

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

Location: Microsoft Teams
Meeting ID: 240 899 963 547
Password: cj63FU9A

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](tel:+15102100967), [600079584#](tel:+15102100967). 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 COMMITTEE 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 VOTE	DESCRIPTION	TIME
I)	Call to order <i>Donna Carey, MD, Chief Medical Officer – Alameda Alliance</i> - Conflict of Interest Check/Disclosure - Agenda Overview	2 min -
II)	Informational Updates <i>Donna Carey, MD, Chief Medical Officer – Alameda Alliance</i> <i>Luke Lim R.Ph, Senior Pharmacy Director – Alameda Alliance</i> - PBM Update - DSNP Update - DHCS Audit - Alameda Alliance for Health 30th Anniversary Celebration	15 min -
III)	Pharmacy Utilization Reports (Quarter 4, 2025) <i>Luke Lim R.Ph., Senior Pharmacy Director – Alameda Alliance</i> - Top 50 Drugs by Cost - Top 50 PA Reviewed Drugs	2 min -
ADJOURN TO CLOSED SESSION (<i>Pursuant to California Government Code Title 5, §54954.5(h)</i>) Discussion will Concern: Review and Recommendations to changes to the AAH Formulary and utilization management for selected drug classes Estimated Date of Public Disclosure: 3/17/2026 (<i>formulary changes only; no trade secrets will be disclosed</i>)		

IV) E-Voting Material/Consent Agenda

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

Luke Lim R.Ph 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.)

Monographs/Class Reviews	Changes
Alcohol Use Disorder Agents Class Review	• No changes
Cystic Fibrosis Agents Class Review	• No changes
First Generation Antihistamines Class Review	• No changes
Fluoride Dental Preparations Class Review	• No changes
Sickle Cell Disease Agents 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)	• Change naming convention to reflect generic availability of Corlanor
Injectable Anticoagulants	• No criteria changes, add enoxaparin 300mg/3mL injection to formulary
Corticosteroids for Duchenne Muscular Dystrophy (DMD)	• Minor grammatical correction
Elmiron (pentosane polysulfate sodium)	• No changes
Ezetimibe (Zetia)	• No changes
Inhaled Corticosteroids/Long-Acting Beta-Agonists (ICS/LABA) Combinations	• No changes
Altoprev (lovastatin ER) and Fluvastatin, Fluvastatin ER	• Remove Altoprev as it has been discontinued
Ophthalmic Antihistamines	• No changes
Histamine H2 Receptor Antagonists	• No changes
Brilinta (ticagrelor) tablet	• Change naming convention to reflect generic availability of Brilinta
GLP-1 Agonists	• Remove Byetta and Bydureon as they have been discontinued and show generic availability of Victoza
DPP-4 Inhibitors and Combinations	• Change naming conventions to reflect generic availability of Onglyza and Kombiglyze XR
SGLT2 inhibitors and Combinations	• No changes
Agents for Atopic Dermatitis	• No changes
Parkinson's Disease Agents	• No changes

10 min EV

Linezolid	• No changes
Pyridostigmine (Mestinon)	• No changes
Long-Acting Muscarinic /Long-Acting Beta Agonist/ Corticosteroid inhaled Triple	• No changes
Corticosteroid Preparations to Treat Hemorrhoids	• No changes
Fexofenadine-pseudoephedrine	• No changes
Savella (milnacipran) tablet	• No changes
Travoprost (Travatan Z) ophthalmic drops	• No changes
Arikayce (amikacin)	• No changes
Zurzuva	• No changes
Dificid	• No changes
Niemann-Pick Disease Type C	• No changes
Physician Administered Drug (PAD) Guidelines	Changes
Rituximab	• No changes
Emergency Use Authorization (EUA) Drugs/Products for COVID-19	• No changes
Primary Hyperoxaluria Agents	• Minor language update in the renewal section for clarity on acceptable improvement endpoints
Reblozyl (luspatercept-aamt)	• No changes
Tzield	• No changes
Gene Therapy for Regular Red Blood Cell (RBC) Transfusion Dependent Beta-Thalassemia	• No changes
Pompe Disease Agents	• No changes
Adzynma	• No changes
Interim Formulary Updates	
• See p. 184 in packet	
Summary of Physician Administered Drug (PAD) Updates	
• See p. 185 in packet	
Pharmacy Policy & Procedure Updates	
• Rx-001 Pharmaceutical Operating	• Q1 2026 Annual Review
• RX-002 Pharmacy Benefit Prior	• Q1 2026 Annual Review
• RX-003 Exception Review Process	• Q1 2026 Annual Review
• RX-004 Formulary Management	• Q1 2026 Annual Review
• RX-005 P&T Committee Roles and Scope	• Q1 2026 Annual Review
• RX-006 Pharmacy Services Staff Description	• Q1 2026 Annual Review
• RX-007 Pharmaceutical Patient Safety, Drug Recalls, Quality Assurance	• Q1 2026 Annual Review
• RX-008 PBM Delegated Audit Oversight	• Q1 2026 Annual Review
• RX-009 Pharmaceutical Emergency Supply Provision	• Q1 2026 Annual Review

• RX-010 Drug Utilization Management	• Q1 2026 Annual Review
• RX-011 Decision and Notification Requirements	• Q1 2026 Annual Review
• RX-012 DU Policies - Pharmacy Portal & DU Access	• Q1 2026 Annual Review
• RX-013 Medical Benefit Physician, Facility-Administered Drugs PAD Prior Authorization Review Process	• Q1 2026 Annual Review
• RX-014 Physician, Facility-Administered Drugs PAD Prior Authorization List Management	• Q1 2026 Annual Review
• RX-016 Self-Administered Drugs Requested Under Medical Benefit	• Q1 2026 Annual Review
ED Oversight	
• None	
90 Day Maintenance List updates	
• Q1 2026 Annual Review	
P&T Meeting Minutes	
• P&T Meeting Minutes Q4 December 16,2025	

V) New Business

Iryna Makukh, PharmD, Pharmacist – PerformRx

New MRG

- Forzinity
- Rhapsido

New PAD

- Papzimeos
- Gene Therapies for Spinal Muscular Atrophy

VI) Class Reviews, Monographs, and Recommendations

Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Insulins Class Review
2. Multiple Sclerosis Agents Class Review

45
min

V

VII) Medication Request Guidelines

Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Pulmonary Biologics for Respiratory and Eosinophilic Conditions
2. Symlin (pramlintide)
3. Biologic Agents for Nasal Polyposis
4. Verquvo
5. Presbyopia Agents

6. Antifibrotic Respiratory Tract Agents
7. Specialty Biologic Agents
8. Tryngolza
9. Immunoglobulin A (IgA) Nephropathy Agents
10. GLP1 Receptor Agonists (Wegovy/Zepbound) for Non-Weight Loss Indications
11. Anti-Obesity Medications

VIII) Physician Administered Drug (PAD) Policies

Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Immunoglobulin Therapy (IVIG)
2. Tryngolza
3. Injectable/Infusible Agents for Osteoporosis and Paget's Disease
4. SMN2 Splicing Modifiers for the Treatment of Spinal Muscular Atrophy (SMA)

10
min

V

IX) Informational Updates on New Developments in Pharmacy

Iryna Makukh, PharmD, Pharmacist – PerformRx

- New Product Review

2
min

V

X) Old Business

- N/A

2
min

-

RECONVENE IN OPEN SESSION

XI) Public Comment

XII) Adjournment

-

ACTION / FOLLOW-UP ITEMS

ITEM	DUE DATE	RESPONSIBLE

FUTURE P&T MEETINGS	
NEXT MEETING	2026 P&T MEETINGS
June 16, 2026	September 15, 2026 December 15, 2026

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 Luke Lim at 510-995-4781 lulim@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.

636 IHSS Top 50 Drugs by Cost for the 4th Quarter 2025

- The top 50 drugs accounted for **1,534 claims** for **885 members** and cost **\$1,721,342**, which is an increase of \$35,831 in spend from the previous quarter.
- Biktarvy remains at number one with 37 claims for 15 members. There was a decrease of 2 claims since the previous quarter.
- Ozempic is at numbers 2, 4, and 5, with 259 total claims for 123 members. There was a decrease of 8 claims from the previous quarter.
- Vemlidy is up at number 3 with 55 claims for 23 members. There was an increase of 3 claims and a decrease of 1 member from the previous quarter. This medication is managed via the Hepatitis B MRG, which requires trial and failure of, intolerance to, or reason not to use, entecavir.
- Skyrizi remains at numbers 6 and 30 with 4 claims for 4 members. There was an increase of 1 claim from the previous quarter. The medication is managed via the Specialty Biologic Agents MRG and is a non-preferred agent, which requires trial and failure of one preferred step 1 agent and one preferred step 2 agent appropriate for the requested use.

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
1	201625	Biktarvy Oral Tablet 50-200-25 MG	37	15	\$150,211.33
2	218338	Ozempic (2 MG/DOSE) Subcutaneous Solution Pen-injector 8 MG/3ML	99	41	\$94,157.63
3	195609	Vemlidy Oral Tablet 25 MG	55	23	\$91,265.58
4	221271	Ozempic (0.25 or 0.5 MG/DOSE) Subcutaneous Solution Pen-injector 2 MG/3ML	84	48	\$79,485.79
5	209911	Ozempic (1 MG/DOSE) Subcutaneous Solution Pen-injector 4 MG/3ML	76	34	\$71,793.12
6	214809	Skyrizi Pen Subcutaneous Solution Auto-injector 150 MG/ML	3	3	\$65,941.08
7	182336	Farxiga Oral Tablet 10 MG	104	44	\$57,457.02
8	206142	Kisqali (600 MG Dose) Oral Tablet Therapy Pack 200 MG	3	1	\$56,007.44
9	223809	Cosentyx UnoReady Subcutaneous Solution Auto-injector 300 MG/2ML	7	2	\$54,224.91
10	189014	Tolvaptan Oral Tablet Therapy Pack 45 & 15 MG	3	1	\$48,825.00
11	177191	Eliquis Oral Tablet 5 MG	83	38	\$47,331.07
12	199758	Verzenio Oral Tablet 100 MG	3	1	\$47,222.25
13	186088	Ofev Oral Capsule 150 MG	3	1	\$42,288.36

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
14	215133	Wegovy Subcutaneous Solution Auto-injector 2.4 MG/0.75ML	31	12	\$40,330.12
15	207962	Rybelsus Oral Tablet 14 MG	38	15	\$35,895.97
16	212379	Cabenuva Intramuscular Suspension Extended Release 600 & 900 MG/3ML	5	3	\$33,605.56
17	207961	Rybelsus Oral Tablet 7 MG	35	17	\$32,587.59
18	184849	Jardiance Oral Tablet 25 MG	54	22	\$29,812.15
19	229072	Mounjaro Subcutaneous Solution Auto-injector 5 MG/0.5ML	29	15	\$29,808.74
20	192096	Odefsey Oral Tablet 200-25-25 MG	8	3	\$29,450.90
21	229078	Mounjaro Subcutaneous Solution Auto-injector 7.5 MG/0.5ML	27	17	\$27,755.78
22	229056	Dupixent Subcutaneous Solution Auto-injector 300 MG/2ML	7	3	\$27,568.94
23	120500	Dasatinib Oral Tablet 20 MG	3	1	\$25,937.43
24	215136	Wegovy Subcutaneous Solution Auto-injector 1.7 MG/0.75ML	20	10	\$25,891.29
25	182335	Farxiga Oral Tablet 5 MG	46	22	\$25,889.14
26	229071	Mounjaro Subcutaneous Solution Auto-injector 2.5 MG/0.5ML	25	17	\$25,729.62
27	218613	Camzyos Oral Capsule 5 MG	3	1	\$23,841.51
28	228573	Livdelzi Oral Capsule 10 MG	2	1	\$23,418.16
29	193380	Sofosbuvir-Velpatasvir Oral Tablet 400-100 MG	3	1	\$23,154.00
30	219135	Skyrizi Subcutaneous Solution Cartridge 360 MG/2.4ML	1	1	\$21,995.36
31	201117	Steglatro Oral Tablet 15 MG	65	24	\$21,483.77
32	190802	Genvoya Oral Tablet 150-150-200-10 MG	5	3	\$20,283.73
33	224365	Comirnaty Intramuscular Suspension Prefilled Syringe 30 MCG/0.3ML	125	125	\$20,138.31
34	229076	Mounjaro Subcutaneous Solution Auto-injector 10 MG/0.5ML	19	11	\$19,463.52

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
35	193035	Ocaliva Oral Tablet 10 MG	2	1	\$19,433.48
36	122702	Januvia Oral Tablet 100 MG	62	27	\$18,837.46
37	225121	Zepbound Subcutaneous Solution Auto-injector 10 MG/0.5ML	18	8	\$18,690.17
38	225062	Xphozah Oral Tablet 30 MG	6	2	\$18,246.12
39	228179	Flublok Intramuscular Solution Prefilled Syringe 0.5 ML	170	170	\$17,680.45
40	215132	Wegovy Subcutaneous Solution Auto-injector 1 MG/0.5ML	13	7	\$16,825.10
41	228549	Nemlurio Subcutaneous Auto-injector 30 MG	4	1	\$16,425.12
42	192525	Descovy Oral Tablet 200-25 MG	6	3	\$16,411.65
43	184045	Erlotinib HCl Oral Tablet 25 MG	2	1	\$15,145.09
44	229075	Mounjaro Subcutaneous Solution Auto-injector 12.5 MG/0.5ML	14	6	\$14,452.88
45	181560	Actemra Subcutaneous Solution Prefilled Syringe 162 MG/0.9ML	3	1	\$14,334.66
46	201116	Steglatro Oral Tablet 5 MG	37	13	\$14,283.22
47	215134	Wegovy Subcutaneous Solution Auto-injector 0.5 MG/0.5ML	11	8	\$14,232.25
48	184848	Jardiance Oral Tablet 10 MG	21	10	\$12,433.61
49	226896	Cimzia (2 Syringe) Subcutaneous Prefilled Syringe Kit 200 MG/ML	2	1	\$11,848.88
50	204204	Shingrix Intramuscular Suspension Reconstituted 50 MCG/0.5ML	52	50	\$11,809.90
TOTAL			1,534	885	\$1,721,342.21

Medi-Cal Top 50 Drugs by Cost for 4th Quarter 2025

- The top 50 drugs accounted for 34,940 claims for 29,605 members and cost \$67,521,651. This represents increases of 3,149 claims, 2,416 members and \$1,462,643 spend from 3Q2025.
- Biktarvy stable utilization 921 vs 907 claims 3Q2025.
- Jardiance both strengths holding steady.
- Skyrizi utilization 143/131 in 2Q2025 compared to 131/125 4Q2025
- Wegovy 2.4mg another 10% increase from 1383 claims to 1526 claims during 4Q2025
- GLP1 for weight loss will be discontinued by Medi-Cal Rx starting 1/1/2026
- Dupixent from 286 claims to 301 (5% increase)

Rank	GCN	Label Name	Claims	Unique Members	Paid Amount	Avg Paid Per Rx
1	44426	BIKTARVY 50-200-25 MG TABLET	921	761	\$7,171,128.35	\$7,786.24
2	49591	SKYRIZI 150 MG/ML PEN	131	125	\$3,416,739.49	\$26,081.98
3	49754	WEGOVY 2.4 MG/0.75 ML PEN	1526	1112	\$3,187,004.85	\$2,088.47
4	36723	JARDIANCE 25 MG TABLET	2325	2117	\$3,183,566.71	\$1,369.28
5	36716	JARDIANCE 10 MG TABLET	2304	2038	\$3,006,224.77	\$1,304.79
6	53536	OZEMPIC 0.25-0.5 MG/DOSE PEN	1855	1445	\$2,342,139.26	\$1,262.61
7	48277	DUPIXENT 300 MG/2 ML PEN	301	246	\$2,193,189.63	\$7,286.34
8	52125	OZEMPIC 2 MG/DOSE (8 MG/3 ML)	1292	985	\$2,112,439.71	\$1,635.02
9	49752	WEGOVY 1 MG/0.5 ML PEN	1144	934	\$1,918,859.00	\$1,677.32
10	48208	OZEMPIC 1 MG/DOSE (4 MG/3 ML)	1196	963	\$1,809,141.57	\$1,512.66
11	49749	WEGOVY 0.5 MG/0.5 ML PEN	1064	898	\$1,702,660.20	\$1,600.24
12	49753	WEGOVY 1.7 MG/0.75 ML PEN	997	764	\$1,685,287.83	\$1,690.36
13	43506	HUMIRA(CF) PEN 40 MG/0.4 ML	112	93	\$1,612,840.26	\$14,400.36
14	42624	VEMLIDY 25 MG TABLET	474	379	\$1,507,050.17	\$3,179.43
15	27418	INVEGA SUSTENNA 234 MG/1.5 ML	229	165	\$1,485,637.60	\$6,487.50
16	49099	CABENUVA ER 600 MG-900 MG SUSP	179	155	\$1,460,089.98	\$8,156.93
17	49748	WEGOVY 0.25 MG/0.5 ML PEN	871	746	\$1,350,394.21	\$1,550.40
18	33935	ELIQUIS 5 MG TABLET	1194	986	\$1,346,974.09	\$1,128.12

Rank	GCN	Label Name	Claims	Unique Members	Paid Amount	Avg Paid Per Rx
19	49468	COSENTYX UNOREADY 300 MG PEN	58	41	\$1,257,058.54	\$21,673.42
20	54989	ZEPBOUND 5 MG/0.5 ML PEN	825	680	\$1,131,183.73	\$1,371.13
21	34394	FARXIGA 10 MG TABLET	781	687	\$1,087,805.22	\$1,392.84
22	54991	ZEPBOUND 7.5 MG/0.5 ML PEN	740	574	\$1,022,140.20	\$1,381.27
23	28159	STELARA 90 MG/ML SYRINGE	26	23	\$984,973.61	\$37,883.60
24	94200	DEXCOM G7 SENSOR	878	751	\$975,591.43	\$1,111.15
25	97724	ENBREL 50 MG/ML SURECLICK	76	60	\$945,984.01	\$12,447.16
26	47136	TRIKAFTA 100-50-75 MG/150 MG	15	12	\$891,774.47	\$59,451.63
27	46966	RYBELSUS 14 MG TABLET	389	350	\$891,327.65	\$2,291.33
28	54988	ZEPBOUND 2.5 MG/0.5 ML PEN	701	584	\$872,652.88	\$1,244.87
29	40953	DESCOVY 200-25 MG TABLET	242	202	\$872,482.73	\$3,605.30
30	40133	TAGRISSO 80 MG TABLET	32	22	\$859,963.94	\$26,873.87
31	49487	APRETUDE ER 600 MG/3 ML VIAL	162	136	\$788,239.77	\$4,865.68
32	44014	HUMIRA(CF) PEN 80 MG/0.8 ML	29	23	\$780,152.98	\$26,901.83
33	56642	BIMZELX 320 MG/2 ML AUTOINJECT	22	17	\$779,139.27	\$35,415.42
34	46965	RYBELSUS 7 MG TABLET	395	351	\$765,664.23	\$1,938.39
35	54456	FERRIPROX 1,000 MG TAB(2X/DAY)	10	9	\$741,333.83	\$74,133.38
36	43699	MAVYRET 100-40 MG TABLET	44	42	\$733,954.76	\$16,680.79
37	37682	ABILIFY MAINTENA ER 400 MG SYR	142	95	\$719,535.52	\$5,067.15
38	43968	SYM TUZA 800-150-200-10 MG TAB	97	74	\$703,633.92	\$7,253.96
39	25200	FREESTYLE LITE TEST STRIP	4011	3864	\$690,509.73	\$172.15
40	54992	ZEPBOUND 10 MG/0.5 ML PEN	490	397	\$683,715.31	\$1,395.34
41	52475	SKYRIZI 360 MG/2.4 ML ON-BODY	29	24	\$644,729.22	\$22,232.04
42	97400	JANUVIA 100 MG TABLET	761	701	\$632,525.91	\$831.18
43	98637	BASAGLAR 100 UNIT/ML KWIKPEN	1298	1087	\$632,464.97	\$487.26

Rank	GCN	Label Name	Claims	Unique Members	Paid Amount	Avg Paid Per Rx
44	38702	INVEGA TRINZA 819 MG/2.63 ML	59	59	\$624,069.03	\$10,577.44
45	52336	MOUNJARO 2.5 MG/0.5 ML PEN	438	367	\$580,568.71	\$1,325.50
46	52337	MOUNJARO 5 MG/0.5 ML PEN	395	337	\$574,732.23	\$1,455.02
47	43167	KISQALI 600 MG DAILY DOSE	27	12	\$567,239.47	\$21,008.87
48	58019	COMIRNATY 2025-26(12Y UP) SYRG	2887	2886	\$550,324.34	\$190.62
49	54994	ZEPBOUND 15 MG/0.5 ML PEN	310	221	\$549,340.90	\$1,772.07
50	43148	ILARIS 150 MG/ML VIAL	6	5	\$495,470.67	\$82,578.45
		Total	34490	29605	\$67,521,650.86	\$577,208.15

Top 50 Prior Authorization Requests by Volume for the 4th Quarter 2025

- Top 50 PA requests = 271. There were 382 total PA requests for quarter 4.
 - 74 requests (27%) were approved. This approval rate is 1% higher than was observed last quarter.
 - 197 requests (73%) were denied or partially approved.
- Lidocaine 5% patch is at number 1 with 27 requests and 3 approvals (11%).
 - Lidocaine requires a diagnosis of neuropathic pain and trial and failure of gabapentin or pregabalin and one other formulary alternative (e.g., duloxetine, venlafaxine, nortriptyline, amitriptyline, etc.) or morphine MME $\geq$ 50/day for 3 months.
- Wegovy is at numbers 2, 5, 10, 17 & 23 with 48 total requests and 14 approvals (29%).
 - Wegovy to reduce excess body weight requires a diagnosis of class III/severe obesity (BMI $\geq$ 40) 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 $\geq$ 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.
 - Wegovy for the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) requires a diagnosis of MASH with moderate to advanced liver fibrosis and prescriber attestation on lifestyle counseling on nutrition and exercise and avoidance of excess alcohol intake.
- Zepbound is at numbers 3, 12, 30 & 36 with 31 total requests and 6 approvals (19%).
 - Zepbound to reduce excess body weight requires a diagnosis of class III/severe obesity (BMI $\geq$ 40) and trial and failure or inability to use Qsymia and Contrives.
 - Zepbound for moderate to severe obstructive sleep apnea requires trial and failure regarding lifestyle changes and behavioral modifications to reach BMI <30 kg/m² and trial and failure or inability to use PAP therapy.
- Jardiance is at numbers 4 & 6 with 28 total requests and 3 approvals (11%).
 - 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 AND documentation of trial and failure, intolerance, contraindication or inability to use one preferred formulary step therapy medication.
- Mounjaro is at number 7 with 8 requests. There were 5 approvals (63%).
 - Mounjaro requires trial and failure of a metformin containing product.

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
1	LIDOCAINE Patch 5%	27	3	11%	24	89%	0	0%
2	WEGOVY Soln Auto-inj 0.25MG/0.5ML	20	1	5%	19	95%	0	0%
3	ZEPBOUND Soln Auto-inj 2.5MG/0.5ML	19	1	5%	18	95%	0	0%
4	JARDIANCE Tablet 10MG	17	2	12%	15	88%	0	0%
5	WEGOVY Soln Auto-inj 2.4MG/0.75ML	12	7	58%	4	33%	1	8%
6	JARDIANCE Tablet 25MG	11	1	9%	6	55%	4	36%
7	MOUNJARO Soln Auto-inj 2.5MG/0.5ML	8	5	63%	3	38%	0	0%
8	VEMLIDY Tablet 25MG	8	6	75%	0	0%	2	25%
9	OZEMPIC (0.25 OR 0.5 MG/DOSE) Soln Pen-inj 2MG/3ML	7	6	86%	1	14%	0	0%
10	WEGOVY Soln Auto-inj 1.7MG/0.75ML	7	4	57%	3	43%	0	0%
11	ZORYVE Cream 0.15%	7	2	29%	4	57%	1	14%
12	ZEPBOUND Soln Auto-inj 7.5MG/0.5ML	6	2	33%	2	33%	2	33%
13	TRANEXAMIC ACID Tablet 650MG	5	1	20%	4	80%	0	0%
14	REPATHA SURECLICK Soln Auto-inj 140MG/ML	5	2	40%	0	0%	3	60%
15	TRETINOIN Cream 0.025%	5	0	0%	5	100%	0	0%
16	CYCLOSPORINE Emulsion 0.05%	5	0	0%	4	80%	1	20%
17	WEGOVY Soln Auto-inj 1MG/0.5ML	5	1	20%	4	80%	0	0%
18	SCOPOLAMINE Patch 72HR 1MG/3DAYS	5	1	20%	4	80%	0	0%
19	EYSUVIS Suspension 0.25%	4	2	50%	2	50%	0	0%
20	DUPIXENT Soln Auto-inj 300MG/2ML	4	0	0%	3	75%	1	25%
21	VEOZAH Tablet 45MG	4	1	25%	3	75%	0	0%
22	LINZESS Capsule 145MCG	4	0	0%	2	50%	2	50%
23	WEGOVY Soln Auto-inj 0.5MG/0.5ML	4	1	25%	3	75%	0	0%
24	TRETINOIN Cream 0.1%	4	0	0%	4	100%	0	0%
25	ZORYVE Foam 0.3%	4	0	0%	3	75%	1	25%
26	TACROLIMUS Ointment 0.1%	3	0	0%	1	33%	2	67%
27	XIIDRA Solution 5%	3	1	33%	2	67%	0	0%
28	TRETINOIN Cream 0.05%	3	1	33%	2	67%	0	0%
29	EZETIMIBE Tablet 10MG	3	3	100%	0	0%	0	0%
30	ZEPBOUND Soln Auto-inj 5MG/0.5ML	3	1	33%	2	67%	0	0%
31	FIDAXOMICIN Tablet 200MG	3	2	67%	1	33%	0	0%
32	TRESIBA FLEXTOUCH Soln Pen-inj 200UNIT/ML	3	0	0%	1	33%	2	67%
33	ICOSAPENT ETHYL Capsule 1GM	3	0	0%	1	33%	2	67%
34	CEQUA Solution 0.09%	3	1	33%	1	33%	1	33%
35	MIEBO Solution 1.338GM/ML	3	1	33%	2	67%	0	0%
36	ZEPBOUND Soln Auto-inj 15MG/0.5ML	3	2	67%	1	33%	0	0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
37	MIRABEGRON ER Tablet ER 24HR 50MG	3	2	67%	1	33%	0	0%
38	OPZELURA Cream 1.5%	3	0	0%	3	100%	0	0%
39	PHENTERMINE HCL Tablet 37.5MG	3	1	33%	0	0%	2	67%
40	SKYRIZI PEN Soln Auto-inj 150MG/ML	2	1	50%	1	50%	0	0%
41	CHORIONIC GONADOTROPIN For Solution 10000UNIT	2	0	0%	1	50%	1	50%
42	TRADJENTA Tablet 5MG	2	1	50%	1	50%	0	0%
43	LISDEXAMFETAMINE DIMESYLATE Capsule 60MG	2	2	100%	0	0%	0	0%
44	BIMZELX Soln Auto-inj 160MG/ML	2	1	50%	1	50%	0	0%
45	ZORYVE Cream 0.3%	2	0	0%	2	100%	0	0%
46	STEGLATRO Tablet 5MG	2	1	50%	0	0%	1	50%
47	PHENTERMINE HCL Capsule 15MG	2	2	100%	0	0%	0	0%
48	UBRELVY Tablet 50MG	2	1	50%	1	50%	0	0%
49	CONTRACE Tablet ER 12HR 8;90MG	2	0	0%	2	100%	0	0%
50	XDEMVEY Solution 0.25%	2	1	50%	0	0%	1	50%
TOTAL		271	74	27%	167	62%	30	11%

Medi-Cal Top 50 Prior Authorization Requests by Volume for 4th Quarter 2025

- The top 50 PA requests = 2,848 (down from 3Q25 3,173)
- #1 most requested item is Freestyle Libre CGM Sensor
- #5 Dexcom G7 Sensor is also CGM item
- #3 Opzelura continues rising from #4 last quarter
- Wegovy dropped from 208 requests 3Q2025 to 160 requests 4Q2025
- Sildenafil – ED indication, 100% denial rate
- Tadalafil – PAH indication so approval rate is higher at 13.8%
- Estradiol valerate, ertapenem have top approval rates
- Ozempic has fourth-lowest approval rate at 20.8%

Rank	Drug Name	Total	Approved		Denied	
1	FREESTYLE LIBRE 3 PLUS SENSOR	306	233	76.1%	73	23.9%
2	WEGOVY	160	103	64.4%	57	35.6%
3	OPZELURA	154	143	92.9%	11	7.1%
4	ALPRAZOLAM	111	87	78.4%	24	21.6%
5	DEXCOM G7 SENSOR	110	90	81.8%	20	18.2%
6	FREESTYLE LIBRE 2 PLUS SENSOR	109	80	73.4%	29	26.6%
7	ZEPBOUND	101	59	58.4%	42	41.6%
8	SILDENAFIL CITRATE	95	0	0.0%	95	100.0%
9	XIFAXAN	93	61	65.6%	32	34.4%
10	OMNIPOD 5 DEXG7G6 PODS (GEN 5)	80	73	91.3%	7	8.8%
11	OZEMPIC	77	16	20.8%	61	79.2%
12	TESTOSTERONE	70	53	75.7%	17	24.3%
13	DUPIXENT PEN	68	62	91.2%	6	8.8%
14	FREESTYLE LIBRE 3 READER	66	52	78.8%	14	21.2%
15	OXYCODONE HCL	58	52	89.7%	6	10.3%

Rank	Drug Name	Total	Approved		Denied	
16	TADALAFIL	58	8	13.8%	50	86.2%
17	DEXCOM G7 RECEIVER	54	37	68.5%	17	31.5%
18	VOQUEZNA	50	21	42.0%	29	58.0%
19	MOUNJARO	46	12	26.1%	34	73.9%
20	ENSURE ORIGINAL	42	37	88.1%	5	11.9%
21	PHENTERMINE HCL	42	39	92.9%	3	7.1%
22	QULIPTA	42	25	59.5%	17	40.5%
23	ESTRADIOL VALERATE	41	41	100.0%	0	0.0%
24	XDEMVI	41	33	80.5%	8	19.5%
25	FREESTYLE LIBRE 3 SENSOR	38	27	71.1%	11	28.9%
26	ERTAPENEM	37	37	100.0%	0	0.0%
27	SACUBITRIL-VALSARTAN	37	34	91.9%	3	8.1%
28	NOVASOURCE RENAL 2 CAL	35	34	97.1%	1	2.9%
29	TRELEGY ELLIPTA	35	25	71.4%	10	28.6%
30	HYDROCODONE-ACETAMINOPHEN	33	29	87.9%	4	12.1%
31	AZELAIC ACID	32	22	68.8%	10	31.3%
32	SCOPOLAMINE	32	21	65.6%	11	34.4%
33	BELSOMRA	31	27	87.1%	4	12.9%
34	OXYCONTIN	31	28	90.3%	3	9.7%
35	SOD SULF-POTASS SULF-MAG SULF	31	27	87.1%	4	12.9%
36	OMNIPOD 5 DEXG7G6 INTRO(GEN 5)	30	23	76.7%	7	23.3%

Rank	Drug Name	Total	Approved		Denied	
37	BOOST	29	26	89.7%	3	10.3%
38	NURTEC ODT	29	24	82.8%	5	17.2%
39	SANTYL	28	22	78.6%	6	21.4%
40	TERBINAFINE	28	13	46.4%	15	53.6%
41	METRONIDAZOLE	27	9	33.3%	18	66.7%
42	REZDIFFRA	27	21	77.8%	6	22.2%
43	WINLEVI	27	4	14.8%	23	85.2%
44	COSENTYX UNOREADY PEN	26	24	92.3%	2	7.7%
45	PIMECROLIMUS	26	9	34.6%	17	65.4%
46	TRIAMCINOLONE ACETONIDE	26	15	57.7%	11	42.3%
47	VRAYLAR	26	24	92.3%	2	7.7%
48	QELBREE	25	15	60.0%	10	40.0%
49	DOXEPIN HCL	24	17	70.8%	7	29.2%
50	NORETHINDRONE ACETATE	24	14	58.3%	10	41.7%
TOTAL		2848	1988	70%	860	30%

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.

