits and risks of DMTs for people with a single clinical demyelinating event with two or more brain lesions that have imaging characteristics consistent with MS. After discussing the risks and benefits, clinicians should prescribe DMT to people with a single clinical demyelinating event and two or more brain lesions characteristic of MS who decide they want this therapy. (Level B)
  - Clinicians may recommend serial imaging at least annually for the first five years and close follow-up rather than initiating DMT in people with CIS or relapsing forms of MS who are not on DMT, have not had relapses in the preceding two years, and do not have active new MRI lesion activity on recent imaging. (Level C)
  - Clinicians should offer DMTs to people with relapsing forms of MS with recent clinical relapses or MRI activity. (Level B)
  - Clinicians should counsel men with MS on their reproductive plans regarding treatment implications before initiating treatment with teriflunomide or cyclophosphamide. (Level B)
  - Because of the high frequency of severe AEs, clinicians should not prescribe mitoxantrone to people with MS unless the potential therapeutic benefits greatly outweigh the risks. (Level B)
  - Clinicians should prescribe alemtuzumab, fingolimod, or natalizumab for people with MS with highly active MS. (Level B)
  - Clinicians may recommend azathioprine or cladribine for people with relapsing forms of MS who do not have access to approved DMTs. (Level C)
  - Clinicians may initiate natalizumab treatment in people with MS with positive anti-JCV antibody indexes above 0.9 only when there is a reasonable chance of benefit compared with the low but serious risk of PML. (Level C)
  - Clinicians should offer ocrelizumab to people with PPMS who are likely to benefit from this therapy unless there are risks of treatment that outweigh the benefits. (Level B)
- Switching DMT: Recommendations
  - Clinicians should monitor MRI disease activity from the clinical onset of disease to detect the accumulation of new lesions in order to inform treatment decisions in people with MS using DMTs. Clinicians should recognize that relapses or new MRI-detected lesions may develop after initiation of a DMT and before the treatment becomes effective in people with MS who are using DMTs. Clinicians should discuss switching from one DMT to another in people with MS who have been using a DMT long enough for the treatment to take full effect and are adherent to their therapy when they experience one or more relapses, two or more

unequivocally new MRI-detected lesions, or increased disability on examination, over a one-year period of using a DMT. (Level B)
  - Clinicians should inquire about medication AEs with people with MS who are taking a DMT and attempt to manage these AEs, as appropriate. Clinicians should discuss a medication switch with people with MS for whom these AEs negatively influence adherence. (Level B)
  - Clinicians should discuss switching DMT or reducing dosage or frequency (where there are data on different doses [e.g., interferons, teriflunomide, azathioprine]) when there are persistent laboratory abnormalities. (Level B)
  - Clinicians should counsel people with MS considering natalizumab, fingolimod, rituximab, ocrelizumab, and dimethyl fumarate about the PML risk associated with these agents. Clinicians should discuss switching to a DMT with a lower PML risk with people with MS taking natalizumab who are or become JCV antibody positive, especially with an index of above 0.9 while on therapy. (Level B)
  - Clinicians should counsel that new DMTs without long-term safety data have an undefined risk of malignancy and infection for people with MS starting or using new DMTs. If a patient with MS develops a malignancy while using a DMT, clinicians should promptly discuss switching to an alternate DMT, especially for people with MS using azathioprine, methotrexate, mycophenolate, cyclophosphamide, fingolimod, teriflunomide, alemtuzumab, or dimethyl fumarate. People with MS with serious infections potentially linked to their DMT should switch DMTs (does not pertain to PML management in people with MS using DMT). (Level B)
  - Clinicians should check for natalizumab antibodies in people with MS who have infusion reactions before subsequent infusions, or in people with MS who experience breakthrough disease activity with natalizumab use. Clinicians should switch DMTs in people with MS who have persistent natalizumab antibodies. (Level B)
  - Physicians must counsel people with MS considering natalizumab discontinuation that there is an increased risk of MS relapse or MRI-detected disease activity within six months of discontinuation. (Level A) Physicians and people with MS choosing to switch from natalizumab to fingolimod should initiate treatment within eight to 12 weeks after natalizumab discontinuation (for reasons other than pregnancy or pregnancy planning) to diminish the return of disease activity. (Level B)
  - Clinicians should counsel women to stop their DMT before conception for planned pregnancies unless the risk of MS activity during pregnancy outweighs the risk associated with the specific DMT during pregnancy. Clinicians should discontinue DMTs during pregnancy if accidental exposure occurs, unless the risk of MS activity during pregnancy outweighs the risk associated with the specific DMT during pregnancy. Clinicians should not initiate DMTs during pregnancy unless the risk of MS activity during pregnancy outweighs the risk associated with the specific DMT during pregnancy. (Level B)
- Stopping DMT: Recommendations
  - In people with RRMS who are stable on DMT and want to discontinue therapy, clinicians should counsel people regarding the need for ongoing follow-up and periodic reevaluation of the decision to discontinue DMT. Clinicians should advocate that people with MS who are stable (that is, no relapses, no disability progression, stable imaging) on DMT should continue their current DMT unless the patient and physician decide a trial off therapy is warranted. (Level B)
  - Clinicians should assess the likelihood of future relapse in individuals with SPMS by assessing patient age, disease duration, relapse history, and MRI-detected activity (e.g., frequency, severity, time since most recent relapse or gadolinium-enhanced lesion). (Level B) Clinicians may advise discontinuation of DMT in people with SPMS who do not have ongoing relapses (or gadolinium-enhanced lesions on MRI activity) and

have not been ambulatory (Expanded Disability Status Scale [EDSS} 7 or greater) for at least two years. (Level C)

- Clinicians should review the associated risks of continuing DMTs versus those of stopping DMTs in people with CIS using DMTs who have not been diagnosed with MS. (Level B)

Recommendation Definitions

Level of Recommendation	Phrasing	Definition
Level A	"Must"	Strongest recommendation level; these recommendations are rare, as they are based on high confidence in the evidence and require both a high magnitude of benefit and low risk.
Level B	"Should"	More common recommendations, as the requirements are less stringent but still based on the evidence and benefit−risk profile.
Level C	"May"	Represents the lowest allowable recommendation level the AAN considers useful within the scope of clinical practice and can accommodate the highest degree of practice variation.

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Rae-Grant A, Day GS, Marrie RA, et al. **Comprehensive systematic review summary: Disease-modifying therapies for adults with multiple sclerosis.** Neurology Apr 2018, 90 (17) 789-800; DOI: 10.1212/WNL.0000000000005345.	This is a summary of the findings of the SR/MA on which the AAN 2018 practice guideline on the efficacy and safety of DMTs in MS is based. Twenty Cochrane reviews and an additional 73 full-text articles were selected for data extraction through an updated systematic review (completed November 2016).	• To review evidence on starting, switching, and stopping DMTs for MS in CIS, RRMS, and progressive MS forms.
Results: For people with RRMS, many DMTs are superior to placebo (annualized relapses rates [ARRs], new disease activity [new MRI T2 lesion burden], and in-study disease progression) (see summary and full text publications). For people with RRMS who experienced a relapse on interferon-β (IFN-β) or glatiramer acetate, alemtuzumab is more effective than IFN-β-1a 44 µg SQ 3 times per week in reducing the ARR. For people with primary progressive MS, ocrelizumab is probably more effective than placebo (in-study disease progression). DMTs for MS have varying adverse effects. In people with CIS, glatiramer acetate and IFN-β-1a SQ 3 times per week are more effective than placebo in decreasing risk of conversion to MS. Cladribine, immunoglobulins, IFN-β-1a 30 µg intramuscular weekly, IFN-β-1b SQ alternate day, and teriflunomide are probably more effective than placebo in decreasing risk of conversion to MS. **Conclusion**: Measures of efficacy such as long-term disability, patient satisfaction, quality of life, and effects on MS symptoms may be important to the decision-making process but ultimately remain inadequately studied. Suggestions for future research include studies considering comparative effectiveness, usefulness of high-efficacy treatment vs stepped-care protocols, and research into predictive biomarkers.		

Citation	Design	Endpoints
Filippini G, Del Giovane C, Clerico M, Beiki O, Mattoscio M, Piazza F, Fredrikson S, Tramacere I, Scalfari A, Salanti G. **Treatment with disease-modifying drugs for people with a first clinical attack suggestive of multiple sclerosis.** Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD012200. DOI: 10.1002/14651858.CD012200.pub2.	This Cochrane systematic review searched the Cochrane Multiple Sclerosis and Rare Diseases of the CNS Group Trials Register, MEDLINE, Embase, CINAHL, LILACS, clinicaltrials.gov, the WHO trials registry, and US FDA reports, and searched for unpublished studies (until December 2016). Randomized and observational studies that evaluated one or more drugs as monotherapy in adult participants with a first clinical attack suggestive of MS were included. The researchers considered evidence on alemtuzumab, azathioprine, cladribine, daclizumab, dimethyl fumarate, fingolimod, glatiramer acetate, immunoglobulins, interferon beta-1b, interferon beta-1a (Rebif®, Avonex®), laquinimod, mitoxantrone, natalizumab, ocrelizumab, pegylated interferon beta-1a, rituximab and teriflunomide. Study data was synthesized using random-effects meta-analyses and indirect comparisons were performed	• To estimate the benefit and safety of disease-modifying drugs that have been evaluated in all studies (randomized or non-randomized) for the treatment of a first clinical attack suggestive of MS compared either with placebo or no treatment. • To assess the relative efficacy and safety of disease-modifying drugs

	between drugs. Odds ratios (OR) and hazard ratios (HR) along with relative 95% confidence intervals (CI) were calculated for all outcomes, and absolute effects were only estimated for primary outcomes. Credibility of the evidence was evaluated using the GRADE system. In total, 10 randomized trials, eight open-label extension studies (OLEs) and four cohort studies published between 2010 and 2016 were included in the review.	according to their benefit and safety. • To estimate the benefit and safety of disease-modifying drugs that have been evaluated in all studies (randomized or non-randomized) for treatment started after a first attack ('early treatment') compared with treatment started after a second attack or at another later time point ('delayed treatment').
Results: The overall risk of bias was high, and the reporting of AEs was scarce. The quality of the evidence associated with the results ranges from low to very low. Early treatment versus placebo during the first 24 months' follow-up: there was a small, non-significant advantage of early treatment compared with placebo in disability-worsening (6.4% fewer participants with disability-worsening with interferon beta-1a (Rebif®) or teriflunomide) and in relapses (10% fewer participants with relapses with teriflunomide). Early treatment was associated with 1.6% fewer participants with at least one serious AE. Participants on early treatment were on average 4.6% times more likely to withdraw from the study due to AEs. This result was mostly driven by studies on interferon beta 1-b, glatiramer acetate and cladribine that were associated with significantly more withdrawals for AEs. Early treatment decreased the hazard of conversion to clinically definite multiple sclerosis (CDMS) (HR 0.53, 95% CI 0.47 to 0.60). Comparing active interventions during the first 24 months' follow-up: indirect comparison of interferon beta-1a (Rebif®) with teriflunomide did not show any difference on reducing disability-worsening (OR 0.84, 95% CI 0.43 to 1.66). No differences were found between the included drugs with respect to the hazard of conversion to CDMS. Interferon beta-1a (Rebif®) and teriflunomide were associated with fewer dropouts because of AEs compared with interferon beta-1b, cladribine and glatiramer acetate (ORs range between 0.03 and 0.29, with substantial uncertainty). Early versus delayed treatment: researchers did not find evidence of differences between early and delayed treatments for disability-worsening at a maximum of five years' follow-up (3% fewer participants with early treatment). There was important variability across interventions; early treatment with interferon beta-1b considerably reduced the odds of participants with disability-worsening during three and five years' follow-up (OR 0.52, 95% CI 0.32 to 0.84 and OR 0.57, 95% CI 0.36 to 0.89). The early treatment group had 19.6% fewer participants with relapses compared to late treatment at a maximum of five years' follow-up and early treatment decreased the hazard of conversion to CDMS at any follow-up up to 10 years (i.e., over five years' follow-up HR 0.62, 95% CI 0.53 to 0.73). No conclusions were drawn on long-term serious AEs or discontinuation due to AEs because of inadequacies in the available data both in the included OLEs and cohort studies. **Conclusion**: Very low-quality evidence suggests a small and uncertain benefit with early treatment compared with placebo in reducing disability-worsening and relapses. The advantage of early treatment compared with delayed on disability-worsening was heterogeneous depending on the actual drug used and based on very low-quality evidence. Low-quality evidence suggests that the chances of relapse are less with early treatment compared with delayed. Early treatment reduced the hazard of conversion to CDMS compared either with placebo, no treatment or delayed treatment, both in short- and long-term follow-up. Low-quality evidence suggests that early treatment is associated		

with fewer participants with at least one serious AE compared with placebo. Very low-quality evidence suggests that, compared with placebo, early treatment leads to more withdrawals or treatment discontinuation due to AEs. Difference between drugs on short-term benefit and safety was uncertain because few studies and only indirect comparisons were available. Long-term safety of early treatment is uncertain because of inadequately reported or unavailable data.		
Citation	**Design**	**Endpoints**
La Mantia L, Di Pietrantonj C, Rovaris M, et al. **Interferons-beta versus glatiramer acetate for relapsing-remitting multiple sclerosis.** Cochrane Database Syst Rev. 2016 Nov 24;11:CD009333. DOI: 10.1002/14651858.CD009333.pub3	This was a Cochrane review update (systematic review) on the same topic first published in 2014. The Trials Register of the Cochrane Multiple Sclerosis and Rare Diseases of the CNS Group (up to August 8, 2016) and the reference lists of retrieved articles were searched as well as authors and pharmaceutical companies were contacted. Search criteria included randomized controlled trials (RCTs) directly comparing IFNs-beta versus glatiramer acetate (GA) in study participants affected by RRMS. Six trials were included, and five trials contributed to this review with data. A total of 2904 participants were randomly assigned to IFNs (1704) and GA (1200). The treatment duration was three years for one study, two years for the other four RCTs while one study was stopped early (after one year). The IFNs analyzed in comparison with GA were IFN-beta 1b 250 mcg (two trials, 933 participants), IFN-beta 1a 44 mcg (three trials, 466 participants) and IFN-beta 1a 30 mcg (two trials, 305 participants). Enrolled participants were affected by active RRMS.	• To assess whether IFNs-beta and GA differ in terms of safety and efficacy in the treatment of people with relapsing-remitting (RR) MS.
Results: Both therapies showed similar clinical efficacy at 24 months, given the primary outcome variables (number of participants with relapse (risk ratio (RR) 1.04, 95% confidence interval (CI) 0.87 to 1.24) or progression (RR 1.11, 95% CI 0.91 to 1.35). However at 36 months, evidence from a single study suggests that relapse rates were higher in the group given IFNs than in the GA group (RR 1.40, 95% CI 1.13 to 1.74, P value 0.002).Secondary magnetic resonance imaging (MRI) outcomes analysis showed that effects on new or enlarging T2- or new contrast-enhancing T1 lesions at 24 months were similar (mean difference (MD) -0.15, 95% CI -0.68 to 0.39, and MD -0.14, 95% CI -0.30 to 0.02, respectively). However, the reduction in T2- and T1-weighted lesion volume was significantly greater in the groups given IFNs than in the GA groups (MD -0.58, 95% CI -0.99 to -0.18, P value 0.004, and MD -0.20, 95% CI -0.33 to -0.07, P value 0.003, respectively).The number of participants who dropped out of the study because of adverse events was similar in the two groups (RR 0.95, 95% CI 0.64 to 1.40).The quality of evidence for primary outcomes was judged as moderate for clinical end points, but for safety and some MRI outcomes (number of active T2 lesions), quality was judged as low. **Conclusion**: The effects of IFNs-beta and GA in the treatment of people with RRMS, including clinical (e.g., people with relapse, risk to progression) and MRI (Gd-enhancing lesions) measures, seem to be similar or to show only small differences. When MRI lesion load accrual is considered, the effect of the two treatments differs, in that IFNs-beta were found to limit the increase in lesion burden as compared with GA. Evidence was insufficient for a comparison of the effects of the two treatments on patient-reported outcomes, such as quality-of-life measures.		
Citation	**Design**	**Endpoints**

Filippini G, Del Giovane C, Vacchi L, et al. **Immunomodulators and immunosuppressants for multiple sclerosis: a network meta-analysis.** Cochrane Database Syst Rev. 2013 Jun 6;(6):CD008933. doi: 10.1002/14651858.CD008933.pub2.	This was a network meta-analysis which searched the Cochrane Database of Systematic Reviews, the Cochrane MS Group Trials Register, and the Food and Drug Administration (FDA) reports for randomized controlled trials (RCTs) that studied one of the 11 treatments available as of February 2012 for use in adults with MS and that reported pre-specified efficacy outcomes. Data synthesis was performed by pairwise meta-analysis and network meta-analysis that was performed within a Bayesian framework. The body of evidence for outcomes within the pairwise meta-analysis was assessed according to GRADE, as very low, low, moderate, or high quality. Forty-four trials were included in this review, in which 17,401 participants had been randomized. Twenty-three trials included relapsing-remitting MS (RRMS) (9096 participants, 52%), 18 trials included progressive MS (7726, 44%), and three trials included both RRMS and progressive MS (579, 3%). The majority of the included trials were short-term studies, with the median duration being 24 months. The results originated mostly from 33 trials on IFNß, glatiramer acetate, and natalizumab that overall contributed outcome data for 9881 participants (66%).	• To estimate the relative efficacy and acceptability of interferon ß-1b (IFNß-1b) (Betaseron), interferon ß-1a (IFNß-1a) (Rebif and Avonex), glatiramer acetate, natalizumab, mitoxantrone, methotrexate, cyclophosphamide, azathioprine, IV immunoglobulins, and long-term corticosteroids versus placebo or another active agent in participants with MS and to provide a ranking of the treatments according to their effectiveness and risk-benefit balance.
Results: From the pairwise meta-analysis, there was high quality evidence that natalizumab and IFNß-1a (Rebif) were effective against recurrence of relapses in RRMS during the first 24 months of treatment compared to placebo (odds ratio (OR) 0.32, 95% confidence interval (CI) 0.24 to 0.43; OR 0.45, 95% CI 0.28 to 0.71, respectively); they were more effective than IFNß-1a (Avonex) (OR 0.28, 95% CI 0.22 to 0.36; OR 0.19, 95% CI 0.06 to 0.60, respectively). IFNß-1b (Betaseron) and mitoxantrone probably decreased the odds of the participants with RRMS having clinical relapses compared to placebo (OR 0.55, 95% CI 0.31 to 0.99; OR 0.15, 95% CI 0.04 to 0.54, respectively) but the quality of evidence for these treatments was graded as moderate. From the network meta-analysis, the most effective drug appeared to be natalizumab (median OR versus placebo 0.29, 95% credible intervals (CrI) 0.17 to 0.51), followed by IFNß-1a (Rebif) (median OR versus placebo 0.44, 95% CrI 0.24 to 0.70), mitoxantrone (median OR versus placebo 0.43, 95% CrI 0.20 to 0.87), glatiramer acetate (median OR versus placebo 0.48, 95% CrI 0.38 to 0.75), IFNß-1b (Betaseron) (median OR versus placebo 0.48, 95% CrI 0.29 to 0.78). However, the confidence was moderate for direct comparison of mitoxantrone and IFNB-1b vs placebo and very low for direct comparison of glatiramer vs placebo. The relapse outcome for RRMS at three years' follow-up was not reported by any of the included trials. Disability progression was based on surrogate markers in the majority of included studies and was unavailable for RRMS beyond two to three years. The pairwise meta-analysis suggested, with moderate quality evidence, that natalizumab and IFNß-1a (Rebif) probably decreased the odds of the participants with RRMS having disability progression at two years' follow-up, with an absolute reduction of 14% and 10%, respectively, compared to placebo. Natalizumab and IFNß-1b (Betaseron) were significantly more effective (OR 0.62, 95% CI 0.49 to 0.78; OR 0.35, 95% CI 0.17 to 0.70, respectively) than IFNß-1a (Avonex) in reducing the number of the participants with RRMS who had progression at two years' follow-up, and confidence in this result was graded as moderate. From the network meta-analyses, mitoxantrone appeared to be the most effective agent in decreasing the odds of the participants with RRMS having		

progression at two years' follow-up, but the confidence was very low for direct comparison of mitoxantrone vs placebo. Both pairwise and network meta-analysis revealed that none of the individual agents included in this review were effective in preventing disability progression over two or three years in patients with progressive MS. There was not a dose-effect relationship for any of the included treatments with the exception of mitoxantrone.
Conclusion: On the basis of high quality evidence, natalizumab and IFNß-1a (Rebif) are superior to all other treatments for preventing clinical relapses in RRMS in the short-term (24 months) compared to placebo. Moderate quality evidence supports a protective effect of natalizumab and IFNß-1a (Rebif) against disability progression in RRMS in the short-term compared to placebo. These treatments are associated with long-term serious adverse events and their benefit-risk balance might be unfavorable. IFNß-1b (Betaseron) and mitoxantrone probably decreased the odds of the participants with RRMS having relapses, compared with placebo (moderate quality of evidence). The benefit-risk balance with azathioprine is uncertain, however this agent might be effective in decreasing the odds of the participants with RRMS having relapses and disability progression over 24 to 36 months, compared with placebo. The lack of convincing efficacy data shows that IFNß-1a (Avonex), IV immunoglobulins, cyclophosphamide and long-term steroids have an unfavorable benefit-risk balance in RRMS. None of the included treatments are effective in decreasing disability progression in patients with progressive MS. It is important to consider that the clinical effects of all these treatments beyond two years are uncertain, a relevant point for a disease of 30 to 40 years duration. Direct head-to-head comparison(s) between natalizumab and IFNß-1a (Rebif) or between azathioprine and IFNß-1a (Rebif) should be top priority on the research agenda and follow-up of the trial cohorts should be mandatory.

Citation	Design	Endpoints
Institute for Clinical and Economic Review (ICER). **Disease-Modifying Therapies for Relapsing-Remitting and Primary-Progressive Multiple Sclerosis: Effectiveness and Value (Final Evidence Report).** Available at https://icer-review.org/wp-content/uploads/2016/08/CTAF_MS_Final_Report_030617.pdf. Epub March 6, 2017.	ICER abstracted evidence from available clinical studies of DMTs in the treatment of RRMS and PPMS, whether in published or abstract form. There were 33 unique randomized trials with 21,768 patients for the RRMS indication and 2 randomized trials for the PPMS indication. The oldest trial was published in 1987 and the most recent trial was published in 2017. This evidence was sufficient to perform network meta-analyses (NMA) that combined direct (head-to-head) and indirect evidence for relapse rate and sustained disability progression. The results of the overall NMA were consistent with the findings of the head-to-head trials for these two outcomes. There was sparse evidence and no consistent outcome measure for MRI and quality of life outcomes, so NMAs were not performed for these outcomes.	• Comparative clinical effectiveness and value of DMTs in the treatment of RRMS and PPMS.

Results/Conclusions:
Performance:
Reduction of relapse-for RRMS, all of the DMTs reduce the number of relapses compared to best supportive care. Alemtuzumab, natalizumab, and ocrelizumab were the most effective. Fingolimod, daclizumab, rituximab, and dimethyl fumarate were the next most effective. The interferons, glatiramer acetate, and teriflunomide were the least effective, but still better than best supportive care. Progression of disability-while all the drugs reduce disability progression (excluding rituximab, for which data on this outcome was not available), there is greater uncertainty in the estimates for the effectiveness on this outcome. Alemtuzumab and ocrelizumab were the most effective drugs at reducing disability progression, followed closely by natalizumab and daclizumab. The next most effective drugs were dimethyl fumarate, peginterferon β-1a, interferon β-

1b, and fingolimod. Teriflunomide, glatiramer acetate, and the remaining interferons were less effective, but were still superior to best supportive care. For PPMS, ocrelizumab reduced progression compared to best supportive care.
Risks: Interferons and glatiramer acetate have more favorable safety profiles compared to more effective agents, while newer agents are more effective but carry greater risks for life threatening infections and autoimmune disease.
Sources of uncertainty: Trial duration testing these drugs were generally not sufficient in length to assess long-term effects of DMTs on disability progression. Patient reported outcomes such as fatigue, mood disorders, and quality of life, were not consistently reported. Patient populations included in trials have changed over many years of research and lead to uncertainty when comparing earlier and later trials.
ICER Evidence Ratings: RRMS-the interferons, glatiramer acetate, and teriflunomide provide incremental net health benefits when compared to best supportive care and are largely similar in their effects on relapse rates and disability progression. There is moderate certainty of small to substantial net health benefit for alemtuzumab, natalizumab, and ocrelizumab compared to the interferons and glatiramer acetate. There is moderate certainty of comparable or better net health benefit for daclizumab, fingolimod, and dimethyl fumarate compared to the interferons and glatiramer acetate. PPMS-there is moderate certainty of small to substantial net health benefit for ocrelizumab compared to best supportive care.
Long-term cost effectiveness at net price: The cost per QALY for alemtuzumab compared to supportive care was $38,000, which represents good value. When compared to glatiramer acetate, alemtuzumab was more effective and less costly over time, though this drug may only be suitable for a subset of patients due to its safety profile. Cost per QALY estimates for the remaining DMTs versus supportive care were above the range for reasonable value, representing poor long-term value for money.

Citation	Design	Endpoints
Kappos L, Bar-Or A, Cree BAC, et al. **Siponimod versus placebo in secondary progressive multiple sclerosis (EXPAND): a double-blind, randomized, phase 3 study.** Lancet. 2018 Mar 31;391(10127):1263-1273. doi: 10.1016/S0140-6736(18)30475-6. Epub 2018 Mar 23. Accessed on March 20, 2019. NCT: 01665144 PMID: 29576505	Randomized (2:1) parallel-group, double-blind, placebo-controlled, event-driven trial enrolled 1645 patients with SPMS defined as progressive increase of disability over at least 6 months. Participants were randomized to receive either once daily oral siponimod 2 mg or placebo. Inclusion criteria: EDSS score of 3.0 to 6.5 and no relapse with corticosteroid treatment within the prior 3 months Exclusion criteria: macular edema, any unstable condition determined by investigator	Primary: The percent of patients with 3-month confirmed disability progression (CDP) events as measured by the EDSS at 3 month intervals up to a maximum of 3 years follow-up

Results/Conclusions:
26% of siponimod patients and 32% of patients receiving placebo had 3-month CDP (hazard ratio 0.79, 95% CI 0.65-0.95; relative risk reduction 21%; p=0.013). The rate of adverse events was similar in both groups, although serious adverse events, including lymphopenia, increased liver transaminase concentration, bradycardia and bradyarrhythmia upon initiation of therapy, macular edema, hypertension, varicella zoster reactivation, and convulsions, occurred at higher rates in the siponimod group. The authors concluded that “siponimod reduced the risk of disability progression with a safety profile similar to that of other S1P modulators and is likely to be a useful treatment for SPMS.”