AD04 is one product near-term in the pipeline for alcohol use disorder, a low-dose ondansetron oral tablet. A serotonin-3 (5HT3) receptor antagonist, ondansetron is used commonly for control of nausea. In the ONWARD clinical trial, use of ondansetron twice daily reduced heavy drinking days in patients with specific genetic mutations in the 5HT3 gene. Approximately one-third of patients with AUD are estimated to have one of these mutations, and a companion diagnostic to identify patients amenable to treatment would accompany the approval. AD04 could receive FDA approval by 2027.

Utilization Findings

There were 6 claims for 5 members, for a total cost of \$262.1, and an average cost per claim of \$43.68. The most highly utilized medication was Naltrexone tablet with 6 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	50 mg orally once daily
	Opioid Dependence	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 $\leq$ 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
 - Are 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, Leher 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, Srisurapanont M, Soyka M. Opioid antagonists for alcohol	Systematic review performed by searching Cochrane Drugs and Alcohol Group (CDAG) Specialized Register, PubMed, EMBASE and CINAHL in January 2010. A search was conducted of all double-blind randomized controlled trials (RCTs) which compared the effects of naltrexone with placebo or active control on	- Primary endpoints: Risk of heavy drinking, number of drinking days - Secondary endpoints: Heavy drinking days, consumed amount of alcohol,

dependence. Cochrane Database Syst Rev. 2010;(12):CD001867.	drinking-related outcomes. A total of 50 RCTs were included with 7,793 patients.	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 (10-01-2025 to 12-31-2025)

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	0	0	0 (0%)	F	No change
Acamprosate 333 mg delayed release (DR) oral tablet	0	0	0	0	0	0 (0%)	F	No change
Opioid Antagonists								
Naltrexone 50 mg oral tablet	6	5	\$262.1	\$43.68	0	0 (0%)	F	No change
Vivitrol® (naltrexone) 380 mg intramuscular injection	0	0	0	0	0	0 (0%)	F	No change
TOTAL	6	5	\$262.1	\$43.68	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

References

1. Lexicomp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on 10/20/2025.
2. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: <https://clinicaltrials.gov/>. Accessed on 10/20/2025.
3. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>. Accessed on 10/20/2025.
4. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: <https://www.ncbi.nlm.nih.gov/pubmed>. Accessed on 10/20/2025.
5. Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on 10/20/2025.
6. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: <http://www.fda.gov/>. Accessed on 10/20/2025.
7. 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.
8. US Department of Veterans Affairs VA/DoD Clinical Practice Guidelines. Management of Substance Use Disorder (SUD) (2021). Available at: <https://www.healthquality.va.gov/guidelines/mh/sud/>. Accessed on November 14, 2024.
9. 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.
10. Miller PM, Book SW, Stewart SH. Medical treatment of alcohol dependence: a systematic review. *Int J Psychiatry Med*. 2011;42(3):227-66.
11. Rösner S, Hackl-herrwerth A, Leucht S, Leher P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. *Cochrane Database Syst Rev*. 2010;(9):CD004332.
12. Rösner S, Hackl-herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev*. 2010;(12):CD001867.

Cystic Fibrosis

Executive Summary

Class Overview

This therapeutic class review examines the cystic fibrosis transmembrane conductance regulator (CFTR) agents, inhaled antibiotics, and mucolytics used by patients with cystic fibrosis (CF) lung disease. The CFTR modulators are indicated for use in patients with specific mutations in the CFTR gene and work to improve processing/function of a defective protein in patients with CF. To date, there are five FDA-approved CFTR modulator therapies targeting various populations in CF by age and type of mutations present. Inhaled antibiotics, aztreonam and tobramycin, are indicated for the management of cystic fibrosis patients with *Pseudomonas aeruginosa* colonization. Mucolytics (acetylcysteine, dornase alfa, mannitol, and sodium chloride) are adjunctive therapies that work to break down the abnormal, viscous pulmonary secretions commonly observed in patients with cystic fibrosis.

In 2012, ivacaftor (Kalydeco®) was the first of a new class of drugs targeted to disease modification. In recent years, advances have given way to development of improved “second-generation” CFTR corrector therapies such as elexacaftor. Combined into a triple-therapy regimen with tezacaftor and ivacaftor and marketed under the trade name Trikafta®, this treatment has shown efficacy and is approved to treat CF patients two years and older whom carry one or more F508del mutations (the most common mutation) in the CFTR gene, or other CFTR gene mutation determined to be responsive to therapy. Thanks to the approval and subsequent broadening of eligible ages and gene mutations, the population of CF patients who can now receive treatment with a disease modifying agent increased from 50% up to approximately 90%.

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®. In clinical trials Alyftrek® demonstrated non-inferiority to Trikafta® for improvement in lung function and showed increased efficacy in reduction of sweat chloride levels (a biomarker of CFTR function and used to diagnose CF) compared to Trikafta®. 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 efficacy in 31 additional CFTR gene mutation types compared to Trikafta®.

With the combination of a large portion of patients eligible for disease modifying therapies and prices averaging \$370,000 annually, the impact from a financial perspective looms largely over the healthcare system. However, CFTR modulator therapies have been transformative to patient quality of life, morbidity and mortality for patients with cystic fibrosis.

An orally inhaled, dry-powdered formulation of mannitol (Bronchitol®) received FDA approval in late 2020 after receiving two previous complete response letters citing issues such as the need for clearer benefit-related data, potential safety concerns, and needs for revised product packaging. Mannitol is thought to improve mucus clearance in the lungs via actions such as stimulating cough, thinning mucus secretions, and increased cilia effectiveness, similarly to dornase alfa and hypertonic saline. Bronchitol clinical trials demonstrated a modest improvement in lung function but failed to demonstrate a reduction in pulmonary exacerbations and may be considered for patients who are unable to use other more established mucolytic therapies.



There are no novel drug therapies in the near term in the cystic fibrosis development pipeline. Novel agents in mid-stage development include several inhaled messenger RNA therapies and antisense oligonucleotides targeted for patients whose CFTR mutations are not amenable to treatment with current disease modifying therapies. In the CFTR modulator class, Trikafta® and Alyftrek® continue working to expand eligible treatment populations to younger patients.

Utilization Findings

There were no claims and no prior authorization requests.

Recommendations

- No changes

Clinical Summary

Cystic fibrosis is an autosomal recessive exocrinopathy that affects multiple epithelial tissues in the lungs, pancreas, and other organ systems. It affects approximately 40,000 people in the United States and around 1,000 new cases are diagnosed annually, according to the Cystic Fibrosis Foundation. Once considered a disease of childhood, the estimated life expectancy for patients in the U.S. today is 38 years of age. This number has increased dramatically over time due to groundbreaking disease modifying therapies, and more than 50% of people with CF born between 2020 and 2024 are predicted to live to at least 65 years.

Cystic fibrosis is caused by reduced quantity or function of the cystic fibrosis transmembrane conductance regulator (CFTR) protein due to gene mutations. Disease severity and rate of progression are determined by the mutation present. The phenylalanine 508 deletion (F508del) is the most common deletion; approximately 50% of patients with CF in the U.S. are homozygous and 40% are heterozygous for this allele. This mutation, when homozygous, is associated with early onset of CF and more rapid disease progression. Approximately 5% of the overall CF population exhibits residual CFTR ion transport due to partial CFTR expression and preserved functioning. These “residual function” gene mutations cause CF with lung disease and a markedly reduced life expectancy but with a slower disease progression than other forms of disease.

Most cystic fibrosis-related morbidity and mortality is due to respiratory compromise. Patients with cystic fibrosis develop hyperviscous and adherent pulmonary secretions that obstruct small- and medium-sized airways. These secretions can be extremely difficult to clear and, subsequently, the lungs become a breeding ground for a variety of bacterial infections including *P. aeruginosa*. Many patients with cystic fibrosis endure lifelong pulmonary infections that become more difficult to eradicate over time. Successfully eradicating organisms such as *P. aeruginosa* early in the disease process may improve prognosis significantly. The pancreas is the other organ prominently affected by cystic fibrosis. In the pancreas, exocrine secretions obstruct pancreatic ducts and impair production and flow of digestive enzymes to the duodenum. This results in chronic malabsorption, poor growth, and fat-soluble vitamin insufficiency. Additionally, diabetes mellitus is observed in over 30% of adults with cystic fibrosis. Other manifestations may include multilobular cirrhosis, intestinal obstructive syndrome, sinusitis, and infertility in men and women.

The diagnosis of cystic fibrosis is based on clinical symptoms, family history, or positive newborn screening. The main diagnostic tests include sweat electrolyte measurements to evaluate chloride levels (markedly elevated chloride levels are seen in cystic fibrosis) and CFTR mutation analysis. The standard of care for outpatients involves multiple medications and therapies which may include exogenous pancreatic enzymes, nutritional supplementation, anti-inflammatory medications, bronchodilators, mucolytics, chronic or periodic oral or inhaled antibiotics, disease-modifying agents (CFTR modulator therapies) in eligible populations, and chest physiotherapy. Acute exacerbations are commonly managed in an inpatient setting with frequent chest physiotherapy and intravenous antibiotics. Despite all these interventions, the disease is progressive. End-stage cystic fibrosis pulmonary failure may be treated with lung transplantation.

Ivacaftor and deutivacaftor are potentiators of the CFTR protein and thereby increase the flux of chloride ions through CFTR channels at the cell surface, but do not increase the expression of the channels. Therefore, potentiators are commonly administered in combination with a so-called “correcting agent” such as tezacaftor, lumacaftor, vanzacaftor or elxacaftor; these improve conformational stability and results in increased processing and trafficking of the mature

protein to the cell surface. Ivacaftor and lumacaftor were the first therapies approved to treat the underlying genetic cause of cystic fibrosis.

Mucolytics are an important component in CF treatment since difficulty clearing purulent secretions is a hallmark of the disease. Dornase alfa is a recombinant human deoxyribonuclease 1 (rhDNase) that hydrolyzes the DNA in sputum and reduces viscoelasticity. This effect helps to improve pulmonary function and reduce exacerbations of infections in patients with cystic fibrosis. Acetylcysteine produces a similar mucolytic effect; however, the exact mechanism by which this occurs is unknown. It is thought that the mucolytic activity of acetylcysteine is related to the sulfhydryl group in the molecule, which “opens” disulfide linkages in mucus thereby lowering viscosity. Nebulized hypertonic saline (3% or 7%) is presumed to work by drawing water from the airway due to its high osmolality, resulting in creation of an aqueous surface layer that is deficient in CF. Mannitol is thought to improve mucus clearance in the lungs via actions such as stimulating cough, thinning mucus secretions, and increased cilia effectiveness, similarly to dornase alfa and hypertonic saline.

Inhaled antibiotics are essential in the treatment of both chronic infections and acute exacerbations of CF and have been shown to improve lung function. Tobramycin and amikacin are aminoglycoside antibiotics that act primarily by disrupting bacteria protein synthesis leading to altered cell membrane permeability, progressive disruption of the cell envelope, and cell death. Aztreonam binds to penicillin-binding proteins of susceptible bacteria, which subsequently leads to inhibition of bacterial cell wall synthesis and cell death. All these inhaled antibiotics have activity against Gram-negative bacteria including *P. aeruginosa*, which is the most common pathogen identified in adults with cystic fibrosis. However, the use of inhaled amikacin (Arikayce®) is only FDA approved for treatment of refractory MAC infections, which can also occur in CF patients.

In 2013, a multidisciplinary committee of the Cystic Fibrosis Foundation updated recommendations regarding the use of chronic medications for lung health maintenance in patients with cystic fibrosis. The authors of the guideline strongly recommended the chronic use of dornase alfa in patients 6 years of age and older with moderate to severe disease, recommended use with a lower level of evidence in patients with mild disease and concluded that evidence is insufficient to recommend for or against the chronic use of inhaled or oral acetylcysteine. Hypertonic saline was recommended in all CF regardless of severity. Regarding inhaled antibiotics, the authors strongly recommended chronic administration of inhaled tobramycin or inhaled aztreonam in patients 6 years and older with moderate to severe disease and *P. aeruginosa* persistently present in airway cultures. Finally, the authors strongly recommended ivacaftor as a chronic treatment to improve lung function and quality of life and reduce exacerbations for patients 6 years and older with at least one G551D CFTR mutation.

In 2014 the Cystic Fibrosis Foundation published a guideline regarding the optimal approach for eradication of initial *P. aeruginosa* infection. In this guideline, the Foundation strongly recommends inhaled antibiotic therapy for the treatment of initial or new *P. aeruginosa* infection from an airway culture. The preferred option is the administration of inhaled tobramycin 300 mg twice daily for 28 days.

In 2018, additional recommendations for two available CFTR modulator therapies at the time, ivacaftor (Kalydeco®) and lumacaftor/ivacaftor (Orkambi®) were released by the Cystic Fibrosis Foundation. Ivacaftor was conditionally recommended for patients age 6 and older with CF gating mutations other than G551D or R117H. For patients with R117H mutations, ivacaftor was conditionally recommended in (a) adults, and (b) ages 6-17 with PPFEV1 > 90%. Additionally for those with R117H mutations, treatment with ivacaftor was conditionally recommended against for



children less than 6 years of age and children 6-17 with PPFEV1 > 90%. Lumacaftor/ivacaftor treatment for patients with 2 copies of the F508del mutation was (a) strongly recommended in CF patients 12 years of age and older with PPFEV1 < 90%, and (b) conditionally recommended for children ages 6-11, and ages 12 and older with PPFEV1 > 90%.

Since these publication dates, significant developments have occurred with new drugs to market and expanded age ranges eligible for therapy with CFTR modulator therapies. Newer disease modifying agents also target an increased number of CFTR mutation types. Future iterations are needed to reflect these changes and determine best practices for the management of cystic fibrosis lung disease.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
CF Transmembrane Conductance Regulator Potentiators		
Kalydeco® (ivacaftor)	Treatment of CF in patients one month and older who have one mutation in the CFTR gene that is responsive to ivacaftor potentiation based on clinical and/or in vitro assay data.	Adults and pediatric patients age 6 years and older: 150 mg by mouth every 12 hours. Pediatric patients 6 months to less than 6 years of age and weighing 5 kg to less than 7 kg: one 25 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours. Pediatric patients 6 months to less than 6 years of age and weighing 7 kg to less than 14 kg: one 50 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours. Pediatric patients 6 months to less than 6 years of age and 14 kg or greater: one 75 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours. Infants 4 to <6 months weighing ≥5 kg: Oral granules: Oral: 25 mg granule packet every 12 hours. Infants <2 months weighing ≥3 kg: Oral granules: Oral: 5.8 mg granule packet every 12 hours. Infants ≥2 to <4 months weighing ≥3 kg: Oral granules: Oral: 13.4 mg granule packet every 12 hours.
Orkambi® (lumacaftor/ivacaftor)	Treatment of CF in patients one year and older who are homozygous for the F508del mutation in the CFTR gene.	Pediatric patients one to two years: Weight 7 to <9 kg: Oral: Lumacaftor 75 mg/ivacaftor 94 mg granule packet: 1 packet every 12 hours. Weight 9 to <14 kg: Oral: Lumacaftor 100 mg/ivacaftor 125 mg granule packet: 1 packet every 12 hours. Weight ≥14 kg: Oral: Lumacaftor 150 mg/ivacaftor 188 mg granule packet: 1 packet every 12 hours. Pediatric patients age 2 through 5 years and weighing less than 14 kg: one packet of granules (each containing lumacaftor 100 mg/ivacaftor 125 mg) mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours.

Medication	Indications	Dosing/Administration
		Pediatric patients age 2 through 5 years and weighing 14 kg or greater: one packet of granules (each containing lumacaftor 150 mg/ivacaftor 188 mg) mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours. Pediatric patients age 6 through 11 years: two tablets (each containing lumacaftor 100 mg/ivacaftor 125 mg) taken orally every 12 hours. Adults and pediatric patients age 12 years and older: 2 tablets (lumacaftor 400 mg/ivacaftor 250 mg) every 12 hours.
Symdeko® (tezacaftor/ivacaftor)	Treatment of patients with CF aged 6 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.	Pediatric patients age 6 to less than 12 years weighing less than 30 kg: one tablet (containing tezacaftor 50 mg/ivacaftor 75 mg) in the morning and one tablet (containing ivacaftor 75 mg) in the evening, approximately 12 hours apart. Adults and pediatric patients ages 12 years and older or pediatric patients age 6 to less than 12 years weighing 30 kg or more: one tablet (containing tezacaftor 100 mg/ivacaftor 150 mg) in the morning and one tablet (containing ivacaftor 150 mg) in the evening, approximately 12 hours apart.
Trikafta® (elexacaftor/tezacaftor/ivacaftor)	Treatment of cystic fibrosis (CF) in patients aged two years and older who have at least one <i>F508del</i> mutation in the <i>CFTR</i> gene or a mutation in the <i>CFTR</i> gene that is responsive based on clinical and/or in vitro data.	Children 2 to <6 years: Oral granules: Weight <14 kg: Elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg per packet and ivacaftor 59.5 mg per packet: Oral: 1 packet (total dose of elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg) in the morning and one ivacaftor 59.5 mg packet in the evening approximately 12 hours apart. Weight ≥14 kg: Elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg per packet and ivacaftor 75 mg packet: Oral: 1 packet (total dose of elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) in the morning and one ivacaftor 75 mg packet in the evening approximately 12 hours apart. Children 6 to <12 years: Oral tablets:

Medication	Indications	Dosing/Administration
		Weight <30 kg: Elexacaftor 50 mg/tezacaftor 25 mg/ivacaftor 37.5 mg per tablet and ivacaftor 75 mg per tablet: Oral: 2 tablets (total dose of elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) in the morning and one ivacaftor 75 mg tablet in the evening, approximately 12 hours apart. Weight ≥30 kg: Elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg per tablet and ivacaftor 150 mg per tablet: Oral: 2 tablets (total dose of elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 150 mg) in the morning and one ivacaftor 150 mg tablet in the evening, approximately 12 hours apart. Adults and pediatric patients aged 12 years and older: Morning dose: two elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg tablets Evening dose (approximately 12 hours later): one ivacaftor 150 mg tablet <i>Reduce dose when co-administered with drugs that are moderate or strong CYP3A inhibitors</i>
Alyftrek® (vanzacaftor, tezacaftor, and deutivacaftor)	For the treatment of cystic fibrosis in patients aged 6 years and older who have at least one F508del mutation or another responsive mutation in the CFTR gene.	Children 6 to <12 years: <40 kg: Vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg per tablet: Oral: 3 tablets once daily (vanzacaftor 12 mg/tezacaftor 60 mg/deutivacaftor 150 mg per dose). ≥40 kg: Vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg per tablet: Oral: 2 tablets once daily (vanzacaftor 20 mg/tezacaftor 100 mg/deutivacaftor 250 mg per dose). Children ≥12 years and older: Oral: 2 tablets once daily (vanzacaftor 20 mg/tezacaftor 100 mg/deutivacaftor 250 mg per dose).
Inhaled Antibiotics		
Cayston® (aztreonam lysine)	To improve respiratory symptoms in CF patients with pulmonary Pseudomonas aeruginosa infections.	75 mg three times daily (at least 4 hours apart) for 28 days; do not repeat for 28 days after completion.

Medication	Indications	Dosing/Administration
	Safety and effectiveness have not been established in pediatric patients below the age of 7 years, patients with FEV1 <25% or >75% predicted, or patients colonized with <i>Burkholderia cepacia</i> .	
Arikayce® (amikacin liposome)	For the treatment of Mycobacterium avium complex (MAC) lung disease as part of a combination antibacterial drug regimen in adult patients who do not achieve negative sputum cultures after a minimum of 6 consecutive months of a multidrug background regimen therapy, and have limited or no alternative treatment options.	Adults: Once daily oral inhalation of the contents of one 590 mg/8.4 mL vial.
tobramycin (Bethkis®, TOBI®, Kitabis Pak®)	Management of cystic fibrosis in adults and pediatric patients 6 years of age and older with <i>Pseudomonas aeruginosa</i> .	300 mg inhalation every 12 hours; administer in repeated cycles of 28 days on drug followed by 28 days off drug.
TOBI Podhaler® (tobramycin)	Management of cystic fibrosis in adults and pediatric patients 6 years of age and older with <i>Pseudomonas aeruginosa</i> .	4 capsules (112 mg) every 12 hours; administer in repeated cycles of 28 days on drug followed by 28 days off drug.
Mucolytics		
acetylcysteine	Adjunct therapy in patients with abnormal, viscid, or inspissated mucous secretions in conditions such as cystic fibrosis (among others).	10% solution (undiluted): 6 to 10 mL given 3 to 4 times/day; dosing range: 2 to 20 mL every 2 to 6 hours. 20% solution (dilute with sodium chloride or sterile water for inhalation): 3 to 5 mL given 3 to 4 times/day; dosing range: 1 to 10 mL every 2 to 6 hours.
Pulmozyme® (dornase alfa)	Management of cystic fibrosis patients, in conjunction with standard therapies, to improve pulmonary function and reduce the risk of respiratory infections requiring parenteral antibiotics in patients with a FVC $\geq$ 40% predicted.	2.5 mg inhalation once daily through selected jet nebulizers. Some patients may benefit from twice daily administration.
sodium chloride	Restores moisture to pulmonary system; loosens and thins congestion caused by colds or allergies; diluent for bronchodilator solutions that require dilution before inhalation.	While labeling does not specify dosing for this particular indication, most studies used 4-10 mL of 3%, 6%, or 7% hypertonic saline once or twice daily.

Medication	Indications	Dosing/Administration
Bronchitol® (mannitol)	An add-on maintenance therapy to improve pulmonary function in adult patients 18 years of age and older with cystic fibrosis.	400 mg (10 capsules) twice a day by oral inhalation, in the morning and evening, with the later dose taken 2-3 hours before bedtime.

Boxed Warnings and Contraindications

Medication	Boxed Warnings	Contraindications
CF Transmembrane Conductance Regulator Potentiators		
Kalydeco® (ivacaftor)	None	None
Orkambi® (lumacaftor/ivacaftor)		
Symdeko® (tezacaftor/ivacaftor)		
Trikafta® (elexacaftor/tezacaftor/ivacaftor) Alyftrek® (vanzacaftor, tezacaftor, and deutivacaftor)	Drug induced liver injury and liver failure	None
Inhaled Antibiotics		
Cayston® (aztreonam lysine)	None	Hypersensitivity to aztreonam or any component of the formulation.
tobramycin (Bethkis®, TOBI®, TOBI Podhaler®, Kitabis Pak®)		Hypersensitivity to tobramycin, other aminoglycosides, or any component of the formulation.
Arikayce® (amikacin liposome)	Risk of increased respiratory adverse reactions.	Known hypersensitivity to any aminoglycoside.
Mucolytics		
acetylcysteine	None	Hypersensitivity to acetylcysteine or any component of the formulation.
Pulmozyme® (dornase alfa)		Hypersensitivity to dornase alfa, Chinese hamster ovary cell products, or any component of the formulation.
sodium chloride		Hypersensitivity to sodium chloride or any component of the formulation.
Bronchitol® (mannitol)		- Hypersensitivity to mannitol or to any of the capsule components - Failure to pass the Bronchitol Tolerance Test (BTT)

Warnings/Precautions

Medication	Warnings/Precautions
CF Transmembrane Conductance Regulator Potentiators	
Kalydeco® (ivacaftor)	• Lens opacities and cataracts have been reported in pediatric patients. • May cause dizziness. • May increase hepatic transaminases; temporarily discontinue if ALT or AST > 5 times ULN; use with caution in patients with hepatic impairment. • Use with caution in patients with severe renal impairment (CrCl ≤ 30 ml/min) or ESRD. • Potentially significant drug interactions may exist.
Orkambi® (lumacaftor/ivacaftor)	• Lens opacities and cataracts have been reported in pediatric patients. • Increased blood pressure has been observed. • May increase hepatic transaminases; temporarily discontinue if ALT or AST > 5 times ULN without concomitant elevated bilirubin or if ALT or AST > 3 times ULN with bilirubin > 2 times ULN; use with caution in patients with hepatic impairment. • Use was associated with an increased incidence of respiratory events. • Use with caution in patients with severe renal impairment (CrCl ≤ 30 ml/min) or ESRD. • Use is not recommended in organ transplant recipients. • Potentially significant drug interactions may exist
Symdeko® (tezacaftor/ivacaftor) Trikafta® (elexacaftor/tezacaftor/ivacaftor)	• Elevated transaminases (ALT or AST): Transaminases (ALT and AST) should be assessed prior to initiating Symdeko®, every 3 months during the first year of treatment, and annually thereafter. In patients with a history of transaminase elevations, more frequent monitoring should be considered. Dosing should be interrupted in patients with significant elevations of transaminases, e.g., patients with ALT or AST > 5 × upper limit of normal (ULN), or ALT or AST > 3 × ULN with bilirubin > 2 × ULN. Following resolution of transaminase elevations, consider the benefits and risks of resuming treatment. • Use with CYP3A inducers: Concomitant use with strong CYP3A inducers (e.g., rifampin, St. John's wort) substantially decrease exposure of ivacaftor and may decrease the exposure of tezacaftor, which may reduce therapeutic effectiveness. Therefore, co-administration is not recommended. • Cataracts: Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with Symdeko®. Baseline and follow-up examinations are recommended in pediatric patients initiating Symdeko® treatment. • Intracranial hypertension has been reported; headache, blurred vision, diplopia, potential vision loss, papilledema on fundoscopy may occur.
Alyftrek® (vanzacaftor, tezacaftor, and deutivacaftor)	• Lens opacities and cataracts have been reported in pediatric patients. • Intracranial hypertension has been reported; headache, blurred vision, diplopia, potential vision loss, papilledema on fundoscopy may occur • Use with caution in patients with hepatic impairment; dosage adjustment recommended in patients with moderate impairment (Child-Pugh class B); use not recommended in severe impairment (Child-Pugh class C) • Use with caution in patients with severe renal impairment (eGFR < 30 mL/minute/1.73 m²) or end-stage renal disease
Inhaled Antibiotics	
Cayston® (aztreonam lysine)	• Rare cross-allergenicity to penicillins, cephalosporins, or carbapenems may occur. • Bronchospasm may occur following nebulization; administer a bronchodilator prior to treatment.