Citation	Design	Endpoints
Giovannoni G, Comi G, Cook S, et al. **A Placebo-Controlled Trial of Oral Cladribine for Relapsing Multiple Sclerosis.** N Engl J Med. 2010 Feb 4;362(5):416-26. doi: 10.1056/NEJMoa0902533. Epub 2010 Jan 20. NCT: 00213135 PMID: 20089960	Phase III, randomized (1:1:1), double-blind, placebo controlled study of adults with definite RRMS as per McDonald criteria and MRI consistent with Fazekas criteria. Patients received one of two cumulative doses of cladribine tablets (either 3.5 mg or 5.25 mg per kilogram of body weight) or matching placebo, given in two or four short courses for the first 48 weeks, then in two short courses starting at week 48 and week 52 (for a total of 8 to 20 days per year). N = 1326 Inclusion criteria: 1 or more relapses within the past 12 months but not within the previous 28 days, EDSS 0 to 5.5, females must be non-pregnant, not breast feeding or attempting to conceive, females must be post-menopausal or surgically sterilized; using a hormonal contraceptive, intrauterine device, or diaphragm/condom with spermicide for the duration of the study, males must use contraception Exclusion criteria: SPMS, PPMS, DMT use within the past 3 months or 2 or more DMT failures due to efficacy, leukopenia, thrombocytopenia, neutropenia within previous 28 days, history of persistent anemia, leukopenia, neutropenia, or thrombocytopenia after immunosuppressive therapy, history of treatment with cladribine, mitoxantrone, total lymphoid irradiation, myelosuppressive therapy, campath-1h, cyclophosphamide, azathioprine, methotrexate or natalizumab, oral or systemic corticosteroids or adrenocorticotropic hormone (ACTH) within previous 28 days, cytokine-based therapy, IV immunoglobulin therapy, or plasmapheresis within previous 3 months, current or prior history of malignancy	Primary: Rate of relapse at 96 weeks Secondary: • Percentage of relapse-free participants • Time to disability progression • Mean number of combined unique (CU) lesions, active time constant 2 (T2) lesions, and active time constant 1 (T1) gadolinium-enhanced (Gd+) lesions per participant per scan • Other: Adverse events
Results/Conclusions: Among patients who received cladribine tablets (either 3.5 mg or 5.25 mg per kilogram), there was a significantly lower annualized rate of relapse than in the placebo group (0.14 and 0.15, respectively, vs. 0.33; P<0.001 for both comparisons), a higher relapse-free rate (79.7% and 78.9%, respectively, vs. 60.9%; P<0.001 for both comparisons), a lower risk of 3-month sustained progression of disability (hazard ratio for the 3.5-mg group, 0.67; 95% confidence interval [CI], 0.48 to 0.93; P=0.02; and hazard ratio for the 5.25-mg group, 0.69; 95% CI, 0.49 to 0.96; P=0.03), and significant reductions in the brain lesion count on magnetic resonance imaging (MRI) (P<0.001 for all comparisons).		

Adverse events that were more frequent in the cladribine groups included lymphocytopenia (21.6% in the 3.5-mg group and 31.5% in the 5.25-mg group, vs. 1.8%) and herpes zoster (8 patients and 12 patients, respectively, vs. no patients). According to the authors, "Treatment with cladribine tablets significantly reduced relapse rates, the risk of disability progression, and MRI measures of disease activity at 96 weeks. The benefits need to be weighed against the risks."		
Citation	**Design**	**Endpoints**
Leist TP, Comi G, Cree BA, et al. **Effect of Oral Cladribine on Time to Conversion to Clinically Definite Multiple Sclerosis in Patients with a First Demyelinating Event (ORACLE MS): A Phase 3 Randomized Trial.** Lancet Neurol. 2014 Mar;13(3):257-67. doi: 10.1016/S1474-4422(14)70005-5. Epub 2014 Feb 4. NCT: 00725985 PMID: 24502830	Phase III, randomized (1:1:1), double-blind, placebo-controlled, multi-center clinical trial of patients with first clinical demyelinating event at high risk of converting to MS. Patients received cladribine tablets at cumulative doses of 5.25 mg/kg or 3.5 mg/kg or placebo. Inclusion criteria: recent first clinical demyelinating event; two clinically silent lesions of ≥ 3 mm on a T2-weighted brain MRI scan); EDSS score 0 to 5.0; negative for active/latent TB Exclusion criteria: Definite MS or any other disease that could better explain symptoms, complete transverse myelitis or bilateral optic neuritis, other autoimmune disease; previous use of any other approved DMT or experimental MS treatment; oral or systemic corticosteroids or ACTH within prior 30 days; previous treatment with any immunomodulatory or immunosuppressive therapy; history of uncontrolled or inadequately controlled seizures; active or chronic infectious or immune compromising disease; prior or current malignancy; abnormal total bilirubin, AST/ALT, or alkaline phosphatase > 2.5 times the ULN; clinically significant hematological abnormalities; positive stool hemoccult test N = 616	Primary – Time to conversion to clinically definite MS according to the Poser criteria
Results/Conclusions: Cladribine was associated with a risk reduction versus placebo for time to conversion to clinically definite MS (hazard ratio [HR] for 5.25 mg/kg=0.38, 95% CI 0.25-0.58, p<0.0001; HR for 3.5 mg/kg=0.33, 0.21-0.51, p<0.0001). Adverse events were reported in 165 (81%) patients in the cladribine 5.25 mg/kg group, 168 (82%) patients in the cladribine 3.5 mg/kg group, and 162 (79%) patients in the placebo group. We noted no increase in risk of adverse events with active treatment versus placebo apart from lymphopenia, which was a severe event in 10 (5%) patients in the 5.25 mg/kg group and four (2%) patients in the 3.5 mg/kg group. Both doses of cladribine significantly delayed MS diagnosis compared with placebo. The safety profile of cladribine was similar to that noted in a trial in patients with relapsing-remitting MS.		
Citation	**Design**	**Endpoints**

Comi G, Kappos L, Selmaj KW, et al. **SUNBEAM Study Investigators. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (SUNBEAM): a multicentre, randomized, minimum 12-month, phase 3 trial.** Lancet Neurol. 2019 Nov;18(11):1009-1020. doi: 10.1016/S1474-4422(19)30239-X. Epub 2019 Sep 3**.** NCT: 02294058 PMID: 31492651	≥ 12-month, double-blind, double-dummy, active-controlled phase 3 trial in which patients with relapsing multiple sclerosis and baseline EDSS 0-5 were randomly assigned (1:1:1) to at least 12 months treatment of either once-daily oral ozanimod 1 mg or 0.5 mg or weekly intramuscular interferon beta-1a 30 µg N = 1346	• Primary – annualized relapse rate (ARR) • Secondary – safety
Results: For relapsing multiple sclerosis patients treated for at least 12 months, ozanimod was well tolerated and demonstrated a significantly lower ARR than interferon beta-1a. Adjusted ARRs were 0.35 (95% CI 0.28-0.44) for interferon beta-1a, 0.18 (95% CI 0.14-0.24) for ozanimod 1.0 mg (rate ratio [RR] of 0.52 [0.41-0.66] vs interferon beta-1a; p<0.0001), and 0.24 (95% CI 0.19-0.31) for ozanimod 0.5 mg (RR 0.69 [0.55-0.86] vs interferon beta-1a; p=0.0013). Few ozanimod-treated participants discontinued treatment because of AEs (2.9% of the ozanimod 1.0 mg group; 1.5% of the ozanimod 0.5 mg group; and 3.6% of the interferon beta-1a group). No first-dose, clinically significant bradycardia or second/third-degree atrioventricular block was reported. Serious AEs occurred with low incidence and at similar rates across treatment groups (2.9% of the ozanimod 1.0 mg group; 3.5% of the ozanimod 0.5 mg group; and 2.5% of the interferon beta-1a group). Ozanimod-treated participants did not experience any serious opportunistic infections. **Conclusions:** The authors concluded that, being well tolerated and having a lower ARR compared to interferon beta-1a, there is evidence to support ozanimod as a treatment option for individuals with relapsing multiple sclerosis.		

Citation	Design	Endpoints
Cohen JA, Comi G, Selmaj KW, et al. **RADIANCE Trial Investigators. Safety and efficacy of ozanimod versus interferon beta-1a in relapsing multiple sclerosis (RADIANCE): a multicentre, randomized, 24-month, phase 3 trial.** Lancet Neurol. 2019 Nov;18(11):1021-1033. doi: 10.1016/S1474-4422(19)30238-8. Epub 2019 Sep 3. NCT: 02047734 PMID: 31492652	24-month, double-blind, double-dummy, placebo-controlled, phase 3 multicenter clinical trial in which patients with relapsing multiple sclerosis and baseline EDSS 0-5 were randomized (1:1:1) to daily oral ozanimod 1.0 mg or 0.5 mg or weekly intramuscular interferon beta-1a 30 µg N = 1320	• Primary – ARR • Secondary – safety
Results: Ozanimod was well tolerated and associated with a significantly lower rate of clinical relapse than intramuscular interferon beta-1a. Adjusted ARRs were 0.17 (95% CI 0.14-0.21) with ozanimod 1.0 mg, 0.22 (95% CI 0.18-0.26) with ozanimod 0.5 mg, and 0.28 (95% CI 0.23-0.32) with interferon beta-1a, with RRs versus interferon beta-1a of 0.62 (95% CI 0.51-0.77; p<0.0001) for ozanimod 1.0 mg and 0.79 (95% CI 0.65-0.96; p=0.0167) for ozanimod 0.5 mg. The incidence of treatment-emergent AEs was higher in the interferon beta-1a group (83%) than in the ozanimod 1.0 mg group (74.7%) and the ozanimod 0.5 mg group (74.3%). More participants in the interferon beta-1a group had treatment-emergent AEs leading to treatment discontinuation than in the ozanimod groups. Infections and serious treatment-emergent AEs occurred at similar rates across all treatment groups. No cases of ozanimod-related symptomatic reduction in heart rate and no second-degree or third-degree cases of atrioventricular block were reported.		

Conclusions: The authors concluded these findings show the potential of ozanimod as a well-tolerated and effective therapy for relapsing multiple sclerosis.		
Citation	**Design**	**Endpoints**
Hauser SL, Bar-Or A, Cohen JA, et al. **Ofatumumab versus Teriflunomide in Multiple Sclerosis.** New England Journal of Medicine. 2020;383(6):546-557. doi:10.1056/nejmoa1917246. NCT: 02792218, 02792231 PMID: 32757523	Two (ASCLEPIOS I and II) randomized, double-blind, double-dummy, active-controlled, multicenter, phase 3 trials of identical design that were conducted concurrently. Arms: Subcutaneous ofatumumab (20 mg every 4 weeks after 20-mg loading doses at days 1, 7, and 14) or oral teriflunomide (14 mg daily) for up to 30 months. Inclusion criteria: Relapsing MS and at least 1 relapse during previous 1 year, 2 relapses during the previous 2 years, or a positive gadolinium-enhancing MRI scan in the previous year; EDSS score 0 to 5.5. Exclusion criteria: PPMS, disease duration > 10 years in patients with an EDSS score of 2 or less; other active chronic immune system disease; at risk or developing or having reactivation hepatitis; active systemic infection or neurological findings consistent with PML N = 1882	• Primary – ARR (defined as the number of confirmed relapses of MS per year) • Secondary – safety
Results: Ofatumumab was associated with lower ARRs than teriflunomide in both ASCLEPIOS I (ARR 0.11 ofatumumab group, 0.22 teriflunomide group; difference -0.11, 95% CI -0.16 to -0.06) and II (ARR 0.10 ofatumumab group, 0.25 teriflunomide group; difference -0.15, 95% CI -0.20 to -0.09) (P<0.001 for both). In the combined analyses, 83.6% in the ofatumumab group reported an adverse event, as compared with 84.2% in the teriflunomide group. Serious adverse events were reported in 9.1% of the patients treated with ofatumumab and 7.9% of those treated with teriflunomide. There was no difference in the rate of infections and infestations between the two groups. Five neoplasms (0.5%) occurred in the ofatumumab group and four (0.4%) in the teriflunomide group. **Conclusion**: The authors concluded "Among patients with multiple sclerosis, ofatumumab was associated with lower annualized relapse rates than teriflunomide."		
Citation	**Design**	**Endpoints**
Kappos L, Fox RJ, Burcklen M, et al**. Ponesimod Compared With Teriflunomide in Patients With Relapsing Multiple Sclerosis in the Active-Comparator Phase 3 OPTIMUM Study: A Randomized Clinical Trial**. JAMA Neurol. 2021 May 1;78(5):558-567. doi: 10.1001/jamaneurol.2021.0405. NCT: 02425644 PMID: 33779698	24-month, multicenter, double-blind, active-comparator, superiority randomized clinical trial in which patients with relapsing multiple sclerosis and baseline EDSS 0-5.5 were randomized (1:1) to once daily oral ponesimod 20 mg or once daily oral teriflunomide 14 mg for 108 weeks N = 1133	Primary: ARR (using confirmed relapses per patient-year from randomization to end of study) Secondary: • Change in fatigue symptoms from baseline to week 108 based on Fatigue Symptom and Impact Questionnaire – Relapsing

		Multiple Sclerosis (FSIQ-RMS) • Cumulative number of combined unique active lesions (CUALs) from baseline to week 108 • Confirmed disability accumulation (CDA) from baseline to end of study • Other: Adverse events
Results: In total, there were 242 confirmed relapses reported for ponesimod compared with 344 for teriflunomide. Ponesimod reduced ARR by 30.5% compared with teriflunomide (mean ARR, 0.202 vs 0.290; rate ratio, 0.695 [99% CI, 0.536-0.902]; p< .001). The change in FSIQ-RMS weekly symptom score from baseline to week 108 was lower (where higher scores indicate more fatigue) for fatigue symptoms in the ponesimod group than the teriflunomide group. The least-square means were 0.01 vs 3.56 (mean difference, −3.57 [95% CI, −5.83 to −1.32]; p = .002). Ponesimod reduced the mean number of CUALs per year on annual brain MRIs from baseline to week 108 by 56% compared with teriflunomide (1.405 vs 3.164; rate ratio, 0.444 [95% CI, 0.364-0.542]; p < .001). The risk of 12-week CDA was not different in the 2 groups (10.1% vs 12.4%; hazard ratio, 0.83 [95% CI, 0.58-1.18]; p = .29), and the formal testing procedure stopped, rendering the subsequent analyses exploratory. In this exploratory analysis, risk of 24-week CDA was also not different (hazard ratio, 0.84 [95% CI, 0.57-1.24]; p = .37). Overall, the proportion of patients who experienced at least 1 treatment-emergent adverse event (TEAE) was similar between the 2 groups (ponesimod, 502 [88.8%]; teriflunomide, 499 [88.2%]). The most common TEAEs (≥10% in either group) were an increased alanine aminotransferase (ALT) level (110 [19.5%] vs 53 [9.4%]), nasopharyngitis (109 [19.3%] vs 95 [16.8%]), headache (65 [11.5%] vs 72 [12.7%]), upper respiratory tract infection (60 [10.6%] vs 59 [10.4%]), and alopecia (18 [3.2%] vs 72 [12.7%]) in the ponesimod vs teriflunomide groups, respectively. **Conclusion**: The authors concluded "OPTIMUM, as the first (to our knowledge) phase 3 study comparing 2 oral DMTs in RMS, showed that ponesimod is superior to teriflunomide, an approved oral DMT, on the primary end point, ARR, and also on 2 of 3 secondary end points: MRI activity and fatigue, a most debilitating MS symptom that until now appears not to have been shown in a prospective phase 3 study to be effectively addressed by other DMTs. Superiority of ponesimod was also shown on the exploratory end points of brain volume loss and NEDA status. Ponesimod was well tolerated, and the safety results were in line with previous observations in its phase 2 dose-finding study and findings on other S1P receptor modulators in controlled studies, including their extensions and post marketing observations."		
Citation	**Design**	**Endpoints**
Śladowska K, Kawalec P, Holko P, Osiecka O. **Comparative safety of high-efficacy disease-modifying therapies in relapsing-remitting multiple sclerosis: a systematic review and network meta-analysis**. Neurol Sci. 2022 Sep;43(9):5479-5500. doi: 10.1007/s10072-022-06197-3. Epub 2022 Jun 17. PMID: 35713731	Systematic review with frequentist network meta-analysis (NMA) performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Included randomized controlled trials (RCTs) with at least 48-week follow-up investigating the use of natalizumab, fingolimod, alemtuzumab, cladribine, ocrelizumab, ofatumumab, ozanimod, and ponesimod, as well as other DMTs, in adult patients with RRMS. Eligible studies were identified by two reviewers in	To compare the safety profile of high-efficacy disease-modifying therapies (DMTs) natalizumab, fingolimod, alemtuzumab, cladribine, ocrelizumab, ofatumumab, ozanimod, as well as a

	MEDLINE (via PubMed), EMBASE, and Cochrane Library. The Cochrane Collaboration tool to assess the risk of bias for RCTs was used.	potentially high-efficacy DMT, ponesimod, in adult patients with relapsing-remitting multiple sclerosis (RRMS) •
Results: A total of 33 RCTs were included in the systematic review and NMA. A higher rate of adverse events (AEs) was revealed for alemtuzumab versus all other high-efficacy DMTs; for alemtuzumab (average probability of an event: 98.2%) versus placebo (86.2%); for cladribine (3.5 mg; 90.5%) versus ozanimod (1 mg; 84.2%) and placebo; as well as for ocrelizumab (95.5%) versus ozanimod, ofatumumab (88.9%), fingolimod (87.4%), natalizumab (82.8%), and placebo. No significant differences were found between drugs in terms of serious AEs except for cladribine (3.5 mg, 17.3%) versus ocrelizumab (10.3%) and ofatumumab (16.6%) versus ocrelizumab. Significant differences in AEs leading to the discontinuation of study drug were found only for ponesimod (10.1%) versus alemtuzumab (12 mg, 3.0%) and placebo (4.2%). No differences were found in terms of upper respiratory tract infections, nasopharyngitis, fatigue, and nausea between individual high-efficacy DMTs as well as between DMTs and placebo. The results of the NMA indicated a higher risk of infections for alemtuzumab (12 mg) versus ocrelizumab, for cladribine (3.5 mg) versus ofatumumab and placebo, and for ofatumumab versus placebo. For serious infections and urinary tract infections, a significant increase was found only for alemtuzumab (12 mg) versus ocrelizumab, while no differences were found between the other DMTs or between DMTs and placebo. Headache was more common for alemtuzumab (12 mg) as compared with all the other high-efficacy DMTs and placebo, as well as for cladribine versus natalizumab and fingolimod versus natalizumab. **Conclusion:** The authors concluded that “the commonly reported AEs are generally similar among high-efficacy DMT; however, based on P scores for most analyzed endpoints, natalizumab and ocrelizumab were shown to be the safest DMTs.”		

PERFORMRx℠

Formulary Placement, Utilization and Cost Experience (10-01-2024 to 12-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Disease Modifying Therapies - Self-administered								
glatiramer (Copaxone®, Glatopa®) 20 mg/mL, 40 mg/mL subcutaneous syringe	3	1	$16,013.49	$5,337.83	0	0 (0%)	F-PA	No change
Extavia® (interferon beta 1b) 0.3 mg subcutaneous vial kit	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Betaseron® (interferon beta 1b) 0.3 mg subcutaneous kit	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Rebif® (interferon beta 1a, albumin) 22 mcg/0.5 mL, 44 mcg/0.5 mL, 8.8 mcg/0.2 mL-22 mcg/0.5 mL subcutaneous syringe	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Rebif Rebidose® (interferon beta 1a, albumin) 8.8 mcg/0.2 mL-22 mcg/0.5 mL, 22 mcg/0.5 mL, 44 mcg/0.5 mL subcutaneous pen injector	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Avonex® (interferon beta 1a) 30 mcg/0.5 mL intramuscular syringe kit	0	0	$0.00	$0.00	0	0 (0%)	F	→F-PA
Avonex ® (interferon beta 1a) 30 mcg/0.5 mL intramuscular pen kit	0	0	$0.00	$0.00	0	0 (0%)	F	→F-PA
Plegridy® (peginterferon beta 1a) 63 mcg/0.5 mL-94 mcg/0.5 mL, 125 mcg/0.5 mL subcutaneous syringe	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Plegridy® (peginterferon beta 1a) 63 mcg/0.5 mL-94 mcg/0.5 mL, 125 mcg/0.5 mL subcutaneous pen injector	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change

Plegridy® (peginterferon beta 1a) 125 mcg/0.5 mL intramuscular syringe	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Kesimpta® (ofatumumab) 20 mg/0.4 mL subcutaneous pen injector	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Teriflunomide (Aubagio®) 7 mg, 14 mg tablets	3	1	$101.04	$33.68	0	0 (0%)	F-PA	→F
Gilenya® (fingolimod) 0.25 mg capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fingolimod (Gilenya®) 0.5 mg capsule	0	0	$0.00	$0.00	0	0 (0%)	F-PA-AL >21	No change
Tascenso ODT® (fingolimod) 0.25, 0.5 mg tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Dimethyl fumarate (Tecfidera®) 120 mg, 240 mg, 120 mg & 240 mg DR capsules	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Bafiertam® (monomethyl fumarate) 95 mg DR capsule	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Vumerity® (diroximel fumarate) 231 mg DR capsule	1	1	$6,751.38	$6,751.38	2	1 (50%)	F-PA	No change
Mayzent® (siponimod) 0.25 mg, 1 mg, 2 mg tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Ponvory® (ponesimod) 20 mg, 14-day starter pack 2-3-4-5-6-7-8-9-10 mg tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Zeposia® (ozanimod) 0.92 mg, 0.23 mg & 0.46 mg capsules	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Mavenclad® (cladribine) 10 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Disease Modifying Therapies - Healthcare professional-administered								
Ocrevus® (ocrelizumab) 30 mg/mL intravenous vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocsq) 920 mg-23,000 units/23 mL subcutaneous vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Lemtrada® (alemtuzumab) 12 mg/1.2 mL intravenous vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Tysabri® (natalizumab) 300 mg/15 mL IV solution, vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Briumvi® (ublituximab-xiiy) 150 mg/6 ml intravenous vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
mitoxantrone 2 mg/mL IV concentrate	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Symptomatic Therapies								
dalfampridine (Ampyra®) 10 mg ER tablet	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Acthar® (corticotropin) 80 unit/mL injection gel	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
TOTAL	7	3	$22,865.91	$3,266.56	2	1 (50%)		

Key (as applicable) F = Formulary, no restrictions; F-QL = Formulary, quantity limit applies; F-AL = Formulary, age limit applies; F-ST = Formulary, step therapy applies; F-PA = Formulary, PA required; NF = Non-formulary; X = Excluded

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Prior Authorization Criteria

Recommendation: Update naming conventions to reflect generic availability of Gilenya and Aubagio, change teriflunomide from F-PA to F, and add to preferred agents in the criteria.

Self-administered Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	
Therapeutic Classes (AHFS)	Immunomodulatory agents
Medications	**Preferred:** **glatiramer acetate (COPAXONE)** **dimethyl fumarate (TECFIDERA)** **teriflunomide (AUBAGIO) ~~(teriflunomide)~~** **Non-preferred:** **fingolimod (GILENYA) (~~fingolimod~~)** **MAYZENT (siponimod)** **Vumerity (diroximel fumarate)** **AVONEX, REBIF (Interferon beta-1a)** **BETASERON, EXTAVIA (Interferon beta-1b)** **COPAXONE (glatiramer acetate)** **glatiramer acetate (GLATOPA)** **PLEGRIDY (Peginterferon beta-1a)** **MAVENCLAD (cladribine)** **ZEPOSIA (ozanimod)** **PONVORY (ponesimod)** **BAFIERTAM (monomethyl fumarate)** **KESIMPTA (ofatumumab)** **Any other newly marketed self-administrable DMT for MS indicated for the listed diagnoses**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Members with primary progressive MS (PPMS) Mavenclad • Clinically Isolated Syndrome (CIS)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Member must be age appropriate per prescribing information (PI) **NOTE: Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	**Initial Approval** — If all of the criteria are met, the request will be approved for 12 months for all agents except Mavenclad (cladribine). If all of the criteria for Mavenclad (cladribine) are met, the request will be approved for 1 course at a time with a lifetime maximum of 2 yearly treatment courses [1 course = (1 cycle per 30 days) two times]. **Later Approval** — 12 months: If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization**

- For all requests, the medication is being prescribed at a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed literature.

Clinically Isolated Syndrome (CIS)

- Diagnosis of CIS
- If the request is for glatiramer, ~~or~~ dimethyl fumarate (Tecfidera), or teriflunomide (Aubagio) approve.
- If the request is for a non-preferred agent, the member must have a documented trial of ~~BOTH~~ two preferred agents or have a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing ~~both~~ two of these therapies (exception Gilenya, see bullet below)

  AND
  - If the request is for fingolimod (Gilenya) ~~(fingolimod)~~, documentation of the following
    - Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination
    - If the request if for fingolimod (Gilenya) ~~(fingolimod)~~ and the member has "highly active" MS, approve WITHOUT requiring trial and failure of both preferred agents
  - If the request is for Mayzent (siponimod), documentation of the following
    - Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination
    - Results of CYP2C9 genotyping AND
      - Member does not have CYP2C9 *3/*3 (**CONTRAINDICATED)**
      - If member has CYP2C9 *1/*3 or *2/*3, dose does not exceed 1 mg daily
  - If the request is for Ponvory (ponesimod) or Zeposia (ozanimod), Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination
  - If the request is for Kesimpta (ofatumumab), documentation that immunizations are up-to-date.