Medication	Warnings/Precautions
	Safety and efficacy has not been established in patients with $FEV_1 < 25\%$ or $> 75\%$ predicted or in patients colonized with <i>Burkholderia cepacia</i>. Reserve for patients with known <i>P. aeruginosa</i>.
Arikayce® (amikacin liposome)	- Hypersensitivity Pneumonitis: Reported with Arikayce® treatment; if hypersensitivity pneumonitis occurs, discontinue Arikayce® and manage patients as medically appropriate. - Hemoptysis: Higher frequency of hemoptysis has been reported with Arikayce® treatment. If hemoptysis occurs, manage the patients as medically appropriate. - Bronchospasm: Higher frequency of bronchospasm has been reported with Arikayce® treatment. Treat patients as medically appropriate if this occurs during treatment. - Exacerbations of Underlying Pulmonary Disease: Higher frequency of exacerbations of underlying pulmonary disease has been reported with Arikayce® treatment. Treat patients as medically appropriate if this occurs during treatment. - Ototoxicity: Higher frequency of ototoxicity has been reported with Arikayce® treatment. Closely monitor patients with known or suspected auditory or vestibular dysfunction. If patients develop tinnitus this may be an early symptom of ototoxicity. - Nephrotoxicity: Aminoglycosides can cause nephrotoxicity. Close monitoring of patients with known or suspected renal dysfunction may be needed when prescribing. - Neuromuscular Blockade: Aminoglycosides may aggravate muscle weakness because of a potential curare-like effect on neuromuscular function. If neuromuscular blockade occurs, it may be reversed by the administration of calcium salts but mechanical assistance may be necessary. - Embryo-Fetal Toxicity: Aminoglycosides can cause total, irreversible, bilateral congenital deafness in pediatric patients exposed in utero.
tobramycin (Bethkis®, TOBI®, TOBI Podhaler®, Kitabis Pak®)	- Bronchospasm may occur. - Nephrotoxicity was not observed during tobramycin inhalation in clinical studies but has been associated with aminoglycosides. - Use with caution in patients with neuromuscular disorders; neuromuscular blockade, respiratory failure, and prolonged respiratory paralysis may occur. - Ototoxicity and vestibular toxicity have occurred.
Mucolytics	
acetylcysteine	- Anaphylactoid reactions have been reported, usually within 30-60 minutes and may resolve spontaneously. - Use caution in patients with asthma or history of bronchospasm; these patients may be at increased risk of hypersensitivity reactions. - Since increased bronchial secretions may develop after inhalation, percussion, postural drainage, and suctioning should follow. If bronchospasm occurs, administer a bronchodilator; discontinue acetylcysteine if bronchospasm progresses.
Pulmozyme® (dornase alfa)	- In patients with pulmonary function $<40\%$ of normal, dornase alfa does not significantly reduce the risk of respiratory infections that require parenteral antibiotics. - Safety studies included children ≥ 3 months, however experience is limited in children <5 years of age.
sodium chloride	None in label for nebulized formulations.
Bronchitol® (mannitol)	Severe bronchospasm; perform the Bronchitol tolerance test prior to use under the supervision of trained professionals. Do not use in patients who fail the Bronchitol tolerance test; patients who pass the tolerance test may still experience bronchospasm

Medication	Warnings/Precautions
	with maintenance use and should premedicate with inhaled short-acting bronchodilators. If bronchospasm occurs, discontinue use immediately. • Hemoptysis: May occur with use; use with caution in patients with history of significant hemoptysis episodes (volume >60 mL); discontinue if hemoptysis occurs. • Renal impairment: Drug is primarily renally eliminated and systemic exposure may be increased; use with caution in patient with renal impairment.

Practice 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 Symdeko®, Trikafta® and Alyftrek® 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 is provided in the tables below. In most 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 benefits.

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

Cystic Fibrosis Foundation pulmonary guidelines. Chronic medications for maintenance of lung health (Am J Respir Crit Care Med. 2013;187(7):680-689)

In 2013, a multidisciplinary committee of the Cystic Fibrosis Foundation updated recommendations regarding the use of chronic medications for lung health maintenance in patients with cystic fibrosis. This review included an assessment of 137 articles describing 84 parallel and cross-over randomized controlled trials. A summary of the recommendations from the panel is provided in the table. This Table includes updated, as well as unchanged, recommendations from the previous 2007 guideline.

Treatment	Recommendation
Unchanged recommendations from the 2007 guideline	
Inhaled tobramycin – moderate to severe disease	Strongly recommends chronic use to improve lung function and quality of life and reduce exacerbations for patients 6 years and older with <i>P. aeruginosa</i> persistently present in airway cultures. (A)
Inhaled tobramycin – mild disease	Recommends chronic use to reduce exacerbations for patients 6 years and older with <i>P. aeruginosa</i> persistently present in airway cultures. (B)
Dornase alfa – moderate to severe disease	Strongly recommends chronic use to improve lung function and quality of life and reduce exacerbations for patients 6 years of age and older. (A)

Treatment	Recommendation
Dornase alfa – mild disease	Recommends chronic use to improve lung function and reduce exacerbations for patients 6 years of age or older. (B)
Inhaled hypertonic saline	Recommends chronic use to improve lung function and quality of life and reduce exacerbations for patients 6 years of age or older. (B)
Inhaled or oral N-acetylcysteine or inhaled glutathione	Insufficient evidence to recommend for or against chronic use. Certainty of benefit is low and cannot estimate magnitude of benefit. (I)
New and modified recommendations since the 2007 guideline	
Ivacaftor	Strongly recommends chronic use to improve lung function and quality of life and reduce exacerbations for patients 6 years and older with at least one G551D CFTR mutation. (A)
Inhaled aztreonam – moderate to severe disease	Strongly recommends chronic use to improve lung function and quality of life for patients 6 years and older with <i>P. aeruginosa</i> persistently present in airway cultures. (A)
Inhaled aztreonam – mild disease	Recommends chronic use to improve lung function and quality of life for patients 6 years and older with <i>P. aeruginosa</i> persistently present in airway cultures. (B)

USPSTF Grade Definitions

Grade	Definition	Suggestions for Practice
A	Recommended: high certainty that the net benefit is substantial.	Offer or provide this service/product
B	Recommended: high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service/product
C	The committee recommends selectively offering or providing this service/product to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service/product for selected patients depending on individual circumstances
D	The committee recommends against the service/product. There is moderate or high certainty that the service/product has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service
I	The committee concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service/product. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	If the service/product is offered, patients should understand the uncertainty about the balance of benefits and harms

Cystic Fibrosis Foundation pulmonary guideline. Pharmacologic approaches to prevention and eradication of initial *Pseudomonas aeruginosa* infection. (Ann Am Thorac Soc. 2014;11(10):1640-1650)

Recommendations:

- The Foundation strongly recommends inhaled tobramycin 300 mg twice daily for 28 days to treat initial or new growth of *P. aeruginosa* from an airway culture. (A)
- The Foundation recommends against the use of prophylactic antipseudomonal antibiotics to prevent the acquisition of *P. aeruginosa*. (D)

U.S. Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of nontuberculous mycobacteria in individuals with cystic fibrosis. Thorax. 2016;71:i1-i22

Recommendations for Treatment:

- Treatment of M. abscessus complex pulmonary disease should involve an intensive phase and a continuation phase.

- The intensive phase should include daily oral macrolide (preferably azithromycin) in conjunction with 3-12 weeks of intravenous (IV) amikacin and one or more of the following: IV tigecycline, imipenem, or cefoxitin, guided but not dictated by drug susceptibility testing. The duration of the intensive phase of therapy should be determined by the severity of infection, the response to treatment, and the tolerability of the regimen.
- The continuation phase should include a daily oral macrolide (preferably azithromycin), and inhaled amikacin, in conjunction with 2-3 of the following additional oral antibiotics: minocycline, clofazimine, moxifloxacin, and linezolid, guided but not directed by susceptibility testing.
- Monotherapy with a macrolide or other antimicrobial should never be used in the treatment of *M. abscessus* complex or *M. avium* complex pulmonary disease.
- Clarithromycin-sensitive *M. avium* complex pulmonary disease should be treated with a daily oral antibiotic regimen containing a macrolide (preferably azithromycin), rifampin, and ethambutol.
- An initial course of IV amikacin should be considered in the treatment of *M. avium* complex pulmonary disease in the presence of one or more of the following:
 - a) AFB smear positive respiratory tract samples
 - b) Radiological evidence of lung cavitation or severe infection
 - c) Systematic signs of illness
- Individuals with CF receiving NTM treatment should have expectorated or induced sputum samples sent for NTM culture every 4-8 weeks throughout the entire course of treatment to assess microbiological response.
- A schedule for detecting drug toxicity (including hearing loss, visual loss, renal impairment, and liver function test abnormalities) should be set in place at the time of treatment initiation and implemented throughout treatment based on the specific drugs prescribed.
- A high-resolution computed tomography scan of the lungs should be performed shortly before starting NTM treatment and at the end of NTM treatment to assess radiological response.
- NTM antibiotic therapy should be prescribed for 12 months beyond culture conversion (defined as three consecutive negative cultures, with the time of conversion being the date of the first of the three cultures) as long as no positive cultures are obtained during these 12 months.
- When amikacin is given intravenously or when streptomycin is given intravenously or intramuscularly, serum levels should be monitored and dosing adjusted to minimize ototoxicity and nephrotoxicity.

Cystic Fibrosis Foundation pulmonary guidelines. Treatment of pulmonary exacerbations. (Am J Respir Crit Care Med. 2009;180(9):802-808)

The Cystic Fibrosis Foundation has also published guidelines that focus on the management of pulmonary exacerbations. Therapy-related recommendations include the following:

- There is insufficient evidence to recommend for or against the continued use of inhaled antibiotics in patients treated with the same antibiotic intravenously for the treatment of an acute exacerbation. (I)
- Continue chronic treatments for maintenance of lung health during treatment of an acute exacerbation. (B)
- There is insufficient evidence to recommend the use of a single antibiotic as being equivalent to the use of more than one antibiotic class for treatment of *Pseudomonas* infection during an acute exacerbation. (I)

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Vanzacaftor–tezacaftor–deutivacaftor versus elexacaftor–tezacaftor–ivacaftor in individuals with cystic fibrosis aged 12 years and older (SKYLINE Trials VX20-121-102 and VX20-121-103): results from two randomized, active-controlled, phase 3 trials PMID: 39756424	N=398 (SKYLINE 102); 573 (SKYLINE 103) Two randomized, active-controlled, double-blind, phase 3 trials in CF patients 12 years and older with: SKYLINE 102: a F508del plus a minimal function mutation SKYLINE 103: two F508del, F508del and a residual function mutation, F508del and a gating mutation, or elexacaftor–tezacaftor–ivacaftor-responsive-non-F508del genotypes Inclusion criteria: • Aged 12 years and older • Confirmed diagnosis of cystic fibrosis with eligible genotypes and stable cystic fibrosis • FEV₁ % predicted at screening had to be 40–80% for those who had not previously received elexacaftor–tezacaftor–ivacaftor, or 40–90% for those who were receiving elexacaftor–tezacaftor–ivacaftor Exclusion criteria: • History of certain comorbidities such as hepatic cirrhosis, solid organ or hematological transplantation, alcohol or drug abuse, or cancer • Abnormal lab values for hemoglobin, total bilirubin, LFTs, renal function per investigators outlined parameters • Recent lung infection • Lung infection with organisms associated with rapid decline in pulmonary status (such as Burkholderia cenocepacia, Burkholderia dolosa, and Mycobacterium abscessus) Interventions: 4-week run-in period, during which subjects received elexacaftor (200 mg once daily), tezacaftor (100 mg once daily), and ivacaftor (150 mg once every 12 h) as two fixed-dose combination tablets in the morning and one ivacaftor tablet in the evening. They were then randomly assigned (1:1) to either elexacaftor (200 mg once daily), tezacaftor	Primary: • Absolute change in FEV₁ % predicted from baseline (most recent value before treatment on day 1) through week 24 (with non-inferiority of vanzacaftor–tezacaftor–deutivacaftor shown if the lower bound of the 95% CI for the primary endpoint was –3.0 or higher) Secondary (Key): • Absolute change from baseline through week 24 in sweat chloride concentration • Proportion of participants with sweat chloride concentration below 60 mmol/L (pooled from both trials) through week 24 • Proportion of participants with sweat chloride concentration below 30 mmol/L (pooled from both trials) through week 24

	(100 mg once daily), and ivacaftor (150 mg once every 12 h) as two fixed-dose combination tablets in the morning and one ivacaftor tablet in the evening, or vanzacaftor (20 mg once daily), tezacaftor (100 mg once daily), and deutivacaftor (250 mg once daily) as two fixed-dose combination tablets in the morning, for the 52-week treatment period.	
Results: SKYLINE 102: - The absolute change in least squares mean FEV₁ % predicted from baseline through week 24 was 0.5 (SE 0.3) percentage points in the vanzacaftor–tezacaftor–deutivacaftor group versus 0.3 (0.3) percentage points in the elexacaftor–tezacaftor–ivacaftor group (least squares mean treatment difference of 0.2 percentage points [95% CI –0.7 to 1.1]; p<0.0001), demonstrating non-inferiority. - The least squares mean treatment difference of absolute change in sweat chloride concentration was –8.4 mmol/L (95% CI –10.5 to –6.3; two-sided p<0.0001) SKYLINE 103: - The absolute change in least squares mean FEV₁ % predicted from baseline through week 24 was 0.2 (SE 0.3) percentage points in the vanzacaftor–tezacaftor–deutivacaftor group versus 0.0 (0.2) percentage points in the elexacaftor–tezacaftor–ivacaftor group (least squares mean treatment difference 0.2 percentage points [95% CI –0.5 to 0.9]; p<0.0001), demonstrating non-inferiority. - The least squares mean treatment difference of absolute change in sweat chloride concentration was – 2.8 mmol/L (–4.7 to –0.9; two-sided p=0.0034) Pooled: - A greater proportion of participants in the vanzacaftor–tezacaftor–deutivacaftor group had sweat chloride concentrations below 60 mmol/L through week 24 (86%) than did those in the elexacaftor–tezacaftor–ivacaftor group (77%); odds ratio 2.21 [95% CI 1.55 to 3.15]; p<0.0001. - A greater proportion of participants across both trials in the vanzacaftor–tezacaftor–deutivacaftor group had sweat chloride concentrations below 30 mmol/L through week 24 (31%) than did those in the elexacaftor–tezacaftor–ivacaftor group (23%); odds ratio 2.87 [95% CI 2.00 to 4.12]; p<0.0001. Conclusion: Study authors concluded vanzacaftor–tezacaftor–deutivacaftor is non-inferior to elexacaftor–tezacaftor–ivacaftor in terms of FEV₁ % predicted and is safe and well tolerated. Once daily dosing with vanzacaftor–tezacaftor–deutivacaftor reduces treatment burden, potentially improving adherence, compared with the twice daily regimen of the current standard of care. The restoration of CFTR function and the potential variants treated are also considerations that should be compared with currently available CFTR modulators.		
Citation	Design	Endpoints
Barry PJ, Mall MA, Álvarez A, et al. Triple Therapy for Cystic Fibrosis <i>Phe508del</i> -Gating and -Residual Function Genotypes. <i>N Engl J Med</i> . 2021;385(9):815-825. doi:10.1056/NEJMoa2100665 PMID: 34437784	N=258 Phase 3, double-blind, randomized, parallel-group trial in CF patients age 12 and older with a single F508del mutation and one gating or residual function mutation. Inclusion criteria: Confirmed diagnosis of CF and is heterozygous for F508del and either a gating or residual function mutation (F/G and F/RF genotypes)	Primary: Absolute change in percent predicted forced expiratory volume in 1 second (ppFEV₁) for ELX/TEZ/IVA group (From Baseline through Week 8) Secondary:

NCT: 04058353	- Forced expiratory volume in 1 second (FEV1) value $\geq 40\%$ and $\leq 90\%$ of predicted mean for age, sex, and height Exclusion criteria: - Clinically significant cirrhosis with or without portal hypertension - Lung infection with organisms associated with a more rapid decline in pulmonary status - Solid organ or hematological transplantation Interventions: All patients received either ivacaftor (Kalydeco®) or tezacaftor/ivacaftor (Symdeko®) for 4 weeks. Participants were then randomized to receive (for 8 weeks): - elexacaftor/tezacaftor/ivacaftor (Trikafta®) (N=132) - remain on run-in regimen of Kalydeco® or Symdeko® (N=126) Baseline measurements were taken after the 4 week run-in period.	- Absolute change from baseline in Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score for ELX/TEZ/IVA group (From Baseline through Week 8) - Absolute change in CFQ-R respiratory domain score for ELX/TEZ/IVA group compared to the control group (From Baseline through Week 8) - Absolute change in ppFEV1 for ELX/TEZ/IVA group compared to the control group (From Baseline through Week 8) - Absolute change in SwCl for ELX/TEZ/IVA group compared to the control group (From Baseline through Week 8) - Absolute change in sweat chloride (SwCl) for ELX/TEZ/IVA group (From Baseline through Week 8) - Safety and tolerability as assessed by number of subjects with adverse events (AEs) and serious adverse events (SAEs) (From Baseline up to Week 12)
Results - The Trikafta® group showed a statistically significant improvement from baseline to week 8 in ppFEV1 of +3.7%(95% confidence interval [CI], 2.8 to 4.6) relative to baseline and higher by 3.5 percentage points (95% CI, 2.2 to 4.7) relative to active control. - Sweat chloride was significantly reduced in patients within in the Trikafta® group from baseline by 22.3 mmol/L (95% CI, 20.2 to 24.5) and lower by 23.1 mmol per liter (95% CI, 20.1 to 26.1) relative to active control. - The change from baseline in the Cystic Fibrosis Questionnaire-Revised respiratory domain score (range, 0 to 100, with higher scores indicating better quality of life) with elexacaftor-tezacaftor-ivacaftor was 10.3 points (95% CI, 8.0 to 12.7) and with active control was 1.6 points (95% CI, -0.8 to 4.1). - Headache occurred in both treatment arms, and was the most common adverse event (15% or more). - Fewer serious ADRs occurred in the Trikafta® group compared to control (3.8% vs. 8.7%, respectively). Conclusion: The addition of the third agent in Trikafta® provides additional clinical benefit over existing therapies in patients in this specific subgroup with once F508del mutation and either a gating or residual function mutation. Safety findings mirrored other clinical trials involving Trikafta®, and it was well tolerated.		

Citation	Design	Endpoints
A Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-445 Combination Therapy in Subjects With Cystic Fibrosis Who Are Homozygous for the F508del Mutation (F/F) NCT: 03525548	N=107 Double-blind, active controlled, randomized clinical trial in CF patients ages 12 and older. Inclusion criteria: • Homozygous for the F508del mutation (F/F). • Forced expiratory volume in 1 second (FEV₁) value ≥40% and ≤90% of predicted mean for age, sex, and height. Exclusion criteria: • Clinically significant cirrhosis with or without portal hypertension. • Glucose-6-phosphate dehydrogenase (G6PD) deficiency. • Lung infection with organisms associated with a more rapid decline in pulmonary status. • Solid organ or hematological transplantation. Other protocol defined Inclusion/Exclusion criteria may apply. Interventions: Participants were randomized to receive one of the following after a 4 week run-in period where all participants received therapy with tezacaftor-ivacaftor: • Experimental: fixed-dose combination of VX-445 (200 mg), tezacaftor (100 mg) and ivacaftor (150 mg) in the morning followed by ivacaftor (150 mg) in the evening • Active control: placebo, tezacaftor (100 mg) and ivacaftor (150 mg) in the morning followed by ivacaftor (150 mg) in the evening	Primary: Mean absolute change in lung function (ppFEV₁) from baseline at week four. Secondary (select): • Absolute change in CF Questionnaire-Revised (CFQ-R) respiratory domain score (from baseline at Week 4) • Absolute change in sweat chloride (SwCl) (from baseline at Week 4)
Results: Mean absolute improvement over active controlled group in ppFEV₁ at 4 weeks was 10% (P<0.0001), which met statistical significance. Secondary endpoints were also met, including 45% absolute difference in reduction of sweat chloride levels at 4 weeks and improvement in CFQ-R respiratory domain from baseline of 17.4% (p<0.0001 for all measures). Conclusion: Compared to currently available CF treatment Symdeko®, triple-therapy with VX-445 showed significant improvements on multiple outcomes including comparatively large increases in ppFEV₁ and sweat chloride reduction in patients with CF 12 years and older with two F508del mutations. The study was not long enough to test whether this translates to reduction in pulmonary exacerbations.		
Citation	Design	Endpoints

A Phase 3, Randomized, Double-blind, Controlled Study Evaluating the Efficacy and Safety of VX-445 Combination Therapy in Subjects With Cystic Fibrosis Who Are Heterozygous for the F508del Mutation and a Minimal Function Mutation (F/MF) NCT: 03525444	N=403 Double-blind, placebo-controlled, randomized clinical trial in CF patients ages 12 and older. Inclusion criteria: • <u>Heterozygous</u> for the F508del mutation (F/MF). • Forced expiratory volume in 1 second (FEV1) value $\geq 40\%$ and $\leq 90\%$ of predicted mean for age, sex, and height. Exclusion Criteria: • Clinically significant cirrhosis with or without portal hypertension. • Glucose-6-phosphate dehydrogenase (G6PD) deficiency. • Lung infection with organisms associated with a more rapid decline in pulmonary status. • Solid organ or hematological transplantation. Interventions: Participants were randomized to receive one of the following: • 200 mg VX-445(elexacaftor)/ 100 mg TEZ/ 150 mg IVA as FDC tablets in the morning and 150 mg IVA as mono tablet in the evening • Matched placebo	Primary: Mean absolute change in lung function (ppFEV1) from baseline at week four. Secondary (select): • Absolute change in ppFEV1 from baseline through Week 24 • Number of pulmonary exacerbations (PEx) from baseline through Week 24 • Absolute change in body mass index (BMI) from baseline at Week 24 • Absolute change in sweat chloride (SwCl) from baseline at Week 4 and through Week 24 • Absolute change in Cystic Fibrosis Questionnaire Revised (CFQ-R) respiratory domain score from baseline at Week 4 and through Week 24
Results: Treatment with the VX-445 triple combination regimen resulted in a mean absolute improvement in ppFEV1 of 13.8 percentage points from baseline at week 4 compared to triple placebo ($p < 0.0001$), and was maintained through 24 weeks of treatment. In addition, statistically significant improvements in all key secondary endpoints were observed, such as a 63% reduction in the number of pulmonary exacerbations through week 24 (rate ratio 0.37, $P < 0.0001$), and absolute change in sweat chloride (-41.8% change through week 24, $P < 0.0001$). Conclusion: VX-445 triple combination regimen showed significant improvements on important cystic fibrosis disease parameters compared to placebo in patients who carry a single F508del mutation and a minimal functions mutation.		
Citation	Design	Endpoints
KONDUCT Moss RB, Flume PA, Elborn JS, et al on behalf of the KONDUCT study group. Efficacy and safety of ivacaftor treatment: randomized trial in subjects with cystic fibrosis	N=69 Double-blind, placebo-controlled, randomized clinical trial. Inclusion criteria: • Age 6 years or older. • Confirmed diagnosis of cystic fibrosis and chronic sinopulmonary disease.	Primary endpoint: Absolute change from baseline in % predicted FEV₁ through week 24. Secondary endpoints:

who have an R117H-CFTR mutation. <i>Lancet Respir Med.</i> 2015;3(7):524-533. NCT: 01614457	- Confirmed R117H mutation on at least one CFTR allele. - FEV₁ ≥ 40%. Exclusion criteria: - CFTR gene mutation leading to CFTR channel with gating defect: G551D, G178R, G551S, S549N, S549R, G970R, G1244E, S1251N, S1255P, or G1349D. - An acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease within 4 weeks before the first dose of study drug. - Abnormal liver function. - Use of any inhibitors or inducers of cytochrome (CYP) P450 3A. - Colonization with organisms associated with a more rapid decline in pulmonary status (for example, <i>Burkholderia cenocepacia</i>, <i>Burkholderia dolosa</i>, and <i>Mycobacterium abscessus</i>) at screening. - Pregnancy. Interventions: Participants were randomized to receive one of the following: Ivacaftor 150 mg twice daily for 24 weeks (N=34) Placebo twice daily for 24 weeks (n=35)	- Changes in sweat chloride concentrations. - Changes in Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain scores. - Change in BMI at week 24. - Time to first pulmonary exacerbation. - Safety.
Results: - Mean absolute change in the percentage of predicted FEV1 from baseline at week 24: +2.6% with ivacaftor vs. +0.5% with placebo; p=0.20. - Change in sweat chloride at week 24: -26.3 mmol/L with ivacaftor vs. -2.3 mmol/L with placebo; p<0.0001. - Change in CFQ-R respiratory domain score at week 24: +7.56 with ivacaftor vs. -0.83 with placebo; p=0.0091. - Time to first pulmonary exacerbation was not statistically different between groups. - There was a non-significant increase in BMI in the ivacaftor group at week 24. - Four participants in the ivacaftor group experienced a serious adverse effect compared with 6 participants in the placebo group. Conclusion: Although this study did not show a significant improvement in % predicted FEV1, ivacaftor did significantly improve sweat chloride and CFQ-R respiratory domain scores and lung function in adult patients with Arg117His-CFTR.		
Citation	Design	Endpoints
KONTINUE Rollover Study of Ivacaftor in Subjects With Cystic Fibrosis and a	N=125	Primary endpoint:

Non G551D CFTR Mutation (KONTINUE) NCT: 01707290	This study is a continuation of previous trials designed to evaluate the safety of long-term ivacaftor. This is an open-label trial in CF patients 6 years and older with a non-G551D CFTR mutation. Inclusion criteria: - Participants from Study 110, Study 111, or Study 113 entering the ivacaftor arm must have completed all study related treatments. - Participants entering the observational arm must have completed at least 4 weeks of study drug treatment in their previous study (Study 110 or Study 111), must have completed the previous study but do not wish to enroll in the ivacaftor arm, or must have completed the previous study but do not meet the inclusion criteria of the ivacaftor arm. - Participants entering the ivacaftor arm must be willing to comply with contraception requirements. Exclusion criteria: - Pregnancy. - Use of moderate or strong inhibitors or inducers of cytochrome P450 (CYP) 3A. - Evidence of cataract or lens opacity at or before the Day 1 Visit. Interventions: Patients who received either ivacaftor or placebo in previous studies either continued on ivacaftor therapy for up to 104 weeks, or no therapy and were observed only for up to 2 years.	Number of participants with treatment-emergent adverse events or serious adverse events up to week 108. Secondary endpoints: - Absolute change from baseline in % predicted FEV₁ through week 104. - Changes in sweat chloride concentrations. - Changes in Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain scores. - Change in BMI through week 104. - Number of pulmonary exacerbation events. - Number of participants with serious adverse events through week 104.
Results: - Of 121 participants in the ivacaftor arm, 117 had a treatment-emergent adverse event over the 2 year study period. Of these, 27 participants experienced serious adverse events. - FEV₁ increases and sweat chloride reductions were maintained through the 2 year study period. - Overall, BMI increased over the 2 year study period. - The positive change in CFQ-R respiratory domain scores continued over the 2 year period. - There were 83 total pulmonary exacerbation events for 121 participants over 2 years. Conclusion: Ivacaftor was well-tolerated up to 104 weeks with no new safety concerns identified. Lung function, CFQ-R respiratory domain scores, and BMI improved.		
Citation	Design	Endpoints

PERSIST McKone EF, Borowitz D, Drevinek P, et al on behalf of the PERSIST study group. Long-term safety and efficacy of ivacaftor in patients with cystic fibrosis who have the Gly551Asp-CFTR mutation: a phase 3, open-label extension study (PERSIST). <i>Lancet Respir Med</i>. 2014;2(11):902-910. NCT: 01117012	N=192 Open label, rollover study extension of the STRIVE and ENVISION trials. Patients were 6 years of age and older with CF and a Gly551Asp-CFTR mutation on at least one allele. Inclusion criteria: • Completion of assigned study treatment in previous study (102 or 103). • Participants of child bearing potential and who are sexually active must meet the contraception requirements and have a negative pregnancy test on day 1. Exclusion criteria: • Pregnancy. • Participants with a history of study treatment intolerance. • Participants taking any inhibitors or inducers of Cytochrome P450 3A4 (CYP3A4), including certain herbal medications (for example, St. John's Wort) and grapefruit/grapefruit juice. Interventions: Patients continued ivacaftor 150 mg Q 12 hours in addition to currently prescribed CF therapies, and those who had been in a placebo group in one of the previous trials initiated ivacaftor therapy for up to 96 weeks.	Primary endpoint: Number of participants with non-serious adverse events and serious adverse events (96 weeks). Secondary endpoints: • Annualized rate of decline in FEV₁ through week 96. • Absolute change in FEV₁ through week 96. • Absolute change in CFQ-R respiratory domain score through week 96. • Annualized pulmonary exacerbation event rate. • Annualized duration of pulmonary exacerbation events. • Absolute change in weight through week 96.
Results: Primary: Across both the STRIVE and ENVISION trials, 38 (20%) patients had a serious AE during the first 48 weeks and 44 (23%) during the subsequent 48 weeks. The most common AEs were pulmonary exacerbation, cough, and upper respiratory tract infection. Mean liver transaminase values were within the normal range at all visits through week 96. Only 3 participants discontinued ivacaftor therapy due to ADRs. Secondary: Sustained improvements in FEV₁, weight, and rate of pulmonary exacerbations were noted up to 144 weeks of treatment. Among adolescents/adults who previously received ivacaftor, the absolute change in FEV₁ at week 96 was 9.4% and the absolute increase in weight was 4.1 kg. Among children, the absolute change in FEV₁ was 10.3% and the absolute increase in weight was 14.8 kg. Conclusion: At 144 weeks of treatment, ivacaftor was well tolerated, with no new safety concerns. Ivacaftor also provided durable effects for 144 weeks in patients who had received active treatment in the placebo-controlled study.		
Citation	Design	Endpoints
TRAFFIC and TRANSPORT Wainwright CE, Elborn JS, Ramsey BW, et al for the TRAFFIC and	N=1108 This paper describes 2 double blind, placebo controlled, multicenter randomized controlled trials.	Primary endpoint: Absolute change from baseline at week 24 in the percentage of predicted FEV₁.

TRANSPORT study groups. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for the Phe508del CFTR. N Engl J Med. 2015;373(3):220-231.	Inclusion criteria: • Age 12 years and older. • Confirmed diagnosis of CF, homozygous for the Phe508del CFTR mutation. • $FEV_1 \geq 40\%$ and $\leq 90\%$ of predicted normal for age, sex, and height. Exclusion criteria: • An acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease within 4 weeks before first dose of study drug. • History of solid organ or hematological transplantation. • History of alcohol or drug abuse in the past year. • Use of strong inhibitors, moderate inducers or strong inducers of Cytochrome P450 3A (CYP3A) within 14 days before Day 1 of dosing. Interventions: 600 mg orally of lumacaftor once daily + 250 mg orally of ivacaftor every 12 hours (n=368) 400 mg of lumacaftor every 12 hours + ivacaftor 250 mg every 12 hours (n=369) placebo (n=371)	Secondary endpoints: • Relative change from baseline in the percentage of predicted FEV1. • Absolute change from baseline at week 24 in BMI. • Absolute change from baseline at week 24 in the patient-reported CFQ-R respiratory domain score. • Percentage of patients with a relative increase from baseline of 5% or higher in the percentage of predicted FEV1. • Number of pulmonary exacerbations through week 24.
Results: Primary: The difference between lumacaftor/ivacaftor and placebo with respect to the mean absolute change in the percentage of predicted FEV1 from baseline at week 24 was significant in all dose groups and ranged from 2.6 to 4.0% ($p < 0.001$ for all comparisons). Secondary: • Mean relative change in FEV1 was also significant and ranged from 4.3 to 6.7%; $p < 0.001$ for all groups. In each study, the percentage of patients who had a relative improvement in the percentage of predicted FEV1 of 5% or higher was greater in the ivacaftor/lumacaftor group as compared to placebo ($p < 0.001$ to $p = 0.002$). • Clinically meaningful reduction in the rates of pulmonary exacerbations was observed in the lumacaftor-ivacaftor groups vs. placebo with a rate ratio ranging from 0.57 to 0.72 ($p < 0.001$ to $p = 0.05$). • Mean BMI increased steadily in both ivacaftor/lumacaftor groups over the 24 weeks; in the pooled analysis, the treatment difference vs. placebo with respect to the absolute change in BMI was 0.24 to 0.28; $p < 0.001$. • In both ivacaftor/lumacaftor groups, there were improvements in the within-group CFQ-R respiratory domain score; the treatment difference vs. placebo was nominally significant. • Serious AEs were reported in 28.6% of the placebo group vs. 17.3% to 22.8% of patients in the ivacaftor/lumacaftor groups; AEs more frequently reported in the ivacaftor/lumacaftor groups included dyspnea and chest tightness.		

Conclusion:

The combination of lumacaftor/ivacaftor improved FEV₁ and reduced the rate of pulmonary exacerbations in patients with cystic fibrosis who were homozygous for the Phe508del CFTR mutation.

Citation	Design	Endpoints
EVOLVE Taylor-Cousar JL, Munck A, McKone E, et al. Tezacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del. <i>N Engl J Med.</i> 2017;377(21):2013-23. NCT: 02347657	N=509 Phase 3, randomized, double-blind, multicenter, placebo-controlled, parallel-group trial. Inclusion criteria: 12 years of age or older. - Confirmed diagnosis of cystic fibrosis; homozygous for F508del CFTR mutation. - FEV₁ ≥ 40% and ≤ 90% of predicted normal for age, sex, and height. - Stable CF disease as judged by the investigator. Exclusion criteria: - Pregnant or nursing females. - An acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease within 28 days before Day 1. Interventions: - tezacaftor 100 mg once daily and ivacaftor 150 mg twice daily for 24 weeks (N=251) - placebo for 24 weeks (N=258)	Primary endpoint: Absolute change in % FEV ₁ predicted through week 24. Secondary endpoints: - Relative change in the % predicted FEV₁ through week 24. - Number of pulmonary exacerbations. - Absolute change in CFQ-R respiratory domain score. - Safety and tolerability. - Time to first pulmonary exacerbation. - Change in sweat chloride. - Change in BMI and body weight.

Results:

Primary: Absolute change in % FEV₁ predicted was 4% greater than placebo; p< 0.001.

Secondary:

- Mean absolute change in FEV₁ from baseline was 3.4% for treatment vs -0.6% for placebo.
- The annualized estimated event rate of pulmonary exacerbations was significantly lower in the treatment group, 0.64 vs 0.99 in the placebo group, a 35% lower rate; p=0.005.
- The risk of pulmonary exacerbation at 24 weeks was 35% in the placebo group and 25% in the treatment group, HR 0.64 (95% CI 0.46-0.88).
- There was no significant difference between groups in BMI at 24 weeks.
- The least-squares mean difference between groups in the CFQ-R respiratory domain score through week 24 was 5.1 points (95% CI, 3.2 to 7.0), favoring tezacaftor-ivacaftor.
- Sweat chloride concentration was also significantly reduced in the treatment group with a between-group difference of -10.1 mmol/L (95% CI -11.4 to -8.8).

- 90.4% of patients in the treatment group and 95% of patients in the placebo group reported at least 1 adverse event; serious adverse events were reported in 31 patients (12.4%) in the tezacaftor–ivacaftor group and in 47 (18.2%) in the placebo group.
- Headache, nausea, and nasopharyngitis were reported more frequently in the treatment group.

Conclusion:

This trial demonstrated efficacy and safety of tezacaftor–ivacaftor in patients 12 years of age or older with CF homozygous for the CFTR F508del mutation. The improved safety profile of combination therapy with tezacaftor–ivacaftor, as compared with currently available therapy, in addition to its effect on multiple efficacy end points, supports its use in a broad range of patients with cystic fibrosis.

Citation	Design	Endpoints
EXPAND Rowe SM, Daines C, Ringshausen FC, et al. Tezacaftor-ivacaftor in residual-function heterozygotes with cystic fibrosis. N Engl J Med.2017; 377(21):2024-35. NCT:02392234	N=246 Phase 3, randomized, multicenter, double-blind, placebo-controlled, crossover trial. Inclusion criteria: • Age 12 years or older. • Confirmed diagnosis of cystic fibrosis; heterozygous for F508del CFTR mutation and a second allele with CFTR mutation with residual function. • FEV₁ ≥ 40% and ≤ 90% of predicted normal for age, sex, and height. • Stable CF disease as judged by the investigator. Exclusion criteria: • Pregnant or nursing females. • An acute upper or lower respiratory infection, pulmonary exacerbation, or changes in therapy (including antibiotics) for pulmonary disease within 28 days before Day 1. • A 12-lead electrocardiogram (ECG) demonstrating corrected QT interval (QTc) greater than (>) 450 milliseconds (msec). • History of solid organ or hematological transplantation. • Colonization with organisms associated with a more rapid decline in pulmonary status. Interventions: Each participant received 2 of the following regimens, each regimen was given for an 8-week treatment period separated by an 8-week washout period: • tezacaftor-ivacaftor combination therapy • ivacaftor monotherapy	Primary endpoint: Absolute change in % predicted FEV₁ from baseline to average of week 4 and week 8. Secondary endpoint: • Absolute change from study baseline to average of week 4 and week 8 in CFQ-R respiratory domain score. • Safety and tolerability. • Relative change from study baseline to average of week 4 and week 8 in % predicted FEV₁. • Absolute change from study baseline to average of week 4 and week 8 in sweat chloride.

- placebo

Results:

Primary: The least-squares mean difference versus placebo in FEV₁ from baseline measurements was 6.8 percentage points (95% CI, 5.7 to 7.8) for tezacaftor–ivacaftor and 4.7 percentage points (95% CI, 3.7 to 5.8) for ivacaftor alone (P<0.001 for both comparisons). The difference between tezacaftor–ivacaftor and ivacaftor alone was significant in favor of tezacaftor–ivacaftor (P<0.001).

Secondary:

- The least-squares mean difference in CFQ-R respiratory domain score vs placebo was 11.1 points (95% CI, 8.7 to 13.6) for tezacaftor–ivacaftor and 9.7 points (95% CI, 7.2 to 12.2) for ivacaftor alone (P <0.001 for both comparisons). The percentage of patients who had a clinically important difference of 4 points or greater was 65% in the tezacaftor–ivacaftor group, 58% in the ivacaftor-alone group, and 33% in the placebo group. The difference in the CFQ-R respiratory domain score between tezacaftor–ivacaftor and ivacaftor alone for either analysis was not significant.
- Sweat chloride concentrations were lower (denoting better CFTR function) in patients receiving tezacaftor–ivacaftor or ivacaftor alone than in those receiving placebo (LS mean difference vs. placebo, –9.5 mmol per liter [95% CI, –11.7 to –7.3] for tezacaftor–ivacaftor and –4.5 mmol per liter [95% CI, –6.7 to –2.3] for ivacaftor alone).
- BMI was increased in both active treatment groups at week 8 but the differences vs. placebo were not statistically significant.
- The difference in annualized pulmonary exacerbations was statistically similar between groups.
- The incidence of adverse events was similar in all three intervention groups.
- Increase in sputum production, nasopharyngitis, diarrhea, and headache were reported more frequently in the tezacaftor-ivacaftor group. Adverse events that were associated with respiratory events or respiratory symptoms were less common in the tezacaftor–ivacaftor group vs placebo.

Conclusion:

Tezacaftor-ivacaftor demonstrated greater efficacy over ivacaftor alone or placebo in improving lung function. Additional efficacy parameters were positive and overall safety measures were similar to the other groups.

Citation	Design	Endpoints
Yang C, Montgomery M. Dornase alfa for cystic fibrosis. Cochrane Database Syst Rev. 2018 Sep 6;9:CD001127. doi: 10.1002/14651858.CD001127.pub4.	N=2565 patients with cystic fibrosis (both children and adults). Cochrane review involving 19 randomized controlled trials. Interventions: Trials compared dornase alfa to placebo, standard therapy, or other medications that improve airway clearance. Dose and frequency of dornase alfa varied among the trials. Comparators included placebo, no treatment, hypertonic saline, hypertonic saline + alternate day dornase alfa, and mannitol + the combination of both drugs.	Objective: To determine whether the use of dornase alfa is associated with improved morbidity and mortality compared to placebo or other medications and to identify any AEs associated with its use.

Results: The following outcomes were improved with dornase alfa as compared to placebo: FEV1 (significant differences at 1, 3, and 6 months and 2 years); lung clearance index (significant at 1 month); pulmonary exacerbations (a decrease noted in trials of longer duration). One trial demonstrated that the cost savings from dornase alfa offset 18% to 38% of the medication costs. When evaluating the trials that compared dornase alfa to other medications that improve airway clearance, the results were mixed. One trial found a greater improvement in FEV1 with dornase alfa as compared to hypertonic saline, while 3 other trials found no such difference. In the 1 trial that evaluated a combination of dornase alfa +mannitol vs. dornase alfa alone, no beneficial effect was observed with the combination. Dornase alfa therapy was not associated with significantly more AEs except for voice alteration and rash.

Conclusion:

Compared with placebo, dornase alfa improves lung function in clinical trials lasting 1 month to 2 years. A reduction in pulmonary exacerbations was noted in trials of 6 month duration or longer. The only more commonly reported AEs with dornase alfa were voice alteration and rash. Data are insufficient to conclude whether or not dornase alfa is superior to hyperosmolar agents with regard to improvement of lung function.

Citation	Design	Endpoints
Tam J, Nash EF, Ratjen F, Tullis E, Stephenson A. Nebulized and oral thiol derivatives for pulmonary disease in cystic fibrosis. <i>Cochrane Database Syst Rev.</i> 2013 Jul 12;(7):CD007168. doi: 10.1002/14651858.CD007168.pub3.	N=255 patients with cystic fibrosis. Cochrane review. Interventions: 3 trials evaluated the effects of nebulized thiol derivatives; 6 trials evaluated oral thiol derivatives. Outcomes for patients who received thiol derivatives were compared to patients receiving no treatment or to control groups including placebo or any other medication. Trials investigating thiol derivatives given at any dose or frequency for a minimum of 4 weeks duration were eligible for inclusion. Thiol derivatives considered for inclusion included acetylcysteine, sodium-2-mercaptoethane sulphonate, carbocysteine, erdosteine, nacystelyn, glutathione, cysteine, and mecysteine.	Primary outcomes: Pulmonary function testing: FEV1 and FVC. Secondary outcomes: • Other pulmonary function testing measurements. • Inflammatory markers. • Quality of life. • Need for oral antibiotics for pulmonary exacerbation. • Need for IV antibiotics for pulmonary exacerbation. • AEs. • Number of days in hospital for respiratory exacerbation. • Adherence. • Acquisition of new respiratory pathogens. • Six-minute walk distance.

Results: No evidence of significant clinical benefit with regard to the primary or secondary outcomes was observed in patients receiving oral or nebulized thiol derivatives for cystic fibrosis; however, these agents were generally well tolerated with no significant AEs.

Conclusion: No evidence to recommend the use of either nebulized or oral thiol derivatives in patients with cystic fibrosis was observed. There are very limited good quality trials investigating the effects of these medications in cystic fibrosis.

Citation	Design	Endpoints
Elkins MR, Robinson M, Rose BR, et al. A controlled trial of long-term inhaled hypertonic saline in patients with cystic fibrosis. N Engl J Med. 2006;354(3): 229-240.	N=164 Randomized, double-blind, parallel-group trial. Inclusion criteria: • 6 years of age or older. • Confirmed diagnosis of cystic fibrosis. Exclusion criteria: • Pregnant or breast-feeding women. • People colonized with Burkholderia cepacia. • Cigarette smokers. Interventions: 7% hypertonic saline 4 ml twice daily for 48 weeks 0.5% saline (control) twice daily for 48 weeks Quinine sulfate was added to each solution to mask the taste and a bronchodilator was given prior to each dose.	Primary endpoint: Rate of change in lung function, as reflected by FVC, FEV₁, and forced expiratory flow at 25 to 75% of FVC during the 48 weeks of treatment. Secondary endpoints: • Number and duration of pulmonary exacerbations. • Total days of antibiotics. • Absenteeism. • Weight and BMI. • Quality of life. • Quantitative microbiology of sputum, cytokine assays of sputum. • Adverse events.

Results:

Primary: The FEV1 fell by a mean of 94 ml in the hypertonic saline group and 16 ml in the control group. FVC and FEV1 appeared to increase during the first four weeks of treatment with hypertonic saline but remained essentially unchanged in the control group. Thereafter, lung function plateaued in the hypertonic-saline group, and a difference in lung function favoring hypertonic saline persisted at all subsequent times. The linear slope of lung function, incorporating FEV1, FVC, and FEF25–75 into a single model, through all times from 0 weeks (baseline) to 48 weeks revealed no significant difference between the two groups ($P = 0.79$). However, the absolute level of lung function, averaged over the period from 4 weeks to 48 weeks after randomization, was higher in the hypertonic-saline group than the control group ($P = 0.03$).

Secondary:

- The mean number of exacerbations per participant in the control group was 0.89, as compared with 0.39 in the hypertonic saline group (difference, 0.5; $p = 0.02$).
- The mean number of days on which participants met this exacerbation definition was 17 days in the control group and 6 days in the hypertonic saline group (difference, 11 days; $p = 0.02$).
- The interval during which participants remained free of exacerbations was significantly longer in the hypertonic saline group than in the control group ($P = 0.03$), with a 48-week exacerbation-free survival rate of 76% in the hypertonic saline group and 62 % in the control group.
- When exacerbations were defined according to signs and symptoms alone, regardless of treatment, results again favored the hypertonic saline group. The mean number of exacerbations defined in this way was 2.74 per participant in the control group and 1.32 in the hypertonic saline group (difference, 1.42; $p < 0.001$).

- The median number of antibiotic-days for exacerbations was 50 in the control group and 11 in the hypertonic saline group; $p < 0.001$.
- Participants in the hypertonic-saline group had significantly fewer days on which they were absent from school or work or unable to participate in other, usual activities: 7 days as compared with 24 in the control group ($p < 0.001$).
- There was no significant difference in weight or body-mass index between the groups. The number of hospitalizations and unscheduled visits to the hospital also did not differ significantly between groups.
- The incidence of acquisition of *P. aeruginosa*, *S. aureus*, *B. cepacia*, *Stenotrophomonas maltophilia*, *Candida albicans*, *aspergillus* species, and *Haemophilus influenzae* did not differ significantly between groups.
- There were significantly fewer adverse events in the hypertonic-saline group than the control group (mean, 2.89 vs. 5.17 per 336 days; $P < 0.001$). However, adverse drug reactions (i.e., adverse events that in the opinion of the examining investigator were directly and temporally related to the inhalation of the trial solution) were significantly more common in the hypertonic saline group ($p = 0.001$).

Conclusion:

Hypertonic saline preceded by a bronchodilator is an inexpensive, safe, additional therapy in patients with cystic fibrosis.

Citation	Design	Endpoints
Wark P and McDonald VM. Nebulized hypertonic saline for cystic fibrosis. Cochrane Database Syst Rev. 2018 Sep 27;9:CD001506. doi: 10.1002/14651858.CD001506.pub4.	N=966 participants age 4 months to 63 years with cystic fibrosis in 17 controlled trials. Inclusion criteria: All controlled trials in any language assessing the effect of hypertonic saline compared to placebo, or other mucolytic therapy, for any duration or dose regimen in people with cystic fibrosis of any age or severity.	Objective: To investigate the effects of treatment with nebulized hypertonic saline on people with CF compared to placebo or other treatments that enhance mucociliary clearance.

Results:

14 of the 17 trials were assessed to have high risk for bias, as participants could discern taste of the saline.

Hypertonic saline 3% to 7% versus placebo: At four weeks, very low-quality evidence from three placebo-controlled trials ($n = 225$) found that hypertonic saline increased the mean change from baseline FEV₁ (% predicted) by 3.44%, but there was no difference between groups in lung clearance index in one small trial ($n = 10$). By 48 weeks the effect was slightly smaller in one trial ($n = 134$), 2.31%. One trial found 0.5 fewer exacerbations requiring antibiotics per person in the hypertonic saline group; the second trial found no difference between groups (low-quality evidence). The rates of different adverse events could not be determined due to insufficient evidence reporting. There was low-quality evidence in four trials hypertonic saline improved sputum clearance.

Hypertonic saline versus mucus mobilizing treatments: There was insufficient evidence from one three-week trial to determine the effects of hypertonic saline vs recombinant deoxyribonuclease (rhDNase) on FEV₁ % predicted (very low-quality evidence). In another trial, rhDNase led to a greater increase in FEV₁ % predicted than hypertonic saline at 12 weeks in participants with moderate to severe lung disease (low-quality evidence). One cross-over trial reported 15 exacerbations during treatment with hypertonic saline and 18 exacerbations in the rhDNase group (low-quality evidence). Increased cough was reported in 13 participants using hypertonic saline and 17 on daily rhDNase in one cross-over trial of 47 people (low-quality evidence). There was insufficient evidence to assess rates of other adverse events reported. One trial (12 participants) compared hypertonic saline to amiloride and one to sodium-2-mercaptoethane sulfonate. Neither trial found a difference between treatments in any measures of sputum clearance; additionally the comparison of hypertonic saline and sodium-2-mercaptoethane sulfonate reported no differences in courses of antibiotics or adverse

events (very low-quality evidence). One trial compared hypertonic saline to mannitol but did not report lung function at relevant time points for this review; there were no differences in sputum clearance, but mannitol was reported to be more 'irritating' (very low-quality evidence).

Conclusion:

Nebulized hypertonic saline improves lung function in the short term (4 weeks) according to clinical trials but the effects do not appear to be sustained after 48 weeks. Most of the evidence was low or very low quality. In comparison to DNase it may be less effective at improving lung function after three months. Nebulized hypertonic saline reduced the frequency of pulmonary exacerbations and may have a small effect on improvement in quality of life in adults, but the same was not found in children under 6 years. rhDNase has questionable improvement in lung function at three months in children. Hypertonic saline as an adjunct to physiotherapy during acute exacerbations of lung disease in adults was found to be effective, but very low to moderate quality evidence supports this.

Formulary Placement, Utilization and Cost Experience (10-01-2025 to 12-31-2025)

UTILIZATION HISTORY			COST			PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Cost/ Month^	Total	Approved (%)	Current	Recommend
CF Transmembrane Conductance Regulator Potentiators									
Trikafta® (elexacaftor/tezacaftor/ivacaftor) 100-50-75 mg/150 mg, 50-25-37.5 mg/75 mg tablets	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Trikafta® 100-50-75 mg/75 mg, 80-40-60 mg/59.5 mg packet, oral granules	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change
Kalydeco® (ivacaftor) 150 mg tablet	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Kalydeco® (ivacaftor) 5.8, 13.4, 25, 50, 75 mg oral granules	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Orkambi® (lumacaftor/ivacaftor) 100-125, 150-188 mg granule packet	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Orkambi® (lumacaftor/ivacaftor) 100-125, 200-125 mg tablet	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Symdeko® (tezacaftor/ivacaftor) 50-75 mg, 100-150 mg tablets	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Alyftrek® (vanzacaftor/tezacaftor/deutivacaftor) 4-20-50 mg, 10-50-125 mg tablets	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Inhaled Antibiotics									
Arikayce® (amikacin liposome) 590 mg/8.4 mL inhalation suspension	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Cayston® (aztreonam lysine) 75 mg/mL vial for nebulization	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Bethkis® (tobramycin) 300 mg/4 mL ampule for nebulization	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change
TOBI® Podhaler (tobramycin) 28 mg capsule, capsule with inhalation device	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
tobramycin (TOBI®, Kitabis Pak®) 300 mg/5 mL ampule for nebulization	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Mucolytics									
acetylcysteine (Mucomyst-10®) 100 mg/mL vial	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change
acetylcysteine (Mucomyst-20®) 200 mg/mL vial	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change

Pulmozyme® (dornase alfa) 1 mg/mL inhalation solution	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Bronchitol® (mannitol) 40 mg inhalation capsules	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
sodium chloride for inhalation (Nebusal®) 3% vial for nebulization	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change
Nebusal® (sodium chloride for inhalation 6% vial for nebulization	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change
Hyper-Sal® (sodium chloride for inhalation) 3.5% vial for nebulization	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change
sodium chloride for inhalation (Hyper-Sal®, Pulmosal™) 7% vial for nebulization	0	0	\$0.00	\$0.00	\$0.00	0	0 (0%)	NF	No change
TOTAL	0	0	\$0.00	\$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 = Excluded

Prior Authorization Criteria

Recommendation: No changes

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 Causton (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	<u>Initial criteria for the use of Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), Symdeko (tezacaftor/ivacaftor), Trikafta (elexacaftor/tezacaftor/ivacaftor), or Alyftrek (vanzacaftor/tezacaftor/deutivacaftor)</u> - 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 <u>Re-authorization criteria for the use of Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), Symdeko (tezacaftor/ivacaftor), Trikafta (elexacaftor/tezacaftor/ivacaftor), or Alyftrek (vanzacaftor/tezacaftor/deutivacaftor)</u>

	• 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. <u>Initial criteria for the use of inhaled tobramycin (Bethkis,Tobi, Kitabis Pak), Pulmozyme (dornase alfa), Tobi Podhaler</u> • 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. <u>Re-authorization criteria for the use of inhaled tobramycin (Bethkis,Tobi, Kitabis Pak), Pulmozyme (dornase alfa), Tobi Podhaler</u> • 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 <u>Initial criteria for the use of Cayston (aztreonam lysine)</u> • 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 <u>Re-authorization criteria for the use of Cayston (aztreonam lysine)</u> • 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) <u>Initial criteria for the use of Bronchitol</u> • 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 <u>Re-authorization criteria for the use of Bronchitol</u>

	- 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, 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 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	<u>3/20253/2026</u>

References

1. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013;187(7):680-689. Accessed on July 28, 2020.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic Fibrosis Foundation pulmonary guideline. Pharmacologic approaches to prevention and eradication of initial *Pseudomonas aeruginosa* infection. *Ann Am Thorac Soc*. 2014;11(10):1640-1650.
3. U.S Department of Health & Human Services NIH Research Portfolio Online Reporting Tools (RePORT). Cystic Fibrosis. Available at <https://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=36>. Accessed January 22, 2018.
4. Cystic Fibrosis Foundation. 2024 Patient Registry Reports. Available at: <https://www.cff.org/managing-cf/understanding-changes-life-expectancy>. Accessed November 10, 2025.
5. MacKenzie T, Gifford AH, Sabadosa K, et al. Longevity of patients with cystic fibrosis in 2000 to 2010 and beyond: survival analysis of the Cystic Fibrosis Foundation patient registry. *Ann Intern Med*. 2014;161(4):233-241.
6. Deeks ED. Lumacaftor/ivacaftor: a review in cystic fibrosis. *Drugs*. 2016;76(12):1191-1201.
7. Flume PA, Mogayzel PJ, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Treatment of pulmonary exacerbations. *Am J Respir Crit Care Med*. 2009;180(9):802-808.
8. Henke MO, Ratjen F. Mucolytics in cystic fibrosis. *Paediatr Respir Rev*. 2007;8(1):24-29.
9. Wark P and McDonald VM. Nebulised hypertonic saline for cystic fibrosis. *Cochrane Database Syst Rev*. 2018 Sep 27;9:CD001506. doi: 10.1002/14651858.CD001506.pub4.
10. Yang C, Montgomery M. Dornase alfa for cystic fibrosis. *Cochrane Database Syst Rev*. 2018 Sep 6;9:CD001127. doi: 10.1002/14651858.CD001127.pub4.
11. Tam J, Nash EF, Ratjen F, Tullis E, Stephenson A. Nebulized and oral thiol derivatives for pulmonary disease in cystic fibrosis. *Cochrane Database Syst Rev*. 2013 Jul 12;(7):CD007168. doi: 10.1002/14651858.CD007168.pub3.
12. Assael BM, Pressler T, Bilton D, et al. Inhaled aztreonam lysine vs. inhaled tobramycin in cystic fibrosis: a comparative efficacy trial. *J Cyst Fibros*. 2013;12(2):130-140.
13. Konstan MW, Flume PA, Kappler M, et al on behalf of the EAGER study investigators. Safety, efficacy and convenience of tobramycin inhalation powder in cystic fibrosis patients: the EAGER trial. *J Cyst Fibros*. 2011;10(1):54-61.
14. Konstan MW, Geller DE, Minic P, Brockhaus F, Zhang J, Angyalosi G. Tobramycin inhalation powder for *P. aeruginosa* infection in cystic fibrosis: the EVOLVE trial. *Pediatr Pulmonol*. 2011;46(3):230-238.
15. Treggiari MM, Retsch-Bogart G, Mayer-Hamblett N, et al. Comparative efficacy and safety of four randomized regimens to treat early *Pseudomonas aeruginosa* infection in children with cystic fibrosis. *Arch Pediatr Adolesc Med*. 2011;165(9):847-856.
16. Ratjen F, Munck A, Kho P, Angyalosi G, for the ELITE study group. Treatment of early *Pseudomonas aeruginosa* infection in patients with cystic fibrosis: the ELITE trial. *Thorax*. 2010;65(4):286-291.
17. Retsch-Bogart GZ, Quittner AL, Gibson RL, et al. Efficacy and safety of inhaled aztreonam lysine for airway *Pseudomonas* in cystic fibrosis. *Chest*. 2009;135(5):1223-1232.
18. McCoy KS, Quittner AL, Oerman CM, Gibson RL, Retsch-Bogart GZ, Montgomery B. Inhaled aztreonam lysine for chronic airway *Pseudomonas aeruginosa* in cystic fibrosis. *Am J Respir Crit Care Med*. 2008;178(9):921-928.
19. Moss RB, Flume PA, Elborn JS, et al on behalf of the KONDUCT study group. Efficacy and safety of ivacaftor treatment: randomized trial in subjects with cystic fibrosis who have an R117H-CFTR mutation. *Lancet Respir Med*. 2015;3(7):524-533.
20. Wainwright CE, Elborn JS, Ramsey BW, et al for the TRAFFIC and TRANSPORT study groups. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for the Phe508del CFTR. *N Engl J Med*. 2015;373(3):220-231.
21. De Boeck K, Munck A, Walker S, et al. Efficacy and safety of ivacaftor in patients with cystic fibrosis and a non-G551D gating mutation. *J Cyst Fibros*. 2014;13(6):674-680.
22. McKone EF, Borowitz D, Drevinek P, et al on behalf of the PERSIST study group. Long-term safety and efficacy of ivacaftor in patients with cystic fibrosis who have the Gly551Asp-CFTR mutation: a phase 3, open-label extension study (PERSIST). *Lancet Respir Med*. 2014;2(11):902-910.
23. Davies JC, Wainwright CE, Canny GJ, et al on behalf of the ENVISION study group. Efficacy and safety of ivacaftor in patients aged 6 to 11 years with cystic fibrosis with a G551D mutation. *Am J Respir Crit Care Med*. 2013;187(11):1219-1225.
24. Ramsey BW, Davies J, McElvaney NG, et al for the VX08-770-102 study group. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. *N Engl J Med*. 2011;365(18):1663-1672.
25. Mayer M. Lumacaftor-ivacaftor (Orkambi) for cystic fibrosis: behind the “breakthrough”. *Evid Based Med*. 2016;21(3):83-86.
26. Taylor-Cousar JL, Munck A, McKone E, et al. Tezacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del. *N Engl J Med*. 2017;377(21):2013-23.
27. Rowe SM, Daines C, Ringshausen FC, et al. Tezacaftor-ivacaftor in residual-function heterozygotes with cystic fibrosis. *N Engl J Med*. 2017;377(21):2024-35.

28. Elkins MR, Robinson M, Rose BR, et al. A controlled trial of long-term inhaled hypertonic saline in patients with cystic fibrosis. *N Engl J Med*. 2006;354(3): 229-240.
29. Institute for Clinical and Economic Review (ICER). Cystic Fibrosis: Final Evidence Report. Available at <https://icer-review.org/material/cf-final-report/>. Accessed on 12/08/2025.
30. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>. Accessed on 12/08/2025.
31. Biomedtracker. Cambridge, MA: Informa Business Intelligence, Inc. <https://www.biomedtracker.com/>. Accessed on 12/08/2025.
32. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: <https://clinicaltrials.gov/>. Accessed on 12/08/2025.
33. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: <https://www.ncbi.nlm.nih.gov/pubmed>. 12/08/2025.
34. Micromedex® (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: <http://www.micromedexsolutions.com/>. Accessed on 12/08/2025.
35. IPD Analytics. Bay Harbor Islands, Florida: IPD Analytics, LLC. <http://www.ipdanalytics.com>. Accessed on 12/08/2025.
36. "DailyMed." DailyMed. N.p., n.d. Web. Available at <https://dailymed.nlm.nih.gov/dailymed/>. Accessed on 12/08/2025.
37. Ren C, Morgan R, Oermann C, et al. Cystic Fibrosis Pulmonary Guidelines: Use of CFTR Modulator Therapy in Patients with Cystic Fibrosis. *Ann Am Thorac Soc*. 2018 Mar. doi: 10.1513/AnnalsATS.201707-539OT.PMID: 29342367. Accessed on 12/08/2025.
38. Floto RA, Olivier KN, Saiman L, Daley CL, Herrmann JL, Nick JA, Noone PG, Bilton D, Corris P, Gibson RL, Hempstead SE, Koetz K, Sabadosa KA, Sermet-Gaudelus I, Smyth AR, van Ingen J, Wallace RJ, Winthrop KL, Marshall BC, Haworth CS, U.S. Cystic Fibrosis Foundation and European Cystic Fibrosis Society. U.S. Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of nontuberculous mycobacteria in individuals with cystic fibrosis. *Thorax*. 2016;71:i1-i22. Accessed on 12/08/2025.
39. Tice JA, Kuntz KM, Wherry K, Chapman R, Seidner M, Pearson SD, Rind DM. Modulator Treatments for Cystic Fibrosis: Effectiveness and Value; Evidence Report. Institute for Clinical and Economic Review, April 27, 2020. <https://icer-review.org/material/cystic-fibrosis-2-evidence-report/>. Accessed on 12/08/2025.
40. Keating C, Yonker LM, Vermeulen F, et al. Vanzacaftor-tezacaftor-deutivacaftor versus elexacaftor-tezacaftor-ivacaftor in individuals with cystic fibrosis aged 12 years and older (SKYLINE Trials VX20-121-102 and VX20-121-103): results from two randomized, active-controlled, phase 3 trials. *Lancet Respir Med*. 2025;13(3):256-271. doi:10.1016/S2213-2600(24)00411-9.
41. Barry PJ, Mall MA, Álvarez A, et al. Triple Therapy for Cystic Fibrosis *Phe508del*-Gating and -Residual Function Genotypes. *N Engl J Med*. 2021;385(9):815-825. doi:10.1056/NEJMoa2100665.