Relapsing Remitting MS (RRMS) and Secondary Progressive MS (SPMS)

- Diagnosis of RRMS or SPMS
- If the request is for glatiramer, ~~or~~ dimethyl fumarate (Tecfidera), or teriflunomide (Aubagio) approve
- If the request is for a non-preferred agent, then the member must have a documented trial of ~~at BOTH~~two preferred agents, or have a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing ~~both~~ two of these therapies (exception Gilenya, see bullet below)

  AND
  - If the request is for fingomod (Gilenya) ~~(fingolimod)~~, documentation of the following
    - Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination

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	▪ If the request if for fingolimod (Gilenya) ~~(fingolimod)~~ and the member has "highly active" MS approve WITHOUT requiring trial and failure of both preferred agents ○ If the request is for Mayzent (siponimod), documentation of the following ▪ Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination ▪ Results of CYP2C9 genotyping AND • Member does not have CYP2C9 *3/*3 (**CONTRAINDICATED)** • If member has CYP2C9 *1/*3 or *2/*3, dose does not exceed 1 mg daily ○ If the request is for Mavenclad (cladribine), documentation of the following ▪ Member's current weight ▪ Results of VZV antibody testing and, if negative, documentation of VZV vaccination ▪ If the member has not tried at least one of the preferred therapies listed above but has a documented medical reason for not utilizing these therapies, the member has tried and failed at least one other DMT for MS ○ If the request is for Ponvory (ponesimod) or Zeposia (ozanimod), Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination ○ If the request is for Kesimpta (ofatumumab), documentation that immunizations are up-to-date. **Reauthorization** CIS • The medication is being prescribed at a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed literature • Documentation was provided that the prescriber has reviewed the risks and benefits of continuing DMT versus stopping. RRMS and SPMS • The medication is being prescribed at a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed literature • Documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit). AND • If the request is for Mavenclad (cladribine) ○ Member's current weight ○ ****NO MORE THAN 2 COURSES IN TOTAL WILL BE APPROVED.**** **Continuation of Therapy/Grandfathering Provision:** Members with history (within the past 90 days or past 12 months for Mavenclad [cladribine]) of a non-preferred product are not required to try a preferred product prior to receiving the non-preferred product.
Criteria Statement	Dimethyl fumarate (Tecfidera), ~~and~~ glatiramer acetate (Copaxone), and teriflunomide (Aubagio) are the preferred agents for multiple sclerosis, dependent on the specific

	sub-type of the disease. Non-preferred agents are reserved for members who have used (or cannot/should not use) two ~~the~~ preferred agents.
Last P&T Review Date	~~12/2024~~3/2025

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Recommendation: Add additional preferred agent teriflunomide (Aubagio)

Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	
Therapeutic Classes (AHFS)	Immunomodulatory agents
Medications	**Non-Preferred** **Ocrevus (ocrelizumab)** **Rituxan (rituximab)** **Ruxience (rituximab-pvvr) - biosimilar** **Truxima (rituximab-abbs) - biosimilar** **Riabni (rituximab-arrx) - biosimilar** **Rituxan Hycela (rituximab/hyaluronidase)** **Lemtrada (alemtuzumab)** **Tysabri (natalizumab)** **Briumvi (ublituximab-xiiy)** **Any other newly marketed healthcare professional administrable DMT for MS indicated for the listed diagnoses**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Tysabri or Briumvi: • Primary Progressive MS (PPMS) Lemtrada: • Primary Progressive MS (PPMS) • Clinically Isolated Syndrome (CIS)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Member must be age appropriate per prescribing information (PI) **NOTE: Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	**Initial Approval** 12 months **Later Approval** 12 months: If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For requests for Tysabri for the indication of Crohn's disease, please see the Specialty Biological Agents for Crohn's Disease policy **** When the biosimilar is indicated, the member must have documented dates of trial and failure, intolerance, inability to use, or contraindication to the biosimilar medication prior to the brand medication approval, OR the currently available biosimilar product does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested, in addition to meeting all applicable criteria below.** **Initial Authorization** Clinically Isolated Syndrome (CIS), Relapsing Remitting MS (RRMS), Secondary Progressive MS (SPMS) ○ Diagnosis of CIS, RRMS, or SPMS ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

	○ Documented trial of ~~BOTH~~ two preferred agents or a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing two of these therapies. ○ Preferred agents: glatiramer, ~~and~~ dimethyl fumarate (Tecfidera), and teriflunomide (Aubagio) OR ○ For members with "highly active" MS requesting Lemtrada (alemtuzumab), Tysabri (natalizumab) or rituximab, a trial with Gilenya (fingolimod) alone will be acceptable. ○ If the request is for Ocrevus (ocrelizumab), Briumvi (ublituximab-xiiy), or rituximab, documentation of the following: ○ Attestation that the member has been screened for and does not have active hepatitis B virus (HBV) ○ Attestation that the member has received all non-live immunizations for rituximab according to immunization guidelines or has a documented medical reason for not receiving recommended immunizations ○ If the request is for Rituxan Hycela (rituximab/hyaluronidase) or brand Rituxan, all of the above AND documented medical reason why the member cannot use a rituximab biosimilar product. ○ If the request is for Tysabri (natalizumab), documentation of the following ○ Member does not have a history of progressive multifocal leukoencephalopathy (PML) ○ Documentation consistent with pharmacy claims data indicating the member is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications Primary Progressive Multiple Sclerosis (PPMS) ○ Diagnosis of PPMS ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature ○ If the request is for Ocrevus (ocrelizumab) or rituximab, documentation of the following has been submitted ○ Attestation that the member has been screened for and does not have active HBV ○ Member has received all non-live immunizations for rituximab, according to immunization guidelines or has a documented medical reason for not receiving recommended immunizations ○ If the request is for Rituxan Hycela (rituximab/hyaluronidase) or brand Rituxan, all of the above AND documented medical reason why the member cannot use a rituximab biosimilar product. **Reauthorization** CIS ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature ○ Documentation was provided that the prescriber has reviewed the risks and benefits of continuing DMT versus stopping.

	PPMS, RRMS, or SPMS ○ Documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit) ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature ○ If the request is for Lemtrada (alemtuzumab), documentation of the following ○ At least 12 months has or will have elapsed since previous treatment ○ If the request is for Tysabri (natalizumab), documentation of the following has been submitted ○ Member does not have a history of PML ○ Documentation consistent with pharmacy claims data was submitted indicating the member is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications **Continuation of Therapy Provision**: Members with history (within the past 90 days) of a non-formulary product (or the past 12 months for Lemtrada) are not required to try a preferred agent prior to receiving the non-preferred product.
Criteria Statement	Ocrevus (ocrelizumab), rituximab, Briumvi (ublituximab-xiiy), Lemtrada (alemtuzumab), and Tysabri (natalizumab) are reserved for members with multiple sclerosis who have tried and failed or have a reason not to use twobeth of the following agents: glatiramer, or dimethyl fumarate (Tecfidera), or teriflunomide (Aubagio). Rituxan/ Rituxan Hycela (rituximab) is reserved for members with multiple sclerosis who have tried and failed or have a reason not to use a rituximab biosimilar product AND both two of the following agents: glatiramer, or dimethyl fumarate (Tecfidera), or teriflunomide (Aubagio).
Last P&T Review Date	6/20243/2025

No changes

dalfampridine (Ampyra)	
Therapeutic Classes (AHFS)	Other miscellaneous therapeutic agents
Medications	Formulary, PA required **dalfampridine (Ampyra)**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	History of seizures. Moderate or severe renal impairment (creatinine clearance ≤ 50mL/minute)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Patient must be 18 years of age or older. **NOTE: Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	**Initial Approval** 6 months **Later Approval** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization:** • Baseline creatinine clearance (within 6 months of request) • Patient has diagnosis of multiple sclerosis (MS), patient is ambulatory (baseline 25 foot walk was submitted with request), AND patient has walking impairment • Documentation was submitted (consistent with pharmacy claims data, OR for new members to the health plan, consistent with chart notes) that patient is currently being treated for MS (e.g. immunomodulator, interferon, immunosuppressive), or documentation of a medical reason (intolerance, hypersensitivity) as to why patient is unable to use one of these agents to treat their medical condition • Drug is being requested at an FDA approved dose **Re-authorization:** • Documentation of improvement (above baseline) in 25 foot walk was submitted with request • Documentation was submitted patient is on MS treatment (e.g. immunomodulator, interferon, immunosuppressive), or documentation of a medical reason (intolerance, hypersensitivity) as to why patient is unable to use one of these agents to treat their medical condition • Drug is being requested at an FDA approved dose
Criteria Statement	**Dalfampridine (Ampyra)** is reserved for members who are ambulatory, have a walking impairment, and are using (or cannot/should not use) disease modifying oral or injectable treatment for multiple sclerosis.
Last P&T Review Date	~~12/2024~~3/2025

No changes

Corticotropin	
Therapeutic Classes (AHFS)	Other miscellaneous therapeutic agents
Medications	Formulary, PA required Preferred: Cortrophin (corticotropin) Non-Preferred: Acthar Gel (corticotropin)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	**Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Diagnosis by a neurologist or a specialist in the condition they are treating
Coverage Duration	**Initial Approval** 4 weeks **Later Approval** 4 weeks If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**All requests must be reviewed by a clinical pharmacist first and then forwarded to AAH for review** **Multiple Sclerosis:** • Documentation was submitted that the member is having an acute attack, with neurologic symptoms and increased disability or impairments in vision, strength or cerebellar function, and has failed therapy with IV methylprednisolone, or a medical reason has been submitted why member is unable to use IV methylprednisolone. • If the request is for a non-preferred product, trial and failure of, contraindication to or medical reason for not using the preferred product is required. **All Other FDA Approved Conditions and Indications:** • Documented trial and failure of IV AND oral corticosteroids, or documented medical reason for why the member cannot use these therapies for treatment **AND** • Documentation was provided that ALL other standard therapies have been used to treat the member's condition as described in medical compendia (Micromedex, AHFS, Drug Points, and package insert) as defined in the Social Security Act and/or per recognized standard of care guidelines OR there is a documented medical reason (i.e. medical intolerance, treatment failure, etc.) for why all other standard therapies could not be used to treat the member's condition. **AND** • If the request is for a non-preferred product, trial and failure of, contraindication to or medical reason for not using the preferred product is required **Appeals/Reconsiderations:** • Requests for appeals/reconsiderations will be sent out for independent medical review.

Criteria Statement	Cortrophin (corticotropin) is reserved for members with a diagnosis of an acute attack of multiple sclerosis who have used (or cannot/should not use) IV methylprednisolone Acthar is reserved for members with a diagnosis of an acute attack of multiple sclerosis who have used (or cannot/should not use) IV methylprednisolone AND Cortrophin.
Last P&T Review Date	~~12/2024~~3/2025

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Antihistamines, Second Generation

Executive Summary

Class Overview

Allergic rhinitis is characterized by sneezing, rhinorrhea, nasal obstruction, and itching of the eyes, nose, and mouth. It is also associated with postnasal drip, cough, and fatigue and occurs in approximately 8% to 30% of individuals in the United States, with the prevalence increasing, particularly in urban areas. Symptoms can be present year round, seasonally, or episodically upon exposure to specific allergens. Urticaria, or hives, involves pruritic erythematous plaques, sometimes accompanied with angioedema, and approximately 20% of the general population will experience it at some point in their lives. Potential triggers may include drugs, food, insect stings/bites, or infection. Allergic conjunctivitis refers to inflammation of the mucous membrane that lines the inside surface of the eye lids caused by airborne allergens contacting the eye. It is usually benign and self-limiting or easily treated with pharmacologic therapy.

Second-generation antihistamines are preferred over first-generation agents for allergic rhinitis and urticaria due to the lower incidence of adverse events. For more severe allergic rhinitis, intranasal corticosteroids have shown superior efficacy. Azelastine and olopatadine are available as prescription nasal sprays, having a more rapid onset of action (15 minutes) than intranasal corticosteroids (may take days or weeks to achieve full response) and therefore can be administered on-demand. These antihistamines are also available as eye drops for allergic conjunctivitis along with a few other drugs exclusively for this indication [e.g. ketotifen (Zaditor®)]. Combination second-generation antihistamines with decongestants (i.e. pseudoephedrine) are also available (Zyrtec®-D, Claritin®-D, Allegra®-D, etc.). Although originally available as prescription drugs, all first- and second-generation antihistamines are now available in some form over the counter.

Utilization Findings

There were 331 claims for 234 members, for a total cost of $2,113.79 and an average cost per claim of $6.39. The most highly utilized medication was Cetirizine tablet, with 149 claims, followed by Loratadine tablet with 96 claims. There were no prior authorization requests.

Recommendations

- Add Fexofenadine-pseudoephedrine 60-120 mg oral tablet and Fexofenadine-pseudoephedrine 180-240 mg oral tablet to F-ST to align with criteria
    - Currently, fexofenadine-psudoephedrine is NF, there is MRG policy that covers these agents with a Step criteria, and there is utilization of Fexofenadine-pseudoephedrine 180-240 mg tablet
    - ST: Documentation of a trial and failure or intolerance to loratadine, cetirizine, OR levocetirizine required
- Change Bepotastine besilate (Bepreve®) 1.5% ophthalmic drops from F to F-PA to match the status in the criteria and for cost savings

- Bepotastine is F-PA in the criteria, there is no utilization, and it's more costly than the preferred alternative on formulary

Clinical Summary

Allergic rhinitis is characterized by sneezing, rhinorrhea, nasal obstruction, and itching of the eyes, nose, and mouth. It is also associated with postnasal drip, cough, and fatigue and occurs in approximately 8% to 30% of individuals in the United States, with the prevalence increasing, particularly in urban areas. Symptoms can be present year round, seasonally, or episodically upon exposure to specific allergens. Urticaria, or hives, involves pruritic erythematous plaques, sometimes accompanied with angioedema, and approximately 20% of the general population will experience it at some point in their lives. Potential triggers may include drugs, food, insect stings/bites, or infection. Allergic conjunctivitis refers to inflammation of the mucous membrane that lines the inside surface of the eye lids caused by airborne allergens contacting the eye. It is usually benign and self-limiting or easily treated with pharmacologic therapy.

Allergic triggers release histamine, which is produced predominantly by mast cells (may also be released by basophils, neutrophils, and platelets). Secretory granule exocytosis rapidly releases histamine after immunoglobulin E (IgE) or non-IgE stimulation, binding to histamine 1-4 (H1-4) receptors located on target cells. H1 receptor binding increases venular permeability, nasal mucus production, heart rate, and cardiac output, and leads to bronchial and intestinal smooth muscle contraction, widened pulse pressure, flushing, and T-cell neutrophil and eosinophil chemotaxis. H2 receptor binding increase venular permeability, gastric acid secretion, and airway mucus production but inhibits neutrophil and eosinophil influx. H3 receptors are found in the brain and some sympathetic nerve fibers but their role is not precisely understood. H4 receptors modulate T-helper response and initiate chemotaxis in eosinophils.

First-generation antihistamines compete with histamine for H1-receptor sites on effector cells in the gastrointestinal tract, blood vessels, and respiratory tract, while having anticholinergic and sedative effects. Second generation antihistamines are more hydrophilic and were developed to avoid the anticholinergic and central nervous system (CNS) side effects of first-generation products. Although sometimes referred to as H1 antagonists, both first and second generation antihistamines downregulate constitutive H1 receptors. They are therefore inverse agonists, shifting equilibrium from the active form of the H1 receptor to the inactive form. This essentially reduces the activity of histamine on afferent C nerve fibers and other receptor sites. Higher doses may also inhibit the release of pruritic mediators from mast cells.

Second-generation agents have a one hour onset of action, with peak serum levels attained in 2 to 3 hours. They are longer-acting than first-generation agents and are dosed once or twice daily. Metabolites of second-generation antihistamines are sometimes referred to as third-generation antihistamines. These include fexofenadine (Allegra®; metabolite of terfenadine), desloratadine [Clarinex®; metabolite of loratadine (Claritin®)], and levocetirizine [Xyzal®; purified isomer of cetirizine (Zyrtec®)]. Although they were developed to have fewer CNS adverse effects than “second-generation” agents, this has yet to be proven. Second-generation antihistamines are preferred over first-generation agents for allergic rhinitis and urticaria due to the lower incidence of adverse events. For more severe allergic rhinitis, intranasal corticosteroids have shown superior efficacy.

Azelastine and olopatadine are available as prescription nasal sprays, having a more rapid onset of action (15 minutes) than intranasal corticosteroids (may take days or weeks to achieve full response) and therefore can be administered on-demand. These antihistamines are also available as eye drops for allergic conjunctivitis along with other products used

exclusively for this indication [e.g. ketotifen (Zaditor®)]. Most recently an ophthalmic formulation of cetirizine (Zerviate®) indicated for allergic conjunctivitis and an intravenous (IV) formulation of cetirizine (Quzyttir®) for acute urticaria have become available. Patients treated with IV cetirizine are often switched to an oral formulation upon discharge. Combination second-generation antihistamines with decongestants (i.e. pseudoephedrine) can be used in patients with allergic rhinitis involving sinus congestion (Zyrtec®-D, Claritin®-D, Allegra®-D, etc.). Although originally available as prescription drugs, all first- and second-generation antihistamines are now available in some form over the counter. Although some meta-analysis have found greater efficacy for cetirizine and levocetirizine, guidelines do not prefer one agent over another. After failure of one agent, a dose increase is often recommended followed by trying another agent or adding on or replacing with intranasal corticosteroids. For moderate to severe symptoms, an intranasal corticosteroid is preferred over both oral and intranasal antihistamines. A leukotriene receptor antagonist or first-generation antihistamine (or H2 antagonist for chronic idiopathic urticaria) may be recommended for patients that fail initial pharmacotherapy. Refractory chronic idiopathic urticaria may be treated with omalizumab (Xolair®), cyclosporine, other anti-inflammatory agents, immunosuppressants, or other biologics.

Indications, Dosing And Administration

Medication	Indications	Dosing/Administration
Oral Dosage Form		
Cetirizine (Zyrtec®) 1 mg/mL oral solution, 5 mg/5mL unit dose cup oral solution Cetirizine 5 mg tablet Cetirizine (Zyrtec®) 10 mg tablet Cetirizine (Zyrtec®) 10 mg softgel capsule Cetirizine (Zyrtec®) 5, 10 mg chewable tablet Quzyttir® (cetirizine) 10 mg/mL IV solution	• Upper respiratory allergies • Urticaria	• Oral: 2.5-10 mg once daily, depending on symptom severity; max 10 mg daily • IV (urticaria only): 10 mg once daily as needed. If symptom control is inadequate, may increase to 10 mg twice daily; switch to scheduled oral dosing when feasible.
Levocetirizine (Xyzal®) 5 mg tablet Levocetirizine (Xyzal®) 2.5 mg/5 mL oral solution	• Allergic rhinitis • Chronic idiopathic urticaria	• Allergic rhinitis: 5 mg once daily in the evening (may use 2.5 mg once daily); max 5 mg daily • Chronic idiopathic urticaria: 5 mg once daily in the evening (may use 2.5 mg once daily; 10 mg twice daily has shown benefit)
Loratadine (Claritin®) 10 mg tablet Loratadine (Claritin®) 5mg/5 mL oral solution Loratadine (Claritin®) 5, 10 mg orally disintegrating tablet Loratadine (Claritin®) 5 mg chewable tablet Claritin (loratadine) 10 mg chewable tablet Claritin® Liqui-gel (loratadine) 10 mg capsule	• Seasonal allergic rhinitis • Urticaria	• 5 mg twice daily or 10 mg once daily
Claritin RediTabs (loratadine) 5, 10 mg orally disintegrating tablet	• Seasonal allergic rhinitis • Urticaria	• 5 mg twice daily or 10 mg once daily

Medication	Indications	Dosing/Administration
Desloratadine (Clarinex®) 5 mg tablet Desloratadine (Clarinex®) 2.5, 5 mg orally disintegrating tablet	• Seasonal or perennial allergic rhinitis • Chronic idiopathic urticaria • NSAID-associated urticaria prophylaxis (off-label)	• Seasonal or perennial allergic rhinitis: 5 mg once daily • Chronic idiopathic urticaria: 5 mg once daily (may use 10 mg twice daily) • NSAID-associated urticaria prophylaxis (off-label): 5 mg 30 minutes before intake of strong COX-1 inhibitor
Fexofenadine (Allegra®) 60, 180 mg tablet Fexofenadine (Allegra®) 30 mg orally disintegrating tablet Fexofenadine (Allegra®) 30 mg/5 mL oral suspension	• Upper respiratory allergies • Chronic idiopathic urticaria (off-label use)	• Upper respiratory allergies: 60 mg every 12 hours (twice daily formulation); max 120 mg/day or 180 mg once daily (once daily formulation); max: 180 mg/day • Chronic idiopathic urticaria (off-label use): 180 mg once daily or 60 mg twice daily; range 20-240 mg twice daily
Combination Pseudoephedrine Products		
Cetirizine-pseudoephedrine (Zyrtec-D) 5 mg-120 mg ER tablet	• Upper respiratory allergies	• One tablet (cetirizine 5 mg/pseudoephedrine 120 mg) twice daily; max 2 tabs (cetirizine 10 mg/pseudoephedrine 240 mg) per day
Fexofenadine-pseudoephrine (Allegra-D) 60 mg-120 mg, 180 mg-240 mg ER tablet		• One tablet (fexofenadine 60 mg/pseudoephedrine 120 mg 12 hr) twice daily • One tablet (fexofenadine 180 mg/pseudoephedrine 240 mg 24 Hour) once daily
Clarinex®-D (desloratadine-pseudoephedrine) 2.5 mg-120 mg		• One tablet (desloratadine 2.5 mg/pseudoephedrine 120 mg) every 12 hours
Loratadine-pseudoephedrine (Claritin-D) 5 mg-120 mg, 10 mg-240 mg ER tablet	• Cold or allergy symptoms	• One tablet (loratadine 5 mg/pseudoephedrine 120 mg) every 12 hours or one tablet (loratadine 10 mg/pseudoephedrine 240 mg) daily; max loratadine 10 mg/pseudoephedrine 240 mg per day
Ophthalmic and Nasal Dosage Forms		

Medication	Indications	Dosing/Administration
Azelastine (Astepro®) 137, 205.5 mcg nasal spray	• Perennial allergic rhinitis (205.5 mcg only) • Seasonal allergic rhinitis • Vasomotor rhinitis (137 mcg only)	• Perennial allergic rhinitis: Two sprays (205.5 mcg) in each nostril twice daily • Seasonal allergic rhinitis: One or two sprays (137 mcg) in each nostril twice daily or two sprays (205.5 mcg) in each nostril once daily • Vasomotor rhinitis: Two sprays (137 mcg) in each nostril twice daily
Azelastine 0.05% drops	• Allergic conjunctivitis	• Instill 1 drop into affected eye(s) twice daily
Olopatadine (Pataday®) 0.1% drops Olopatadine (Pataday®) 0.2% drops Pataday® (olopatadine) 0.7% drops	• Allergic conjunctivitis	• Instill 1 drop into each affected eye twice daily (allowing 6 to 8 hours between doses for 0.1% only)
Lastacaft® (alcaftadine) 0.25% drops		• Instill 1 drop into each eye once daily
Bepotastine (Bepreve®) 1.5% drops		• Instill 1 drop into the affected eye(s) twice daily
Epinastine (Elestat®) 0.05% drops		• Instill 1 drop into each eye twice daily; continue throughout period of exposure, even in the absence of symptoms
Ketotifen (Zaditor®) 0.025% drops		• Instill 1 drop into the affected eye(s) twice daily every 8 to 12 hours; max 2 applications per day
Zerviate® (cetirizine) 0.24% drops		• Instill 1 drop in affected eye(s) twice daily (~8 hours apart)

Boxed Warnings And Contraindications

Medication	Boxed Warnings	Contraindications
Cetirizine (Zyrtec®) solution, tablet, capsule, chewable tablet, orally disintegrating tablet Quzyttir® (cetirizine) IV solution	None	Hypersensitivity to cetirizine, hydroxyzine, or any component of the formulation
Levocetirizine (Xyzal®) tablet, solution		• Hypersensitivity to levocetirizine, cetirizine, or any component of the formulation • End-stage renal disease (CrCl <10 mL/min) • Infants and children 6 months or 11 years of age with renal impairment
Loratadine (Claritin®, Claritin® RediTabs) tablet, solution, orally disintegrating tablet, chewable tablet, capsule		Hypersensitivity to loratadine or any component of the formulation
Desloratadine (Clarinex®) tablet, orally disintegrating tablet		Hypersensitivity to desloratadine, loratadine, or any component of the formulation
Fexofenadine (Allegra®) tablet, orally disintegrating tablet, suspension		History of allergic reaction to fexofenadine or any component of the formulation
Combination Pseudoephedrine Products		
Cetirizine-pseudoephedrine (Zyrtec-D) tablet	None	• Hypersensitivity to cetirizine, pseudoephedrine, hydroxyzine, or any component of the formulation • Use with or within 2 weeks of discontinuing MAO inhibitor therapy
Fexofenadine-pseudoephedrine (Allegra-D) tablet		• Hypersensitivity to fexofenadine, pseudoephedrine, adrenergic agents or other drugs of similar structure, or any component of the formulation • Narrow-angle glaucoma • Urinary retention • During or within 14 days of MAO inhibitor therapy • Severe hypertension or coronary heart disease
Clarinex®-D (desloratadine-pseudoephedrine) tablet		

Loratadine-pseudoephedrine (Claritin®-D) ER tablet		• Hypersensitivity to loratadine, pseudoephedrine, or any component of the formulation • During or within 14 days of MAOI therapy; severe hypertension or coronary heart disease
Ophthalmic and Nasal Dosage Forms		
Azelastine (Astepro®) nasal spray	None	None
Azelastine drops		Hypersensitivity to azelastine or any component of the formulation
Olopatadine (Pataday®) drops		Hypersensitivity to olopatadine or any component of the formulation
Lastacaft® (alcaftadine) drops		Hypersensitivity to alcatadine or any component of the formulation
Bepotastine (Bepreve®) drops		Hypersensitivity to bepotastine or any component of the formulation
Epinastine (Elestat®) drops		None
Ketotifen (Zaditor®) drops		Hypersensitivity to ketotifen or any component of the formulation
Zerviate® (cetirizine) drops		None

Warnings/Precautions

Medication	Warnings/Precautions
Oral Dosage Form	
Cetirizine (Zyrtec®) solution, tablet, capsule, chewable tablet, orally disintegrating tablet Quzyttir® (cetirizine) IV solution	**Concerns related to adverse effects:** • May cause CNS depression **Disease-related concerns:** • Use with caution in patients with hepatic or renal impairment **Concurrent drug therapy issues:** • Potentially significant interactions may exist **Special populations:** • Use with caution in elderly patients
Levocetirizine (Xyzal®) tablet, solution	**Concerns related to adverse effects:** • May cause CNS depression • Rebound pruritis may occur within several days after stopping levocetirizine **Disease-related concerns:** • Use with caution in patients with renal impairment • Urinary retention may occur **Concurrent drug therapy issues:** • Potentially significant interactions may exist **Special populations:** • Use with caution in the elderly
Loratadine (Claritin®, Claritin® RediTabs) tablet, solution, orally disintegrating tablet, chewable tablet, capsule	**Disease-related concerns:** • Use with caution in patients with hepatic or renal impairment **Concurrent drug therapy issues:** • Sedative effect may be potentiated when used with other sedative drugs or ethanol **Dosage form specific issues:** • Some dosage forms may contain sodium benzoate/benzoic acid, a metabolite of benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates • Some products may contain phenylalanine