Antihistamines, First Generation

Executive Summary

Class Overview

First-generation antihistamines have been used reliably for decades to treat a variety of histamine-mediated disorders such as allergic rhinitis, urticaria, and motion sickness. They are also used as premedication to prevent anaphylactic reactions prior to intravenous infusions, including some chemotherapy regimens. These drugs are available in prescription and over-the-counter formulations at a relatively low cost. While still used for a wide variety of ailments, they are often recommended as alternatives to first-line therapies (i.e. second-generation antihistamines) due to significant adverse events. This may include sedation, urinary retention, mental confusion, and other anticholinergic effects. Due to the paucity of new data and lack of new drug releases, this review will focus on consensus guidelines and systematic reviews.

Utilization Findings

There were 135 claims for 101 members, for a total cost of \$892.74, and an average cost per claim of \$6.61. The most highly utilized medication was Hydroxyzine tablets with 78 claims, followed by Promethazine-DM oral syrup with 28 claims. There were no prior authorization requests.

Recommendations

- No changes

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 10-30% of individuals in the United States, with the prevalence increasing particularly in urban areas. Urticaria, or hives, involves pruritic erythematous plaques sometimes accompanied with angioedema and has a prevalence of 20% in the general population. 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 and is 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 mucous 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 increases venular permeability, gastric acid secretion, and airway mucous 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, respiratory tract, and central nervous system, leading to their anticholinergic and sedative effects. 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.

First generation antihistamines are indicated for many allergic, histamine-mediated conditions such as allergic rhinitis, conjunctivitis, urticaria, as an adjunct for treating anaphylactic reactions, premedication for IV infusions, and nausea and vomiting related to motion sickness, anesthesia, and labor. Unlike second generation antihistamines, they are lipophilic and readily cross the blood brain barrier, leading to somnolence. This may be beneficial for patients who suffer from exacerbations of pruritis at bedtime. While not recommended by the American Academy of Sleep Medicine, diphenhydramine is also used routinely in the treatment of chronic insomnia. Daytime sedation may be hazardous for some patient populations (e.g. elderly). Due to unfavorable adverse effect profiles, first generation antihistamines are generally reserved for more severe allergic reactions, prophylaxis, or in scenarios where somnolence is not concerning or desired. However, this class is preferred in the treatment and prevention of infusion reactions, motion sickness, and severe allergic reactions.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
Single-Drug First Generation Antihistamine Products		
Doxylamine (Nighttime Sleep-Aid, Sleep Aid, Unisom®, Wal-Som®) 25 mg oral tablet	Insomnia, sleep onset or sleep maintenance	Insomnia, sleep onset or sleep maintenance: 25 mg once daily 30 minutes before bedtime, as needed.
Diphenhydramine (Aler-Caps®, Allergy, Allergy Medication, Allergy Relief, Banophen®, Benadryl®, Complete Allergy, Wal-Dryl® Allergy, Pharmedryl®) 25 mg, 50 mg oral capsule Diphenhydramine (Alka-Seltzer Plus Allergy, Aller-G-Time, Allergy, Allergy Medicine, Allergy Relief, Banophen®, Benadryl® Allergy, Complete Allergy, Diphen®, Geri-Dryl®, Total Allergy, Wal-Dryl® Allergy) 25 mg oral tablet, caplet, minitab Diphenhydramine (Children's Allergy Relief, Allergy Relief) 12.5, 25 mg chewable tablet Diphenhydramine (Allergy, Allergy Relief, Children's Allergy, Children's Benadryl® Allergy, Children's Wal-Dryl®, Diphedryl®, Geri-Dryl®, M-Dryl®, MAXAllergy™ Kids) 12.5 mg/5 mL oral solution Diphenhydramine (Naramin®) 12.5 mg/5 mL oral liquid in packet Diphenhydramine (Diphen®) 12.5 mg/5 mL oral elixir, cup Diphenhydramine 50 mg/mL IV syringe Diphenhydramine (Children's Allergy Relief, Children's Wal-Dryl® Allergy) 12.5 mg orally disintegrating tablet	- Symptomatic relief of allergic symptoms caused by histamine release including nasal allergies and allergic dermatosis - Antitussive - Insomnia, occasional - Prevention or treatment of motion sickness - Management of Parkinsonian syndrome including drug-induced extrapyramidal symptoms (dystonic reactions) alone or in combination with centrally acting anticholinergic agents - Anaphylaxis, severe [adjunct to epinephrine; second-line (off-label)]	Allergic reactions: 25-50 mg every 4 to 8 hours; max 300 mg daily Rhinitis, sneezing due to common cold: 25 to 50 mg every 4 to 6 hours; maximum 300 mg daily Antitussive: 25 mg every 4 hours; maximum 150 mg daily Insomnia, occasional: 50 mg at bedtime Motion sickness treatment or prophylaxis: 25-50 mg every 6 to 8 hours (take 30 minutes prior to motion for prophylaxis) Parkinsonism: 25 to 50 mg 3 or 4 times daily Anaphylaxis, severe [adjunct to epinephrine; second-line (off-label)]: IV: 25-50 mg over 10-15 minutes IM, IV (Parkinsonism, allergic reactions): 10 to 50 mg per dose; single doses up to 100 mg may be used if needed; not to exceed 400 mg daily

Medication	Indications	Dosing/Administration
Diphenhydramine (NightTime Sleep Aid, Sleep Aid, Sleep Time, Unisom® SleepMinis, Wal-Sleep Z, ZzzQuil®, NightTime Sleep Gel, Unisom® SleepGels, Wal-Som®) 25, 50 mg oral capsule, softgel Diphenhydramine (NightTime Sleep Aid, Nytol QuickCaps®, Rest Simply, Simply Sleep, Sleep Aid, Sleep II, Sleep-Tabs, Sominex®, Sominex® Maximum Strength) 25 mg oral tablet, caplet Diphenhydramine (Sleep Aid, Sleep Time, Wal-Sleep Z, ZzzQuil®) 50 mg/30 mL oral solution Diphenhydramine (Unisom® SleepMelts, Wal-Sleep Z) 25 mg orally disintegrating tablets		
Hydroxyzine HCL 10 mg, 25 mg, 50 mg oral tablet Hydroxyzine HCL 10 mg/5 mL oral syrup Hydroxyzine HCL intramuscular solution 25 mg/mL, 50 mg/mL Hydroxyzine pamoate 25 mg, 50 mg, 100 mg oral capsule	• Antiemetic • Anxiety • Peripartum adjunct • Pruritis	• Antiemetic: 25 - 100 mg/dose IM • Anxiety: 50 -100 mg PO 4 times daily or 50-100 mg IM every 4 to 6 hours as needed • Peripartum adjunct: 25-100 mg IM • Perioperative adjunct: 50-100 mg PO or 25-100 mg IM one time • Pruritus: 25 mg PO 3 to 4 times a day

Medication	Indications	Dosing/Administration
Carbinoxamine 4 mg oral tablet Carbinoxamine (Ryvent®) 6 mg oral tablet Carbinoxamine 4 mg/5 mL oral liquid	• Symptomatic treatment of seasonal and perennial allergic rhinitis • Vasomotor rhinitis • Allergic conjunctivitis • Mild, uncomplicated allergic skin manifestations of urticaria and angioedema • Dermatographism • As adjunctive therapy for anaphylactic reactions • Amelioration of the severity of allergic reactions to blood or plasma	• Immediate release: 4-8 mg 3-4 times daily • Extended release: 6-16 mg every 12 hours
Promethazine 12.5, 25, 50 mg oral tablet Promethazine (Phenergan®) 25 mg/mL, 50 mg/mL IV ampule Promethazine 6.25 mg/5 mL oral syrup Promethazine (Promethegan™) 12.5 mg, 25 mg, 50 mg rectal suppository	• Perennial and seasonal allergic rhinitis • Vasomotor rhinitis • allergic conjunctivitis due to inhalant allergens and foods • mild, uncomplicated allergic skin manifestations of urticaria and angioedema • amelioration of allergic reactions to blood or plasma • Dermographism • Adjunct therapy for anaphylactic reactions • Prevention and control of nausea and vomiting associated with anesthesia and surgery • Active and prophylactic treatment of motion sickness • Surgical analgesia/hypnotic, pre-post-op adjunct • Sedation • Preop, postop, and obstetric sedation • Nausea and vomiting of pregnancy (off-label)	• Allergic conditions, treatment: oral, rectal: 25 mg at bedtime or 12.5 mg before meals and at bedtime (usual range: 6.25 to 12.5 mg 3 times daily); IM, IV: 25 mg, may repeat in 2 hours when necessary • Motion sickness: oral, rectal: 25 mg 30 to 60 minutes before departure; repeat 8 to 12 hours later as needed; maintenance: 25 mg twice daily • Nausea and vomiting (including pregnancy): Oral, IM, IV, rectal: 12.5-25 mg every 4 to 6 hours as needed • Labor, adjunct to analgesia: IM, IV: Early labor: 50 mg; Established labor: 25-75 mg in combination with analgesic at reduced dosage; may repeat every 4 hours for up to 2 additional doses; max: 100 mg/day while in labor • Surgical analgesia/hypnotic; pre-/postoperative adjunct: IM, IV: 25-50 mg in combination with analgesic or hypnotic (at reduced dosage) • Sedation: Oral, IM, IV, rectal: 25-50 mg/dose

Medication	Indications	Dosing/Administration
Cyproheptadine 4 mg oral tablet Cyproheptadine 2 mg/5 mL, 4 mg/10 mL oral syrup	• Perennial and seasonal allergic rhinitis • Vasomotor rhinitis • allergic conjunctivitis • Mild, uncomplicated allergic skin manifestations of urticaria and angioedema • Amelioration of allergic reactions to blood or plasma • Cold urticaria • Dermatographism • Adjunctive anaphylactic therapy • Decreased appetite secondary to chronic disease (off-label) • Serotonin syndrome (off-label) • Spacticity associated with spinal cord damage (off-label)	• Allergic conditions: 4 mg three times daily; maintenance: 4-20 mg daily in divided doses; max 0.5 mg/kg/day • Decreased appetite secondary to chronic disease (off-label): 2 mg four times per day for one week, then 4 mg four times per day • Serotonin syndrome (off-label): 12 mg one time, then 2 mg every 2 hours or 4-8 mg every 6 hours as needed for symptom control • Spacticity associated with spinal cord damage (off-label): 2-4 mg every 8 hours; max 8 mg every 8 hours
Dexbrompheniramine (Ala-Hist® IR) 2 mg oral tablet Dexbrompheniramine (Pediavent®) 2 mg/5 mL oral liquid Dexchlorpheniramine (Ryclora®) 2 mg/5 mL oral solution	• Symptomatic treatment of seasonal and perennial allergic rhinitis or upper respiratory allergies	• Allergic rhinitis: 2 mg every 4 to 6 hours; max 18 mg/day
Tripolidine (Flonase® Night Allergy Relief) oral tablet 2.5 mg Tripolidine (Miclara® LQ) 1.25 mg/5 mL, 2.5 mg/5 mL oral syrup Tripolidine (PediaClear® PD, Histex® PD, Histex® PDX) 0.625 mg/mL, 0.938 mg/mL, 1.25 mg/mL oral drops Tripolidine (Histex®) 2.5 mg/5 mL oral syrup	• Symptomatic treatment of seasonal and perennial allergic rhinitis or upper respiratory allergies	• Allergies: 2.5 mg every 4 to 6 hours; max: 10 mg/day

Medication	Indications	Dosing/Administration
Chlorpheniramine (Aller-Chlor, Allergy, Allergy Relief, ChlorHist®, Pharbechlor®, Wal-Finate) 4 mg oral tablet Chlorpheniramine 12 mg oral tablet Chlorpheniramine (Ed Chlorped® Jr) 2 mg/5 mL oral syrup	• Allergic symptoms • Symptomatic treatment of seasonal and perennial allergic rhinitis • Urticaria • Pruritis • Motion sickness (off-label)	• Immediate release: 4 mg every 4 to 6 hours; max 24 mg in 24 hours • Extended release: 12 mg every 12 hours; max 24 mg in 24 hours
Clemastine (Dayhist® Allergy) 1.34 mg, 2.68 mg oral tablet Clemastine 0.5 mg/5 mL oral syrup	• Symptomatic treatment of seasonal and perennial allergic rhinitis • Urticaria/angioedema • Common cold, hay fever, upper respiratory allergies (OTC labeling)	• 1.34 mg twice daily; may be increased as needed to a max of 2.68 mg three times a day (8.04 mg/day) • OTC labeling: 1.34 mg twice daily; max 2.68 mg/day
Pyrilamine (PediaClear-8®) 12.5 mg/15 mL oral syrup	• Temporarily relieves runny nose and alleviates sneezing, itching of the nose or throat, and itchy, watery eyes due to hay fever or other upper respiratory allergies.	• Children 6 to under 12 years: 30 mL (2 dose cups) every 6 to 8 hours, not to exceed 4 doses in 24 hours, or as directed by a doctor
Prescription-Only First Generation Antihistamine Combination Products		
Promethazine-codeine oral solution 6.25-10 mg/5 mL	• Cough and upper respiratory symptoms	• Cough and upper respiratory symptoms: 5 mL every 4 to 6 hours (maximum: 30 mL [codeine 60 mg/promethazine 37.5 mg/phenylephrine 30 mg] per 24 hours).
Brompheniramine-pseudoephedrine-dextromethorphan (BIO Dtuss DMX, Bromfed® DM) 1 mg-30 mg-10 mg/5 mL, 2 mg-30 mg-10 mg/5 mL oral syrup	• Cough and upper respiratory symptoms	• Cough and upper respiratory symptoms: Brompheniramine 2 mg, pseudoephedrine 30 mg, and dextromethorphan 10 mg per 5 mL: 10 mL every 4 hours (maximum: 60 mL/24 hours)
Promethazine/dextromethorphan (promethazine-DM) 6.25 mg-15 mg/5 mL oral syrup	• Cough and upper respiratory symptoms:	• Cough and upper respiratory symptoms: 5 mL every 4 to 6 hours; maximum: 30 mL in 24 hours

Boxed Warnings and Contraindications

Medication	Boxed Warnings	Contraindications
Single-Drug First Generation Antihistamine Products		
Doxylamine (Nighttime Sleep-Aid, Sleep Aid, Unisom®, Wal-Som®) 25 mg oral tablet	None	Do not use in children <12 years of age.
Diphenhydramine (Aler-Caps®, Allergy, Allergy Medication, Allergy Relief, Banophen®, Benadryl®, Complete Allergy, Wal-Dryl® Allergy, Pharbedryl®) 25 mg, 50 mg oral capsule Diphenhydramine (Alka-Seltzer Plus Allergy, Aller-G-Time, Allergy, Allergy Medicine, Allergy Relief, Banophen®, Benadryl® Allergy, Complete Allergy, Diphen®, Geri-Dryl®, Total Allergy, Wal-Dryl® Allergy) 25 mg oral tablet, caplet, minitab Diphenhydramine (Children's Allergy Relief, Allergy Relief) 12.5, 25 mg chewable tablet Diphenhydramine (Allergy, Allergy Relief, Children's Allergy, Children's Benadryl® Allergy, Children's Wal-Dryl®, Diphedryl®, Geri-Dryl®, M-Dryl®, MAXAllergy™ Kids) 12.5 mg/5 mL oral solution Diphenhydramine (Naramin®) 12.5 mg/5 mL oral liquid in packet Diphenhydramine (Diphen®) 12.5 mg/5 mL oral elixir, cup Diphenhydramine 50 mg/mL IV syringe	None	- Neonates or premature infants - Breast-feeding - When used for self-medication, do not use in children <6 years, to make a child sleep, or with any other diphenhydramine-containing products

Medication	Boxed Warnings	Contraindications
Diphenhydramine (Children's Allergy Relief, Children's Wal-Dryl® Allergy) 12.5 mg orally disintegrating tablet Diphenhydramine (NightTime Sleep Aid, Sleep Aid, Sleep Time, Unisom® SleepMinis, Wal-Sleep Z, ZzzQuil®, NightTime Sleep Gel, Unisom® SleepGels, Wal-Som®) 25, 50 mg oral capsule, softgel Diphenhydramine (NightTime Sleep Aid, Nytol QuickCaps®, Rest Simply, Simply Sleep, Sleep Aid, Sleep II, Sleep-Tabs, Sominex®, Sominex® Maximum Strength) 25 mg oral tablet, caplet Diphenhydramine (Sleep Aid, Sleep Time, Wal-Sleep Z, ZzzQuil®) 50 mg/30 mL oral solution Diphenhydramine (Unisom® SleepMelts, Wal-Sleep Z) 25 mg orally disintegrating tablets		
Hydroxyzine HCL 10 mg, 25 mg, 50 mg oral tablet Hydroxyzine HCL 10 mg/5 mL oral syrup Hydroxyzine HCL intramuscular solution 25 mg/mL, 50 mg/mL Hydroxyzine pamoate 25 mg, 50 mg, 100 mg oral capsule	None	- Early pregnancy - Prolonged QT interval - Hypersensitivity to cetirizine or levocetirizine - Injection should not be used SQ, IA, or IV
Carbinoxamine 4 mg oral tablet Carbinoxamine (Ryvent®) 6 mg oral tablet Carbinoxamine 4 mg/5 mL oral liquid	None	- Coadministration with monoamine oxidase inhibitors (MAOIs) - Children <2 years of age - Breast-feeding women

Medication	Boxed Warnings	Contraindications
Promethazine 12.5, 25, 50 mg oral tablet Promethazine (Phenergan®) 25 mg/mL, 50 mg/mL IV ampule Promethazine 6.25 mg/5 mL oral syrup Promethazine (Promethegan™) 12.5 mg, 25 mg, 50 mg rectal suppository	- Respiratory depression in pediatric patients: Promethazine should not be used in pediatric patients younger than 2 years because of the potential for fatal respiratory depression - Severe tissue injury including gangrene (injection): Promethazine injection can cause severe chemical irritation and damage to tissues regardless of the route of administration. Due to the risks of intravenous (IV) injection, the preferred route of administration of promethazine is deep intramuscular (IM) injection. SQ injection is contraindicated.	- Coma - Treatment of lower respiratory tract symptoms, including asthma - Children <2 years of age - Intra-arterial or subcutaneous administration
Cyproheptadine 4 mg oral tablet Cyproheptadine 2 mg/5 mL, 4 mg/10 mL oral syrup	None	- Use in newborn or premature infants or breast-feeding mothers - Concomitant use of monoamine oxidase inhibitor therapy - Angle-closure glaucoma - Stenosing peptic ulcer - Symptomatic prostatic hypertrophy - Bladder neck obstruction - Pyloroduodenal obstruction - Elderly, debilitated patients
Dexbrompheniramine (Ala-Hist® IR) 2 mg oral tablet Dexbrompheniramine (Pediavent®) 2 mg/5 mL oral liquid Dexchlorpheniramine (Ryclora®) 2 mg/5 mL oral solution	None	- When used for self-medication, do not use with or within 14 days of stopping an MAOI - Use in newborns or premature infants - Breast-feeding mothers - Treatment of lower respiratory tract symptoms, including asthma - Concomitant MAOI therapy

Medication	Boxed Warnings	Contraindications
Triprolidine (Flonase® Night Allergy Relief) oral tablet 2.5 mg Triprolidine (Miclara® LQ) 1.25 mg/5 mL, 2.5 mg/5 mL oral syrup Triprolidine (PediaClear® PD, Histex® PD, Histex® PDX) 0.625 mg/mL, 0.938 mg/mL, 1.25 mg/mL oral drops Triprolidine (Histex®) 2.5 mg/5 mL oral syrup	None	When used for self-medication, do not use if you are taking sedatives or tranquilizers or with any other triprolidine-containing products
Chlorpheniramine (Aller-Chlor, Allergy, Allergy Relief, ChlorHist®, Pharbechlor®, Wal-Finate) 4 mg oral tablet Chlorpheniramine 12 mg oral tablet Chlorpheniramine (Ed Chlorped® Jr) 2 mg/5 mL oral syrup	None	- Narrow-angle glaucoma - Bladder neck obstruction - Symptomatic prostate hypertrophy - During acute asthmatic attacks - Stenosing peptic ulcer - Pyloroduodenal obstruction - Avoid use in premature and term newborns due to possible association with SIDS
Clemastine (Dayhist® Allergy) 1.34 mg, 2.68 mg oral tablet Clemastine 0.5 mg/5 mL oral syrup	None	- Concomitant use with monoamine oxidase inhibitors - Newborn or premature infants - Breast-feeding women - Lower respiratory tract symptoms (e.g. asthma)
Pyrilamine (PediaClear-8®) 12.5 mg/15 mL oral syrup	None	None
Prescription-Only First Generation Antihistamine Combination Products		

Medication	Boxed Warnings	Contraindications
Promethazine-codeine oral solution 6.25-10 mg/5 mL	- Addiction, abuse, and misuse - Life-threatening respiratory depression - Accidental ingestion - Ultra-rapid metabolism of codeine and other risk factors for life-threatening respiratory depression in children - Promethazine and respiratory depression in children - Risk of medication errors - Interactions with drugs affecting cytochrome P450 isoenzymes: - Risks from concomitant use with benzodiazepines or other CNS depressants - Neonatal opioid withdrawal syndrome	- Idiosyncratic reaction to promethazine or other phenothiazines - Pediatric patients <12 years of age - Postoperative management in pediatric patients <18 years of age who have undergone tonsillectomy and/or adenoidectomy - Significant respiratory depression - Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment - GI obstruction (known or suspected), including paralytic ileus - Narrow angle glaucoma - Urinary retention - Severe hypertension - Severe coronary artery disease - Peripheral vascular insufficiency - Concurrent use with monoamine oxidase inhibitors (MAOIs) or use of MAOIs within the last 14 days
Brompheniramine-pseudoephedrine-dextromethorphan (BIO Dtuss DMX, Bromfed® DM) 1 mg-30 mg-10 mg/5 mL, 2 mg-30 mg-10 mg/5 mL oral syrup	None	- Severe hypertension or coronary artery disease - Concomitant or within 2 weeks of MAO inhibitor therapy - Newborns or premature infants - Breast-feeding - Treatment of lower respiratory tract conditions, including acute asthma
Promethazine/dextromethorphan (promethazine-DM) 6.25 mg-15 mg/5 mL oral syrup	Respiratory depression - Pediatrics: promethazine should not be used in pediatric patients <2 years of age because of the potential for fatal respiratory depression.	- Coma - Treatment of lower respiratory tract symptoms, including asthma - Use with or within 14 days of monoamine oxidase inhibitor therapy - Children <2 years of age

Warnings/Precautions

Medication	Warnings/Precautions
Single-Drug First Generation Antihistamine Products	
Doxylamine (Nighttime Sleep-Aid, Sleep Aid, Unisom®, Wal-Som®) 25 mg oral tablet	Concerns related to adverse effects: • CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving). • Sleeplessness: If sleeplessness persists for >2 weeks, consult health care provider. Disease-related concerns: • Increased intraocular pressure/glaucoma: Use with caution in patients with increased intraocular pressure or angle-closure glaucoma. • Prostatic hyperplasia/urinary obstruction: Use with caution in patients with prostatic hyperplasia and/or GU obstruction. • Respiratory disease: Use with caution in patients with asthma or other chronic breathing disorders. Concurrent drug therapy issues: • Sedatives: Effects may be potentiated when used with other sedative drugs or ethanol. Special populations: • Pediatric: Do not use for insomnia in children <12 years of age. Antihistamines may cause paradoxical excitation in young children.

Medication	Warnings/Precautions
Diphenhydramine (Aler-Caps [®] , Allergy, Allergy Medication, Allergy Relief, Banophen [®] , Benadryl [®] , Complete Allergy, Wal-Dryl [®] Allergy, Pharbedryl [®]) 25 mg, 50 mg oral capsule	• Concerns related to adverse effects: may cause CNS depression • Disease-related concerns: use caution in patients with asthma, cardiovascular disease, increased intraocular pressure/glaucoma, prostatic hyperplasia/urinary obstruction, pyloroduodenal obstruction, thyroid dysfunction • Concurrent drug therapy issues: Potentially significant drug interactions may exist • Dosage form specific issues: some oral liquid products may contain alcohol; some dosage forms may contain sodium benzoate/benzoic acid, a metabolite of benzyl alcohol; large amounts of benzyl alcohol have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; some dosage forms may contain polysorbate 80 (also known as Tweens) which has been associated with hypersensitivity reactions following exposure; some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated hyperosmolality, lactic acidosis, seizures, and respiratory depression; some products may contain phenylalanine; subcutaneous or intradermal use has been associated with tissue necrosis; some preparations contain soy protein • Special populations: may cause excitation in young children • Other warnings/precautions: do not use with other products containing diphenhydramine; oral products are not for OTC use in children <6 years of age
Diphenhydramine (Alka-Seltzer Plus Allergy, Aller-G-Time, Allergy, Allergy Medicine, Allergy Relief, Banophen [®] , Benadryl [®] Allergy, Complete Allergy, Diphen [®] , Geri-Dryl [®] , Total Allergy, Wal-Dryl [®] Allergy) 25 mg oral tablet, caplet, minitab	
Diphenhydramine (Children's Allergy Relief, Allergy Relief) 12.5, 25 mg chewable tablet	
Diphenhydramine (Allergy, Allergy Relief, Children's Allergy, Children's Benadryl [®] Allergy, Children's Wal-Dryl [®] , Diphedryl [®] , Geri-Dryl [®] , M-Dryl [®] , MAXAllergy [™] Kids) 12.5 mg/5 mL oral solution	
Diphenhydramine (Naramin [®]) 12.5 mg/5 mL oral liquid in packet	
Diphenhydramine (Diphen [®]) 12.5 mg/5 mL oral elixir, cup	
Diphenhydramine 50 mg/mL IV syringe	
Diphenhydramine (Children's Allergy Relief, Children's Wal-Dryl [®] Allergy) 12.5 mg orally disintegrating tablet Diphenhydramine (NightTime Sleep Aid, Sleep Aid, Sleep Time,	

Medication	Warnings/Precautions
Unisom® SleepMinis, Wal-Sleep Z, ZzzQuil®, NightTime Sleep Gel, Unisom® SleepGels, Wal-Som®) 25, 50 mg oral capsule, softgel Diphenhydramine (NightTime Sleep Aid, Nytol QuickCaps®, Rest Simply, Simply Sleep, Sleep Aid, Sleep II, Sleep-Tabs, Sominex®, Sominex® Maximum Strength) 25 mg oral tablet, caplet Diphenhydramine (Sleep Aid, Sleep Time, Wal-Sleep Z, ZzzQuil®) 50 mg/30 mL oral solution Diphenhydramine (Unisom® SleepMelts, Wal-Sleep Z) 25 mg orally disintegrating tablets	
Hydroxyzine HCL 10 mg, 25 mg, 50 mg oral tablet Hydroxyzine HCL 10 mg/5 mL oral syrup Hydroxyzine HCL intramuscular solution 25 mg/mL, 50 mg/mL Hydroxyzine pamoate 25 mg, 50 mg, 100 mg oral capsule	• Concerns related to adverse effects: acute generalized exanthematous pustulosis; CNS depression; QT prolongation/torsades de pointes • Disease-related concerns: use caution in patients with increased intraocular pressure/glaucoma, prostatic hyperplasia/urinary obstruction, respiratory disease • Concurrent drug therapy issues: Potentially significant drug interactions may exist • Dose form specific issues: some dosage forms may benzyl alcohol; large amounts of benzyl alcohol have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated hyperosmolality, lactic acidosis, seizures, and respiratory depression • Other warnings/precautions: appropriate administration (IM use only; no SQ, IA, or IV); Severe injection-site reactions have been reported with IM administration (eg, extensive tissue damage, necrosis, gangrene) requiring surgical intervention; the effectiveness of hydroxyzine for long-term use (>4 months) has not been assessed
Carbinoxamine 4 mg oral tablet Carbinoxamine (Ryvent®) 6 mg oral tablet Carbinoxamine 4 mg/5 mL oral liquid	• Concerns related to adverse effects: may cause CNS depression • Disease-related concerns: use caution in patients with asthma, cardiovascular disease, increased intraocular pressure, prostatic hyperplasia/urinary obstruction, pyloroduodenal obstruction, thyroid dysfunction • Concurrent drug therapy issues: Potentially significant drug interactions may exist • Special populations: use is contraindicated in children <2 years of age • Dosage form specific issues: some products may contain sodium metabisulfite, which may cause allergic-type reactions including anaphylaxis and life-threatening or less severe asthmatic episodes, in susceptible patients

Medication	Warnings/Precautions
Promethazine 12.5, 25, 50 mg oral tablet Promethazine (Phenergan®) 25 mg/mL, 50 mg/mL IV ampule Promethazine 6.25 mg/5 mL oral syrup Promethazine (Promethegan™) 12.5 mg, 25 mg, 50 mg rectal suppository	• Concerns related to adverse effects: altered cardiac conduction; anticholinergic effects; CNS depression; extrapyramidal symptoms; neuroleptic malignant syndrome; orthostatic hypotension; photosensitivity; serious tissue injury with injection (boxed warning); impaired core body temperature regulation; • Disease-related concerns: use caution in patients with bone marrow suppression, cardiovascular disease, increased intraocular pressure/glaucoma, hepatic impairment, myasthenia gravis, Parkinson disease, respiratory disease, seizure history or risk • Concurrent drug therapy issues: Potentially significant drug interactions may exist • Special populations: respiratory depression has been reported in children younger than 2 (boxed warning) • Dosage form specific issues: some dosage forms may benzyl alcohol; large amounts of benzyl alcohol have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; injection may contain sodium metabisulfite which may cause allergic reaction
Cyproheptadine 4 mg oral tablet Cyproheptadine 2 mg/5 mL, 4 mg/10 mL oral syrup	• Concerns related to adverse effects: may cause CNS depression; elderly patients may be more susceptible to adverse effects; may cause excitation in young children • Disease-related concerns: use caution in patients with cardiovascular disease, increased intraocular pressure, respiratory disease, thyroid dysfunction • Concurrent drug therapy issues: Potentially significant drug interactions may exist • Special populations: elderly patients may be more susceptible to adverse effects; antihistamines may cause excitation in young children
Dexbrompheniramine (Ala-Hist® IR) 2 mg oral tablet Dexbrompheniramine (Pediavent®) 2 mg/5 mL oral liquid Dexchlorpheniramine (Ryclora®) 2 mg/5 mL oral solution	• Concerns related to adverse effects: may cause CNS depression, which may impair physical or mental abilities • Disease related concerns: use with caution in patients with cardiovascular disease (including hypertension), diabetes, increased intraocular pressure/glaucoma, prostatic hyperplasia/urinary obstruction, respiratory disease, and thyroid dysfunction • Concurrent drug therapy issues: potentially significant drug interactions may exist • Special populations: use with caution in the elderly and pediatric patients • Other warnings/precautions: when used for self-medication (OTC), discontinue use and contact health care provider if symptoms do not improve within 7 days or are accompanied by fever, new symptoms appear, or if nervousness, dizziness or sleeplessness occur

Medication	Warnings/Precautions
Tripolidine (Flonase® Night Allergy Relief) oral tablet 2.5 mg Tripolidine (Miclara® LQ) 1.25 mg/5 mL, 2.5 mg/5 mL oral syrup Tripolidine (PediaClear® PD, Histex® PD, Histex® PDX) 0.625 mg/mL, 0.938 mg/mL, 1.25 mg/mL oral drops Tripolidine (Histex®) 2.5 mg/5 mL oral syrup	• Concerns related to adverse effects: may cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks that require mental alertness (e.g. operating machinery, driving) • Concurrent drug therapy issues: potentially significant drug interactions may exist • Special populations: may cause excitation in children • Dosage form specific issues: Some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated with hyperosmolality, lactic acidosis, seizures, and respiratory depression • Other warnings/precautions: Prior to self-medication (OTC use), contact health care provider if you have breathing problems (e.g. chronic bronchitis, emphysema), glaucoma, or difficulty urinating because of enlarged prostate
Chlorpheniramine (Aller-Chlor, Allergy, Allergy Relief, ChlorHist®, Pharbechlor®, Wal-Finate) 4 mg oral tablet Chlorpheniramine 12 mg oral tablet Chlorpheniramine (Ed Chlorped® Jr) 2 mg/5 mL oral syrup	• Concerns related to adverse effects: may cause CNS depression • Disease-related concerns: use caution in patients with cardiovascular disease, increased intraocular pressure, prostatic hyperplasia/urinary obstruction, respiratory disease, thyroid dysfunction • Concurrent drug therapy issues: Effects may be potentiated when used with other sedative drugs or ethanol • Special populations: Antihistamines may cause excitation in young children; not for OTC use in children <2 years of age • Dosage form specific issues: some dosage forms may contain sodium benzoate/benzoic acid, a metabolite of benzyl alcohol; large amounts of benzyl alcohol have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates
Clemastine (Dayhist® Allergy) 1.34 mg, 2.68 mg oral tablet Clemastine 0.5 mg/5 mL oral syrup	• Concerns related to adverse effects: may cause CNS depression • Disease-related concerns: use caution in patients with asthma, cardiovascular disease, increased intraocular pressure, prostatic hyperplasia/urinary obstruction, pyloroduodenal obstruction, thyroid dysfunction • Concurrent drug therapy issues: Potentially significant drug interactions may exist
Pyrilamine (PediaClear®-8) 12.5 mg/15 mL oral syrup	• Ask a doctor before use if the child has a breathing problem such as emphysema or chronic bronchitis, glaucoma • Ask a doctor before use if the child is taking sedatives or tranquilizers • When using this product marked drowsiness may occur, sedatives and tranquilizers may increase drowsiness, excitability may occur, especially in children
Prescription-Only First Generation Antihistamine Combination Products	
Promethazine-codeine oral solution 6.25-10 mg/5 mL	• Concerns related to adverse effects: Altered cardiac conduction, anticholinergic effects, CNS depression, constipation, extrapyramidal symptoms, hypotension, neuroleptic malignant syndrome (NMS), phenanthrene hypersensitivity, photosensitivity, respiratory depression [US Boxed Warning], temperature regulation • Disease-related concerns: Abdominal conditions, adrenal insufficiency, biliary tract impairment, bone marrow suppression, Cardiovascular disease, Delirium tremens, head trauma, hepatic impairment, myasthenia gravis, obesity, Parkinson disease, prostatic

Medication	Warnings/Precautions
	hyperplasia/urinary stricture, psychosis, renal impairment, respiratory disease, seizures, sleep-related disorders, thyroid disease • Concurrent drug therapy issues: Benzodiazepines or other CNS depressants: [US Boxed Warning], cytochrome P450 interactions: [US Boxed Warning] • Special populations: CYP2D6 "ultrarapid metabolizers", cachectic or debilitated patients: Avoid use caution in cachectic or debilitated patients; there is a greater potential for critical respiratory depression, even at therapeutic dosages, elderly, Neonatal withdrawal syndrome: [US Boxed Warning], pediatrics • Dosage forms related issues: Benzyl alcohol and derivatives, propylene glycol • Other warnings/precautions: Abrupt discontinuation/withdrawal, abuse/misuse/diversion: [US Boxed Warning], accidental ingestion: [US Boxed Warning], appropriate use, medication errors: [US Boxed Warning], naloxone access, surgery
Brompheniramine-pseudoephedrine-dextromethorphan (BIO Dtuss DMX, Bromfed® DM) 1 mg-30 mg-10 mg/5 mL, 2 mg-30 mg-10 mg/5 mL oral syrup	• Concerns related to adverse effects: CNS depression • Disease-related concerns: Cardiovascular disease, GI obstruction, GU dysfunction, Increased intraocular pressure, respiratory disease, seizures, thyroid dysfunction • Concurrent drug therapy issues: Sedatives • Special populations: CYP2D6 poor metabolizers, pediatric • Other warnings/precautions: cough, self-medication (OTC use)
Promethazine/dextromethorphan (promethazine-DM) 6.25 mg-15 mg/5 mL oral syrup	• Concerns related to adverse effects: altered cardiac conduction, anticholinergic effects, CNS depression, extrapyramidal symptoms, neuroleptic malignant syndrome, orthostatic hypotension, temperature regulation • Disease-related concerns: Bone marrow suppression, cardiovascular disease, glaucoma, hepatic impairment, myasthenia gravis, Parkinson disease, respiratory disease, seizures • Special populations: CYP2D6 poor metabolizers, debilitated patients, pediatric • Other warnings/precautions: Abuse/Misuse

Practice Guidelines

Allergic Rhinitis

American College of Allergy, Asthma & Immunology Guidelines (2020 Update)
Dykewicz MS, Wallace DV, Amrol DJ, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol. 2020;146(4):721-767.

- 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
- Should not prescribe a first-generation antihistamine and are in favor of a second-generation antihistamine when prescribing an oral antihistamine for the treatment of AR

American Academy of Otolaryngology – Head and Neck Surgery Allergic Rhinitis Guidelines (2015)

Seidman MD, Gurgel RK, Lin SY, et al. Clinical practice guideline: Allergic rhinitis. American Academy of Otolaryngology – Head and Neck Surgery. 2015; 152(2):197-206.

Recommendation	Grade of Recommendation
Clinicians should recommend oral second-generation/less-sedating antihistamines for patients with allergic rhinitis and primary complaints of sneezing and itching	Strong Recommendation: based on randomized, controlled trials with minor limitations and a preponderance of benefit over harm
Clinicians may offer intranasal antihistamines for patients with seasonal, perennial, or episodic allergic rhinitis	Option: based on randomized, controlled trials with minor limitations and observational studies, with equilibrium of benefit over harm
Clinicians may offer combination pharmacologic therapy in patients with allergic rhinitis who have inadequate response to pharmacologic monotherapy	Option: based on randomized, controlled trials with minor limitations and observational studies, with equilibrium of benefit over harm

Urticaria

American Family Physician (AFP) Acute and Chronic Urticaria: Evaluation and Treatment (2017)

Schaefer P. Acute and Chronic Urticaria: Evaluation and Treatment. Am Fam Physician. 2017;95(11):717-724.

- Second-generation antihistamines are considered first-line agents in the management of chronic urticaria
- For patients not responding to monotherapy with a second-generation antihistamine one of the following strategies may be employed:
 - Increase the dose of the second-generation antihistamine
 - Add another second-generation antihistamine
 - Add a H₂-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

Infusion Reaction Prophylaxis

European Society for Medical Oncology (EMSO) Guidelines for the Management of Infusion Reactions to Systemic Anticancer Therapy (2017)

Rosella S, Blasco I, Garcia FL, et al. Management of infusion reactions to systemic anticancer therapy: ESMO Clinical Practice Guidelines. Annals of Oncology. 2017; 28(4): 100-118.

Recommendation	Grade of Recommendation
If pre-medications are to be taken orally, oncology nurses should check that the patient has actually taken them	V, C
In the management of infusion reaction, the combined use of H ₁ and H ₂ antagonists is superior to the use of either class alone.	I, B
Diphenhydramine (1-2 mg/kg or 25-50 mg) may be given slowly via IV in combination with ranitidine (50 mg in 20 ml diluent) IV over 5 minutes.	V, C
After all symptoms have resolved, rechallenge with a reduced infusion rate and additional premedication (corticosteroids/antihistamines)	V, C

Recommendation definitions

Class/Level	Definition
I	Evidence from at least one large randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies

V	Studies without control group, case reports, expert opinions
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages, optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

Extrapyramidal Side Effects Associated With Second-Generation Antipsychotics

Canadian Alliance for Monitoring Effectiveness and Safety of Antipsychotics in Children (CAMESA) Guideline Group (2011)

Pringsheim T, Doja A, Belanger S, et al. Treatment recommendations for extrapyramidal side effects associated with second-generation antipsychotic use in children and youth. *Pediatric Child Health*. 2011; 16(9):590-598.

Recommendation	Grade of Recommendation
For the treatment of neuroleptic-induced acute dystonia, administer diphenhydramine. The patient and family can be advised that if an acute dystonic reaction occurs, they can self-administer an oral dose of diphenhydramine while seeking medical care. Treatment for two to five days to prevent recurrence may be considered.	High
For the treatment of neuroleptic-induced acute dystonia, an anticholinergic (benztropine) may be administered.	Very low

Insomnia

VA/Dod Clinical Practice Guidelines: The Management of Chronic Insomnia Disorder and Obstructive Sleep Apnea (Insomnia/OSA) (2025)

Va.gov: Veterans Affairs [Internet]. 2025 [cited 2025 Oct 28]. Available from: <https://www.healthquality.va.gov/guidelines/CD/insomnia/index.asp>

- Suggest against the use of diphenhydramine for the treatment of chronic insomnia disorder
- Lack of rigorous data supporting the effectiveness of these antihistamines as nighttime sleep aids for chronic insomnia

Antiemetics

American Academy of Family Physicians Antiemetics Guidelines (2015)

Flake ZA, Linn BS, and Hornecker JR. Practical selection of antiemetics in the ambulatory setting. American Academy of Family Physicians. 2015; 91(5):293-296.

- Antihistamines and anticholinergics are the preferred treatments for motion sickness. (Evidence rating C)
- When combined with aspirin, metoclopramide reduces nausea associated with migraine headaches. (Evidence rating B)
- Ondansetron significantly reduces the need for intravenous rehydration in children with gastroenteritis. (Evidence rating B)
- Pyridoxine with or without doxylamine is recommended to reduce pregnancy-induced nausea and vomiting. (Evidence rating C)

Class/Level	Definition
A	Consistent, good-quality, patient-oriented evidence
B	Inconsistent or limited-quality patient-oriented evidence
C	Consensus, disease-oriented evidence, usual practice, expert opinion, or case series

Clinical Trials/Systematic Reviews/Meta-Analyses*

Citation	Design	Endpoints
Bender BG, Berning S, Dudden R, et al. Sedation and performance impairment of diphenhydramine and second-generation antihistamines: a meta-analysis. 2003; 111(4): 770-776.	Meta-analysis of 18 articles to compare the sedating and performance-impairing effects of diphenhydramine relative to placebo and second-generation antihistamines. Search using MEDLINE limited to studies that included patients with atopic disease and control subjects, blinded and randomized clinical trials, objective examination of alertness and psychomotor performance, and reported means and variances	Primary endpoint: Alertness and psychomotor performance
Results: Diphenhydramine impaired performance relative to placebo control and second-generation antihistamines, including acrivastine, astemizole, cetirizine, fexofenadine, loratadine, and terfenadine. There was a high variance, the average sedating effect of diphenhydramine was modest, and some tests of performance showed less sedation with diphenhydramine than in the control and second-generation antihistamine groups. There was a significant average effect size indicating a mild sedating effect of second-generation antihistamines compared to placebo. Conclusion: Diphenhydramine-induced sedation was not consistently found in the selected studies, with some designs intended to increase the probability of this outcome with higher diphenhydramine doses. Although this sedating effect has been established in the literature, this meta-analysis does not draw a clear distinction between sedating and nonsedating antihistamines.		
Citation	Design	Endpoints
Cho H, Myung J, Suh HS, et al. Antihistamine use and the risk of injurious falls or fracture in elderly patients: a systematic review and meta-analysis. 2018; 29(1):2163-2170.	Meta-analysis using MEDLINE, EMBASE, and local databases through November 2016 that observed the association between antihistamine use and the risk of injurious falls or fractures among elderly populations. A random effects model was used and heterogeneity was examined based on I-square and Cochran's Q test. Of the 473 identified studies, 5 were included in the analysis.	Primary endpoint: Risk of injurious falls or fractures

Results: First generation antihistamines had an increased risk of injurious falls or fracture (odds ratio [OR] 2.03, 95% confidence interval [CI] 1.49-2.76, heterogeneity: $p = 0.41$, $I^2 = 0\%$). Among studies that included all generations of antihistamines, the association was statistically significant without heterogeneity (OR 2.89, 95% CI 1.71-4.89, heterogeneity: $p = 0.42$, $I^2 = 0\%$).

Conclusion: First generation antihistamines may considerably increase the risk of injurious falls or fractures among the elderly and should be prescribed with caution in this patient population.

*Reliable clinical trial data, systematic reviews, and meta-analyses investigating first generation antihistamines are limited due to their conduction prior to digital recording and their general acceptance as being safe and efficacious.

Formulary Placement, Utilization and Cost Experience (10-01-2025 to 12-31-2025)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Single-Drug First Generation Antihistamine Products								
Chlorpheniramine (Aller-Chlor, Allergy, Allergy Relief, ChlorHist®, Pharbechlor®, Wal-Finate) 4 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Chlorpheniramine 12 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Chlorpheniramine (Ed Chlorped® Jr) 2 mg/5 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Dexbrompheniramine (Ala-Hist® IR) 2 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Dexbrompheniramine (Pediavent®) 2 mg/5 mL oral liquid	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Dexchlorpheniramine (Ryclora®) 2 mg/5 mL oral solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Triprolidine (Flonase® Night Allergy Relief) oral tablet 2.5 mg	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Triprolidine (Miclara® LQ) 1.25 mg/5 mL, 2.5 mg/5 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Triprolidine (PediaClear® PD, Histex® PD, Histex® PDX) 0.625 mg/mL, 0.938 mg/mL, 1.25 mg/mL oral drops	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Triprolidine (Histex®) 2.5 mg/5 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Carbinoxamine 4 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Carbinoxamine (Ryvent®) 6 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Carbinoxamine 4 mg/5 mL oral liquid	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Carbinoxamine (Karbinal® ER) 4 mg/5 mL extended release oral suspension	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Clemastine (Dayhist® Allergy) 1.34 mg, 2.68 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Clemastine 0.5 mg/5 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Diphenhydramine (Aler-Caps®, Allergy, Allergy Medication, Allergy Relief, Banophen®, Benadryl®, Complete Allergy, Wal-Dryl® Allergy, Pharbedryl®) 25 mg, 50 mg oral capsule	10	6	\$6.35	\$0.64	0	0 (0%)	F	No change
Diphenhydramine (Alka-Seltzer Plus Allergy, Aller-G-Time, Allergy, Allergy Medicine, Allergy Relief, Banophen®, Benadryl® Allergy, Complete Allergy, Diphen®, Geri-Dryl®, Total Allergy, Wal-Dryl® Allergy) 25 mg oral tablet, caplet, minitab	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (Children's Allergy Relief, Allergy Relief) 12.5, 25 mg chewable tablet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (Allergy, Allergy Relief, Children's Allergy, Children's Benadryl® Allergy, Children's Wal-Dryl®, Diphedryl®, Geri-Dryl®, M-Dryl®, MAXAllergy™ Kids) 12.5 mg/5 mL oral solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (Naramin®) 12.5 mg/5 mL oral liquid in packet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (Diphen®) 12.5 mg/5 mL oral elixir, cup	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change

Diphenhydramine 50 mg/mL IV syringe	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (Children's Allergy Relief, Children's Wal-Dryl® Allergy) 12.5 mg orally disintegrating tablet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Pyrilamine (PediaClear-8®) 12.5 mg/15 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Promethazine 12.5, 25, 50 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Promethazine (Phenergan®) 25 mg/mL, 50 mg/mL IV ampule	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Promethazine 6.25 mg/5 mL oral syrup	8	7	\$95.25	\$11.91	0	0 (0%)	F	No change
Promethazine (Promethegan™) 12.5 mg, 25 mg, 50 mg rectal suppository	2	2	\$140.14	\$70.07	0	0 (0%)	F	No change
Cyproheptadine 4 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Cyproheptadine 2 mg/5 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Hydroxyzine HCL 10 mg, 25 mg, 50 mg oral tablet	78	52	\$310.32	\$3.98	0	0 (0%)	F	No change
Hydroxyzine HCL 10 mg/5 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Hydroxyzine HCL intramuscular solution 25 mg/mL, 50 mg/mL	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Hydroxyzine pamoate 25 mg, 50 mg, 100 mg oral capsule	7	7	\$28.74	\$4.11	0	0 (0%)	F	No change
Doxylamine (Nighttime Sleep-Aid, Sleep Aid, Unisom®, Wal-Som®) 25 mg oral tablet	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Diphenhydramine (NightTime Sleep Aid, Sleep Aid, Sleep Time, Unisom® SleepMinis, Wal-Sleep Z, ZzzQuil®, NightTime Sleep Gel, Unisom® SleepGels, Wal-Som®) 25, 50 mg oral capsule, softgel	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (NightTime Sleep Aid, Nytol QuickCaps®, Rest Simply, Simply Sleep, Sleep Aid, Sleep II, Sleep-Tabs, Sominex®, Sominex® Maximum Strength) 25 mg oral tablet, caplet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (Sleep Aid, Sleep Time, Wal-Sleep Z, ZzzQuil®) 50 mg/30 mL oral solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Diphenhydramine (Unisom® SleepMelts, Wal-Sleep Z) 25 mg orally disintegrating tablets	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Prescription-Only First Generation Antihistamine Combination Products								
Promethazine-codeine 6.25-10 mg/5 mL oral solution	2	1	\$17.80	\$8.90	0	0 (0%)	F-QL (240/30)	No change
Promethazine-dextromethorphan (promethazine-DM) 6.25 mg-15 mg/5 mL oral syrup	28	26	\$294.14	\$10.51	0	0 (0%)	F-QL (240/30) AL (>12)	No change
Brompheniramine-pseudoephedrine-dextromethorphan (BIO Dtuss DMX, Bromfed® DM) 1 mg-30 mg-10 mg/5 mL, 2 mg-30 mg-10 mg/5 mL oral syrup	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Total	135	101	\$892.74	\$6.61	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

References

1. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: <https://www.ncbi.nlm.nih.gov/pubmed>. Accessed on October 28, 2025.
2. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>. Accessed on October 28, 2025.
3. "DailyMed." DailyMed. N.p., n.d. Web. 11 Nov 2021. Available at <https://dailymed.nlm.nih.gov/dailymed/>
4. "Micromedex Products." Micromedex Products. N.p., n.d. Web. 11 Nov 2011. Available at <http://www.micromedexsolutions.com/micromedex2/librarian/>
5. Seidman MD, Gurgel RK, Lin SY, et al. Clinical practice guideline: Allergic rhinitis. American Academy of Otolaryngology – Head and Neck Surgery. 2015; 152(2):197-206.
6. Rosella S, Blasco I, Garcia FL, et al. Management of infusion reactions to systemic anticancer therapy: ESMO Clinical Practice Guidelines. Annals of Oncology. 2017; 28(4): 100-118.
7. Pringsheim T, Doja A, Belanger S, et al. Treatment recommendations for extrapyramidal side effects associated with second-generation antipsychotic use in children and youth. Pediatric Child Health. 2011; 16(9):590-598.
8. Flake ZA, Linn BS, and Hornecker JR. Practical selection of antiemetics in the ambulatory setting. American Academy of Family Physicians. 2015; 91(5):293-296.
9. Bender BG, Berning S, Dudden R, et al. Sedation and performance impairment of diphenhydramine and second-generation antihistamines: a meta-analysis. 2003; 111(4): 770-776.
10. Cho H, Myung J, Suh HS, et al. Antihistamine use and the risk of injurious falls or fracture in elderly patients: a systematic review and meta-analysis. 2018; 29(1):2163-2170.
11. Dykewicz MS, Wallace DV, Amrol DJ, et al. Rhinitis 2020: A practice parameter update. J Allergy Clin Immunol. 2020;146(4):721-767.
12. Schaefer P. Acute and Chronic Urticaria: Evaluation and Treatment. Am Fam Physician. 2017;95(11):717-724.
13. Va.gov: Veterans Affairs [Internet]. 2025 [cited 2025 Oct 28]. Available from: <https://www.healthquality.va.gov/guidelines/CD/insomnia/index.asp>



Fluoride Dental Preparations

Utilization Findings

There were no claims and no prior authorization requests from 10/1/2025 to 12/31/2025.

Recommendations

- No changes



Formulary Placement, Utilization and Cost Experience (10-01-2025 to 12-31-2025)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Fluoride Dental Preparations								
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 = Excluded

Sickle Cell Disease

Executive Summary

Class Overview

Sickle cell disease (SCD) is an inherited red blood cell (RBC) disorder characterized by vascular occlusion and hemolytic anemia, which leads to severe acute and chronic complications affecting numerous organ systems. Patients with SCD have an abnormal type of hemoglobin called HbS, with the letter "S" referring to the sickle shape of affected RBCs. Those who receive two sickle cell genes, one from each parent, are affected. Prevalence of SCD is estimated to be about 100,000 people in the United States and disproportionately affects African Americans and, to a lesser degree, the Hispanic population. Approximately 1 in 13 Black babies are born with SCD. SCD is considered a rare disease given its prevalence in less than 200,000 in the United States. The signs and symptoms of SCD usually begin in early childhood. While the severity may vary, characteristic features include low red blood cells, chronic episodes of pain, and frequent infections. Acute episodes are categorized as vaso-occlusive crises (VOCs) and are the primary cause of health care encounters. Major complications include recurrent pain episodes, life-threatening infections because of splenic infarction, acute chest syndrome, pulmonary hypertension, stroke, and cumulative multi-organ damage.

The National Heart, Lung, and Blood Institute has provided recommendations for the management of SCD, however, these clinical guidelines have not been updated since 2014. In 2019, The American Society of Hematology (ASH) convened 5 guideline panels to develop clinical practice recommendations addressing 5 management areas of highest importance to individuals living with sickle cell disease: pain, cerebrovascular complications, pulmonary and kidney complications, transfusion, and hematopoietic stem cell transplant. Although the ASH recommendation serve as guidance for specific scenarios, with a particular focus on cardiopulmonary and renal complications, the guidelines do not provide treatment recommendations for SCD as a whole. The only curative therapy for SCD is hematopoietic cell transplantation (HCT). Hydroxyurea, which includes brand names Siklos®, Droxia®, and Xromi®, is usually a first-line therapy in individuals with SCD who have frequent painful episodes, including infants <9 months, children, and adults. Other pharmacological treatment options include Endari® (L-glutamine) and Adakveo® (crizanlizumab). In 2023, two gene therapies were approved for the treatment of SCD, Casgevy® (exagamglogene autotemcel) and Lyfgenia® (lovotibeglogene autotemcel). Casgevy is approved for the treatment of SCD in patients 12 years of age and older with recurrent VOCs, while Lyfgenia is approved for the treatment of patients 12 years of age and older with SCD and a history of VOC events. Both treatments are administered as one-time infusions and are made from a patient's own blood stem cells, which are modified and returned to the patient.

Utilization Findings

There were no claims and no prior authorization requests.

Recommendations

- No changes

Clinical Summary

Sickle cell disease (SCD) is an inherited red blood cell (RBC) disorder. Patients with SCD have an abnormal type of hemoglobin called HbS, with the letter “S” referring to the sickle shape of affected RBCs. Those who receive two sickle cell genes, one from each parent, are affected. Homozygous HbS is usually the most severe form of SCD while a milder form is typically associated with a sickle cell gene (“S”) from one parent and an abnormal hemoglobin “C” from the other parent. The beta thalassemia gene can also be inherited, affecting beta globin production. The prevalence of SCD is estimated to be about 100,000 people in the United States and disproportionately affects African Americans and, to a lesser degree, the Hispanic population. The signs and symptoms of SCD usually begin in early childhood. While the severity of symptoms vary, characteristic features include low RBCs, chronic episodes of pain, and frequent infections. Diagnosis may occur in various settings including prenatal testing, newborn screening, or patients presenting with symptoms. Prenatal testing involves DNA-testing of placental tissue. Newborns with SCD are typically asymptomatic until hemoglobin levels decline; screening involves blood sampling and analysis of hemoglobin patterns. Although targeted screening of high-risk populations has been performed, universal screening is recommended by a National Institutes of Health consensus panel due to superior detection of the disease and prevention of mortality.

SCD is primarily characterized by vascular occlusion and hemolytic anemia, which lead to severe acute and chronic complications affecting numerous organ systems. The vaso-occlusive process is multifactorial and believed to comprise multiple interactions between sickled RBCs, activated leukocytes, endothelial cells, platelets, and plasma proteins. Acute episodes are categorized as vaso-occlusive crises (VOC) and are the primary cause of health care encounters. Major complications include recurrent pain episodes, life-threatening infections because of splenic infarction, pulmonary hypertension, stroke, and cumulative multi-organ damage. Acute chest syndrome, an episode of new pulmonary infiltrate with symptoms of fever, chest pain, hypoxemia, wheezing, cough, and/or respiratory distress, may also occur and is another major cause of hospitalization and mortality.

The National Heart, Lung, and Blood Institute has provided recommendations for the management of SCD, however, these clinical guidelines have not been updated since 2014. In 2019, The American Society of Hematology (ASH) convened 5 guideline panels to develop clinical practice recommendations addressing 5 management areas of highest importance to individuals living with sickle cell disease: pain, cerebrovascular complications, pulmonary and kidney complications, transfusion, and hematopoietic stem cell transplant. Although the ASH recommendation serve as guidance for specific scenarios, with a particular focus on cardiopulmonary and renal complications, the guidelines do not provide treatment recommendations for SCD as a whole. Hematopoietic stem cell transplant (HSCT) is the only potentially curative intervention for SCD but is associated with significant risk and therefore, risk-benefit analysis and decision-making should be highly individualized. Treatment primarily consists of hydroxyurea with or without L-glutamine to reduce painful crises and VOCs, blood transfusions, vaccines, and supportive care. Hydroxyurea is used first-line for the management of SCD. Hydroxyurea comes in a few formulations and brand names including Droxia®, Siklos® and Xromi®. Droxia® (hydroxyurea) is indicated to reduce the frequency of painful crises and the need for blood transfusions. Siklos® (hydroxyurea) tablets have the same indication but are also approved in pediatric patients 2 years of age and older. Xromi® (hydroxyurea) is an oral solution that was approved in 2024. Xromi® is indicated to reduce the frequency of painful crises and reduce the need for blood transfusions in pediatric patients 6 months to less than 2 years of age with sickle cell anemia with recurrent moderate to severe painful crises. Endari® (L-glutamine), approved in 2017, is an amino acid indicated to reduce acute complication of SCD in adults and pediatrics 5 years of age and older. L-glutamine is available as a dietary supplement, which has been used off-label for SCD. Endari® is a pharmaceutical-grade L-glutamine that has shown efficacy in clinical trials. It may be used second line for patients in whom treatment with hydroxyurea was not effective or who were

intolerant. Adakveo® (crizanlizumab-tmca), approved in 2019, is an infusible selectin blocker indicated to reduce the frequency of VOCs in adults and pediatric patients aged 16 years and older with sickle cell disease. It is typically used as an add on treatment to hydroxyurea, or as monotherapy for patients that are unable to tolerate hydroxyurea.

In 2023, two gene therapies were approved for the treatment of SCD, Casgevy® (exagamglogene autotemcel) and Lyfgenia® (lovotibeglogene autotemcel). Casgevy is approved for the treatment of SCD in patients 12 years of age and older with recurrent VOCs, while Lyfgenia is approved for the treatment of patients 12 years of age and older with SCD and a history of VOC events. Both treatments are administered as one-time infusions and are made from a patient's own blood stem cells, which are modified and returned to the patient. Casgevy® received a label expansion in January 2024 for transfusion-dependent beta thalassemia.