Medication	Warnings/Precautions
Desloratadine (Clarinex®) tablet, syrup, orally disintegrating tablet	**Concerns related to adverse effects:** • Hypersensitivity reactions have been reported with use **Disease-related concerns:** • Use with caution in patients with hepatic or renal impairment **Concurrent drug therapy issues:** • Effects may be potentiated when used with other sedative drugs or ethanol. **Special populations:** • Use with caution in patients known to be slow metabolizers of desloratadine (incidence of side effects may be increased). **Dosage form specific issues:** • Some dosage forms may contain sodium benzoate/benzoic acid, a metabolite of benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates • Some products may contain phenylalanine
Fexofenadine (Allegra®) tablet, orally disintegrating tablet, suspension	**Disease-related concerns:** • Use with caution in patients with renal impairment **Concurrent drug therapy issues:** • Potentially significant interactions may exist **Dosage form specific issues:** • Some products may contain phenylalanine **Other warnings/precautions:** • When used for self-medication (OTC), do not exceed recommended dosage or administer at the same time with aluminum or magnesium antacids or with fruit juices.
Combination Pseudoephedrine Products	
Cetirizine-pseudoephedrine (Zyrtec-D) ER tablet	**Concerns related to adverse effects:** • May cause CNS depression **Disease-related concerns:** • Use with caution in patients with cardiovascular disease (including hypertension and heart disease), diabetes mellitus, hepatic impairment, increased intraocular pressure/glaucoma, prostatic hyperplasia/urinary retention, renal impairment, or thyroid dysfunction **Concurrent drug therapy issues:** • Potentially significant interactions may exist **Special populations:** • Use with caution in the elderly • Antihistamines may cause excitation in young children **Other warnings/precautions:** • When used for self-medication (OTC), do not exceed the recommended doses; discontinue use and contact healthcare provider if symptoms do not improve within 7 days or are accompanied by fever; if nervousness, dizziness, or sleeplessness occur; or if an allergic reaction to the formulation occurs

Medication	Warnings/Precautions
Fexofenadine-pseudoephedrine (Allegra-D) ER tablet	**Disease-related concerns:** • Use with caution in patients with cardiovascular disease (including hypertension and heart disease), diabetes mellitus, increased intraocular pressure/glaucoma, prostatic hyperplasia/urinary retention, renal impairment, seizure disorder, or thyroid dysfunction **Concurrent drug therapy issues:** • Potentially significant interactions may exist
Clarinex®-D (desloratadine-pseudoephedrine) tablet	**Concerns related to adverse effects:** • CNS stimulation and/ or seizures may occur due to sympathomimetic amine • Hypersensitivity reactions have been reported with use of desloratadine • Tachycardia may occur due to sympathomimetic amine (pseudoephedrine); cardiovascular collapse with hypotension may also occur. **Disease-related concerns:** • Use with caution in patients with cardiovascular disease (contraindicated in patients with severe hypertension or severe coronary artery disease), diabetes mellitus, hepatic or renal impairment, increased intraocular pressure, prostatic hyperplasia, or hypothyroidism **Concurrent drug therapy issues:** • Potentially significant interactions may exist **Special populations:** • Use with caution in elderly patients; may be more sensitive to adverse effects
Loratadine-pseudoephedrine (Claritin®-D) ER tablet	**Disease-related concerns:** • Use with caution in patients with cardiovascular disease (including hypertension and heart disease), diabetes mellitus, hepatic impairment, increased intraocular pressure/glaucoma, prostatic hyperplasia/urinary retention, renal impairment, or thyroid dysfunction **Concurrent drug therapy issues:** • Potentially significant interactions may exist **Other warnings/precautions:** • When used for self-medication (OTC), do not exceed the recommended doses; discontinue use and contact healthcare provider if symptoms do not improve within 7 days or are accompanied by fever; if nervousness, dizziness, or sleeplessness occur; or if an allergic reaction to the formulation occurs
Ophthalmic and Nasal Dosage Forms	
Azelastine (Astepro®) nasal spray	**Concerns related to adverse effects:** • May cause CNS depression **Concurrent drug therapy issues:** • Potentially significant interactions may exist
Azelastine drops	**Dosage form specific issues:** • Solution contains benzalkonium chloride; remove lens prior to administration and wait at least 10 minutes before reinserting. Do not use contact lenses if eyes are red.
Olopatadine (Pataday®) drops	**Dosage form specific issues:** • Solution contains benzalkonium chloride; remove lens prior to administration and wait at least 10 minutes before reinserting. Do not use contact lenses if eyes are red.

Medication	Warnings/Precautions
Lastacaft® (alcaftadine) drops Bepotastine (Bepreve®) drops	**Special populations:** • Solution contains benzalkonium chloride; remove lens prior to administration and wait at least 10 minutes before reinserting. Do not use contact lenses if eyes are red. **Other warnings/precautions:** • For topical ophthalmic use only
Ketotifen (Zaditor®) drops	**Special populations:** • Solution contains benzalkonium chloride; remove lens prior to administration and wait at least 10 minutes before reinserting. Do not use contact lenses if eyes are red. • When used for self-medication (OTC), notify healthcare provider if symptoms worsen or do not improve within 3 days **Concurrent drug therapy issues:** • Potentially significant interactions may exist
Epinastine (Elestat®) drops	**Concerns related to adverse effects:** • Inadvertent contamination of multiple-dose ophthalmic solutions has caused bacterial keratitis **Special populations:** • Contains benzalkonium chloride which may be absorbed by contact lenses; remove contact lenses prior to use and wait 10 minutes before reinserting. **Other warnings/precautions:** • For topical ophthalmic use only
Zerviate® (cetirizine) drops	**Special populations:** • Contact lens wearers: Contains benzalkonium chloride, which may be absorbed by contact lenses; remove lenses prior to administration and wait 10 minutes before reinserting. **Other warnings/precautions:** • Appropriate use: For topical ophthalmic use only. To avoid eye injury and contamination, do not touch dropper tip of the bottle or single-use container to eyelids, surrounding area, or any surface.

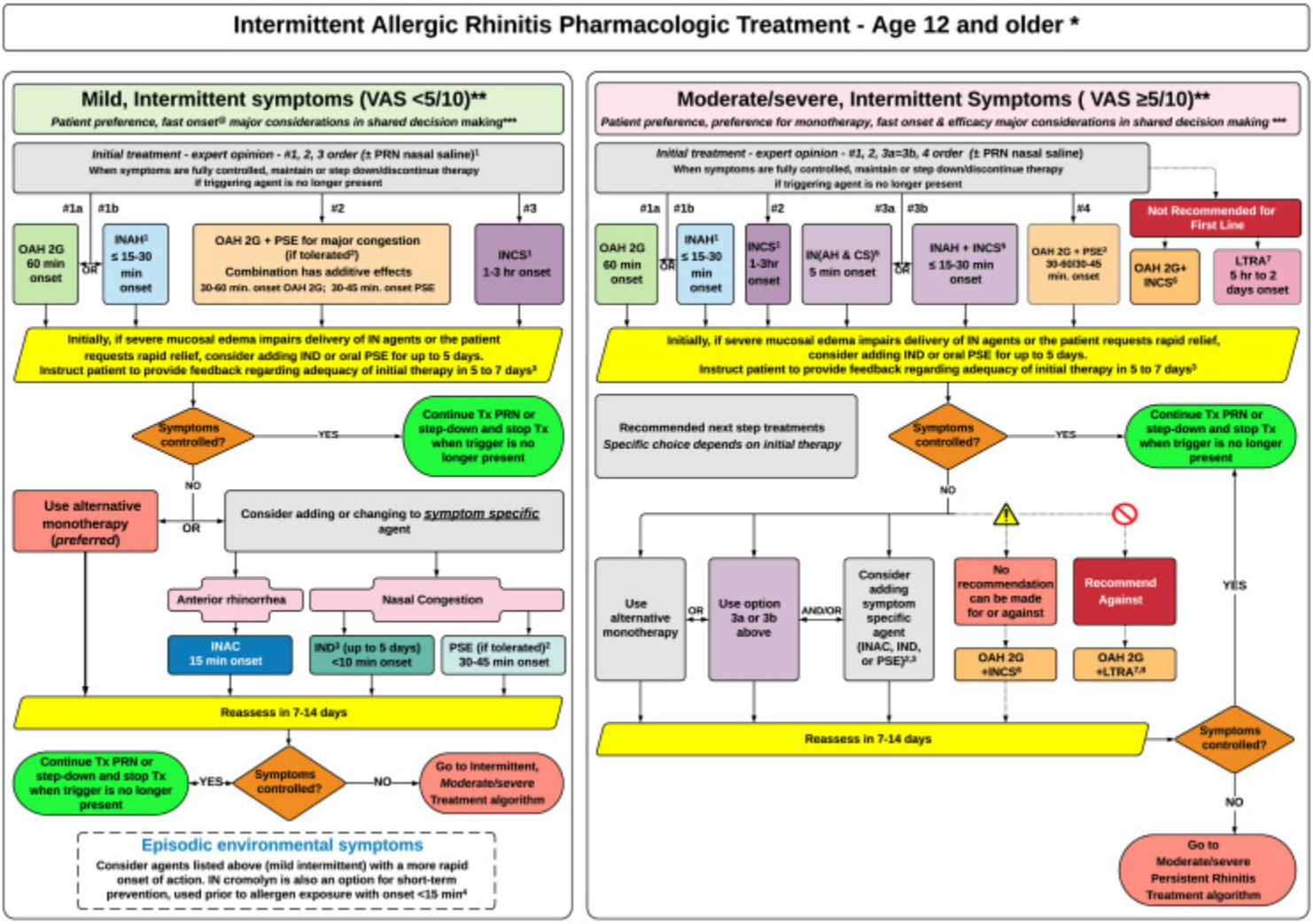
Practice Guidelines

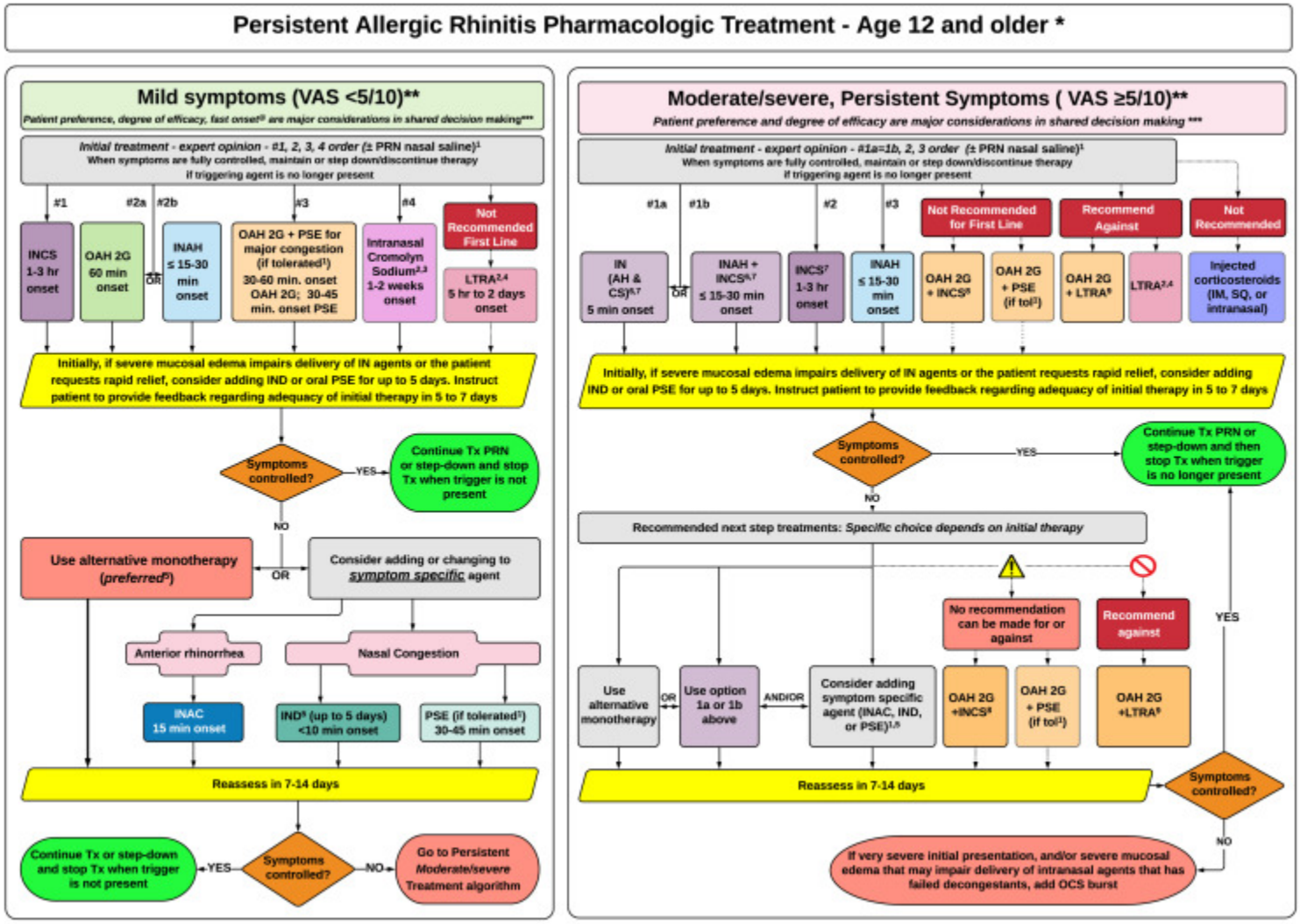
Allergic rhinitis

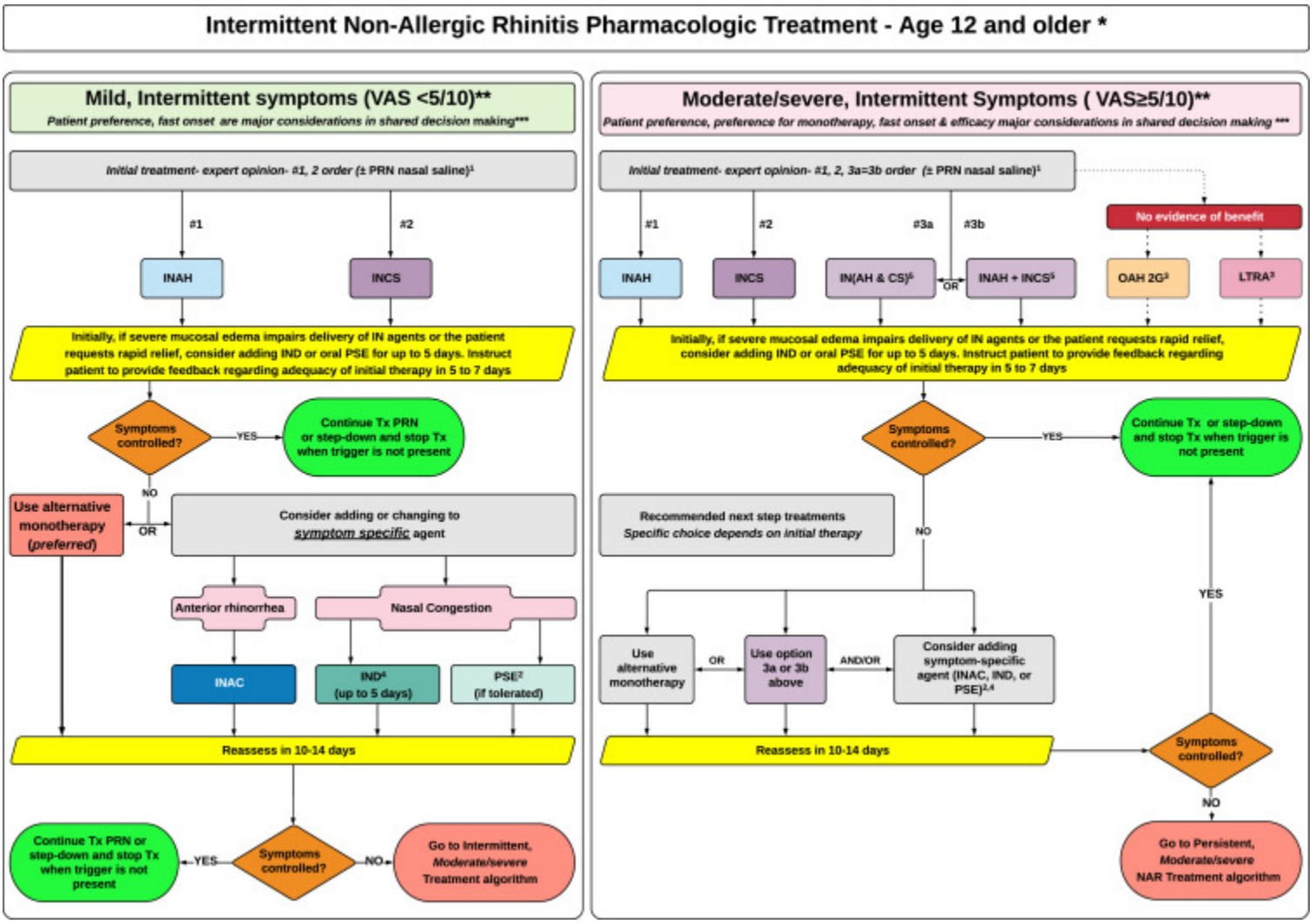
Joint Task Force on Practice Parameters: Dykewicz MS, Wallace DV, Amrol DJ, Baroody FM, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol. 2020 Oct;146(4):721-767.

Summary of updates:

- Four new algorithms based on a combination of evidence and expert opinion can guide the clinician in the treatment of intermittent and persistent allergic rhinitis (AR) and nonallergic rhinitis (NAR)
- Cough is emphasized as a common symptom present in both AR and NAR
- New information is presented about local allergic rhinitis (LAR), possibly present in up to 25% of patients with rhinitis, and its response to both subcutaneous allergy immunotherapy (SCIT) and sublingual immunotherapy (SLIT), although more research is needed
- We recommend that food allergy testing not be performed in the routine evaluation of possible AR (Recommendation 4)
- We recommend that the oral leukotriene receptor antagonist (LTRA) montelukast should only be used for AR in patients who have an inadequate response or intolerance to alternative therapies (Recommendation 7)
- Either intranasal antihistamines (INAH) or intranasal corticosteroids (INCS) may be offered as first-line monotherapy for NAR (Recommendations 12, 32)
- Since the 2008 rhinitis update, additional studies support the use of combination INCS and INAH in AR and NAR (Recommendations 22-24)
- Oral decongestants should be avoided during the first trimester of pregnancy (Recommendation 19)
- Additional information is presented as to why first-generation antihistamines should not be used in AR, especially on a chronic basis, due to potential sedation, performance impairment, poor sleep quality, anticholinergic-medicated symptoms, and increased risk of dementia (Recommendation 6)
- We continue to suggest that the use of intranasal decongestants generally be limited to short-term use to prevent rebound congestion that may occur with longer use; however, in limited circumstances discussed in the document, patients on regimens that include an INCS may be offered combination therapy with addition of an intranasal decongestant for up to 4 weeks (Recommendations 16, 26)
- SCIT and SLIT tablets are both effective for the treatment of AR and may help prevent and/or treat allergic asthma (Recommendation 34)
- Neither acupuncture nor herbal medications have adequate studies to support a recommendation to use them in the treatment of AR (Recommendations 36, 37)







Emeryk A, Emeryk-Maksymiuk J, Janeczek K. New guidelines for the treatment of seasonal allergic rhinitis. Advances in Dermatology and Allergology. 2019; 36(3): 255-260.

Summary of updates: (GCin=intranasal glucocorticoids, AHpo: oral antihistamines, AHin (intranasal antihistamine [e.g. azelastine])

- For the initial treatment of moderate/severe SAR in patients aged 12 years or older, clinicians should routinely prescribe monotherapy with a GCin rather than a combination of a GCin and an AHpo (Strong)

- For the initial treatment of moderate/severe SAR in patients aged 15 years or older, clinicians should prescribe monotherapy with a GCin over montelukast (Strong)
- For the initial treatment of moderate/severe SAR in patients aged 12 years or older, clinicians may recommend the combination of a GCin and AHin (Weak)

Recommendation Definitions

Class/Level	Definition
Strong	Consistent, good-quality, patient-oriented evidence
Weak	Inconsistent or limited-quality patient-orientated evidence
Consensus	Consensus, disease-oriented evidence, usual practice, expert opinion, or case series

Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: An evidence-based focused 2017 guideline update. Annals of Allergy Asthma and Immunology. 2017;119(6):489-511.

Summary of recommendations:

- Should routinely prescribe monotherapy with an intranasal corticosteroid rather than a combination of an intranasal corticosteroid with an oral antihistamine
- Should recommend an intranasal corticosteroid over a leukotriene receptor antagonist (for >15 years of age)
- For moderate to severe symptoms, may recommend the combination of an intranasal corticosteroid and an intranasal antihistamine

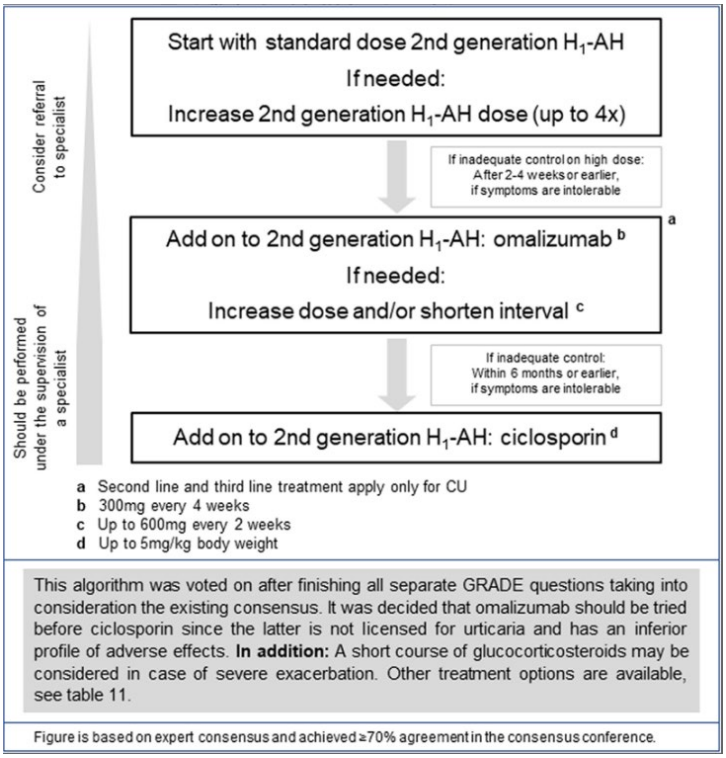
Chronic Idiopathic Urticaria

Zuberbier T, Abdul-Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. European Journal of Allergy and Clinical Immunology, 2022; 77(3):734-766.

Summary of guidelines:

- We recommend aiming at complete symptom control in urticaria, considering as much as possible the safety and the quality of life of each individual patient. (Strong consensus, Expert consensus)
- We recommend advising patients with chronic spontaneous urticaria to discontinue medication that is suspected to worsen the disease, for example, NSAIDs. (Strong consensus, Expert consensus)
- We recommend a 2nd generation H1-antihistamine as first-line treatment for all types of urticaria. (Strong Consensus, Evidence- and consensus-based)

- We recommend up-dosing of a 2nd generation H1-antihistamine up to fourfold in patients with chronic urticaria unresponsive to a standard-dosed 2nd generation H1-antihistamines as second-line treatment before other treatments are considered. (Strong Consensus, Evidence- and consensus-based)
- We suggest 2nd generation H1-antihistamines to be taken regularly for the treatment of patients with chronic urticaria. (Strong Consensus, Evidence- and consensus-based)
- We suggest against using different H1-antihistamines at the same time. (Consensus, Evidence- and consensus-based)
- We recommend against using higher than fourfold standard-dosed H1-antihistamines in chronic urticaria. (Strong consensus, Evidence- and consensus-based)



Recommendation Definitions

Class/Level	Definition
Strong recommendation for the use of an intervention	We believe that all or almost all informed people would make a choice in favor of using this intervention. Clinicians will not have to spend as much time on the process of decision-making with the patient and may devote that time instead to overcoming barriers to implementation and adherence. In most clinical situations, the recommendation can be adopted as a policy.
Weak recommendation for the use of an intervention	We believe that most informed people would make a choice in favor of using this intervention, but a substantial number would not. Clinicians and other healthcare providers will need to devote more time to the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making will require substantial debate.

Class/Level	Definition
No recommendation with respect to an intervention	Currently, a recommendation in favor of or against using this intervention cannot be made due to certain circumstances (eg, unclear or balanced benefit-risk ratio, no data available).

Bernstein JA, Lang DM, Khan DA, et al. American Academy of Allergy, Asthma & Immunology (AAAAI), American College of Allergy, Asthma & Immunology (ACAAI), and the Joint Council of Allergy, Asthma & Immunology Joint Task Force on Practice Parameters: The diagnosis and management of acute and chronic urticaria: 2014 update. Journal of Allergy and Clinical Immunology. 2014; 133(5):1270-1277.

Summary of recommendations:

- Second-generation antihistamines are considered first-line agents in the management of chronic urticaria. Avoidance of triggers (e.g. NSAIDs) and relevant physical factors if physical urticaria/angioedema syndrome is present
- For patients not responding to monotherapy with a second-generation antihistamine one or more of the following strategies may be employed:
    - Increase the dose of the second-generation antihistamine
    - Add another second-generation antihistamine
    - Add a H_2-antagonist
    - Add a leukotriene receptor antagonist
    - Add a first-generation antihistamine
- For patients still uncontrolled after the second step, a potent antihistamine such as hydroxyzine or doxepin should be utilized
- Refractory chronic urticaria may be treated with omalizumab, cyclosporine, other anti-inflammatory agents, immunosuppressants, or biologics

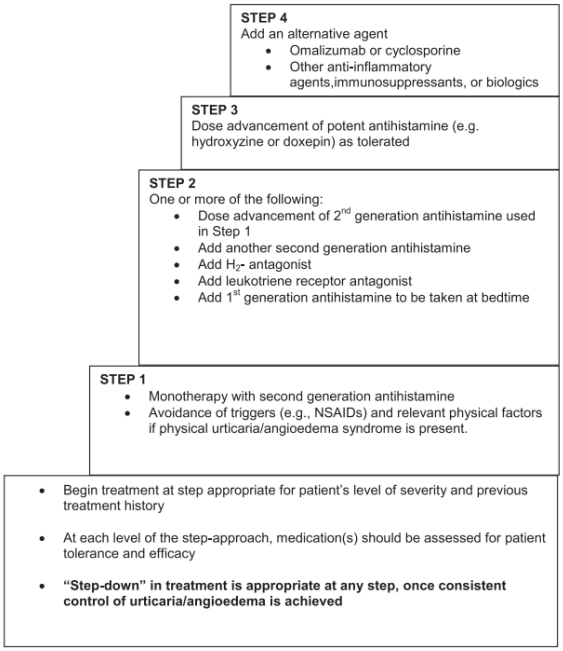


FIG 1. Step-care approach to the treatment for CU.