In August 2023, Institute for Clinical and Economic Review (ICER) released an updated evidence report indicating that gene therapies for sickle cell disease, Casgevy® and Lyfgenia®, would be cost-effective if priced up to \$2.05 million per treatment. ICER compared the treatments with each other and with standard of care which included hydroxyurea, blood transfusions, and other supportive care, and found that Lyfgenia® may provide at least an incremental net health benefit or may provide a substantial net health benefit compared with standard of care. Because the data for Casgevy® are not as robust since data from fewer patients are available, ICER indicated that Casgevy® may be comparable to stand of care, or result in an incremental or substantial net benefit. The report noted that safety continues to be a major concern with these products, particularly due to the myeloablative busulfan conditioning required prior to treatment with both products.

In September 2024, Oxbryta® (voxelotor) was voluntarily discontinued by Pfizer based on the totality of clinical data that indicated the overall benefit of Oxbryta no longer outweighs the risk in the SCD patient population. The data suggest an imbalance in VOCs and fatal events which require further assessment.

There are a few products in the Pipeline for support and treatment of SCD. Pyrukynd® (mitapivat), which is already FDA approved for hemolytic anemia, is an oral pyruvate kinase activator that works by increasing the affinity of hemoglobin in the sickled cells for oxygen. Pyrukynd® is in Phase III development for SCD with expected approval in 2026. This product would primarily compete with Adakveo® and Endari® in patients who fail or are unable to tolerate hydroxyurea. Another oral pyruvate kinase activator, FT-4202 (etavopivat), is also in Phase III development. FT-4202 would also compete with Adakveo®, Endari®, and Pyrukynd® (if approved). Based on the Phase II/III trial date, approval of FT-4202 before 2027 is unlikely. Inclacumab is an intravenous selectin inhibitor in Phase III development. Inclacumab may compete with Adakveo® or could be approved as adjunctive therapy. Patients in the inclacumab clinical trials were permitted to be on a stable dose of hydroxyurea, Oxbryta®, or Endari®. Pfizer had been planning for a 2026 approval for inclacumab, however the approval timeline is unclear since the primary endpoint of the GBT2104-131 trial was missed. Another Phase III Pipeline product, GBT601 (osivelotor), is an oral hemoglobin-oxygen affinity enhancer with potential approval in 2028. Lastly, in June 2025, the FDA granted orphan drug designation to Wayrilz® (rilzabrutinib) for SCD. Wayrilz® is an oral, reversible bruton's tyrosine kinase (BTK) inhibitor that works through multi-immune modulation to reduce VOCs associated with inflammation in SCD. Based on clinical trial timeline, approval is unlikely before 2028.

Indications, Dosing and Administration

Medication	Indications	Dosing/Administration
Droxia® (hydroxyurea)	To reduce the frequency of painful crises and to reduce the need for blood transfusions in patients with sickle cell anemia with recurrent moderate to severe painful crises.	Initial dose: 15 mg/kg once daily. Monitor the patient's blood count every two weeks. Blood counts in an acceptable range (Note: acceptable range is neutrophils ≥ 2500 cells/mm³, platelets $\geq 95,000$/mm³, hemoglobin > 5.3 g/dL, reticulocytes $\geq 95,000$/mm³ if the hemoglobin is concentration is < 9 g/dL): - The dose may be increased by 5 mg/kg/day every 12 weeks until a maximum tolerated dose or 35 mg/kg/day is reached if blood counts are in an acceptable range. - Increase dosing only if blood counts are in an acceptable range - Do not increase if myelosuppression occurs Blood counts between acceptable and toxic range (Note: toxic range is neutrophils < 2000 cells/mm³, platelets $< 80,000$/mm³, hemoglobin < 4.5 g/dL, reticulocytes $< 80,000$/mm³ if the hemoglobin is concentration is < 9 g/dL): - Do not increase the dose - If blood counts are considered toxic, discontinue the medication Dosing after hematologic recovery: - Reduce dose by 2.5 mg/kg/day - May titrate up or down every 12 weeks in 2.5 mg/kg/day increments - The patient should be at a stable dose with no hematologic toxicity for 24 weeks Discontinue the treatment permanently if a patient develops hematologic toxicity twice
Siklos® (hydroxyurea)	To reduce the frequency of painful crises and to reduce the need for blood transfusions in pediatric patients, 2 years of age and older, with sickle cell anemia with recurrent moderate to severe painful crises.	Initial dose: 15 mg/kg in adults and 20 mg/kg in children once daily. Monitor the patient's blood count every two weeks. Blood counts in an acceptable range (Note: acceptable range is neutrophils ≥ 2000 cells/mm³, platelets $\geq 80,000$/mm³, hemoglobin > 5.3 g/dL, reticulocytes $\geq$

Medication	Indications	Dosing/Administration
		80,000/mm³ if the hemoglobin is concentration is < 9 g/dL): • The dose may be increased by 5 mg/kg/day every 8 weeks until a maximum tolerated dose or 35 mg/kg/day is reached if blood counts are in an acceptable range. • Increase dosing only if blood counts are in an acceptable range • May increase if a painful crisis occurs. Do not increase if myelosuppression occurs. Blood counts between acceptable and toxic range (Note: toxic range is neutrophils < 2000 cells/mm³, platelets < 80,000/mm³, hemoglobin < 4.5 g/dL, reticulocytes < 80,000/mm³ if the hemoglobin is concentration is < 9 g/dL): • If blood counts are considered toxic, discontinue the medication until hematologic recovery Dosing after hematologic recovery: • Reduce dose by 5 mg/kg/day • May titrate up or down every 8 weeks in 5 mg/kg/day increments • The patient should be at a stable dose with no hematologic toxicity for 24 weeks Discontinue the treatment permanently if a patient develops hematologic toxicity twice
Xromi® (hydroxyurea)	To reduce the frequency of painful crises and reduce the need for blood transfusions in pediatric patients 6 months of age and older with sickle cell anemia with recurrent moderate to severe painful crises.	Initial dose: 15 mg/kg orally once daily. Monitor the patient's blood count every two weeks. The dose may be increased by 5 mg/kg/day every 8 to 12 weeks until a maximum tolerated dose or 35 mg/kg/day is reached if blood counts are in an acceptable range. Renal impairment: Reduce the dose by 50% in patients with creatinine clearance less than 60 mL/min.
Adakveo® (crizanlizumab-tmca)	To reduce the frequency of vasoocclusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease.	5 mg/kg by intravenous infusion over a period of 30 minutes at Week 0, Week 2, and every 4 weeks thereafter. May be given with or without hydroxyurea.

Medication	Indications	Dosing/Administration
Endari® (glutamine)	To reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older.	Administer Endari orally, twice per day at the dose based on body weight. < 30kg: 5g (1 packet) per dose 30-65kg: 10g (2 packets) per dose > 65kg: 15g ((3 packets) per dose
Casgevy® (exagamglogene autotemcel)	For the treatment of patients aged 12 years and older with: - sickle cell disease (SCD) with recurrent vaso-occlusive crises - transfusion-dependent β-thalassemia (TDT)	For autologous use only. For intravenous use only. The minimum recommended dose of Casgevy is 3×10^6 CD34 cells/kg. Casgevy is provided as a single dose for infusion containing a suspension of CD34 cells in one or more vials. See the Lot Information Sheet provided with the product shipment for additional information pertaining to the number of vials required to achieve the patient-specific dose. Administer all vials.
Lyfgenia™ (lovotibeglogene autotemcel)	For the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events.	For autologous use only. For intravenous use only. Lyfgenia is provided as a single dose for infusion containing a suspension of CD34+ cells in one to four infusion bags. The minimum recommended dose of Lyfgenia is 3×10^6 CD34+ cells/kg.

Boxed Warnings and Contraindications

Medication	Boxed Warnings	Contraindications
Droxia® (hydroxyurea)	- Myelosuppression - Malignancies	Patients who have demonstrated a previous hypersensitivity to hydroxyurea or any other component of its formulation.
Siklos® (hydroxyurea)	- Myelosuppression - Malignancies	Patients who have demonstrated a previous hypersensitivity to hydroxyurea or any other component of its formulation
Xromi® (hydroxyurea)	- Myelosuppression - Malignancies	Patients who have demonstrated a previous hypersensitivity to hydroxyurea or any other component of its formulation.
Adakveo® (crizanlizumab-tmca)	None	None
Endari® (glutamine)	None	None
Casgevy® (exagamglogene autotemcel)	None	None
Lyfgenia™ (lovotibeglogene autotemcel)	Hematologic Malignancies	None

Warnings/Precautions

Medication	Warnings/Precautions
Droxia® (hydroxyurea)	Myelosuppression: Hydroxyurea causes severe myelosuppression. Treatment with hydroxyurea should not be initiated if bone marrow function is markedly depressed. Bone marrow suppression may occur, and leukopenia is generally its first and most common manifestation. Thrombocytopenia and anemia occur less often and are seldom seen without a preceding leukopenia. Hemolytic Anemia: Cases of hemolytic anemia in patients treated with hydroxyurea for myeloproliferative diseases have been reported. Patients who develop acute jaundice or hematuria in the presence of persistent or worsening of anemia should have laboratory tests evaluated for hemolysis (e.g., measurement of serum lactate dehydrogenase, haptoglobin, reticulocyte, unconjugated bilirubin levels, urinalysis, and direct and indirect antiglobulin [Coombs] tests). Malignancies: Hydroxyurea is a human carcinogen. In patients receiving long-term hydroxyurea for myeloproliferative disorders, secondary leukemia has been reported. Secondary leukemia has also been reported in patients treated with long-term hydroxyurea for sickle cell disease. Leukemia has also been reported in patients with sickle cell disease and no prior history of treatment with hydroxyurea. Skin cancer has also been reported in patients receiving long-term hydroxyurea. Advise protection from sun exposure and monitor for the development of secondary malignancies. Embryo-Fetal toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception. Vasculitic toxicities: Institute treatment and discontinue medication if this occurs. Live Vaccinations: Avoid live vaccine use in a patient taking this medication. Concomitant use of this medication with a live virus vaccine may potentiate the replication of the virus and/or may increase the adverse reaction of the vaccine because normal defense mechanisms may be suppressed by hydroxyurea. Vaccination with live vaccines in a patient receiving this medication may result in severe infection. Patient's antibody response to vaccines may be decreased. Risks with concomitant use of antiretroviral drugs: Pancreatitis, hepatotoxicity, and neuropathy have occurred. Monitor for signs and symptoms in patients with HIV infection using antiretroviral drugs; discontinue medication and implement treatment. Macrocytosis: This medication may cause macrocytosis, which is self-limiting, and is often seen early in the course of treatment. The morphologic change resembles pernicious anemia but is not related to vitamin B12 or folic acid deficiency. This may mask the diagnosis of pernicious anemia. Prophylactic administration of folic acid is recommended. Pulmonary toxicity: Interstitial lung disease including pulmonary fibrosis, lung infiltration, pneumonitis, and alveolitis/allergic alveolitis (including fatal cases) have been reported in patients treated for myeloproliferative neoplasm. Safety and effectiveness have not been established for the use of hydroxyurea in the treatment of myeloproliferative neoplasms and the use is not approved by the FDA. Monitor patients developing pyrexia, cough, dyspnea, or other respiratory symptoms frequently, investigate and treat promptly. Discontinue medication and manage with corticosteroids. Laboratory test interference: Interference with Uric Acid, Urea, or Lactic Acid Assays is possible, rendering falsely elevated results of these in patients treated with hydroxyurea.
Siklos® (hydroxyurea)	Embryo-Fetal toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception.

Medication	Warnings/Precautions
	Cutaneous vasculitic toxicities (e.g. leg ulcers): Institute treatment and discontinue treatment and/or reduce dose if this occurs. Risks with concomitant use of antiretroviral drugs: Pancreatitis, hepatotoxicity, and neuropathy have occurred. Monitor for signs and symptoms patients with HIV infection using antiretroviral drugs; discontinue medication, and implement treatment. Concomitant use with live virus vaccine: Avoid use of live virus vaccine in patients taking this medication. Concomitant use of hydroxyurea with a live virus vaccine may potentiate the replication of the vaccine virus and/or may increase the adverse reactions of the vaccine virus and result in severe infections. Patient's antibody response to vaccines may be decreased. Macrocytosis: This medications may cause macrocytosis, which is self-limiting, and is often seen early in the course of treatment. The morphologic change resembles pernicious anemia, but is not related to vitamin B12 or folic acid deficiency. This may mask the diagnosis of pernicious anemia. Prophylactic administration of folic acid is recommended. Laboratory test interference: Interference with Uric Acid, Urea, or Lactic Acid Assays is possible, rendering falsely elevated results of these in patients treated with hydroxyurea.
Xromi® (hydroxyurea)	Myelosuppression: Hydroxyurea causes severe myelosuppression. Treatment with hydroxyurea should not be initiated if bone marrow function is markedly depressed. Bone marrow suppression may occur, and leukopenia is generally its first and most common manifestation. Thrombocytopenia and anemia occur less often and are seldom seen without a preceding leukopenia. Hemolytic Anemia: Cases of hemolytic anemia in patients treated with hydroxyurea for myeloproliferative diseases have been reported. Patients who develop acute jaundice or hematuria in the presence of persistent or worsening of anemia should have laboratory tests evaluated for hemolysis (e.g., measurement of serum lactate dehydrogenase, haptoglobin, reticulocyte, unconjugated bilirubin levels, urinalysis, and direct and indirect antiglobulin [Coombs] tests). In the setting of confirmed diagnosis of hemolytic anemia and in the absence of other causes, discontinue Xromi. Malignancies: Hydroxyurea is a human carcinogen. In patients receiving long-term hydroxyurea for myeloproliferative disorders, secondary leukemia has been reported. Secondary leukemia has also been reported in patients treated with long-term hydroxyurea for sickle cell disease. Leukemia has also been reported in patients with sickle cell disease and no prior history of treatment with hydroxyurea. Skin cancer has also been reported in patients receiving long-term hydroxyurea. Advise protection from sun exposure and monitor for the development of secondary malignancies. Embryo-Fetal toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception. Vasculitic toxicities: Cutaneous vasculitic toxicities, including vasculitic ulcerations and gangrene, have occurred in patients with myeloproliferative disorders during therapy with hydroxyurea. These vasculitic toxicities were reported most often in patients with a history of, or currently receiving, interferon therapy. If cutaneous vasculitic ulcers occur, institute treatment and discontinue Xromi. Live Vaccinations: Avoid live vaccine use in a patient taking this medication. Concomitant use of this medication with a live virus vaccine may potentiate the replication of the virus and/or may increase the adverse reaction of the vaccine because normal defense mechanisms may be suppressed by hydroxyurea. Vaccination with live vaccines in a patient receiving this medication may result in severe infection. Patient's antibody response to vaccines may be decreased.

Medication	Warnings/Precautions
	Risks with concomitant use of antiretroviral drugs: Pancreatitis, hepatotoxicity, and peripheral neuropathy have occurred when hydroxyurea was administered concomitantly with antiretroviral drugs, including didanosine and stavudine. Macrocytosis: This medication may cause macrocytosis, which is self-limiting, and is often seen early in the course of treatment. The morphologic change resembles pernicious anemia but is not related to vitamin B12 or folic acid deficiency. This may mask the diagnosis of pernicious anemia. Prophylactic administration of folic acid is recommended. Pulmonary toxicity: Interstitial lung disease including pulmonary fibrosis, lung infiltration, pneumonitis, and alveolitis/allergic alveolitis (including fatal cases) have been reported in patients treated for myeloproliferative neoplasm. Safety and effectiveness have not been established for the use of hydroxyurea in the treatment of myeloproliferative neoplasms and the use is not approved by the FDA. Monitor patients developing pyrexia, cough, dyspnea, or other respiratory symptoms frequently, investigate and treat promptly. Discontinue medication and manage with corticosteroids. Laboratory test interference: Interference with Uric Acid, Urea, or Lactic Acid Assays is possible, rendering falsely elevated results of these in patients treated with hydroxyurea. Hydroxyurea may falsely elevate sensor glucose results from certain continuous glucose monitoring (CGM) systems and may lead to hypoglycemia if sensor glucose results are relied upon to dose insulin.
Adakveo® (crizanlizumab-tmca)	Infusion-related reactions: Monitor patients for signs and symptoms of infusion-related reactions, which may include fever, chills, nausea, vomiting, fatigue, dizziness, pruritus, urticaria, sweating, shortness of breath or wheezing. Discontinue infusion for severe reactions and institute appropriate medical care. Laboratory test interference: Interference with automated platelet counts (platelet clumping) has been observed following administration of medication, in particular, when blood samples were collected in tubes containing ethylenediaminetetraacetic acid (EDTA). Mitigation strategies are recommended.
Endari® (glutamine)	Hepatic impairment: Use with caution in patients with hepatic impairment. Renal impairment: Use with caution in patients with renal impairment.
Casgevy® (exagamglogene autotemcel)	Neutrophil Engraftment Failure: There is potential risk of neutrophil engraftment failure after treatment with Casgevy. In the clinical trials, all treated patients achieved neutrophil engraftment and no patients received rescue CD34 cells. Monitor absolute neutrophil counts (ANC) and manage infections according to standard guidelines and medical judgement. In the event of neutrophil engraftment failure, patients should be infused with rescue CD34 cells. Delayed Platelet Engraftment: Delayed platelet engraftment has been observed with Casgevy treatment. There is an increased risk of bleeding until platelet engraftment is achieved. In the clinical trials, there was no association observed between incidence of bleeding events and time to platelet engraftment. Monitor patients for bleeding according to standard guidelines and medical judgement. Conduct frequent platelet counts until platelet engraftment and platelet recovery are achieved. Perform blood cell count determination and other appropriate testing whenever clinical symptoms suggestive of bleeding arise. Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylaxis, can occur due to dimethyl sulfoxide (DMSO) or dextran 40 in the cryopreservation solution. Monitor patients for hypersensitivity reactions during and after infusion. Off-Target Genome Editing Risk: The risk of unintended, off-target editing in an individual's CD34 cells cannot be ruled out due to genetic variants. The clinical significance of potential off-target editing is unknown.

Medication	Warnings/Precautions
Lyfgenia™ (lovotibeglogene autotemcel)	Hematologic Malignancy: Hematologic malignancy has occurred in patients treated with Lyfgenia. The additional hematopoietic stress associated with mobilization, conditioning, and infusion of Lyfgenia, including the need to regenerate the hematopoietic system, may increase the risk of a hematologic malignancy. Patients with sickle cell disease have an increased risk of hematologic malignancy as compared to the general population. Patients treated with Lyfgenia may develop hematologic malignancies and should have lifelong monitoring. Monitor for hematologic malignancies with a complete blood count (with differential) at least every 6 months for at least 15 years after treatment with Lyfgenia, and integration site analysis at Months 6, 12, and as warranted. Delayed Platelet Engraftment: Delayed platelet engraftment has been observed with Lyfgenia. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia. Patients should be made aware of the risk of bleeding until platelet recovery has been achieved. Monitor patients for thrombocytopenia and bleeding according to standard guidelines. Conduct frequent platelet counts until platelet engraftment and platelet recovery are achieved. Perform blood cell count determination and other appropriate testing whenever clinical symptoms suggestive of bleeding arise. Neutrophil Engraftment Failure: There is a potential risk of neutrophil engraftment failure after treatment with Lyfgenia. Neutrophil engraftment failure is defined as failure to achieve three consecutive absolute neutrophil counts (ANC) $\geq 0.5 \times 10^9$ cells/L obtained on different days by Day 43 after infusion of Lyfgenia. Monitor neutrophil counts until engraftment has been achieved. If neutrophil engraftment failure occurs in a patient treated with Lyfgenia, provide rescue treatment with the back-up collection of CD34+ cells. Insertional Oncogenesis: There is a potential risk of lentiviral vector-mediated insertional oncogenesis after treatment with Lyfgenia. Hypersensitivity Reactions: Allergic reactions may occur with the infusion of LYFGENIA. The dimethyl sulfoxide (DMSO) or dextran 40 in Lyfgenia may cause hypersensitivity reactions, including anaphylaxis. Anti-retroviral Use: Patients should not take prophylactic HIV anti-retroviral medications for at least one month prior to mobilization and until all cycles of apheresis are completed. There are some long-acting anti-retroviral medications that may require a longer duration of discontinuation for elimination of the medication. Hydroxyurea Use: Patients should not take hydroxyurea for at least 2 months prior to mobilization and until all cycles of apheresis are completed. If hydroxyurea is administered between mobilization and conditioning, discontinue 2 days prior to initiation of conditioning. Iron Chelation: Do not administer myelosuppressive iron chelators for 6 months post-treatment with Lyfgenia. Interference with PCR-based Testing: Patients who have received Lyfgenia are likely to test positive by polymerase chain reaction (PCR) assays for HIV due to integrated BB305 LVV proviral DNA, resulting in a possible false-positive PCR assay test result for HIV. Therefore, patients who have received Lyfgenia should not be screened for HIV infection using a PCR-based assay.

Practice Guidelines

The National Heart, Lung, and Blood Institute: Management of Sickle Cell Disease: Summary of the 2014 Evidence Based Report by Expert Panel Members (2014)

- Clinical guidelines and recommendations for the management of sickle cell disease have not been updated since the approval of gene therapies.
- Current treatment recommendations for sickle cell disease primarily revolve around management of complications and the use of hydroxyurea or blood transfusions.
- Hydroxyurea therapy is recommended for adults with any of the following:
 - For adults with 3 or more severe vasoocclusive crises during any 12-month period (strong recommendation, high quality of evidence)
 - Sickle cell disease pain or chronic anemia interfering with daily activities or quality of life (strong recommendation, moderate quality of evidence)
 - Severe or recurrent episodes of acute chest syndrome. (strong recommendation, moderate quality of evidence)
- Treatment with hydroxyurea without regard to the presence of symptoms should be offered for infants, children, and adolescents. (strong/moderate recommendation, high/moderate quality of evidence)
- Addition of hydroxyurea therapy is recommended in adults and children with sickle cell disease and chronic kidney disease on erythropoietin, to improve anemia. (weak recommendation, low quality of evidence)
- In patients with sickle cell anemia, transfuse red blood cells to bring hemoglobin level to 10 g/dL prior to undergoing a surgical procedure involving general anesthesia. (strong recommendation, moderate quality of evidence)
- In patients with sickle cell anemia who receive transfusions long-term, the goal of transfusion should be to maintain an HbS level of <30% prior to the next transfusion. (moderate recommendation, moderate quality of evidence)

Recommendation Definitions

Grade of Recommendation	Clarity of Risk/Benefit	Quality of Supporting Evidence	Implications
Strong recommendation; High-quality evidence	Benefits clearly outweigh harms and burdens, or vice versa	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies*	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 harms and burdens, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise evidence), or unusually strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation; Low-quality evidence	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one critical outcome from observational studies, from RCTs with serious flaws, or indirect evidence	Recommendation may change when higher quality evidence becomes available. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to

Grade of Recommendation	Clarity of Risk/Benefit	Quality of Supporting Evidence	Implications
			change the estimate.
Strong recommendation; Very low-quality evidence (very rarely applicable)	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one of the critical outcomes from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher quality evidence becomes available; any estimate of effect, for at least one critical outcome, is very uncertain.
Weak recommendation; High-quality evidence	Benefits closely balanced with harms and burdens	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patient or societal values. Further research is very unlikely to change our confidence in the estimate of effect.
Weak recommendation; Moderate-quality evidence	Benefits closely balanced with harms and burdens	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise evidence), or unusually strong evidence from unbiased observational studies	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak recommendation; Low-quality evidence	Uncertainty in the estimates of benefits, harms, and burdens; benefits may be closely balanced with harms and burdens	Evidence for at least one critical outcome from observational studies, from RCTs with serious flaws, or indirect evidence	Other alternatives may be equally reasonable. 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.
Weak recommendation; Very low-quality evidence	Major uncertainty in the estimates of benefits, harms, and burdens; benefits may or may not be balanced with harms and burdens	Evidence for at least one critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least one critical outcome, is very uncertain.

* Exceptionally strong evidence from unbiased observational studies includes: (1) evidence from studies that yield estimates of the treatment effect that are large and consistent; (2) evidence in which all potential biases may be working to underestimate an apparent treatment effect, and therefore, the actual treatment effect is likely to be larger than that suggested by the study data; and (3) evidence in which a dose-response gradient exists

Clinical Trials/Systematic Reviews/Meta-Analyses

Citation	Design	Endpoints
Niihara Y, Miller ST, Kanter J, et al; A phase 3 trial of l-glutamine in sickle cell disease. N Engl J Med. 2018;379(3):226-235.	This study was a multi-center, randomized, placebo-controlled, double-blind, phase 3 trial. They tested the efficacy of pharmaceutical-grade l-glutamine (0.3 g/kg/dose) administered twice daily by mouth, as compared with placebo, in reducing the incidence of pain crises among patients with sickle cell anemia or sickle β^0-thalassemia and a history of two or more pain crises during the previous year. Therapy was continued through the 48-week treatment period for those receiving hydroxyurea at stable dose for at least 3 months before screening. N = 230; Age range: 5 to 58 years; 53.9% female; Randomized 2:1 - l-glutamine group (N = 152) - Placebo (N = 78) Inclusion criteria: Patient is at least five years of age, patient has been diagnosed with sickle cell anemia or sickle β^0-thalassemia (documented by hemoglobin electrophoresis), patient has had at least two documented episodes of sickle cell crises within 12 months of the screening visit, if the patient has been treated with an anti-sickling agent within three months of the screening visit, the therapy must have been continuous for at least three months with the intent to continue for the duration of the study, patient or the patient's legally authorized representative has given written informed consent, if the patient is a female of child-bearing potential, she agrees to avoid pregnancy during the study and is willing and agrees to practice a recognized form of birth control during the course of the study (e.g. barrier, birth control pills, abstinence). Exclusion criteria: Patient has a significant medical condition that required hospitalization (other than sickle cell crisis) within two months of the screening visit, patient has prothrombin time INR > 2.0, patient has serum albumin < 3.0 g/dl, patient has received any blood products within three weeks of the Screening Visit, patient has uncontrolled liver disease or renal insufficiency, patient is pregnant or lactating or has the intention of becoming pregnant during the study (if female and of child-bearing potential), patient is currently taking or has been treated with any form of glutamine supplement within 30 days of the screening visit, patient has been treated with an experimental anti-sickling medication/ treatment within 30 days of the screening visit	Primary endpoint: The number of pain crises through week 48. Secondary endpoints: The number of hospitalizations for sickle cell-related pain, the number of visits to an ED (or outpatient treatment center) for sickle cell-related pain, and changes in hematologic measures (hemoglobin and hematocrit levels and reticulocyte count) from baseline through week 48.

	(with the exception of hydroxyurea in pediatric patients), patient is currently taking or has been treated with an investigational drug within 30 days of the screening visit (with the exception of hydroxyurea in pediatric patients), patient is currently enrolled in an investigational drug or device study and/or has participated in such a study within 30 days of the screening visit, there are factors that would, in the judgment of the investigator, make it difficult for the patient to comply with the requirements of the study.	
Results: There were significantly fewer pain crises in the l-glutamine group than the placebo group (P=0.005). The l-glutamine group had a median of 3.0 compared to 4.0 in the placebo group. Additionally, the l-glutamine group had fewer hospitalizations than placebo (P=0.005) as demonstrated by a median of 2.0 in the l-glutamine group and 3 in the placebo group. Concomitant use of hydroxyurea was seen in two-thirds of patients. The l-glutamine group experienced a greater frequency of low-grade nausea, non-cardiac chest pain, fatigue, and musculoskeletal pain. Conclusion: Over the 48-week period, the median number of pain crises was lower among children and adults with sickle cell anemia receiving therapy with l-glutamine alone or with hydroxyurea as compared to placebo (with or without hydroxyurea).		
Citation	Design	Endpoints
SUSTAIN Trial Ataga KI, Kutlar J, Liles D, et al. Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease. N Engl J Med. 2017 Feb 2;376(5):429-439	This study was a Phase 2, multicenter, randomized, placebo-controlled, double-blind, 12-month study to assess safety and efficacy of crizanlizumab with or without hydroxyurea therapy in sickle cell disease patients with sickle cell-related pain crises. N = 198; Median age: 29 years older; 55% female; Randomized 1:1:1 - Low-dose crizanlizumab (2.5 mg/kg) via IV infusion once every 4 weeks through week 50 (n=66) - High-dose crizanlizumab (5.0 mg/kg) via IV infusion once every 4 weeks through week 50 (n=67) - Placebo via IV infusion once every 4 weeks through week 50 (n=65) Inclusion criteria: - Sickle Cell Disease (HbSS, HbSC, HbSβ⁰-thalassemia, or HbSβ⁺-thalassemia) - If receiving hydroxyurea or erythropoietin, treatment must have been prescribed for at least 6 months, with the dose stable for at least 3 months - Between 2 and 10 sickle cell-related pain crises in the past 12 months Exclusion criteria: - On a chronic transfusion program or planning on exchange transfusion during the study - Hemoglobin <4.0 g/dL	Primary endpoint: The annual rate of sickle cell–related pain crises with high-dose crizanlizumab versus placebo. Secondary endpoints: The annual rate of days hospitalized, the times to first and second crises, annual rates of uncomplicated crises (defined as crises other than the acute chest syndrome, hepatic sequestration, splenic sequestration, or priapism) and the acute chest syndrome, and patient-reported outcomes were also assessed.

	Planned initiation, termination, or dose alteration of hydroxyurea during the study	
	Receiving chronic anticoagulation therapy (e.g. warfarin, heparin) other than aspirin	
Results: The median rate of crises per year was 1.63 with high-dose crizanlizumab compared to 2.98 with placebo (indicating a 45.3% lower rate with high-dose crizanlizumab, $P = 0.01$). The median rate of days hospitalized was 4.00 per year in the high-dose crizanlizumab group and 6.87 per year in the placebo group (representing a 41.8% lower rate with high-dose crizanlizumab than with placebo, although the difference was not statistically significant, $P=0.45$). The median time to the first crisis was significantly longer with high-dose crizanlizumab than with placebo (4.07 vs. 1.38 months, $P=0.001$). The median time to the second crisis was also significantly longer with high-dose crizanlizumab compared to placebo (10.32 vs. 5.09 months, $P=0.02$). The median rate of uncomplicated crises per year was 1.08 with high-dose crizanlizumab compared to 2.91 with placebo (indicating a 62.9% lower rate with high-dose crizanlizumab, $P=0.02$). Adverse events that occurred in 10% or more of the patients in either active-treatment group and at a frequency that was at least twice as high as that in the placebo group were arthralgia, diarrhea, pruritus, vomiting, and chest pain Conclusion: A significantly lower rate of sickle cell-related pain crises was seen with crizanlizumab therapy compared to placebo with a low incident of adverse.		