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Mosges R, Konig V, Koberlein J. The effectiveness of modern antihistamines for treatment of allergic rhinitis – an IPD meta-analysis of 140,853 patients. Allergology International. 2013; 62:215-222.	Meta-analysis: Database containing ten open-label prospective observational studies including raw data from 140,853 patients with allergic rhinitis taking desloratadine, ebastine, fexofenadine, or levocetirizine).	• Primary endpoint: symptomatology variables
Results: Monotherapy with second generation antihistamines achieved total symptom and total nasal symptom scores that were significantly better than those from patients taking combination therapy with intranasal steroids. Monotherapy with levocetirizine was significantly more effective in lowering total symptom score and total nasal symptom score than the other antihistamines. A greater positive effect of levocetirizine was demonstrated in relation to the severity of the clinical symptoms of allergic rhinitis. **Conclusion**: Levocetirizine was more effective than desloratadine, ebastine, or fexofenadine and should be recommended in patients with severe cases of allergic rhinitis.		
Citation	**Design**	**Endpoints**
Xiao J, Wu WX, Ye YY, et al. A network meta-analysis of randomized controlled trials focusing on different allergic rhinitis medications. American Journal of Therapeutics. 2016; 23(6):e1568-e1578.	Meta-analysis: 386 high-quality randomized controlled trials were screened and 13 were selected containing a combined 6,867 patients with allergic rhinitis taking loratadine, cetirizine, montelukast, and desloratadine.	• Primary endpoint: rhinoconjunctivitis quality of life questionnaire scores
Results: Compared with placebo, all four drugs treated allergic rhinitis effectively. Cetirizine was the most optimal drug for allergic rhinitis. **Conclusion**: Cetirizine is the most effective treatment for allergic rhinitis compared with loratadine, montelukast, and desloratadine, significantly reducing the functional problems in patients with this condition.		
Citation	**Design**	**Endpoints**

Sharma M, Bennet C, Cohen SN, et al. H1-antihistamines for chronic spontaneous urticaria. Cochrane Database of Sytematic Reviews. 2014; (11):CD006137.	Systematic Review: Included 73 randomized controlled trials of 9,759 patients taking H1-antihistamines (monotherapy or combination therapy) for chronic spontaneous urticaria for short-term (2 weeks) or longer than two weeks and up to 3 months (intermediate-term)	• Primary endpoint: Proportion of participants with complete suppression of urticaria (good or excellent response and adverse events)
Results: Cetirizine 10 mg and desloratadine 5mg once daily in the short term and intermediate term led to complete suppression of urticaria over placebo. Desloratadine 20 mg was favored over cetirizine 10 mg for short term therapy but no difference was seen for 5 mg and 10 mg desloratadine. Levocetirizine 20 mg short term was more effective for complete suppression of urticaria compared to placebo and at 5mg was effective in the long term (not effective in the short term). The 10 mg dose was not effective in the short term. Loratadine 10 mg vs. emedastine 2 mg showed no statistical difference for complete suppression or for adequate response. No difference in short-term treatment was found between loratadine 10 mg and hydroxyzine 25 mg for complete suppression. Levocetirizine 5-20 mg was more effective than desloratadine 5-20 mg. More patients in the cetirizine group showed complete suppression of urticaria compared to fexofenadine. Adverse events were comparable among all agents. **Conclusion**: No single antihistamine stands out as most effective for spontaneous urticaria and all have comparable adverse effects. Higher doses tended to have a better complete response or maintain a longer response.		
Citation	**Design**	**Endpoints**
Quzyttir® [prescribing information]. Pfizer, Rocky Mount, NC; September, 2020.	Randomized, double-blind, parallel group, active controlled, multicenter, phase 3 trial comparing cetirizine 10 mg IV push to diphenhydramine 50 mg IV push over ~2 minutes for 262 patients with acute urticaria presenting to emergency departments (ED) or urgent care centers.	• Primary endpoint: Change from baseline in patient-rated pruritis score assessed 2 hours post treatment • Secondary endpoints: need to return to any ED or clinic after patients discharge; time spent at treatment center
Results: Pruritis score change from baseline for cetirizine was -1.5 (SD 0.984) compared to -1.61 (SD 0.944) with an adjusted difference between treatments (95% CI) of -0.06 (-0.28, 0.40), which met the non-inferiority margin. The proportion of patients returning to any ED or clinic was lower in the cetirizine group (6%) compared to the diphenhydramine group (14%). The time spent in the treatment center was shorter in the cetirizine group (1.7 hours spent reported as mean [SD 0.9]) compared to diphenhydramine (2.1 hours spent reported as mean [SD 1.1]). **Conclusion**: IV cetirizine is non-inferior to IV diphenhydramine in the treatment of acute urticaria and may have a quicker onset and longer-lasting effect.		

PERFORMRx℠

Formulary Placement, Utilization And Cost Experience (10-01-2024 to 12-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Oral Dosage Forms								
Cetirizine (Zyrtec®, Allergy Relief, Children's All Day Allergy, Wal-Zyr™) 1 mg/mL oral solution, 5 mg/5 mL unit dose cup oral solution	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Cetirizine (Zyrtec®, All Day Allergy, CVS Allergy, Wal-Zyr™) 10 mg softgel capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Cetirizine (Zyrtec®, Allergy Relief, 24Hour Allergy, Wal-Zyr™) 5 mg, 10 mg tablet	149	102	$224.20	$1.50	0	0 (0%)	F	No change
Cetirizine (Children's Zyrtec®, Children's Wal-Zyr™) 2.5, 5, 10 mg chewable tablet	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Quzyttir® (cetirizine hydrochloride injection) 10 mg/ml vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Desloratadine (Clarinex®) 5 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Desloratidine 2.5, 5 mg ODT	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fexofenadine (Allegra® Allergy, Allergy Relief, Wal-Fex®, Aller-Ease, Aller-Fex) HCL 60, 180 mg oral tablet	15	11	$101.94	$6.80	0	0 (0%)	F	No change
Children's Allegra Allergy® (fexofenadine) 30 mg/5 ml oral solution	0	0	$0.00	$0.00	0	0 (0%)	F	No change

Children's Allegra Allergy® (fexofenadine) 30 mg ODT	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Levocetirizine dihydrochloride (Xyzal®, 24Hour Allergy, Allergy Relief) 5 mg oral tablet	4	2	$16.93	$4.23	0	0 (0%)	F	No change
Levocetirizine (Xyzal®) 2.5 mg/5 ml oral solution	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Claritin® (loratadine) 10 mg liqui-gel capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Loratadine (Claritin®, Allerclear, Allergy Relief, Loradamed, Wal-Itin®) 10 mg oral tablet	96	67	$135.01	$1.41	0	0 (0%)	F	No change
Loratadine (Children's Allergy Relief, Children's Claritin®, Claritin®) 5, 10 mg chewable tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Loratadine (Allergy Relief, Children's Allergy, Children's Allergy Relief, Children's Claritin®) 5 mg/5 ml oral solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Loratadine (CVS Allergy, Claritin®, Alavert®) 5, 10 mg ODT	0	0	$0.00	$0.00	0	0 (0%)	F-QL (30/30)	No change
Combination Pseudoephedrine Products								
Cetirizine HCL-pseudoephedrine (12 Hour Allergy-D®, All Day Allergy-D®, Aller-Tec D®, Cetiri-D®, Wal-Zyr™, Zyrtec®) 5-120 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Loratadine-pseudoephedrine (Alavert® D-12 Allergy, Allerclear® D-12hr, Allergy Relief D-24hr, Wal-Itin® D 12 Hour) 5-120 mg 12 hour tablet	0	0	$0.00	$0.00	0	0 (0%)	F	No change

Loratadine-pseudoephedrine (Allerclear® D-24hr, Allergy Relief D-24hr, Claritin®, Lorata-Dine, Wal-Itin® D 24 Hour) 24 hour tablet	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Clarinex-D® 12 Hr (desloratadine-pseudoephedrine) 2.5-120 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fexofenadine-pseudoephedrine (Allegra®, Allergy Relief-D, 24Hr Allergy) 60-120 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	→**F-ST**
Fexofenadine-pseudoephedrine (Allegra®, CVS Allergy Relief D24, Wal-Fex®) 180-240 mg oral tablet	3	1	$149.40	$49.8	0	0 (0%)	NF	→ **F-ST**
Ophthalmic and Nasal Dosage Forms								
Lastacaft® Once Daily Relief (alcaftadine) 0.25% ophthalmic drops	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Azelastine HCL 0.05% ophthalmic drops	17	12	$465.17	$27.36	0	0 (0%)	F	No change
Bepotastine besilate (Bepreve®) 1.5% ophthalmic drops	0	0	$0.00	$0.00	0	0 (0%)	F	→**F-PA**
Zerviate® (cetirizine) 0.24% ophthalmic drops	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Epinastine HCL 0.05% ophthalmic drops	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Ketotifen fumarate (Alaway®, CVS Allergy, Children's Alaway®, Zaditor®) 0.25% ophthalmic drops	15	14	$102.11	$6.81	0	0 (0%)	F-QL (10ml/30)	No change
Olopatadine (Pataday®) HCL 0.1% ophthalmic drops	5	5	$42.34	$8.47	0	0 (0%)	F-QL (5ml/30)	No change
Olopatadine (Pataday®) HCL 0.2% ophthalmic drops	7	6	$58.54	$8.36	0	0 (0%)	F-QL (2.5ml/30)	No change

Pataday® Once Daily (olopatadine) 0.7% ophthalmic drops	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Azelastine 0.1% (137 mcg) nasal spray	20	14	$818.15	$40.91	0	0 (0%)	F	No change
Azelastine 0.15% nasal spray	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Olopatadine 665 mcg nasal spray	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	331	234	$2,113.79	$6.39	0	0 (0%)		

Key (as applicable) F = Formulary, no restrictions; F-QL = Formulary, quantity limit applies; F-AL = Formulary, age limit applies; F-ST = Formulary, step therapy applies; F-PA = Formulary, PA required; NF = Non-formulary; X = Excluded

Prior Authorization Criteria

Recommendation: No changes to the criteria, but the Fexofenadine-pseudoephedrine is currently NF, recommend adding to formulary with ST to match the criteria.

Fexofenadine-pseudoephedrine	
Therapeutic Classes (AHFS)	Second generation antihistamines
Medications	Formulary, step therapy required Fexofenadine-pseudoephedrine tablet extended release
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Reauthorization** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Fexofenadine-pseudoephedrine tablet extended release step therapy criteria: • Documentation of a trial and failure or intolerance to loratadine, cetirizine, OR levocetirizine required.
	Fexofenadine-pseudoephedrine tablet extended release is reserved for members who have used (or cannot/should not use) loratadine, cetirizine, OR levocetirizine.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation:

- Update ketotifen available strength formulation
- Change bepotastine from F to F-PA formulary status to match the criteria

Ophthalmic Antihistamines	
Therapeutic Classes (AHFS)	Antiallergic Agents (EENT)
Medications	Formulary, with restrictions ((quantity limit may apply) • Azelastine 0.05% drops • Ketotifen (Zaditor) 0.0~~2~~3~~5~~% drops (QL 10/30) • Olopatadine 0.1% (Pataday Twice Daily) (QL 5/30) • Olopatadine 0.2% (Pataday Once Daily) (QL 2.5/30) Formulary, PA required • Lastacaft (alcaftadine) • Bepotastine (Bepreve) • Pataday Once Daily (olopatadine) 0.7% • Zerviate (cetirizine) 0.24% • Epinastine (Elestat) Any newly marketed ophthalmic antihistamine agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), and the Drug Package Insert.
Exclusion Criteria	N/A
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** If the criteria are met, the request will be approved for 1 bottle per 30 days for up to a 12 month duration; **Later Approvals** If the criteria are met, the request will be approved for 1 bottle per 30 days for up to a 12 month duration If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	**CRITERIA FOR AUTHORIZATION** Formulary, prior authorization required medications are approved when the following criteria are met: • Documented trial and failure, contraindication, or intolerance to at least 3 alternatives: ketotifen, azelastine, olopatadine 0.1%, olopatadine 0.2% for at least 2 weeks (14 days) of therapy. **For requests over the quantity limit:** • The member must have a documented treatment failure with the drug prescribed at the health plan's quantity limit **OR** the member requires a dose within prescribing guidelines that exceeds the plan's quantity limit. **AND**

	• The provider has submitted a medical reason why the plan's quantity limit will be inadequate based on the member's condition and treatment history. **AND** • The dose requested is supported by the Medical Compendia or current treatment guidelines.
Criteria Statement	**Pataday Once Daily 0.7%, bepotastine (Bepreve), Lastacaft, epinastine (Elestat), and Zerviate~~:~~** Pataday Once Daily 0.7%, bepotastine (Bepreve), Lastacaft, epinastine (Elestat), and Zerviate are reserved for members who have used (or cannot/should not use) at least 3 of the following eye drops: ketotifen, azelastine, olopatadine 0.1%, or olopatadine 0.2%.
Last P&T Review Date	~~3/2024~~3/2025

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Drug Name: Alyftrek (vanzacaftor/tezacaftor/deutivacaftor)

Manufacturer: Vertex

Approval Date: 12/20/2024

Marketing Date: 1/1/2025

Recommendation

Update Prior Authorization Criteria for Cystic Fibrosis Agents and add Alyftrek to formulary with PA.

Prescribing Information

Indication

Alyftrek is a combination of deutivacaftor, a CFTR potentiator, tezacaftor, and vanzacaftor indicated for the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one F508del mutation or another responsive mutation in the CFTR gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one indicated mutation.

Mechanism of Action

Vanzacaftor and tezacaftor bind to different sites on the CFTR protein and have an additive effect in facilitating the cellular processing and trafficking of select mutant forms of CFTR (including F508del-CFTR) to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone. Deutivacaftor potentiates the channel open probability (or gating) of the CFTR protein at the cell surface. The combined effect of vanzacaftor, tezacaftor and deutivacaftor is increased quantity and function of CFTR at the cell surface, resulting in increased CFTR activity as measured both by CFTR mediated chloride transport in vitro and by sweat chloride in patients with CF.

Dosage and Administration

Recommended Dosage for Adult and Pediatric Patients Aged 6 Years and Older (with fat-containing food) (2.2)

Age	Weight	Once Daily Oral Dosage
6 to less than 12 years old	Less than 40 kg	Three tablets of vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg
	Greater than or equal to 40 kg	Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg
12 years and older	Any Weight	Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg

Black Box Warning

WARNING: DRUG-INDUCED LIVER INJURY AND LIVER FAILURE

Elevated transaminases have been observed in patients treated with Alyftrek. Cases of serious and potentially fatal drug-induced liver injury and liver failure were reported in patients who were taking a fixed-dose combination drug containing elexacaftor, tezacaftor, and ivacaftor, which contains the same or similar active ingredients as Alyftrek. Liver injury has been reported within the first month of therapy and up to 15 months following initiation of elexacaftor/tezacaftor/ivacaftor.

Assess liver function tests (ALT, AST, alkaline phosphatase, and bilirubin) in all patients prior to initiating Alyftrek, every month during the first 6 months of treatment, then every 3 months for the next 12 months, then at least annually thereafter. Consider more frequent monitoring for patients with a history of liver disease or elevated liver function tests at baseline.

Interrupt Alyftrek for significant elevations in liver function tests or in the event of signs or symptoms of liver injury. Consider referral to a hepatologist. Follow patients closely with clinical and laboratory monitoring until abnormalities resolve. If abnormalities resolve, resume treatment only if the benefit is expected to outweigh the risk. Closer monitoring is advised after resuming Alyftrek.

Alyftrek should not be used in patients with severe hepatic impairment (Child-Pugh Class C). Alyftrek is not recommended in patients with moderate hepatic impairment (Child-Pugh Class B) and should only be considered when there is a clear medical need, and the benefit outweighs the risk. If used, monitor patients closely.

Adverse Reactions

Most common (≥5% of patients and at a frequency higher than ELX/TEZ/IVA by ≥1%): cough, nasopharyngitis, upper respiratory tract infection, headache, oropharyngeal pain, influenza, fatigue, increased ALT, rash, increased AST, and sinus congestion

Serious: drug-induced liver injury and liver failure, hypersensitivity reactions, reduced effectiveness in patients with concomitant use with CYP3A inducers, adverse reactions with concomitant use with CYP3A inhibitors, cataracts

Use in Specific Populations, Pregnancy

There are no available data on Alyftrek use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Although there are no animal reproduction studies with the concomitant administration of vanzacaftor, tezacaftor, and deutivacaftor, separate reproductive and developmental studies were conducted with vanzacaftor and tezacaftor in pregnant rats and rabbits. Deutivacaftor is a deuterated isotopologue of ivacaftor with a toxicity profile similar to ivacaftor. Reproductive and development studies were conducted with ivacaftor in pregnant rats and rabbits.

In animal embryo fetal development (EFD) studies, oral administration of vanzacaftor to pregnant rats and rabbits during organogenesis demonstrated no adverse developmental effects at doses that produced maternal exposures up to approximately 30 times the exposure at the maximum recommended human dose (MRHD) in rats and 22 times the MRHD in rabbits. Oral administration of tezacaftor to pregnant rats and rabbits during organogenesis demonstrated no adverse developmental effects at doses that produced maternal exposures up to approximately 3 times the exposure at the MRHD in rats and 0.2 times the MRHD in rabbits (based on summed AUCs of tezacaftor and the metabolite M1-TEZ). Oral administration of ivacaftor to pregnant rats and rabbits during organogenesis demonstrated no adverse developmental effects at doses that produced maternal exposures up to approximately 8 and 9 times the exposure at the MRHD, respectively (based on AUC of ivacaftor for rats and rabbits). No adverse developmental effects were observed after oral administration of vanzacaftor, tezacaftor, or ivacaftor to pregnant rats from the period of organogenesis through lactation at doses that produced maternal exposures approximately 18 times, 1 time, and 8 times the exposures at the MRHD, respectively (based on AUCs of vanzacaftor, tezacaftor and M1-TEZ, and ivacaftor)

Drug Interactions

- Strong or moderate CYP3A inducers: Concomitant use with Alyftrek is not recommended.
- Strong or moderate CYP3A inhibitors: Reduce Alyftrek dosage with concomitant use. Avoid food or drink containing grapefruit.

How Supplied

Tablets:

- Fixed-dose combination containing vanzacaftor 4 mg, tezacaftor 20 mg, and deutivacaftor 50 mg.
- Fixed-dose combination containing vanzacaftor 10 mg, tezacaftor 50 mg, and deutivacaftor 125 mg.

Price

$30,433

(Per month, based on WAC.)

Clinical Studies

Completed

Title	SKYLINE 102: A Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-121 Combination Therapy in Subjects with Cystic Fibrosis (CF) Who Are	SKYLINE 103: A Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-121 Combination Therapy in Subjects with Cystic Fibrosis Who Are Homozygous for F508del, Heterozygous for

	Heterozygous for F508del and a Minimal Function Mutation (F/MF) NCT: 05033080	F508del and a Gating (F/G) or Residual Function (F/RF) Mutation, or Have At Least 1 Other Triple Combination Responsive CFTR Mutation and No F508del Mutation NCT: 05076149
Design	Two 52-week randomized, double-blind, active-controlled trials comparing Alyftrek and a fixed-dose combination drug containing elexacaftor, tezacaftor, and ivacaftor (ELX/TEZ/IVA; Symdeko)	
Population	N=398 Mean age of 30.8 years, 59% male, 97.5% White, 1.3% Black/African American, 0.3% Asian, 0.3% other race, and 6% Hispanic or Latino ethnicity. After the 4_week run-in, the mean ppFEV1 at baseline was 67.1% and the mean sweat chloride at baseline was 53.9 mmol/L.	N= 573 Mean age of 33.7 years, 51.1% male, 92.8% White, 0% Black/African American, 0.3% Asian, 0.2% American Indian or Alaska Native, 0.3% Other race, and 1.6% Hispanic or Latino ethnicity. After the 4-week run-in, the mean ppFEV1 at baseline was 66.8% and the mean sweat chloride at baseline was 42.8 mmol/L.
Arms	Patient received a daily dose of ELX/TEZ/IVA (elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 150 mg in the am and ivacaftor 150 mg in the pm) for a 4-week run-in period, and were then randomized 1:1 to one of the following arms for 52 weeks: • Alyftrek once daily (vanzacaftor 20 mg/tezacaftor 100 mg/deutivacaftor 250 mg) • ELX/TEZ/IVA in the same dose as the run-in period	
Endpoint(s)	Primary: • Non-inferiority in mean absolute change in ppFEV1 from baseline through Week 24 Secondary: • The mean absolute change from baseline in sweat chloride through Week 24 • Percentage of Participants With SwCl <30 mmol/L (pooled data from SKYLINE 102 & 103) (From Baseline Through Week 24) • Percentage of Participants With SwCl <60 mmol/L (pooled data from SKYLINE 102 & 103) (From Baseline Through Week 24)	
Inclusion Criteria	• Age 12 years or older • Heterozygous for F508del and a minimal function mutation (F/MF genotype)	• Age 12 years or older • Participant has one of the following genotypes: ○ Homozygous for F508del;

	• Forced expiratory volume in 1 second (FEV1) value >=40% and <=90% of predicted mean for age, sex, and height for participants currently receiving ELX/TEZ/IVA therapy; FEV1 >=40% and <=80% for participants not currently receiving ELX/TEZ/IVA	○ Heterozygous for F508del and a gating (F/G) mutation; ○ Heterozygous for F508del and a residual function (F/RF) mutation; ○ At least 1 other TCR CFTR gene mutation identified as responsive to ELX/TEZ/IVA and no F508del mutation • Forced expiratory volume in 1 second (FEV1) value >=40% and <=90% of predicted mean for age, sex, and height for participants currently receiving CFTR protein modulator therapy; FEV1 >=40% and <=80% for participants not currently receiving CFTR protein modulator therapy
Exclusion Criteria	• History of intolerance to ELX/TEZ/IVA • History of solid organ or hematological transplantation • Hepatic cirrhosis with portal hypertension, moderate hepatic impairment (Child Pugh Score 7 to 9), or severe hepatic impairment (Child Pugh Score 10 to 15) • Lung infection with organisms associated with a more rapid decline in pulmonary status • Pregnant or breast-feeding females	• History of solid organ or hematological transplantation • Hepatic cirrhosis with portal hypertension, moderate hepatic impairment (Child Pugh Score 7 to 9), or severe hepatic impairment (Child Pugh Score 10 to 15) • Lung infection with organisms associated with a more rapid decline in pulmonary status • Pregnant or breast-feeding females

Results

Table 9: Efficacy Results in Patients Aged 12 Years and Older with CF Who Had at Least One *F508del* Mutation or Responsive Mutation in the *CFTR* Gene (Trials 1 and 2)

Analysis*	Statistic	Trial 1		Trial 2	
		ALYFTREK N = 196	ELX/TEZ/IVA N = 202	ALYFTREK N = 284	ELX/TEZ/IVA N = 289
Primary Endpoint					
Absolute change from baseline in ppFEV$_1$ through Week 24 (percentage points)	n	187	193	268	276
	LS mean (SE)	0.5 (0.3)	0.3 (0.3)	0.2 (0.3)	0.0 (0.2)
	LS mean difference, 95% CI§	0.2 (-0.7, 1.1)		0.2 (-0.5, 0.9)	
Key Secondary Endpoint					
Absolute change from baseline in SwCl through Week 24 (mmol/L)	n	185	194	270	276
	LS mean (SE)	-7.5 (0.8)	0.9 (0.8)	-5.1 (0.7)	-2.3 (0.7)
	LS mean difference, 95% CI	-8.4 (-10.5, -6.3)		-2.8 (-4.7, -0.9)	
	P-value (2-sided)	< 0.0001		0.0034	

ppFEV$_1$: percent predicted Forced Expiratory Volume in 1 second; CI: Confidence Interval; SE: Standard Error; SwCl: sweat chloride
Note: Analyses were based on the full analysis set (FAS). FAS was defined as all randomized subjects who carry the intended CFTR allele mutation and received at least 1 dose of study drug.
* A 4-week ELX/TEZ/IVA run-in-period was performed to establish an on-treatment baseline.
§ The pre-specified non-inferiority margin was -3.0 percentage points.

For the pooled analysis:

- A greater proportion of participants in the Alyftrek group had sweat chloride concentrations below 60 mmol/L through week 24 (399 [86%] of 465) than did those in the Trikafta group (367 [77%] of 479; odds ratio 2·21 [95% CI 1·55 to 3·15]; p<0·0001]).
- A greater proportion of participants across both trials in the Alyftrek group had sweat chloride concentrations below 30 mmol/L through week 24 (142 [31%] of 465) than did those in the Trikafta group (108 [23%] of 479; odds ratio 2·87 [95% CI 2·00 to 4·12; p<0·0001).

Safety information:

- Most adverse events were mild or moderate, with the most common being infective pulmonary exacerbation (133 [28%] of 480 participants in the pooled vanzacaftor–tezacaftor–deutivacaftor group *vs* 158 [32%] of 491 in the pooled elexacaftor–tezacaftor–ivacaftor group), cough (108 [23%] *vs* 101 [21%]), COVID-19 (107 [22%] *vs* 127 [26%]), and nasopharyngitis (102 [21%] *vs* 95 [19%]).
- Based on laboratory values for alanine aminotransferase and aspartate aminotransferase, among 480 participants in the pooled vanzacaftor–tezacaftor–deutivacaftor group, 29 (6%), 12 (3%), and six (1%) had alanine aminotransferase or aspartate aminotransferase concentrations that were greater than three times, five times, and eight times the upper limit of normal (ULN), respectively, compared with 15 (3%), six (1%), and one (<1%) of 491 participants in the pooled elexacaftor–tezacaftor–ivacaftor group.

Conclusion	Alyftrek is non-inferior to Trikafta in terms of FEV_1 % predicted, and is safe and well tolerated. Once daily dosing with Alyftrek reduces treatment burden, improving adherence, compared with the twice daily regimen of the current standard of care. The restoration of CFTR function and the variants treated are also considerations that should be compared with currently available CFTR modulators.
Interpretation	Alyftrek was as effective at improving lung function parameters (ppFEV1) as standard of care therapy Trikafta but was better at reducing sweat chloride levels in both trials, with a greater proportion of patients in both trials able to reach sweat chloride levels under the threshold for diagnosing cystic fibrosis (60 mmol/L) and levels considered normal (30 mmol/L). Sweat chloride levels are indicative of CFTR function, but further study is needed to determine if such additional reduction as demonstrated in these trials will translate to improved clinical outcomes for patients.

Ongoing

Title	RIDGELINE 105: A Phase 3 Study Evaluating the Pharmacokinetics, Safety, and Tolerability of VX-121/Tezacaftor/Deutivacaftor Triple Combination Therapy in Cystic Fibrosis Subjects 1 Through 11 Years of Age NCT: 05422222
Design	An ongoing, single arm, open label trial examining safety and tolerability of Alyftrek in younger patients (1 through 11 years).
Completion Date	06/2030

Guidelines

Cystic Fibrosis Foundation Pulmonary Guidelines. Use of cystic fibrosis transmembrane conductance regulator modulator therapy in patients with cystic fibrosis. (Ann Am Thorac *Soc*. 2018 Mar. doi: 10.1513/AnnalsATS.201707-539OT.PMID: 29342367)

The Cystic Fibrosis Foundation released guidelines specific to the use of two available CFTR modulator therapies, ivacaftor (Kalydeco®) and lumacaftor/ivacaftor (Orkambi®) using a multidisciplinary panel of CF caregivers and patient representatives. The newer agents Alyftrek®, Symdeko® and Trikafta® are not included in these guidelines. The panel sought to address three questions specific to a CFTR modulator therapy vs no CFTR modulator therapy in certain groups of CF patients respective to their genetic mutations. Recommendations were made based on grading of currently available clinical evidence and were stratified according to age and varying levels of pulmonary function. A review of the recommendations for each group are provided in the below tables. In the majority of situations, the panel felt in favor of

recommending (at least conditionally) the applicable CFTR modulator therapies, given a small amount of evidence of clinical benefit, and that most patients and caregiver groups would be in favor of using these therapies, but noted cost may play a part in the decision-making process. Exceptions where CFTR modulators were recommended against include situations where data had demonstrated unfavorable clinical outcomes for certain groups, and where the cost of therapy and risk for side-effects potentially outweighed possible benefit.

Ivacaftor for patients with cystic fibrosis due to gating mutations other than G551D or R117H

Age (years)	$PPFEV_1$ (%)	Certainty	Recommendation
0-2	N/A	N/A	No recommendation
2-5	N/A	N/A	Recommend for
6-11	<40	Very low	Conditional for
6-11	40-90	Low	Conditional for
6-11	>90	Low	Conditional for
12-17	<40	Low	Conditional for
12-17	40-90	Moderate	Conditional for
12-17	>90	Moderate	Conditional for
18+	<40	Low	Conditional for
18+	40-90	Moderate	Conditional for
18+	>90	Moderate	Conditional for

Ivacaftor for patients with cystic fibrosis with the R117H mutation

Age (years)	$PPFEV_1$ (%)	Certainty	Recommendation
0-5	N/A	Very low	Conditional against
6-11	<40	Very low	Conditional for
6-11	40-90	Very low	Conditional for
6-11	>90	Low	Conditional against
12-17	<40	Very low	Conditional for
12-17	40-90	Very low	Conditional for
12-17	>90	Very low	Conditional against
18+	<40	Very low	Conditional for
18+	40-90	Moderate	Conditional for
18+	>90	Low	Conditional for

Ivacaftor/lumacaftor for patients with cystic fibrosis with two copies of F508del

Age (years)	$PPFEV_1$ (%)	Certainty	Recommendation
0-5	N/A	N/A	No recommendation
6-11	<40	Very low	Conditional for
6-11	40-90	Very low	Conditional for
6-11	>90	Very low	Conditional for
12-17	<40	Moderate	Strong for
12-17	40-90	Moderate	Strong for
12-17	>90	Low	Conditional for
18+	<40	Moderate	Strong for
18+	40-90	Moderate	Strong for
18+	>90	Low	Conditional for

Grading Strength Interpretation

Implications	Strong Recommendation	Conditional Recommendation
For patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that clinicians must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals make decisions consistent with their values and preferences
For policy makers	The recommendation can be adapted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders

Clinical Opinions

Cystic fibrosis (CF) is a rare, progressive, life-threatening disease that results in the formation of thick mucus that builds up in the lungs, digestive tract, and other parts of the body. It leads to severe respiratory and digestive problems along with other complications such as infections and diabetes. The prevalence of CF in the United States is approximately 40,000 people, with 1,000 new cases diagnosed annually. CF is caused by a defective protein that results from mutations in the CFTR gene. While there are approximately 2,000 known mutations of the CFTR gene, the most common mutation is the F508del mutation. Recent advances in pharmacologic therapies for CF, specifically the emergence of the CFTR modulator class, have increased life expectancy of these individuals from young adulthood now into the fifth decade of life. The CFTR modulators are indicated for use in patients with specific mutations in the CFTR gene and work to improve processing and function of the defective protein.

Alyftrek is the newest CFTR modulator therapy approved for CF, and a triple therapy agent. Vanzacaftor is considered a next-generation CFTR corrector, deutivacaftor is a unique once-daily CFTR potentiator, and tezacaftor is the same CFTR corrector used in Trikafta and Symdeko. Alyftrek demonstrated non-inferiority to Trikafta in clinical trials in change in percent-predicted forced expiratory volume in 1 second (ppFEV1), a measure of lung function. Alyftrek also demonstrated increased efficacy in reducing sweat chloride levels compared to Trikafta, which is a biomarker of CFTR function and is used to diagnose CF. Whether the additional reduction in sweat chloride levels seen with Alyftrek will translate to improved clinical outcomes in patients with CF is not clear and requires further study.

Alyftrek also offers patients the convenience of once daily dosing and has efficacy in 31 additional CFTR gene mutations compared to Trikafta. Existing CFTR modulator therapies already covered mutations for approximately 90% of the CF patient population, meaning impact in terms of newly eligible CF patients who can now benefit form CFTR modulator therapy should be minimal. However, the convenient dosing schedule and potential for improved long term clinical benefit may drive interest from patients and providers to switch from other existing CFTR modulator therapies to Alyftrek. Alyftrek's list price is approximately 7% more than Trikafta, which will be a contributor to increased spending for payers in the CF space. Drug induced liver injury and liver failure occurrences with Trikafta prompted the FDA to

issue a black box warning and increased monitoring recommendations for both Trikafta and Alyftrek since these agents contain some identical or highly similar drugs. Transaminase elevations occurred in 9% of patients in the clinical trials taking Alyftrek, and approximately 1.5% of these patients needed to discontinue therapy. Rates of these occurrences were slightly lower with Trikafta. This could create some hesitation amongst providers considering switching Trikafta patients to Alyftrek if patients' liver function is within normal range and responding positively to therapy.

Alternatives

Drug Name^	Formulary Status	Dosage Form	Price*
Trikafta® (elexacaftor/tezacaftor/ivacaftor)	F-PA	100 mg-50 mg-75 mg/150 mg, 50 mg-25 mg-37.5 mg/75 mg oral tablets and 100 mg-50 mg-75 mg/75 mg, 80 mg-40 mg-60 mg/59.5 mg oral granule packets	$28,442
Kalydeco® (ivacaftor)	F-PA	150 mg oral tablets and 5.8 mg, 13.4 mg, 25 mg, 50 mg, 75 mg oral granule packets	$28,442
Orkambi® (lumacaftor/ivacaftor)	F-PA	100 mg-125 mg, 200 mg-125 mg oral tablets and 75 mg-94 mg, 100 mg-125 mg, 150 mg-188 mg oral granule packets	$24,899
Symdeko® (tezacaftor/ivacaftor)	F-PA	50 mg/75 mg-75 mg, 100 mg/150 mg-150 mg oral tablets	$26,661

^The manner in which the Drug Name is listed implies its availability. The generic name is listed first, with brand in parenthesis, if the product is available as a generic. The brand name is listed first, with the generic name in parenthesis, if the product is available as a brand only.

**Price per month unless otherwise noted. Pricing for multi-source generic medications based on National Average Drug Acquisition Cost (NADAC). Pricing for single-source branded medications and generic drugs without NADAC data based on Wholesale Acquisition Cost (WAC).*

PA Criteria

Recommendation: Add Alyftrek as the newest CFTR modulator indicated for the treatment of cystic fibrosis in patients 6 years and older who have at least one F508del mutation or another responsive mutation in the CFTR gene.

Cystic Fibrosis Agents	
Therapeutic Classes (AHFS)	Cystic Fibrosis (CFTR) Potentiators, Misc. Beta-lactam antibiotics, Mucolytic agents
Medications	Formulary, PA required Kalydeco (ivacaftor) oral granules, tablet Orkambi (lumacaftor/ivacaftor) tablet, granule packet Symdeko (tezacaftor/ivacaftor) tablets Trikafta (elexacaftor/tezacaftor/ivacaftor) tablets Alyftrek (vanzacaftor/tezacaftor/deutivacaftor) tablets Cayston (aztreonam lysine) vial for nebulization TOBI Podhaler (tobramycin) capsule, capsule with inhalation device tobramycin (TOBI) ampule for nebulization tobramycin (Kitabis Pak) ampule for nebulization tobramycin (Bethkis) ampule for nebulization Pulmozyme (dornase alfa) inhalation solution Bronchitol (mannitol) *Or any other newly marketed dosage form, strength, or medication used to treat cystic fibrosis
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a pulmonologist, or specialist in the treatment of cystic fibrosis
Coverage Duration	**Initial Approval** 6 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Initial criteria for the use of Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), Symdeko (tezacaftor/ivacaftor), ~~or~~ Trikafta (elexacaftor/tezacaftor/ivacaftor), or Alyftrek (vanzacaftor/tezacaftor/deutivacaftor) • Documentation provided includes a copy of the FDA-cleared cystic fibrosis (CF) mutation test OR documentation from the National Cystic Fibrosis Registry (e.g. screen shot) with member's genetic mutations. • The request is appropriate for member (e.g. age/weight/degree of liver function) per package insert or standard of care guidelines • Baseline liver transaminase levels were submitted with request (within 90 days of request) • The request is for an FDA approved indication for the member's genotype and within dosing guidelines

	Re-authorization criteria for the use of Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), Symdeko (tezacaftor/ivacaftor), ~~or~~ Trikafta (elexacaftor/tezacaftor/ivacaftor), or Alyftrek (vanzacaftor/tezacaftor/deutivacaftor) • Documentation has been submitted that patient has obtained clinical benefit from medication (i.e. improvement in FEV1, BMI, decrease in number or frequency of pulmonary exacerbations, or improvement in quality of life) • MD attests that liver function testing/monitoring has been completed per the package labeling • The medication is being prescribed at a dose that is within FDA approved guidelines. Initial criteria for the use of inhaled tobramycin (Bethkis,Tobi, Kitabis Pak), Pulmozyme (dornase alfa), Tobi Podhaler • The request is appropriate for member (e.g. age/weight) • If the request is for a brand name tobramycin product, documentation has been provided why member is unable to use generic tobramycin • The medication is being prescribed at a dose that is within FDA approved guidelines. Re-authorization criteria for the use of inhaled tobramycin (Bethkis,Tobi, Kitabis Pak), Pulmozyme (dornase alfa), Tobi Podhaler • The request is appropriate for member (e.g. age/weight) • The medication is being prescribed at a dose that is within FDA approved guidelines. • Documentation has been submitted that patient has obtained clinical benefit from medication Initial criteria for the use of Cayston (aztreonam lysine) • The medication is being prescribed for a cystic fibrosis patient colonized with P. aeruginosa • Documentation has been provided why member is unable to use generic tobramycin • The medication is being prescribed at a dose that is within FDA approved guidelines Re-authorization criteria for the use of Cayston (aztreonam lysine) • The medication is being prescribed for a cystic fibrosis patient colonized with P. aeruginosa • The medication is being prescribed at a dose that is within FDA approved guidelines • Documentation has been submitted that patient has obtained clinical benefit from medication (i.e. improvement in FEV1, decrease in number or frequency of pulmonary exacerbations) Initial criteria for the use of Bronchitol • The medication is being prescribed at a dose that is within FDA approved guidelines • The prescriber attests that the patient has not had an episode of hemoptysis (>60 mL) in the 3 months prior to beginning therapy

	• The prescriber attests that the Bronchitol Tolerance Test (BTT) will be administered and performed under the supervision of a qualified healthcare practitioner Re-authorization criteria for the use of Bronchitol • The medication is being prescribed at a dose that is within FDA approved guidelines • Documentation has been submitted that patient has obtained clinical benefit from medication (i.e. decrease in number or frequency of pulmonary exacerbations)
Criteria Statement	For the treatment of cystic fibrosis, Kalydeco, Orkambi, Symdeko, ~~or~~ Trikafta, or Alyftrek are reserved for members with documented genetic mutations and who have documented baseline liver transaminase levels within 90 days of request. For the treatment of cystic fibrosis, inhaled tobramycin (Bethkis, Tobi, Kitabis Pak), Pulmozyme (dornase alfa), and Tobi Podhaler are reserved for members of appropriate age, indication, and dosing who have used (or cannot/should not use) generic tobramycin. For the treatment of cystic fibrosis in members colonized with P. aeruginosa, Cayston is reserved for members who have used (or cannot/should not use) generic tobramycin. For the treatment of cystic fibrosis, Bronchitol is reserved for members of appropriate age, indication, and dosing, who have or will have had the Bronchitol Tolerance Test (BTT) performed, and who have not had an episode of hemoptysis (>60 mL) in the 3 months prior to beginning therapy.
Last P&T Review Date	~~3/2024~~3/2025

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Alameda MRGs for review Q1 2025 P&T

Recommendation:

- Change naming convention to reflect Emflaza availability as a generic deflazacort
- Add trial and failure with generic deflazacort before Agamree as it is more cost effective and there is no preference per guidelines
- No utilization of these products

Corticosteroids for Duchenne Muscular Dystrophy (DMD)	
Therapeutic Classes (AHFS)	Glucocorticoids
Medications	Formulary, PA required Deflazacort (Emflaza) ~~(deflazacort)~~ Agamree (vamorolone)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a neurologist or provider who specializes in the treatment of DMD
Coverage Duration	**Initial Approval** 6 months **Later Approval** 12 months; If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**For Approval:** • Confirmed diagnosis of Duchenne Muscular Dystrophy (such as documented mutation of dystrophin gene~~)~~, genetic sequencing indicating mutations attributed to Duchene Muscular Dystrophy, muscle biopsy indicating absence of dystrophin protein, etc.), and copies of testing were submitted with request • Trial and failure with prednisone for at least 12 months, and documented medical reason why prednisone cannot be continued • If the request is for Agamree, trial and failure of, intolerance, or inability to use generic deflazacort • The request is for an FDA approved dose **Reauthorization:** • Documentation or attestation of clinical benefit (such as improved muscle strength, muscle function, or overall symptom improvement) • The request is for an FDA approved dose
Criteria Statement	Deflazacort~~Emflaza~~ and Agamree are reserved for members who have Duchenne Muscular Dystrophy who have used (or cannot/should not use) prednisone for 12 months. Additionally, Agamree is reserved for members who have used (or cannot/should not use) generic deflazacort.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation:

- Change Eucrisa and Rinvoq placement in the criteria to match current placement on formulary: Eucrisa is on formulary with PA and Rinvoq is NF.
- Add Ebglyss—new IL-13 inhibitor SC injection indicated for the treatment of adult and pediatric patients 12 years and older who weigh at least 40 kg with moderate to severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- Add Nemluvio—IL-31 receptor antagonist SC injection that received an expanded indication for the treatment of moderate to severe atopic dermatitis.
- Add Vtama--topical cream, an aryl hydrocarbon receptor agonist, that received an expanded indication for the treatment of atopic dermatitis.
- Add Zoryve—topical cream recently approved for the treatment of mild to moderate atopic dermatitis in adult and pediatric patients 6 years of age and older. It is a topical phosphodiesterase-4 (PDE4) inhibitor like Eucrisa.
- Expand prescriber restriction to all drugs in the policy. The only drugs that have been left out of this restriction are the TCIs (tacrolimus and pimecrolimus), however, considering their side effect profile, they would be appropriate to be managed by a specialist as well.
- Add Vtama and Zoryve to the "For Opzelura: 8 weeks" coverage duration section, as trial safety and efficacy endpoints for both were also assessed at 8 weeks.
- Combine four FDA-approved topicals into one section as none are preferred for efficacy or safety per guidelines and are of comparable cost.
- Remove Rinvoq from Dupixent criteria as it is more in line with Cibinqo in terms of cost, formulation and indication.
- Add Adbry to formulary with PA and combine with Dupixent criteria requirements to qualify for preferred pricing.
- Add separate sections for Nemluvio and Ebglyss due to their higher cost.
- Remove the previous step therapy through TCSs and TCIs from Nemluvio, Ebglyss and all therapies further down the line as it is redundant (patients would have already stepped through these agents in the previous section for topicals: Eucrisa/Opzelura/Vtama or Zoryve).
- Combine Cibinqo and Rinvoq as they are both oral formulations indicated for refractory AD not controlled by other systemic drugs and simplify the requirements.

Agents for Atopic Dermatitis	
Therapeutic Classes (AHFS)	Skin and mucous membrane agents, anti-inflammatory agents, misc (skin)
Medications	**Formulary, Step therapy required:** Tacrolimus (Protopic) Pimecrolimus (Elidel) **Formulary, Prior Authorization Required:** Dupixent (dupilumab) Eucrisa (crisaborole) ~~Rinvoq (upadacitinib)~~ Adbry (tralokinumab-ldrm) **Non-formulary:** Rinvoq (upadacitinib) ~~Eucrisa (crisaborole)~~ Opzelura (ruxolitinib) ~~Adbry (tralokinumab-ldrm)~~ Cibinqo (abrocitinib)

	Ebglyss (lebrikizumab-lbkz) Nemluvio (nemolizumab-ilto) Vtama (tapinarof) Zoryve (roflumilast) Any other newly marketed agent for atopic dermatitis
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Tacrolimus (Protopic), pimecrolimus (Elidel), and Opzelura (ruxolitinib): Immunocompromised members
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	~~Dupixent, Rinvoq, Adbry, Cibinqo and Opzelura requests: Provider must be a p~~Prescribed by, or in consultation with, a pediatrician, family practitioner (for members under 21 years of age), dermatologist, immunologist, or allergist
Coverage Duration	For Opzelura, Vtama, and Zoryve: If the criteria are met, the request will be approved with up to an 8 week duration and all reauthorization requests will be approved for up to a 6 month duration. For all others: If the criteria are met, the request will be approved with up to a 6 month duration; if the criteria are not met, the request will be referred to a clinical reviewer for medical necessity review.
PA Review Criteria	**Initial Authorization:** **Criteria for approval for pimecrolimus (Elidel)** • Diagnosis of mild to moderate atopic dermatitis • For mild atopic dermatitis: trial and failure of, intolerance, or inability to use, one formulary medium to high potency topical corticosteroid • For moderate atopic dermatitis: trial and failure of, intolerance, or inability to use, one formulary medium to high potency topical corticosteroid AND topical tacrolimus **Criteria for approval of tacrolimus (Protopic)** • Diagnosis of moderate to severe atopic dermatitis • Trial and failure of, intolerance, or inability to use, one formulary medium to high potency topical corticosteroid **Criteria for approval for Eucrisa, Opzelura, Vtama, or Zoryve** • Diagnosis of atopic dermatitis (AD) • Trial and failure of, intolerance, or contraindication to, ALL of the following: o One formulary medium to high potency topical corticosteroid o One formulary topical calcineurin inhibitor • For Opzelura requests, trial and failure of, intolerance, or contraindication to Eucrisa **A MAXIMUM OF ONE 60gm TUBE OF OPZELURA MAY BE APPROVED PER WEEK** ~~• Diagnosis of mild to moderate atopic dermatitis~~ ~~• Trial and failure of, intolerance, or inability to use, one formulary medium to high potency topical corticosteroid~~ ~~• Trial and failure of, intolerance, or inability to use tacrolimus or pimecrolimus~~

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Criteria for approval for Dupixent ~~or Rinvoq~~ or Adbry:

- Provider attestation of diagnosis of moderate to severe atopic dermatitis
- Trial and failure of ONE of the following:
  - One formulary medium to high potency topical corticosteroid
  - Topical tacrolimus or pimecrolimus
  - Eucrisa (crisaborole)

Criteria for approval for ~~Adbry~~Nemluvio:

- Diagnosis of moderate to severe atopic dermatitis (AD)
- Trial and failure of, intolerance, or contraindication to, ONE of the following:
  - Eucrisa
  - Opzelura
  - Vtama
  - Zoryve
- ~~For moderate AD: Trial and failure, or contraindication/intolerance to ALL of the following:~~
  - ~~One formulary medium to high potency topical corticosteroid~~
  - ~~Topical tacrolimus or pimecrolimus~~
  - ~~Eucrisa (crisaborole)~~
- ~~For severe AD: Trial and failure of, or contraindication/intolerance to, ALL of the following:~~
  - ~~One formulary topical medium to high potency topical corticosteroid~~
  - ~~Topical tacrolimus~~

Criteria for approval for Ebglyss:

- Diagnosis of moderate to severe AD
- Trial and failure of, intolerance, or contraindication to, ONE of the following:
  - Adbry
  - Dupixent
  - Nemluvio

Criteria for approval for Cibingo or Rinvoq:

- Diagnosis of refractory, moderate to severe~~,~~ AD
- Trial and failure of, intolerance, or contraindication to, another systemic drug product for AD
- ~~For moderate AD: Trial and failure of, or contraindication to, ALL of the following:~~
  - ~~One formulary topical medium to high potency topical corticosteroid~~
  - ~~Topical tacrolimus or pimecrolimus~~
  - ~~Eucrisa (crisaborole)~~
- ~~For severe AD: Trial and failure of, or contraindication to ALL of the following:~~
  - ~~One formulary medium to high potency topical corticosteroid~~
  - ~~Topical tacrolimus~~
- ~~Trial and failure of, intolerance to, or contraindication to another systemic drug product~~

~~**Criteria for approval for Opzelura:**~~

- ~~Diagnosis of mild to moderate atopic dermatitis~~
- ~~Member must have 3% to 20% of BSA atopic dermatitis involvement (excluding scalp)~~
- ~~Trial and failure of, intolerance, or inability to use to ALL of the following:~~
  - ~~One formulary medium to high potency topical corticosteroid~~
  - ~~Topical tacrolimus or pimecrolimus~~

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	~~o Eucrisa (crisaborole)~~ ~~**A MAXIMUM OF ONE 60gm TUBE OF OPZELURA MAY BE APPROVED PER WEEK**~~ **Reauthorization:** • Prescriber attests that the member has experienced improvement in symptoms (e.g. significant clearing of the skin, reduction in itching)
Criteria Statement	For mild to moderate atopic dermatitis pimecrolimus is reserved for members who have used (or cannot/should not use) one topical steroid. For moderate atopic dermatitis pimecrolimus is reserved for members who have used (or cannot/should not use) one topical steroid and tacrolimus. For moderate to severe atopic dermatitis tacrolimus is reserved for members who have used (or cannot/should not use) one topical steroid. For mild to ~~moderate~~ severe atopic dermatitis Eucrisa, Opzelura, Vtama, ~~or~~ Zoryve are~~is~~ reserved for members who have used (or cannot/should not use) one topical steroid and tacrolimus or pimecrolimus. Additionally, Opzelura is reserved for members who have used (or cannot/should not use) Eucrisa. For moderate to severe atopic dermatitis Dupixent ~~or Rinvoq are~~ or Adbry are reserved for members who have used (or cannot/ ~~should not use~~) ONE of the following: one topical steroid, tacrolimus or pimecrolimus, or Eucrisa. For moderate to severe atopic dermatitis ~~Adbry~~ Nemluvio ~~is~~ is reserved for members who have used (or cannot/ ~~should not use~~) ONE of the following: Eucrisa, Opzelura, Vtama, or Zoryve. ~~ALL of the following: one topical steroid, tacrolimus or pimecrolimus, and Eucrisa.~~ For moderate to severe atopic dermatitis ~~Adbry~~Ebglyss is reserved for members who have used (or cannot/should not use) ~~ALL~~ ONE of the following: ~~one topical steroid and tacrolimus.~~Adbry, Dupxent, or Nemluvio. For refractory moderate to severe atopic dermatitis Cibinqo and Rinvoq are ~~is~~ reserved for members who have used (or cannot/should not use) ~~ALL of the following: one topical steroid, tacrolimus or pimecrolimus, and Eucrisa AND another systemic drug product.~~another systemic drug product for AD. ~~For severe atopic dermatitis Cibinqo is reserved for members who have used (or cannot/should not use) ALL of the following: one topical steroid and tacrolimus AND another systemic drug product.~~ ~~For mild to moderate atopic dermatitis Opzelura is reserved for members who have used (or cannot/should not use) ALL of the following: one topical steroid, tacrolimus or pimecrolimus, and Eucrisa.~~
Last P&T Review Date	~~3/2024~~3/2025

Recommendation:

- Add new product Alvaiz—thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in adult and pediatric patients 6 years and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy; for the treatment of thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy; for the treatment of adult patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.
- Add trial and failure of Promacta before Alvaiz since it is the most established, cost-effective agent in this class.

Thrombocytopenia Agents	
Therapeutic Classes (AHFS)	Hematopoietic agents
Medications	Formulary, PA required Promacta (eltrombopag) tablets Mulpleta (lusutrombopag) Nplate (romiplostim) Doptelet (avatrombopag) Alvaiz (eltrombopag) Non-Formulary Promacta (eltrombopag) powder packets Tavalisse (fostamatinib)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber is a hematology specialist or working in consultation with a hematologist
Coverage Duration	**Initial Approval** If the criteria are met, the request will be approved for 12 months for Promacta, Nplate, Doptelet (for the indication of chronic immune thrombocytopenia), Alvaiz and Tavalisse. Doptelet will be approved for a maximum of 5 days (for the indication of chronic liver disease-associated thrombocytopenia) Mulpleta will be approved for a maximum of 7 days. If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	For all indications below, the medication is prescribed at an FDA-approved dose for indication and age **Chronic immune (idiopathic) thrombocytopenia (ITP):** • Platelet count < 30,000 cells/microL • Documented trial and failure, intolerance, or contraindication to use ONE of the following: glucocorticoids, intravenous immune globulin (IVIG), rituximab or splenectomy • For Doptelet, Nplate, Alvaiz or Tavalisse, the member must also have a documented trial and failure, intolerance, or contraindication to Promacta tablets

	Severe aplastic anemia: Promacta & Alvaiz only: • Documented trial and failure, intolerance or contraindication to at least one immunosuppressive agent **OR** is being prescribed in conjunction with at least one immunosuppressive agent **AND** • Platelet count < 20,000 cells/microL OR < 30,000 cells/microL with bleeding OR reticulocyte count < 20,000 cells/microL OR absolute neutrophil count < 500 cells/microL • For Alvaiz, member must also have a documented trial and failure, intolerance, or contraindication to Promacta tablets **Thrombocytopenia in patients with Hepatitis C infection:** Promacta & Alvaiz only: • Diagnosis of chronic hepatitis C **AND** • Documented treatment with interferon-based therapy **AND** • Patient's degree of thrombocytopenia prevents the initiation or limits the ability to maintain interferon-based therapy **AND** • Medical reason for why patient needs to be treated with interferon over new DAA medication **AND** • Platelet count < 50,000 cells/microL • For Alvaiz, member must also have a documented trial and failure, intolerance, or contraindication to Promacta tablets **Thrombocytopenia associated with chronic liver disease in adult patients requiring elective surgery** Doptelet and Mulpleta only: • Patient has a diagnosis of chronic liver disease and is scheduled to undergo a procedure **AND** • Platelet count < 50,000 cells/microL **AND** • For Mulpleta, approve if there is documentation of trial and failure, intolerance, or contraindication to use Doptelet For Promacta powder, approve if there is a documentation of trial and failure, intolerance or contraindication to use Promacta tablets, and all other Promacta criteria above are met.
Criteria Statement	Promacta is reserved for members with chronic immune (idiopathic) thrombocytopenia (ITP), who have used (or cannot/ should not use) one of the following: glucocorticoids, intravenous immune globulin (IVIG), rituximab, or splenectomy. Doptelet, Nplate, Alvaiz and Tavalisse are reserved for members with chronic immune (idiopathic) thrombocytopenia (ITP), who have used (or cannot/ should not use) Promacta tablets. Promacta is reserved for members with severe aplastic anemia who have used (or cannot/ should not use) an immunosuppressive agent or is being used in conjunction with an immunosuppressive agent. Alvaiz is reserved for members with severe aplastic anemia who have used (or cannot/should not use) Promacta tablets.

	Promacta is reserved for members with hepatitis C infection in patients who must be treated with interferon-based therapy. Alvaiz is reserved for members with hepatitis C infection in patients who must be treated with interferon-based therapy who have used (or cannot/should not use) Promacta tablets. Doptelet is reserved for members who have thrombocytopenia associated with chronic liver disease in adult patients requiring elective surgery. Mulpleta is reserved for members who have thrombocytopenia associated with chronic liver disease in adult patients requiring elective surgery and who have used (or cannot/ should not use) Doptelet.
Last P&T Review Date	~~3/2024~~3/2025

Recommendation:

- Change asthma to respiratory conditions in the name of the criteria due to new indication of Dupixent as an add-on COPD maintenance treatment of adult patients with inadequately controlled COPD and an eosinophilic phenotype
- Reword prescriber restrictions section for more clarity
- Add COPD indication for Dupixent with appropriate requirements per inclusion criteria from the trials and PI
- Add Fasenra to eosinophilic granulomatosis with polyangiitis (EGPA) indication, and trial and failure of Fasenra if the request is for Nucala for cost effectiveness
- Add COPD to clinical benefits in reauthorization section

Pulmonary Biologics for ~~Asthma~~ Respiratory and Eosinophilic Conditions	
Therapeutic Classes (AHFS)	Interleukin antagonists
Medications	Nucala (mepolizumab) Fasenra (benralizumab) Cinqair (reslizumab) Dupixent (dupilumab) Tezspire (tezepelumab) Any other newly marketed agents
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), and the Drug Package Insert.
Exclusion Criteria	• When being used for relief of acute bronchospasm or status asthmaticus • In combination with another monoclonal antibody for the treatment of ~~asthma~~ respiratory or eosinophilic conditions
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	Per Package Insert Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be ~~prescribed by or in consultation with~~ an allergist, pulmonologist, immunologist, rheumatologist, gastroenterologist, dermatologist, or other provider who specializes in the treatment of asthma or eosinophilic conditions, or in consultation with one of these specialists
Coverage Duration	Initial Approval 4 months Later Approvals 6 months If conditions are not met, the request will be sent to a clinical reviewer

PA Review Criteria	**Initial Authorization:**
	
	Asthma:
	• Confirmed diagnosis of one of the following:
	  ○ Nucala, Fasenra, and Cinqair: Severe Eosinophilic Asthma
	  ○ Dupixent: Moderate-to-Severe eosinophilic asthma
	  ○ Tezspire: Severe Asthma
	• Documentation has been provided of blood eosinophil count within ONE of the following ranges:
	  ○ Nucala and Dupixent: ≥ 150 cells/mcL (within 6 weeks of request) OR ≥ 300 cells/mcL (within the past 12 months)
	  ○ Fasenra: ≥ 150 cells/mcL (within the past 12 months)
	  ○ Cinqair: ≥ 400 cells/mcL (within the past 12 months)
	  ○ Tezspire: No baseline blood eosinophil counts are required
	• The member has a documented baseline FEV_1 < 80% of predicted with evidence

of reversibility by bronchodilator response.
    - Tezspire ONLY: If age is < 18 years, the member has a documented baseline FEV_1 < 90% of predicted with evidence of reversibility by bronchodilator response
- Documentation has been provided indicating that that the member continues to experience significant symptoms while compliant on a maximally tolerated inhaled corticosteroid with long-acting beta2 agonist (ICS/LABA) AND long-acting muscarinic antagonist (LAMA) (or a documented medical reason must be provided why the member is unable to use these therapies) and ONE of the following:
    - Nucala: ≥ 2 exacerbations in the past 12 months
    - Fasenra: ≥ 1 exacerbation in the past 12 months
    - Cinqair: ≥ 1 exacerbation in the past 12 months requiring systemic corticosteroids
    - Dupixent: ≥ 1 exacerbation in the past 12 months requiring systemic corticosteroids or hospitalization
    - Tezspire: ≥ 2 exacerbations requiring systemic corticosteroids OR ≥ 1 exacerbation in the past 12 months requiring hospitalization
- The prescribed dose is within FDA approved dosing guidelines

Chronic Obstructive Pulmonary Disease (COPD) (*Dupixent only*):
- Confirmed diagnosis of COPD
- Documentation has been provided of blood eosinophil count ≥ 300 cells/mcL
- The member has a documented post-bronchodilator FEV_1/FVC ratio < 0.7 and post-bronchodilator FEV_1 of 30% to 70% predicted
- Documentation has been provided indicating that the member continues to experience significant symptoms (i.e., chronic productive cough) while compliant on maintenance triple therapy consisting of a long-acting muscarinic antagonist (LAMA), long-acting beta2 agonist (LABA), and inhaled corticosteroid (ICS) (or a documented medical reason must be provided why the member is unable to use these therapies) and ONE of the following:
    - ≥ 2 exacerbations in the past 12 months, where systemic corticosteroids were required for at least one of them
    - ≥ 1 exacerbation in the past 12 months requiring hospitalization
- The prescribed dose is within FDA approved dosing guidelines

Oral Corticosteroid Dependent Asthma: (*Dupixent only*)
- Confirmed diagnosis of oral corticosteroid (OCS) dependent asthma with at least 5 mg oral prednisone or equivalent per day for at least 4 weeks within the last 3 months
- The patient has a documented baseline FEV1 < 80% of predicted with evidence of reversibility by bronchodilator response.
- Documentation has been provided indicating patient still is having significant symptoms with ≥ 1 exacerbations in the previous 12 months requiring additional medical treatment, (emergency room visits, hospital admissions) while compliant on a high-dose inhaled corticosteroid with a long-acting B2 agonist AND a long-acting muscarinic antagonist (LAMA). If the patient has not utilized these therapies, a documented medical reason must be provided why patient is unable to do so.
- The prescribed dose is within FDA approved dosing guidelines

Eosinophilic Esophagitis (EoE) (*Dupixent only):*
- Confirmed diagnosis of EoE by endoscopic biopsy indicating ≥15 intraepithelial eosinophils per high-power field (eos/hpf)
- Documentation of baseline esophageal intraepithelial eosinophil count and Dysphagia Symptom Questionnaire (DSQ) scores

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- Member has a history of at least 2 episodes of dysphagia (with intakes of solids) per week in the last 4 weeks
- Documented trial and failure, intolerance, or contraindication to one proton pump inhibitor at a maximally tolerated dose for a minimum of 8 weeks
- Member has a documented weight greater than or equal to 40 kg
- The prescribed dose is within FDA approved dosing guidelines

Prurigo Nodularis (PN) (*Dupixent only*):

- Confirmed diagnosis of PN lasting for at least three months prior to request
- Member has a Worst-itch Numeric Rating Scale (WI-NRS) score of 7 or higher indicating severe or very severe itching
- Member has at least 20 PN lesions in total
- Documented trial and failure, intolerance, or contraindication to at least two of the following for a minimum of two weeks:
  - One medium to super-high potency topical corticosteroid
  - One topical calcineurin inhibitor
  - UVB phototherapy or psoralen plus UVA phototherapy
- The prescribed dose is within FDA approved dosing guidelines

Eosinophilic granulomatosis with polyangiitis (EGPA) (*Nucala & Fasenra only*):

- Confirmed diagnosis of EGPA and eosinophilic asthma lasting for ≥6 months
- Member has a history of relapsing disease defined as at least one EGPA relapse requiring additional corticosteroids or immunosuppressant or hospitalization within the past 2 years OR member has a history of refractory disease defined as failure to attain remission in the prior 6 months following induction treatment with standard therapy
- Member must be on a stable dose of oral corticosteroids for at least 4 weeks prior to request
- Member has a blood eosinophil count ≥1,000 cells/mcL OR > 10% of total leukocyte count
- Documented trial and failure, intolerance, or contraindication to cyclophosphamide, rituximab, azathioprine, methotrexate, OR mycophenolate mofetil
- If the request is for Nucala, member must also have a documented trial and failure, intolerance, or contraindication to Fasenra
- The prescribed dose is within FDA approved dosing guidelines

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Hypereosinophilic Syndrome (HES) (*Nucala only*):

- Confirmed diagnosis of FIP1 like 1-platelet derived growth factor receptor alpha (FIP1L1-PDGFRA)-negative HES lasting for ≥6 months without an identifiable non-hematologic secondary cause
- Member has a history of two or more HES flares (worsening of HES-related symptoms necessitating therapy escalation or ≥2 courses of rescue oral corticosteroids) within the past 12 months
- Member has a blood eosinophil count ≥1,000 cells/mcL
- Documented trial and failure, intolerance, or contraindication to oral corticosteroids AND at least one second-line agent (e.g. hydroxyurea, interferon, imatinib, methotrexate, cyclophosphamide, cyclosporine, azathioprine) (member must be on stable dose of at least one agent for at least 4 weeks prior to request)

Criteria for re-authorization:

- Documented submitted indicates the member has had a positive clinical response (e.g. Asthma & COPD: improved FEV1, reduced exacerbations; HES: symptomatic improvement, reduced oral corticosteroid dose; EGPA:

	reduction in relapse frequency or severity, disease remission, symptomatic improvement, reduced oral corticosteroid dose; EoE: histological remission, improvement in DSQ scores; PN: improvement in WI-NRS score, symptomatic improvement) • The prescribed dose is within FDA approved dosing guidelines
Criteria Statement	For asthma, Nucala, Dupixent, Fasenra, ~~and~~ Cinqair, and Tezspire are reserved for members who have used (or cannot/should not use) a maximally tolerated inhaled corticosteroid with a long acting B2 agonist (ICS/LABA) AND a long-acting muscarinic antagonist (LAMA), who have eosinophils in the treatment range per package insert, and who have had asthma exacerbations during the previous 12 months. For COPD, Dupixent is reserved for members with a diagnosis of COPD, eosinophil count ≥ 300 cells/mcL, who continue to experience significant symptoms while compliant on maintenance triple therapy consisting of LAMA, LABA, and ICS, and who have had COPD exacerbations in the previous 12 months. For oral corticosteroid dependent asthma, Dupixent is reserved for members with a diagnosis of oral corticosteroid dependent asthma, who have used (or cannot/should not use) a high-dose inhaled corticosteroid with a long acting B2 agonist (ICS/LABA) AND a long-acting muscarinic antagonist (LAMA), and who have been using oral corticosteroids for at least 4 weeks within the past 3 months and who have had asthma exacerbations during the previous 12 months. For eosinophilic esophagitis (EoE), Dupixent is reserved for members with a diagnosis of eosinophilic esophagitis with a history of at least 2 episodes of dysphagia (with intakes of solids) per week in the last 4 weeks, who have used (or cannot/should not use) one proton pump inhibitor at a maximum dose for 8 weeks, with a weight greater than or equal to 40kg. For prurigo nodularis (PN), Dupixent is reserved for members with a diagnosis of prurigo nodularis with a Worst-itch Numeric Rating Scale (WI-NRS) score of 7 or higher indicating severe or very severe itching AND at least 20 PN lesions in total AND who have used (or cannot/should not use) at least two of the following: one medium to super-high potency topical corticosteroid or one topical calcineurin inhibitor or UVB phototherapy or psoralen plus UVA phototherapy. For eosinophilic granulomatosis with polyangiitis (EGPA), Nucala and Fasenra are~~is~~ reserved for members with a diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA), with a history of relapsing disease, who have used (or cannot/should not use) cyclophosphamide, rituximab, azathioprine, methotrexate, OR mycophenolate mofetil. Additionally, Nucala is reserved for members who have used (or cannot/should not use) Fasenra. For hypereosinophilic syndrome (HES), Nucala is reserved for members with a diagnosis of hypereosinophilic syndrome, who have a history of 2 or more flares within the past 12 months, who have used (or cannot/should not use) oral corticosteroids AND at least one second-line agent (e.g. hydroxyurea, interferon, imatinib, methotrexate, cyclophosphamide, cyclosporine, or azathioprine).
Last P&T Review Date	~~3/2024~~3/2025

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Recommendation: Add exclusion criteria of a BBW of multiple endocrine neoplasia syndrome type 2 and medullary thyroid carcinoma for Zepbound, Wegovy, and Saxenda

Anti-Obesity Medications	
Therapeutic Classes (AHFS)	GI drugs, miscellaneous; anorexigenic agents
Medications	Alli (orlistat) Xenical (orlistat) Phentermine (phentermine hcl) (Adipex-P) Phentermine (phentermine hcl) (Lomaira) Qsymia (phentermine/topiramate) Contrave (naltrexone/bupropion) Saxenda (liraglutide) Wegovy (semaglutide) Zepbound (tirzepatide) Any other newly marketed agent ****Please Note: If the request is for Wegovy to reduce the risk of major adverse cardiovascular events please refer to the Wegovy criteria*****
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	~~N/A~~ For Zepbound, Wegovy, and Saxenda: • Personal or family history of medullary thyroid carcinoma • Multiple Endocrine Neoplasia syndrome type 2
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to 6 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	**INITIAL CRITERIA FOR APPROVAL** Phentermine HCL (Adipex-P) • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc) or history of heart attack, despite diet and exercise. • For phentermine (Lomaira): trial and failure or medical reason for not using generic phentermine (Adipex-P) Alli: • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack despite diet and exercise. Qsymia • **For adults:** Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack, despite diet and exercise. **OR**

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	○ **For pediatrics**: BMI in the ≥95th percentile standardized for age and sex ▪ https://www.cdc.gov/healthyweight/bmi/calculator.html • Documented trial and failure, contraindication, or intolerance to use phentermine HCL (Adipex-P) and topiramate as separate ingredients <u>Contrave</u> • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack, despite diet and exercise. • Documented trial and failure, contraindication, or intolerance to use Qsymia <u>Saxenda, Wegovy, and Zepbound</u> • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack, despite diet and exercise • Documented trial and failure, contraindication, or intolerance to use Qsymia AND Contrave <u>Xenical:</u> • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one cardiovascular comorbidity (such as diabetes, controlled hypertension, history of heart attack, etc.) despite diet and exercise. • Documented trial and failure, contraindication, or intolerance to Alli dosed at 120 mg (2 capsules) three times daily. **<u>REAUTHORIZATION CRITERIA FOR APPROVAL</u>** • Documented weight loss of 5% of body weight or more, compared with baseline • If a weight-related comorbidity was previously noted, an objective improvement compared with baseline is documented (e.g. reduction in blood pressure, cholesterol, hemoglobin A1c, etc.)
Criteria Statement	Phentermine is reserved for members who are obese with body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes or hypertension. Generic Lomaira is reserved for members who have used (or cannot/should not use) generic Adipex-P. Alli is reserved for members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack. Qsymia is reserved for adult members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack or pediatric members who are obese with a BMI in the ≥95th percentile standardized for age and sex and who have used (or cannot/should not use) phentermine and topiramate as separate ingredients. Contrave is reserved for members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack and who have used (or cannot/should not use) Qsymia. Saxenda,Wegovy, and Zepbound are reserved for members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack and who have used (or cannot/should not use) Qsymia and Contrave.

	Xenical is reserved for obese members with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack and who have used (or cannot/should not use) Alli.
Last P&T Review Date	~~6/2024~~3/2025

Alameda Q1 2025 PADs for Review Changes

Recommendation:

- Add age requirements to pemphigus vulgaris and GPA/MPA indications for consistency
- For GPA and MPA diagnoses:
    - Remove requirement for diagnosis classification of either severe or non-severe disease since EULAR guidelines do not use the "non-severe" and "severe" language because this puts patients at risk of being undertreated. The EULAR guideline uses "organ-threatening" or "non-organ threatening" language instead.
    - Remove requirement of trial and failure of methotrexate OR cyclophosphamide for non-severe disease since per EULAR guidelines rituximab is recommended regardless of organ status/disease severity. Methotrexate can be used as an alternative to rituximab in non-organ-threatening disease, but rituximab is preferred due to higher rates of sustained remission.

Rituximab	
Medications	Ruxience (rituximab-pvvr) - biosimilar Truxima (rituximab-abbs) - biosimilar Riabni (rituximab-arrx) - biosimilar RITUXAN (rituximab) RITUXAN HYCELA (rituximab and hyaluronidase)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “Other Criteria” below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	See “Other Criteria” below
Coverage Duration	See “Other Criteria” below
Maximum Billable Units	Variable
Other Criteria	**** When this biosimilar is indicated, the member must have documented dates of trial and failure, intolerance, inability to use, or contraindication to the biosimilar medication prior to the brand medication approval, in addition to meeting all applicable criteria below, unless the currently available biosimilar product does not have the same appropriate use (per the references outlined in “Covered Uses”) as the reference biologic drug being requested.** **ONCOLOGY INDICATIONS** **Initial Authorization:** • The medication is being recommended and prescribed by an oncologist. • The medication is being requested for a labeled indication OR an indication supported by NCCN category 1 or 2A level of evidence. ○ If the request is for a category 2B recommendation then the medical documentation has been provided as to why member is unable to utilize a treatment regimen with a higher level of evidence (e.g. allergic reaction, contraindication). • The requested indication is CD20 positive • Documentation provided of results of all required laboratory values and patient specific information (e.g. weigh, ALT/AST, creatinine kinase, etc.) when recommended/required per drug package insert.

	• Documentation indicating that the patient has been screened for HBV (hepatitis B virus) prior to initiation of treatment. • The medication is being prescribed at a dose that is within FDA approved guidelines and/or is supported by the medical compendium as defined by the Social Security Act and/or the National Comprehensive Cancer Network (NCCN) or American Society of Clinical Oncology (ASCO) standard of care guidelines. • For requests for IV medications: attestation medication is administered by a healthcare professional (Medi-Cal only). If all of the above conditions are met, the request will be approved for up to a 3 month duration **Reauthorization** • The medication is being recommended and prescribed by an oncologist. • Rituximab is being prescribed at a dose that is within FDA approved guidelines and/or is supported by the medical compendium as defined by the Social Security Act and/or per the NCCN or ASCO standard of care guidelines. If all of the above conditions are met, the request will be approved for up to a 3 month duration. **RHEUMATOID ARTHRITIS INDICATIONS** **Initial Authorization** • The medication is being recommended and prescribed by a rheumatologist. • The patient is an adult (≥18 y/o) and has a documented clinical diagnosis of rheumatoid arthritis. • The patient has a documented (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) adequate trial (including dates and doses) of 3 months or more of therapy with one conventional (non-biologic) DMARD (e.g. methotrexate, leflunomide, sulfasalazine, hydroxychloroquine) or has a documented medical reason (e.g. intolerance, hypersensitivity) for not utilizing any of these therapies to manage their medical condition. • Documentation indicating that the patient has been screened for Hepatitis B Virus (HBV) prior to initiation of treatment. • Rituximab is being prescribed at an FDA approved dosage. If all of the above conditions are met, the request will be approved for up to a 1 month duration. **Reauthorization** • The member has been receiving rituximab and documentation is provided that a rheumatologist has reevaluated the member and recommends continuation of therapy. • Documentation was provided indicating that the patient had clinical benefit from receiving rituximab therapy. • At least 16 weeks (4 months) has elapsed since the previous course of rituximab therapy. • Rituximab is being prescribed at an FDA approved dosage. If all of the above conditions are met, the request will be approved for up to a 1 year duration. **MULTIPLE SCLEROSIS INDICATIONS**

- Refer to “Healthcare Professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)”

NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD):

- Refer to “Neuromyelitis Optica Spectrum Disorder (NMOSD) Agents”

PEMPHIGUS VULGARIS

Initial Approval

- The medication is being recommended and prescribed by a rheumatologist or dermatologist
- The patient is an adult (≥18 y/o) and has a diagnosis of moderate to severe pemphigus vulgaris
- Documentation the patient will be receiving *P. jirovecii pneumonia* (PCP) prophylaxis (ex. TMP/SMX, dapsone, atovaquone) or the prescriber has provided a medical reason for not prescribing PCP prophylaxis
- Rituximab is being used in combination with a tapering course of glucocorticoids
- Documentation indicating that the patient has been screened for HBV (hepatitis B virus) prior to initiation of treatment.
- Rituximab is prescribed at an FDA approved dose/frequency

If all of the above conditions are met, the request will be approved for up to a 3 month duration

Reauthorization

- Documentation of clinical benefits (e.g. absence of new lesions) with rituximab therapy was provided by a rheumatologist or dermatologist
- Documentation the patient will continue to receive *P. jirovecii pneumonia* (PCP) prophylaxis (ex. TMP/SMX, dapsone, atovaquone) or the prescriber has provided a medical reason for not prescribing PCP prophylaxis
- Rituximab is being prescribed at an FDA approved dose/frequency

If all of the above conditions are met, the request will be approved for up to a 1 year duration.

GRANULOMATOSIS WITH POLYANGIITIS (GPA) (WEGENER’S GRANULOMATOSIS) AND MICROSCOPIC POLYANGIITIS (MPA)

Initial Approval

- The medication is being recommended and prescribed by a rheumatologist or nephrologist.
- The patient is 2 years of age or older and has a documented clinical diagnosis of granulomatosis with polyangiitis (GPA) (Wegener’s Granulomatosis), eosinophilic granulomatosis with polyangiitis (EGPA), or microscopic polyangiitis (MPA) ~~AND the prescriber indicates a diagnosis classification of either severe or non-severe disease.~~
- ~~The patient has a documented (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) adequate trial (including dates, doses) of glucocorticoid (i.e. prednisone) along with methotrexate OR cyclophosphamide (Cytoxan) or a documented medical reason (intolerance, hypersensitivity, etc.) why patient is not able to use these therapies to manage their medical condition.~~
  - ~~If the member has severe GPA/MPA, then this is not required.~~
- Documentation indicating that rituximab is being used concurrently with glucocorticoids.

	• Documentation the patient will be receiving *P. jirovecii pneumonia* (PCP) prophylaxis (ex. TMP/SMX, dapsone, atovaquone) during treatment or the prescriber has provided a medical reason for not prescribing PCP prophylaxis • Documentation indicating that the patient has been screened for HBV (hepatitis B virus) prior to initiation of treatment. • Rituximab is being prescribed at an FDA approved dosage. If all of the above conditions are met, the request will be approved for up to a 3 month duration. **Reauthorization** • The medication is being recommended and prescribed by a rheumatologist or nephrologist. • Documentation the patient will continue to receive *P. jirovecii pneumonia* (PCP) prophylaxis (ex. TMP/SMX, dapsone, atovaquone) or the prescriber has provided a medical reason for not prescribing PCP prophylaxis • Rituxan is being prescribed at an FDA approved dose. If all of the above conditions are met, the request will be approved for up to a 1 year duration. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2024~~3/2025

Recommendation:

- Remove the requirement for trial and failure of a biosimilar before Avastin because the American Academy of Ophthalmology strongly recommends against including these in step therapy regimens and/or as replacement for the reference product, bevacizumab, in the absence of sufficient clinical studies for eye disease. The Academy has stated that neither available biosimilar has been studied for ophthalmic indications and that their inactive ingredients have not all been approved for use in the eye. Also, they state that ophthalmic use of these products could create safety risks because small variations in excipients can lead to significant and potentially blinding inflammatory complications when injected intravitreally.
- Add two additional indications for ophthalmic use.

Ophthalmic indications for bevacizumab	
Medications	Avastin (bevacizumab) Mvasi (bevacizumab-awwb) - biosimilar Zirabev (bevacizumab-bvzr) - biosimilar
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber must be an ophthalmologist
Coverage Duration	A 3 month duration for initial approval and 12 months for renewal
Maximum Billable Units	Variable
Other Criteria	~~** When this biosimilar is indicated, the member must have documented dates of trial and failure, intolerance, inability to use, or contraindication to the biosimilar medication prior to the brand medication approval, in addition to meeting all applicable criteria below unless the currently available biosimilar product does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested.~~ • Member must have a diagnosis for an ophthalmic indication accepted in a nationally recognized compendia ○ Age related macular degeneration - Choroidal retinal neovascularization ○ Branch retinal vein occlusion with macular edema ○ Central retinal vein occlusion with macular edema ○ Choroidal retinal neovascularization, secondary to pathologic myopia ○ Macular edema due to diabetes mellitus ○ Retinopathy due to diabetes mellitus ○ Retinopathy of prematurity • Must be prescribed at a dose that is consistent with nationally recognized compendia If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2024~~3/2025

Recommendation:

- Add Alyglo IVIG indicated for the treatment of primary humoral immunodeficiency in adults.
- Correct grammar in acute Idiopathic Thrombocytopenic Purpura indication
- Correct maximum dose for Multifocal Motor Neuropathy indication: Gammagard dose is 0.5-2.4 g/kg/month per PI

Immunoglobulin Therapy (IVIG)	
Medications	Bivigam (IV) (Immune Globulin) Cuvitru (SQ) (Immune Globulin) Flebogamma (IV) (Immune Globulin) Gamastan (IM) (Immune Globulin) Gamastan SD (IM) (Immune Globulin) Gammagard liquid (IV or SQ) (Immune Globulin) Gammagard SD (IV) (Immune Globulin) Gammaked (IV or SQ) (Immune Globulin) Gammaplex (IV) (Immune Globulin) Gamunex-C (IV or SQ) (Immune Globulin) Hizentra (SQ) (Immune Globulin) Octagam (IV) (Immune Globulin) Privigen (IV) (Immune Globulin) Asceniv (IV) (Immune Globulin-slra) Cutaquig (SQ) (Immune Globulin-hipp) Panzyga (IV) (Immune Globulin-ifas) Hyqvia (SQ) (Immune Globulin Human/Recombinant Human Hyaluronidase) Xembify (SQ) (Immune Globulin-klhw) Alyglo (IV) (Immune Globulin-stwk)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “Other Criteria” below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	See “Other Criteria” below
Coverage Duration	If the criteria are met the request will be approved for a 3 month duration unless otherwise specified in the diagnosis specific “Other Criteria” section below.
Maximum Billable Units	Variable

Other Criteria	**All Requests:**
	• Diagnosis has been confirmed by one of the specialist types, listed below
	  ○ Immunologist
	  ○ Neurologist
	  ○ Oncologist/Hematologist
	• Documentation of patient weight
	• Member has tried and failed, or has a documented medical reason for not using, all other standard of care therapies as defined per recognized guidelines.
	
	Primary Immunodeficiency*:
	• Patient’s IgG level is provided and is below normal for provided indication
	• Clinically significant deficiency of humoral immunity as evidenced by ONE of the following:
	  ○ Inability to produce an adequate immunologic response to specific antigens.

	○ History of recurrent infections despite prophylactic antibiotics • Dose is consistent with FDA approved package labeling, nationally recognized compendia, or peer-reviewed literature • If criteria are met, approve for 6 months. *Primary Immunodeficiency includes, but is not limited to, the following: Congenital agammaglobulinemia. Hypogammaglobulinemia (Common Variable Immunodeficiency, CVID), Severe combined immunodeficiency (SCID), Wiskott-Aldrich syndrome, X-linked agammaglobulinemia or Bruton's agammaglobulinemia, Hypergammaglobulinemia, X-linked Hyper IgM syndrome **Idiopathic Thrombocytopenic Purpura, acute and chronic**: • Acute: (active bleeding, patients requiring an urgent invasive procedure, to defer splenectomy, or platelet counts < 20,000/ul at risk for intra-cerebral hemorrhage or has life threatening bleeding~~)~~, or has an inadequate increase in platelets from corticosteroids or is unable to tolerate corticosteroids) ○ Dose does not exceed 1g/kg daily for up to 2 days, or 400mg/kg daily for 5 days • Chronic: ○ Duration of illness is greater than 12 months ○ Member has documented trial and failure of corticosteroids and splenectomy, or has a documented medical reason why they are not able to use corticosteroids or member is at high risk for post-splenectomy sepsis. ○ Dose does not exceed 1g/kg daily for up to 2 days, or 400mg/kg daily for 5 days • If criteria are met, approve for up to 5 days **Kawasaki disease:** • Immunoglobulin is being given with high dose aspirin • Requested dose does not exceed a single 2g/kg dose within 10 days of the diagnosis • If criteria is met, approve for a single dose **Chronic B-cell lymphocytic leukemia:** • Patient's IgG level has been provided, and is < 500mg/dL • The patient has history of severe bacterial infections • Dose does not exceed 400mg/kg every 3-4 weeks • If criteria are met, approve for 3 months. **Bone marrow transplantation:** • Patient requires a bone marrow transplant • Patient's IgG level is < 400mg/dL • Dose does not exceed 500mg/kg/wk for the first 100 days post- transplant or 500 mg/kg/dose every 3-4 weeks for greater than 100 days post- transplant • If criteria are met, approve for 3 months. **Pediatric HIV**: • Diagnosis of HIV • Patient is < 13 years of age • Either patient's IgG level is < 400mg/dL or

	• If patient's IgG level is ≥ 400 mg/dL than significant deficiency of humoral immunity as evidenced by ONE of the following:
	  ○ Inability to produce an adequate immunologic response to specific antigens.
	  ○ History of recurrent bacterial infections despite prophylactic antibiotics
	• Dose does not exceed 400mg/kg/dose every 14 days
	
	• If criteria are met, approve for 3 months.
	
	Multifocal motor neuropathy (MMN):
	• Duration of symptoms has been at least 1 month with disability.
	• Nerve conduction studies were completed to rule out other possible conditions, and confirms the diagnosis of MMN.
	• Dose does not exceed 2.4g/kg/month. This dose can be given over two to five days.
	
	• If criteria is met, approve for up to 5 days for 3 months.
	
	Chronic inflammatory demyelinating polyneuropathy (CIDP):
	• Duration of symptoms has been at least 2 months with disability.
	• Nerve conduction studies or a nerve biopsy were completed in order to rule out other possible conditions, and confirms the diagnosis of CIDP.
	• Patient has tried and failed, or has a medical reason for not using, corticosteroids.
	  ○ If the patient has severe and fulminant CIDP a trial of corticosteroids is not required
	  ○ If the patient has pure motor CIPD a trial of corticosteroids in not required
	• Dose is consistent with FDA approved package labeling, nationally recognized compendia, or peer-reviewed literature
	
	• If criteria are met, approve for up to 5 days for 3 months
	
	Guillain-Barre syndrome:
	• Patient has severe disease with the inability to walk without aid
	• Onset of symptoms within the last 4 weeks
	• Dose does not exceed 2g/kg given in divided doses over 2-5 days
	
	• If criteria are met, approve for up to 5 days for 3 months
	
	Myasthenia Gravis (DM):
	• Acute:
	  ○ Patient has an acute myasthenic exacerbation (i.e. acute episode of respiratory muscle weakness, difficulty swallowing, etc.) or is in preparation for thymoma surgery to prevent myasthenic exacerbation
	  ○ Dose does not exceed 2 g/kg administered over 2-5 days
	
	  ○ If criteria are met, approve for up to 5 days for 3 months
	• Chronic:
	  ○ Diagnosis of refractory generalized myasthenia gravis
	  ○ Patient has tried and failed, or has a documented medical reason for not using 2 or more immunosuppressive therapies (i.e. corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil)

	○ Dose does not exceed 2 g/kg/month administered over 2-5 days ○ If criteria are met, approve for 3 months **<u>Dermatomyositis (DM)</u>:** • One of the following: ○ Bohan and Peter score of 3 (i.e. definite DM) ○ Bohan and Peter score of 2 (i.e. probable DM) AND concurring diagnostic evaluation by ≥ 1 specialist (e.g. neurologist, rheumatologist, dermatologist) • Patient does NOT have any of the following: ○ Cancer (CA) associated myositis defined as myositis within 2 years of CA diagnosis (except basal or squamous cell skin cancer or carcinoma in situ of the cervix that has been excised and cure) ○ Active malignancy ○ Malignancy diagnosed within the previous 5 years ○ Breast CA within the previous 10 years • For a diagnosis of DM, one of the following: ○ Patient has tried and failed, or has a documented medical reason for not using both of the following: ▪ methotrexate (MTX) OR azathioprine ▪ rituximab ○ Patient has severe, life-threatening weakness or dysphagia • For a diagnosis of cutaneous DM (i.e. amyopathic DM, hypomyopathic DM): ○ Patient has tried and failed, or has a documented medical reason for not using all of the following: MTX and mycophenolate mofetil. • Dose does not exceed 2 g/kg administered over 2-5 days every 4 weeks. • If criteria are met, approve for 3 months If all of the above criteria are not met per diagnosis, the request is referred to a Clinical Reviewer for medical necessity review.
Last Review Date	~~3/2024~~3/2025

Recommendation:

- Change initial authorization coverage duration to 6 months to align better with the assessment of outcomes in clinical trials.
- Streamline abbreviations.
- For Reauthorization section, change time frame for hemoglobin increase and reduction in RBC transfusions to 8-12 weeks as that is the definition of an erythroid response and were also the endpoints used in trials to assess efficacy.

Reblozyl (luspatercept-aamt)	
Medications	Reblozyl (luspatercept-aamt) vial for subcutaneous injection
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Members are excluded if they have hemoglobin S/beta-thalassemia, isolated alpha-thalassemia
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Member must be 18 years of age or older Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a hematologist or oncologist
Coverage Duration	Initial requests will be approved for ~~3~~6 months. Reauthorization requests will be approved for 6 months.
Maximum Billable Units	Variable

Other Criteria	**Criteria for initial approval:**
	• Requested dose is appropriate per labeling
	• The member's weight has been provided with the request
	• The member's most recent hemoglobin level (within the last month) has been provided with the request
	• Diagnosis appropriate per Covered Uses
	• For requests for anemia due to beta thalassemia, documentation of all of the following is required:
	  ○ Member requires regular red blood cell (RBC) transfusions (defined as no transfusion-free period of more than 35 days over the last 6 months)
	• For requests for anemia due to myelodysplastic syndrome, documentation of all of the following is required:
	  ○ Myelodysplastic Syndrome Revised International Prognostic Scoring System (IPSS-R) categorization as very low, low, or intermediate risk of progression.
	  ○ Member has required transfusion of 2 or more ~~red blood cell (~~RBC~~)~~ units within an 8 week period in the last 4 months
	  ○ Hemoglobin less than 10 g/dl
	
	Reauthorization:
	• For diagnosis of anemia due to beta thalassemia, documentation of the following:
	  ○ Fewer transfusions compared with baseline
	  AND
	  ○ A reduction in transfusion requirement of at least 2 ~~red cell~~RBC units compared with baseline
	• Diagnosis of anemia due to myelodysplastic syndrome: documentation of ONE

	of the following: ○ Hemoglobin increase of at least 1.5 g/dl from baseline over a period of ~~3-6 months~~8-12 weeks OR ○ Reduction in ~~red blood cell~~RBC transfusion by at least 4 units over a period of ~~3-6 months~~ 8-12 weeks compared with baseline transfusion requirement • Prescriber states that the member did not experience a Grade 3 or 4 hypersensitivity reaction. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2024~~3/2025

Recommendation: Retire criteria since Zulresso was discontinued.
Sage Therapeutics announced in its 3Q 2024 earnings report that it will discontinue Zulresso, effective December 31, 2024. The company plans to focus its resources on the commercialization of Zurzuvae.

Zulresso	
Medications	Zulresso (brexanalone)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a psychiatrist or an obstetrician-gynecologist
Coverage Duration	If all of the criteria are met, the initial request will be approved for a one-time administration of Zulresso per postpartum period. Reauthorization will not be permitted
Other Criteria	**Initial Authorization:** • Physician attestation of moderate to severe postpartum depression (PPD) diagnosis and submission of validated screening tool result(s) (e.g. Edinburgh Postnatal Depression Scale, Hamilton Depression Rating Scale) • Onset of a major depressive episode within 6 months of delivery • Medication is prescribed at an FDA approved dose • Healthcare facility and patient must be enrolled in the Zulresso REMS program prior to initiation of medication • Patient's weight has been provided If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.
Last P&T Review Date	3/2024

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Vyalev	foscarbidopa and foslevodopa subcutaneous solution 240-12 mg/ml	Abbvie	• For the treatment of motor fluctuations in adults with advanced Parkinson's disease	$14,430 (for maximum dose)	Duopa	Non-formulary (see new MRG policy)
Vyloy	zolbetuximab-clzb intravenous solution reconstituted 100 mg	Astellas Pharma US	• For use in combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction adenocarcinoma whose tumors are claudin (CLDN) 18.2 positive as determined by an FDA-approved test.	$22,400 (for BSA of 1.74, dosing is BSA dependent)	Keytruda, Opdivo (both as part of FOLFOX regimen)	Non-formulary
Erzofri	paliperidone palmitate intramuscular suspension prefilled syringe 39mg/0.25ml, 78mg/0.5ml, 117mg/0.75ml, 156mg/ml, 234mg/1.5ml, 351mg/2.25ml	Luye Innomind Pharma	• Treatment of schizophrenia in adults. • Treatment of schizoaffective disorder in adults as monotherapy and as an adjunct to mood stabilizers or antidepressants.	$3,896 (for max dose of 234mg per month)	Invega Sustenna, Invega Trinza, Abilify Maintena, other long acting antipsychotics	Non-formulary
Ebglyss	lebrikizumab subcutaneous solution auto-injector 250 mg/2ml	Eli Lilly	• For the treatment of adults and pediatric patients 12 years of age and older who weigh at least 40 kg with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Ebglyss can be used with or without topical corticosteroids.	$3,500	Dupixent, Adbry	Non-formulary (see updated MRG policy)
Pavblu	Aflibercept-ayyh intravitreal solution and prefilled syringe 2mg/0.05ml	Amgen	• Treatment of neovascular (Wet) Age-Related macular Degeneration (AMD). • Treatment of macular Edema Following Retinal Vein Occlusion (RVO). • Treatment of diabetic Macular Edema (DME). • Treatment of diabetic Retinopathy (DR).	$1,665 per 0.05ml	Eylea, Lucentis, Byooviz, Cimerli	Non-formulary

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Itovebi	Inavolisib 3mg, 9mg oral tablet	Genentech	• Treatment of adults with endocrine-resistant, PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth-factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy.	$24,500	Piqray, Truqap	Non-formulary
Hympavzi	marstacimab-hncq subcutaneous solution auto-injector 150 mg/ml	Pfizer	For routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with: • hemophilia A (congenital factor VIII deficiency) without factor VIII inhibitors, or • hemophilia B (congenital factor IX deficiency) without factor IX inhibitors	$61,200	Hemlibra, Altuviiio	Non-formulary
Lumakras	Sotorasib oral tablet 240mg	Amgen	• For the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC), as determined by an FDA-approved test, who have received at least one prior systemic therapy. This indication is approved under accelerated approval based on overall response rate (ORR) and duration of response (DOR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).	$21,116	Krazati	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Augtyro	Repotrectinib 160mg oral capsule	Bristol-Myers Squibb	• Treatment of adult patients with locally advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) • Treatment of adult and pediatric patients 12 years of age and older with solid tumors that: ○ have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion and ○ are locally advanced or metastatic or where surgical resection is likely to result in severe morbidity ○ have progressed following treatment or have no satisfactory alternative therapy This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.	$30,739	Rozlytrek, Xalkori	Non-formulary
Aurlumyn	Iloprost intravenous solution 100 mcg/ml	Eicos Sciences	• For the treatment of severe frostbite in adults to reduce the risk of digit amputations. Effectiveness was established in young, healthy adults who suffered frostbite at high altitudes	$25,344 (per 80kg patient for max dose of 8 days of tx)	None	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Azmiro	Testosterone cypionate intramuscular solution prefilled syringe 200 mg/ml	Slayback Pharma	• For testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone Limitations of use: • Safety and efficacy of Azmiro in men with "age- related hypogonadism" (also referred to as "late-onset hypogonadism") • Safety and effectiveness in pediatric patients below the age of 12 years have not been established	$500 per month (for dose of 200mg every 2 weeks)	AndroGel, Testopel, Jatenzo, etc.	Non-formulary
Opipza	Aripiprazole oral film 2mg, 5mg, 10mg	Xiamen LP	• Treatment of schizophrenia in patients ages 13 years and older • Adjunctive treatment of major depressive disorder (MDD) in adults • Irritability associated with autistic disorder in pediatric patients 6 years and older • Treatment of Tourette's disorder in pediatric patients 6 years and older	$1,895 - $6,886	Abilify, Saphris, Latuda, Seroquel (and other atypical antipsychotics)	Non-formulary
Emrosi	Minocycline hydrochloride oral capsule extended release 24 hour 40mg	Journey Medical Corporation	• Indicated to treat inflammatory lesions (papules and pustules) of rosacea in adults Limitations of use: This formulation of minocycline has not been evaluated in the treatment or prevention of infections. To reduce the development of drug-resistant bacteria and to maintain the effectiveness of other antibacterial drugs, use Emrosi only as indicated.	$1,297	Oracea	Non-formulary
Revuforj	Revumenib oral tablet 110mg, 160mg	Syndax Pharmaceuticals	• For the treatment of relapsed or refractory acute leukemia with a lysine methyltransferase 2A gene (KMT2A) translocation in adult and pediatric patients 1 year and older	$79,000 (for max dose per month)	Venclexta	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Aucatzyl	Obecabtagene autoleucel intravenous suspension 410000000 cells	Autolus Inc.	• For the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)	$525,000 one time treatment	Tecartus	Non-formulary
Danziten	Nilotinib 71mg, 95mg oral tablet	Azurity Pharmaceuticals	• Treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase. • Treatment of adult patients with chronic phase (CP) and accelerated phase (AP) Ph+ CML resistant to or intolerant to prior therapy that included imatinib.	$19,200	Tasigna	Non-formulary
Ziihera	zanidatamab-hrii intravenous solution reconstituted 300 mg	Jazz Pharmaceuticals	• For the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).	$28,440 (60kg patient)	Enhertu	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Nypozi	Filgrastim-txid injection solution prefilled syringe 300 mcg/0.5ml, 480mcg/0.8ml	Tanvex BioPharma	• Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever • Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML) • Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT) • Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis • Reduce the incidence and duration of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia • Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome)	$249 per syringe	Neupogen, Zarxio, Nivestym, Releuko, Granix	Non-formulary
Attruby	Acoramidis oral tablet therapy pack 356 mg	BridgeBio Pharma Inc.	• For the treatment of the cardiomyopathy of wild-type or variant transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular death and cardiovascular-related hospitalization.	$20,098	Vyndaqel, Vyndamax	Non-formulary

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Simlandi	Adalimumab-ryvk (2 Syringe) Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	Teva Pharmaceuticals	• Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, Uveitis	$519 per dose	Humira, Amjevita, Hadlima, Cylezo, Yusimry, Hulio, Hyrimoz, Idacio, Yuflyma, Abrilada	F-QL (Already added via CRF) (QL: 4 syringes/28 days, LD: 8 syringes)
Boruzu	Bortezomib Injection Solution 3.5 MG/1.4ML	Amneal Pharmaceuticals	• Treatment of adult patients with multiple myeloma • Treatment of adult patients with mantle cell lymphoma	$893 per vial (dose is BSA and cycle specific)	Velcade	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^

Hercessi	Trastuzumab-strf intravaneous solution reconstituted 150mg, 420mg	Accord BioPharma Inc.	• Adjuvant Breast Cancer: in adults for adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer
			  ○ as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
			  ○ as part of a treatment regimen with docetaxel and carboplatin
			  ○ as a single agent following multi-modality anthracycline based therapy
			• Metastatic Breast Cancer
			  ○ In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
			  ○ As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease.
			• Metastatic Gastric Cancer: in combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma who have not received prior treatment for metastatic disease.
				$3,704 (every 3 weeks for 70kg patient)	Herceptin and its biosimilars (Herzuma, Kanjinti, Ogivri, Trazimera, etc.)	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Axtle	Pemetrexed dipotassium intravenous solution 100mg, 500mg	Avyxa Pharma	• Indicated in combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous NSCLC. • Indicated as a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. • Indicated as a single agent for the treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy. Limitations of Use: Axtle is not indicated for the treatment of patients with squamous cell, non-small cell lung cancer. • Initial treatment, in combination with cisplatin, of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.	$7,900 every 21 days (for BSA 1.9, dose varies depending on BSA)	Pemfexy, Alimta, Pemrydi RTU	Non-formulary
Imkeldi	Imatinib mesylate oral solution 80mg/ml	Shorla Oncology	• Certain forms of leukemia and other cancers *Note: Imkeldi has many approved indications. See full prescribing information for details of each indication.*	$2,349 per bottle	Gleevec, Tasigna, Scemblix, Bosulif, Sprycel, Iclusig	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Bimzelx	Bimekizumab-bkzx 320mg/ml auto injector and syringe	UBC, Inc.	• Treatment of moderate to severe plaque psoriasis (PSO) in adults who are candidates for systemic therapy or phototherapy • Treatment of adults with active psoriatic arthritis (PsA) • Treatment of adults with active non-radiographic axial spondyloarthritis (nraxSpA) with objective signs of inflammation • Treatment of adults with active ankylosing spondylitis (AS) • Treatment of adults with moderate to severe hidradenitis suppurativa	$7,553	Taltz, Cosentyx	Non-formulary
Qlosi	Pilocarpine HCl ophthalmic solution 0.4%	Orasis Pharmaceuticals	• For the treatment of presbyopia in adults	$79	Vuity	Non-formulary
Wezlana	Ustekinumab-auub subcutaneous solution 45 mg/0.5ml Ustekinumab-auub intravenous solution 130 mg/26ml Ustekinumab-auub subcutaneous solution prefilled syringe 45 mg/0.5ml Ustekinumab-auub subcutaneous solution prefilled syringe 90 mg/ml	Amgen	Adult patients with: • moderate to severe plaque psoriasis (Ps) who are candidates for phototherapy or systemic therapy • active psoriatic arthritis (PsA) • moderately to severely active Crohn's disease (CD) • moderately to severely active ulcerative colitis Pediatric patients 6 years and older with: • moderate to severe plaque psoriasis, who are candidates for phototherapy or systemic therapy • active psoriatic arthritis (PsA)	$5,568-$27,564 every 12 weeks (for dose of 90mg) (dose is weight and indication specific)	Stelara, Skyrizi, Tremfya, Ilumya, other Stelara biosimilars (once they launch)	Non-formulary
Alyftrek	vanzacaftor/ tezacaftor/ deutivacator oral tablet 4-20-50mg, 10-50-125mg	Vertex Pharmaceuticals	• For the treatment of cystic fibrosis (CF) in patients aged 6 years and older who have at least one F508del mutation or another responsive mutation in the CFTR gene	$28,404 per 28 day pack	Trikafta	Add to F-PA (see updated MRG criteria)

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Crenessity	crinecerfont oral capsule 50mg, 100mg crinecerfont oral solution 50mg/ml	Neurocrine BioSciences	• Adjunctive treatment to glucocorticoid replacement to control androgens in adults and pediatric patients 4 years of age and older with classic congenital adrenal hyperplasia (CAH)	$38,330 (per month for adult dosing)	None	Non-formulary
Bizengri	zenocutuzumab-zbco (750 mg dose) intravenous solution therapy pack 375 mg/18.75mL	Partner Therapeutics	• Treatment of adults with advanced, unresectable or metastatic non-small cell lung cancer (NSCLC) harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy.* • Treatment of adults with advanced, unresectable or metastatic pancreatic adenocarcinoma harboring a neuregulin 1 (NRG1) gene fusion with disease progression on or after prior systemic therapy.* *This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).	$23,750	None	Non-formulary
Tryngolza	Olezarsen subcutaneous solution auto-injector 80 mg/0.8ml	Ionis Pharmaceuticals	• Adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)	$49,584	None	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Opdivo Qvantig	Nivolumab and hyaluronidase-nvhy subcutaneous solution 600-10000 mg-ut/5ml	Bristol-Myers Squibb Company	• Renal Cell Carcinoma (RCC) • Melanoma • Non-Small Cell Lung Cancer (NSCLC) • Squamous Cell Carcinoma of the Head and Neck (SCCHN) • Colorectal Cancer • Hepatocellular Carcinoma (HCC) • Esophageal Cancer • Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma Note: Opdivo Qvantig has many approved indications. See full prescribing information for details of each indication.	$15,575 (for most common dose of 1,200 mg/20,000 units every 4 weeks)		Non-formulary
Kebilidi	Eladocagene exuparvovec-tneq injection suspension 280000000000 vg/0.5ml	PTC Therapeutics	• For the treatment of adult and pediatric patients with aromatic 13 L-amino acid decarboxylase (AADC) deficiency This indication is approved under accelerated approval based on change from baseline in gross motor milestone achievement at 48 weeks post-treatment. Continued approval for this indication may be contingent upon verification 18 and description of clinical benefit in a confirmatory clinical trial.	$3.8 million for one time treatment	None	Non-formulary
Gabarone	Gabapentin oral tablet 100mg, 400mg	Ina Pharmaceuticals	• Postherpetic neuralgia in adults • Adjunctive therapy in the treatment of partial onset seizures, with and without secondary generalization, in adults and pediatric patients 3 years and older with epilepsy	$510	Neurontin, Gralise, Lyrica	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Adalimumab-adaz	Adalimumab-adaz subcutaneous solution auto-injector 80 mg/0.8ml	Sandoz	• Rheumatoid Arthritis • Juvenile Idiopathic Arthritis • Psoriatic Arthritis • Ankylosing Spondylitis • Crohn's Disease • Ulcerative Colitis • Plaque Psoriasis • Hidradenitis Suppurativa • Uveitis Note: Adalimumab-adaz has many approved indications. See full prescribing information for details of each indication.	$1,331 per pen	Humira, Amjevita, Idacio, Cyltezo, Hyrimoz, Yusimry, Yuflyma, Hadlima and other biosimilars	Non-formulary

*	Pricing reflects Wholesale Acquisition Cost (WAC) per month unless otherwise noted.
^	The recommendation may be affected by state specific requirements including carve out lists and individual state mandates.
†	Pricing based on standard twice-monthly dosing for most indications.
‡	Pricing is per each kit on items listed as a kit.

Alameda March Q1 2025 P&T Old Business

Pharmacists to prescribe Naloxone at POS

- Title 16 California Code of Regulations section 1746.3 allows a pharmacist to furnish naloxone without a prescription in the following forms:
    - IM injection
    - Intranasal Spray
    - Autoinjector
    - Any FDA approved product form
- Furnishing pharmacist MUST
    - Complete required CE/training
    - Screen recipient appropriately
    - Provide recipient with training, counseling, naloxone fact sheet
    - Notify PCP if recipient gives consent
    - Maintain documentation for at least 3 years
- IPS, our third party conducting audits will monitor Naloxone claims during audit and will validate the pharmacy is following requirements
- Only formulary products will be covered by the plan with or without a prescription
- Pharmacist can submit their own NPI if available
- Pharmacist can submit the pharmacy NPI along with SCC code 42

- Need plan approval on pharmacist to prescribe naloxone at POS
- Need clarification on how plan would like to proceed if pharmacy is not following the requirements (we suggest recoupment of claims that do not meet requirements)