Citation	Design	Endpoints
European Sickle Cell Disease Cohort - Hydroxyurea (ESCORT-HU)	The European Sickle Cell Disease Cohort study (ESCORT-HU) assessed the efficacy of Siklos®. This was an open-label single-arm study of 405 pediatric patients with sickle cell disease from 2-18 years of age, of which 141 had not been previously treated with hydroxyurea prior to enrollment. At least 12 months of follow-up was required.	Primary endpoint: Change in hemoglobin after 6 and 12 months of Siklos® treatment Secondary endpoints: SCD events (e.g. vaso-occlusive episodes, acute chest syndrome, hospitalization)
Results: Siklos® use resulted in an increase in hemoglobin F for the analyzable pediatric population ($n=141$). Median (range) hemoglobin F percentages were 5.6% (1.3, 15.0) at baseline and 12.8% (2.1, 37.2) at least 6 months after initiation of Siklos® treatment, with median (range) change of 5.9% (-2.2, 34.7) in 47 patients. Median (range) hemoglobin levels were 8.2 g/dL (3.7, 14.2) at baseline, 8.8 g/dL (0.7, 13.1) at 6 months (the value closest to 6 months collected between 5 and 7 months), and 8.9 g/dL (5.5, 13.2) at 12 months (the value closest to 12 months collected between 10 and 14 months) after initiation of Siklos® treatment. The median (range) change was 0.5 g/dL (-4.6, 6.1) in 63 patients at 6 months and 0.7 g/dL (-6.4, 6.0) in 83 patients at 12 months after initiation of Siklos® treatment. Among pediatric patients not previously treated with hydroxyurea prior to enrollment and analyzable for efficacy ($N=141$), the percentage of patients with at least one vaso-occlusive episode, one episode of acute chest syndrome, one hospitalization due to SCD or one blood transfusion decreased after 12 months of Siklos® treatment. Most common adverse reactions (incidence $>10\%$) include infections and neutropenia. Conclusion: Treatment with Siklos® resulted in increased fetal hemoglobin (hemoglobin F or HbF) concentration. After 12 months of treatment, there was a significant reduction in the number of pediatric patients experiencing at least one painful crisis in the 12 months prior to treatment with Siklos®.		
Citation	Design	Endpoints

Multicenter Study of Hydroxyurea in Sickle Cell Anemia	A randomized, double-blind, placebo-controlled trial that evaluated 299 adult patients (≥ 18 years) with moderate to severe disease (≥ 3 painful crises yearly). The Data Safety Monitoring Committee stopped the trial after accrual was completed but before the scheduled 24 months of follow-up was completed in all patients, based on observations of fewer painful crises among patients receiving hydroxyurea.	Median yearly rate of painful crises, median yearly rate of painful crises requiring hospitalization, median time to first painful crisis (months), median time to second painful crisis (months), incidence of chest syndrome (# episodes), number of patients transfused, number of units of blood transfused
Results: Compared to placebo treatment, treatment with hydroxyurea resulted in a significant decrease in the yearly rate of painful crises (percent change versus placebo -46), the yearly rate of painful crises requiring hospitalization (percent change versus placebo -60), the incidence of chest syndrome (percent change versus placebo -45 episodes), the number of patients transfused (percent change versus placebo -30), and units of blood transfused (percent change versus placebo -37). Hydroxyurea treatment significantly increased the median time to both first (percent change versus placebo +104 months) and second (percent change versus placebo +59 months) painful crises. Conclusion: Most of the benefit in crisis reduction was seen in the patients with 6 or more painful crises during the preceding 12 months even though patients with 3 or more painful crises were included in the study. Fetal hemoglobin (HbF) increased 4 to 12 weeks after initiation of treatment in patients with sickle cell anemia treated with hydroxyurea. In general, average HbF levels correlate with dose and plasma level with possible plateauing at higher dosages. No clear relationship between reduction in crisis frequency and increased HbF or F-cell levels was demonstrated. The dose-related cytorreductive effects of hydroxyurea, particularly on neutrophils, was the factor most strongly correlated with reduced crisis frequency.		

Formulary Placement, Utilization and Cost Experience (10-01-2025 to 12-31-2025)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Sickle Cell Agents								
Siklos® (hydroxyurea) 100 mg, 1000 mg oral tablets	0	0	\$0.00	\$0.00	0	0 (0%)	F-PA	No change
Droxia® (hydroxyurea) 200 mg, 300 mg, 400 mg oral capsule	0	0	\$0.00	\$0.00	0	0 (0%)	F	No change
Xromi® (hydroxyurea) 100 mg/ml oral solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
L-glutamine (Endari®) 5 gram oral powder packet	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Adakveo® (crizanlizumab-tmca) 10 mg/mL intravenous solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Casgevy® (exagamglogene autotemcel) intravenous suspension	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Lyfgenia™ (lovotibeglogene autotemcel) intravenous suspension	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 = Excluded

Prior Authorization Criteria

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 <u>OR</u> • 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	3/20253/2026

Recommendation: No changes

Endari	
Therapeutic Classes (AHFS)	Other Miscellaneous Therapeutic Agents
Medications	Non-formulary L-Glutamine (Endari)
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	N/A
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	Initial/Later Approval If all of the conditions are met, requests will be approved for a 12 months. If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Initial: - Member has diagnosis of sickle cell disease - Documentation was provided that the member had 2 or more crises in the last 12 months - Documentation was provided the member has been on hydroxyurea at the maximum tolerated dose and was compliant within the last 6 months (or a medical reason was provided why member is unable to use hydroxyurea) - Request is for an FDA approved dose Reauthorization: - Prescriber attests member had reduction in number of sickle cell crises - Request is for an FDA approved dose
Criteria Statement	L-Glutamine (Endari) is reserved for members who have unstable sickle cell disease and are taking the highest tolerated dose of hydroxyurea or cannot/should not take hydroxyurea.
Last P&T Review Date	~~12/2025~~ 3/2026

Recommendation: No changes

Adakveo	
Medications	Adakveo (crizanlizumab-tmca)
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	Check AAH active CCS cases for members < 21 years of age for MCAL Member must be 16 years of age or older
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	If the criteria are met, the initial request will be approved for up to a 12 month duration; reauthorization requests will be approved for up to 12 months.
Maximum Billable Units	Variable
Other Criteria	Initial Authorization: • Member has a confirmed diagnosis of sickle cell disease • Documentation was provided that the member has had 2 or more pain crises in the last 12 months • Documentation was provided that the member has been taking hydroxyurea at the maximum tolerated dose and has been compliant within the last 6 months (or a medical reason was provided why the patient is unable to use hydroxyurea) • Documentation of the member's current weight • Request is for an FDA-approved dose Reauthorization: • Documentation has been submitted that the member has demonstrated or maintained ONE of the following changes from baseline: ○ Reduction in pain crises ○ Increased time between crises ○ Decrease in days hospitalized • Documentation of the member's current 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 Review Date	9/20253/2026

Recommendation: No changes

Gene Therapy for Sickle Cell Disease	
Medications	Casgevy (exagamglogene autotemcel), Lyfgenia (lovotibeglogene 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 or specialist in the treatment of sickle cell disease
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 sickle cell disease - Member has experienced at least 2 severe vaso-occlusive crises/events (VOE) per year in the past 2 years defined as either: - VOE requiring a hospitalization or multiple visits to an emergency department/urgent care over 72 hours and receiving intravenous medications at each visit - priapism lasting > 2 hours and requiring a visit to a medical facility - acute chest syndrome - splenic sequestration - hepatic sequestration - Documentation was provided that the member has been taking hydroxyurea at the maximum tolerated dose and has been compliant within the last 6 months (or a medical reason was provided why the patient is unable to use hydroxyurea) - Documentation was provided that the member had a trial and failure of, or a medical reason was provided why the patient is unable to trial one of the following agents: - L-Glutamine (Endari) - Adakveo - Prescriber attests pregnancy has been ruled out prior to initiation of treatment (if applicable) - Patient has not had a prior HSCT or gene therapy treatment The safety and effectiveness of repeat administration of Casgevy or Lyfgenia 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	12/20253/2026

References

1. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: <https://clinicaltrials.gov/>. Accessed on October 28, 2025.
2. Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on October 28, 2025.
3. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: <https://www.ncbi.nlm.nih.gov/pubmed>.
4. Accessed on October 28, 2025.
5. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>. Accessed on October 28, 2025.
6. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: <http://www.fda.gov/>. Accessed on October 28, 2025.
7. IPD Analytics. Bay Harbor Islands, Florida: IPD Analytics, LLC. <http://www.ipdanalytics.com>. Accessed on October 28, 2025.
8. Biomedtracker. Cambridge, MA: Informa Business Intelligence, Inc. <https://www.biomedtracker.com/>. Accessed on October 28, 2025.
9. Institute for Clinical and Economic Review (ICER Crizanlizumab, Voxelotor, and L-Glutamine for Sickle Cell Disease: Effectiveness and Value (Evidence Report). Available at: https://icer-review.org/wp-content/uploads/2019/08/ICER_SCD_Evidence-Report_031220.pdf
10. Vichinsky E, Hoppe CC, Ataga KI, et al. A Phase 3 Randomized Trial of Voxelotor in Sickle Cell Disease. *N Engl J Med*. 2019;381(6):509-519.
11. Yawn BP, Buchanan GR, Afeniyi-annan AN, et al; National Heart, Lung and Blood Institute. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *JAMA*. 2014; 312(10): 1033-48.
12. Adakveo® [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2024.
13. Endari (glutamine) [prescribing information]. Torrance, CA: Emmaus Medical Inc; June 2025.
14. Droxia (hydroxyurea) [prescribing information]. Rahway, NJ: Waylis Therapeutics LLC; September 2025.
15. Siklos (hydroxyurea) [prescribing information]. Rosemont, PA: Medunik USA Inc; November 2023.
16. Casgevy (exagamglogene autotemcel) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Incorporated; August 2025.
17. Xromi (hydroxyurea) [prescribing information]. Franklin, TN: Rare Disease Therapeutics Inc; December 2024.
18. Lyfgenia (lovotibeglogene autotemcel) [prescribing information]. Somerville, MA: Bluebird Bio, Inc; December 2023.
19. Howard J, Ataga KJ, Brown RC, et al. Voxelotor in adolescents and adults with sickle cell disease (HOPE): long-term follow-up results of an international, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Haematol*. 2021;8(5):e323-e333. doi:10.1016/S2352-3026(21)00059-4
20. Estep JH, Kalpatthi R, Woods G, et al. Safety and efficacy of voxelotor in pediatric patients with sickle cell disease aged 4 to 11 years. *Pediatr Blood Cancer*. 2022 Aug;69(8):e29716. doi: 10.1002/pbc.29716. Epub 2022 Apr 21. PMID: 35451176.
21. Leonard A, Tisdale JF. Gene therapy for sickle cell disease. *Hematology Am Soc Hematol Educ Program*. 2023 Dec 8;2023(1):542-547. doi: 10.1182/hematology.2023000487. PMID: 38066927; PMCID: PMC10727030.
22. Nikitin D, Beaudoin FL, Thokala P, McKenna A, Nhan E, Rind DM, Pearson SD. Gene therapies for sickle cell disease: Effectiveness and value. *J Manag Care Spec Pharm*. 2023 Nov;29(11):1253-1259. doi: 10.18553/jmcp.2023.29.11.1253. PMID: 37889869; PMCID: PMC10609928.
23. Pfizer Press Release. Pfizer Voluntarily Withdraws All Lots of Sickle Cell Disease Treatment Oxbryta from Worldwide Markets. September 25, 2024. <https://www.pfizer.com/news/press-release/press-release-detail/pfizer-voluntarily-withdraws-all-lots-sickle-cell-disease>

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

Approval Date: November 19, 1946

Marketing Date: Unknown

Recommendation

- No changes
 - The current formulary status is F
 - There was no utilization of this medication and no prior authorization requests from 10/1/2025 to 12/31/2025

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

\$127

(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.

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)
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).

References

1. Methergine [prescribing information]. Novel Laboratories, Somerset, NJ; May, 2025.
2. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: <https://clinicaltrials.gov/>. Accessed on December 30, 2025.
3. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: <https://www.ncbi.nlm.nih.gov/pubmed>. Accessed on December 30, 2025.
4. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: <http://www.fda.gov/>. Accessed on December 30, 2025.
5. IPD Analytics. Bay Harbor Islands, Florida: IPD Analytics, LLC. <http://www.ipdanalytics.com>. Accessed on December 30, 2025.
6. American College of Obstetrics and Gynecologists (ACOG) Practice Bulletin No. 183: Postpartum Hemorrhage. Obstet Gynecol. 2017;130(4):e168-e186.
7. Şentürk Ş, Kağıtçı M, Balık G, Arslan H, Kır Şahin F. The Effect of the Combined Use of Methylergonovine and Oxytocin during Caesarean Section in the Prevention of Post-partum Hemorrhage. Basic Clin Pharmacol Toxicol. 2016 May;118(5):338-43.

Alameda MRGs for review Q1 2026 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	<u>FORMULARY STATUS: Formulary, Pays at Point-of-Sale (first line)</u> 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 <u>FORMULARY STATUS: Formulary, Requires Prior Authorization (second line)</u> 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 <u>FORMULARY STATUS: Formulary, Requires Prior Authorization (third line)</u> 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 <u>AND</u> 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	~~3/2025~~ 3/2026

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	<u>3/20253/2026</u>

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	3/20253/2026

Recommendation: Change naming convention to reflect generic availability of Corlanor as ivabradine

Ivabradine (Corlanor) (ivabradine)	
Therapeutic Classes (AHFS)	Cardiac drugs, miscellaneous
Medications	Formulary, PA required: ivabradine (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 ivabradine (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. • Ivabradine (Corlanor) may not be approved if the request indicates any of the following: ○ Severe hypotension (less than 90/50 mmHg) ○ Severe hepatic impairment (Child-Pugh class C) ○ 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 $\leq$ 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	<u>Ivabradine</u> (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. <u>Ivabradine</u> (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	<u>3/20253/2026</u>

Recommendation: No criteria changes, add enoxaparin 300mg/3mL injection to formulary as it is missing from formulary and is priced comparatively.

Injectable Anticoagulants	
Therapeutic Classes (AHFS)	Anticoagulants
Medications	<u>Preferred:</u> 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. <u>Non-Preferred:</u> 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.

Injectable Anticoagulants	
	PA CRITERIA FOR APPROVAL FOR USE IN MEMBER WITH CANCER: • The medication is being prescribed for the prevention or treatment of a VTE for 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 formulary oral 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	<u>3/20253/2026</u>

Recommendation: No changes, minor grammatical correction

Corticosteroids for Duchenne Muscular Dystrophy (DMD)	
Therapeutic Classes (AHFS)	Glucocorticoids
Medications	Formulary, PA required deflazacort (Emflaza) 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 Duchenne 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 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	3/20253/2026

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	<u>3/20253/2026</u>

Recommendation: No changes

Ezetimibe (Zetia)	
Therapeutic Classes (AHFS)	Cholesterol Absorption Inhibitors
Medications	<u>Formulary, step therapy required</u> 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 Later Approvals 12 months 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	~~3/2025~~ 3/2026

Recommendation: No changes

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 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	<u>Asthma</u> - 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) <u>COPD</u> - 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), 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	3/20253/2026

Recommendation: Remove Altoprev as it has been discontinued

Altopen (lovastatin ER) and Fluvastatin, and Fluvastatin ER	
Therapeutic Classes (AHFS)	Antihyperlipidemic – HMG CoA reductase inhibitors
Medications	Non-formulary (non-preferred, requires prior authorization): ~~Altopen (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	~~Altopen, f~~ 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	~~Altopen, f~~ 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	~~3/2025~~ 3/2026

Recommendation: No changes

Ophthalmic Antihistamines	
Therapeutic Classes (AHFS)	Antiallergic Agents (EENT)
Medications	Formulary, with restrictions ((quantity limit may apply) - Azelastine 0.05% drops - Ketotifen (Zaditor) 0.035% 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	3/20253/2026

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	3/20253/2026

Recommendation: Change naming convention to reflect generic availability of Brilinta as ticagrelor

Ticagrelor (Brilinta) (ticagrelor) tablet	
Therapeutic Classes (AHFS)	Platelet aggregation inhibitors
Medications	Formulary, PA required ~~ticagrelor (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	<u>Ticagrelor (Brilinta)</u> is reserved for members with a diagnosis of stable coronary artery disease with a high risk for cardiovascular events. <u>Ticagrelor (Brilinta)</u> is reserved for members with a diagnosis of minor ischemic stroke (NIHSS score ≤ 5) or high-risk transient ischemic attack (ABCD2 score ≥ 4). <u>Ticagrelor (Brilinta)</u> 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	<u>3/20253/2026</u>

Recommendation: Remove Byetta and Bydureon as they have been discontinued and show generic availability of Victoza

GLP-1 Agonists	
Therapeutic Classes (AHFS)	GLP-1 Agonists
Medications	<u>Formulary, Step therapy required (prior use of metformin)</u> • Trulicity (dulaglutide) • Ozempic (semaglutide) • Rybelsus (semaglutide) • Mounjaro (tirzepatide) <u>Formulary, PA required</u> • ~~Byetta, Bydureon~~, Bydureon Bcise (exenatide) • <u>liraglutide</u> (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	<u>Criteria for Type 2 Diabetes</u> 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	3/20253/2026

Recommendation: Change naming conventions to reflect generic availability of Onglyza and Kombiglyze XR

DPP-4 Inhibitors and Combinations	
Therapeutic Classes (AHFS)	Dipeptidyl Peptidase-4 (DPP-4) Inhibitors
Medications	<u>Formulary, Step therapy required (prior use of metformin)</u> • Alogliptin (Nesina) • Alogliptin/metformin (Kazano) • Alogliptin/pioglitazone (Oseni) • Januvia (sitagliptin) • Janumet, Janumet XR (sitagliptin/metformin) <u>Formulary, PA required/ Non-formulary</u> • Tradjenta (lingagliptin) • Jentadueto, Jentadueto XR (linagliptin/metformin) • ~~saxagliptin~~ (Onglyza) ~~(saxagliptin)~~ • ~~saxagliptin/metformin~~ (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	<u>Criteria for Type 2 Diabetes</u> 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	3/20253/2026

Recommendation: No changes

SGLT2 inhibitors and Combinations	
Therapeutic Classes (AHFS)	Glucose Cotransport 2 Inhibitors (SGLT2 inhibitors)
Medications	<u>Formulary, step therapy required</u> • Steglatro (ertugliflozin) • Segluromet (ertugliflozin/metformin) • Farxiga (dapagliflozin) • Xigduo XR (dapagliflozin/metformin) <u>Formulary, PA required/Non-formulary</u> • Jardiance (empagliflozin) • Synjardy/Synjardy XR (empagliflozin/metformin) • Dapagliflozin (Farxiga) • Dapagliflozin/metformin (Xigduo XR) • Invokana (canagliflozin) • 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	<u>Formulary, step therapy required medications</u> 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 <u>Formulary, PA required/Non-formulary medications</u> 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	<u>~~3/2025~~3/2026</u>

Recommendation: No changes

Agents for Atopic Dermatitis	
Therapeutic Classes (AHFS)	Skin and mucous membrane agents, anti-inflammatory agents, misc (skin)
Medications	<u>Formulary, Step therapy required:</u> Tacrolimus (Protopic) Pimecrolimus (Elidel) <u>Formulary, Prior Authorization Required:</u> Dupixent (dupilumab) Eucrisa (crisaborole) Adbry (tralokinumab-ldrm) <u>Non-formulary:</u> Rinvoq (upadacitinib) Opzelura (ruxolitinib) 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	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	<u>Initial Authorization:</u> 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: ○ One formulary medium to high potency topical corticosteroid ○ 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** Criteria for approval for Dupixent 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 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 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 Cibinqo or Rinvoq: • Diagnosis of refractory, moderate to severe AD • Trial and failure of, intolerance, or contraindication to, another systemic drug product for AD <u>Reauthorization:</u> • Prescriber attests that the member has experienced improvement in symptoms (e.g. significant clearing of the skin, reduction in itching)
Criteria Statement	For mild 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 severe atopic dermatitis Eucrisa, Opzelura, Vtama, or Zoryve are 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 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 Nemluvio is reserved for members who have used (or cannot/should not use) ONE of the following: Eucrisa, Opzelura, Vtama, or Zoryve. For moderate to severe atopic dermatitis Ebglyss is reserved for members who have used (or cannot/should not use) ONE of the following: Adbry, Dupxent, or Nemluvio. For refractory moderate to severe atopic dermatitis Cibinqo and Rinvoq are reserved for members who have used (or cannot/should not use) another systemic drug product for AD.
Last P&T Review Date	~~3/2025~~ 3/2026

Recommendation: No changes

Parkinson's Disease Agents	
Therapeutic Classes (AHFS)	DOPAMINE PRECURSORS
Medications	<u>Formulary, Step Therapy Required</u> Carbidopa-levodopa-entacapone (Stalevo) oral tablet Entacapone (Comtan) oral tablet <u>Formulary, Prior Authorization</u> 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	~~3/2025~~ 3/2026

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 to 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	3/20253/2026

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	~~3/2025~~ 3/2026

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	~~3/2025~~ 3/2026

Recommendation: No changes

Corticosteroid Preparations to Treat Hemorrhoids	
Therapeutic Classes (AHFS)	Corticosteroids (skin, mucous membrane)
Medications	<u>Formulary</u> Hydrocortisone acetate (Anucort-HC) rectal suppository 25 Mg Hydrocortisone (Proctozone-HC) topical cream with perineal applicator 2.5 % <u>Formulary, PA required</u> 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	<u>Initial criteria for authorization for formulary, PA-required medications:</u> - Documented trial and failure, intolerance, inability to use, or contraindication to one preferred formulary medication <u>Re-approval criteria for formulary, PA-required medications</u> - 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	3/20253/2026

Recommendation: No changes

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 Reauthorization 12 months 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	<u>Fexofenadine-pseudoephedrine tablet extended release step therapy criteria:</u> 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	<u>3/2025</u> 3/2026

Recommendation: No changes

Savella (milnacipran) tablet	
Therapeutic Classes (AHFS)	Fibromyalgia Agents
Medications	<u>Formulary, step therapy required</u> 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	<u>Savella tablet step therapy criteria:</u> 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	<u>3/2025</u> 3/2026

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	<u>Travoprost (Travatan Z) ophthalmic drops step therapy criteria:</u> 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	<u>3/2025</u> 3/2026

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	<u>Initial criteria for the use of Arikayce (amikacin liposome) inhalation suspension</u> - 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	~~3/2025~~ 3/2026

Recommendation: No changes

Zurzuva	
Therapeutic Classes (AHFS)	Antidepressants, Miscellaneous
Medications	Zurzuva (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 Zurzuva per postpartum period. Reauthorization will not be permitted.
PA Review Criteria	<u>Initial Authorization:</u> - 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	Zurzuva 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	~~3/2025~~ 3/2026

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	<u>Authorization for initial Clostridium difficile infection:</u> 1. Documentation provided for intolerance or medical reason why patient is unable to use oral vancomycin 2. Dose requested follows FDA labeling <u>Authorization for recurrent Clostridium difficile infection:</u> 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	3/20253/2026

Recommendation: No changes

Niemann-Pick Disease Type C	
Therapeutic Classes (AHFS)	Other Miscellaneous Therapeutic Agents
Medications	Miplyffa (arimoclomol), Aqneursa (levacetylucine)
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	3/20253/2026

Alameda PADs for review Q1 2026 P&T Consent Agenda

Recommendation: No changes

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. <u>ONCOLOGY INDICATIONS</u> <u>Initial Authorization:</u> • 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 <u>Reauthorization</u>

- 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)
- 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	~~3/2025~~ 3/2026

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	<u>3/2025</u> 3/2026

Recommendation: Minor language update in the renewal section for clarity on acceptable improvement endpoints.

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	<u>Initial Authorization</u> • 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 <u>Reauthorization</u> • 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 <u>oxalate, urinary oxalate:creatinine ratio</u>, 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	3/20253/2026

Recommendation: No changes

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 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 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 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 8-12 weeks OR - Reduction in RBC transfusion by at least 4 units over a period of 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	~~3/2025~~ 3/2026

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	<u>Initial Authorization:</u> - 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	~~3/2025~~ 3/2026

Recommendation: No changes

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	~~3/2025~~ 3/2026

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	<u>Initial Authorization:</u> 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) <u>Re-Authorization:</u> • 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	~~3/2025~~ 3/2026

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	<u>Initial Authorization</u> • 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 <u>Reauthorization</u> • 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	3/20253/2026

Alameda Alliance for Health (IHSS)

Q1 2026 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
PAZOPanib HCl Oral Tablet 400 MG	NF to F-PA
Cladribine (8 Tabs) Oral Tablet Therapy Pack 10 MG	NF to F-PA
Cladribine (10 Tabs) Oral Tablet Therapy Pack 10 MG	NF to F-PA
Cladribine (5 Tabs) Oral Tablet Therapy Pack 10 MG	NF to F-PA
Cladribine (4 Tabs) Oral Tablet Therapy Pack 10 MG	NF to F-PA
Cladribine (9 Tabs) Oral Tablet Therapy Pack 10 MG	NF to F-PA
Cladribine (7 Tabs) Oral Tablet Therapy Pack 10 MG	NF to F-PA
Cladribine (6 Tabs) Oral Tablet Therapy Pack 10 MG	NF to F-PA
Mavenclad (8 Tabs) Oral Tablet Therapy Pack 10 MG	F-PA to NF
Mavenclad (10 Tabs) Oral Tablet Therapy Pack 10 MG	F-PA to NF
Mavenclad (5 Tabs) Oral Tablet Therapy Pack 10 MG	F-PA to NF
Mavenclad (4 Tabs) Oral Tablet Therapy Pack 10 MG	F-PA to NF
Mavenclad (9 Tabs) Oral Tablet Therapy Pack 10 MG	F-PA to NF
Mavenclad (7 Tabs) Oral Tablet Therapy Pack 10 MG	F-PA to NF
Mavenclad (6 Tabs) Oral Tablet Therapy Pack 10 MG	F-PA to NF
Shingrix Intramuscular Suspension Prefilled Syringe 50 MCG/0.5ML	NF to F-QL-AL (QL: 1 syringe/1 dose, member allowed 2 fills per lifetime; AL: 18 years old and above)
Wegovy Oral Tablet 1.5 MG	NF to F-PA-QL (30 tabs/30 days)
Wegovy Oral Tablet 4 MG	NF to F-PA-QL (30 tabs/30 days)
Wegovy Oral Tablet 9 MG	NF to F-PA-QL (30 tabs/30 days)
Wegovy Oral Tablet 25 MG	NF to F-PA-QL (30 tabs/30 days)

Alameda Alliance for Health Q1 2026 PAD Updates

This list only includes summary of changes to prior authorization (PA) for physician administered drugs for quarter 1 2026 and is not comprehensive.

HCPCS Code	HCPCS Description	Action
J9183	GEMCITABINE INTRAVESICAL SYSTEM (INLEXZO)	Add PA
J9277	PEMBROLIZUMAB, 1 MG AND BERAHYALURONIDASE ALFA-PMPH (KEYTRUDA QLEX)	Add PA
J9003	LEUPROLIDE INJECTABLE (CAMCEVI ETM)	Add PA
Q5161	DENOSUMAB-KYQQ (AUKELSO/BOSAYA) BIOSIMILAR	Add PA
Q5162	DENOSUMAB-NXXP (BILDYOS/BILPREVDA) BIOSIMILAR	Add PA
J3404	ZOPAPOGENE IMADENOVEC-DRBA (PAPZIMEOS)	Add PA
J9601	INVOSELTAMAB-GCPT (LYNOZYFIC)	Add PA
J1553	IMMUNE GLOBULIN (YIMMUGO)	Add PA
J9019	ASPARAGINASE (ERWINAZE), 1,000 IU ERWINAZE	Remove PA
J9020	ASPARAGINASE, 10,000 UNITS, NOT OTHERWISE SPECIFIED	Remove PA
J1562	IMMUNE GLOBULIN (VIVAGLOBIN)	Remove PA
Q5109	INFLIXIMAB-QBTX BIOSIMILR (IXIFI)	Remove PA
Q5131	ADALIMUMAB-AACF (IDACIO), BIOSIMILAR	Remove PA



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

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
Administrative Oversight Committee Approval Date	~~5/21/2025~~ 3/3/2026

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.IX. 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.X. 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. Darwin: Point-of-sale system used to verify claimshistory
 - 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.XI. 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, 5/21/2025, 3/3/2026

REFERENCES

- NCQA UM ~~1210~~, 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.



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

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
Administrative Oversight Committee Approval Date	~~5/21/2025~~ 3/4/2026

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. Prior Authorizations may be submitted electronically to the PBM using Covermymeds. 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~~¹⁹²) 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:

draft

- 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 at least annually 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 (unless treating gender dysphoria or alleviating mental health or substance use):
 - (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) recent (no more than 5-years old) peer reviewed articles published in major scientific journals.
- 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

draft

(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**). For more information on appeals, refer to **G&A-008 Adverse Benefit Determination Appeal Process**.

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.

Draft

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

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-005 P&T Committee Roles and Scope](#)
RX-006 Pharmacy Services Staff Description
RX-008 PBM Delegated Audit Oversight
RX-009 Pharmaceutical Emergency Supply Provision
[RX-011 Review and Notification Time Frames](#)

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 APPROVAL 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, 5/21/2025, [9/2025, 3/4/2026](#)

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—Medi-Cal 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

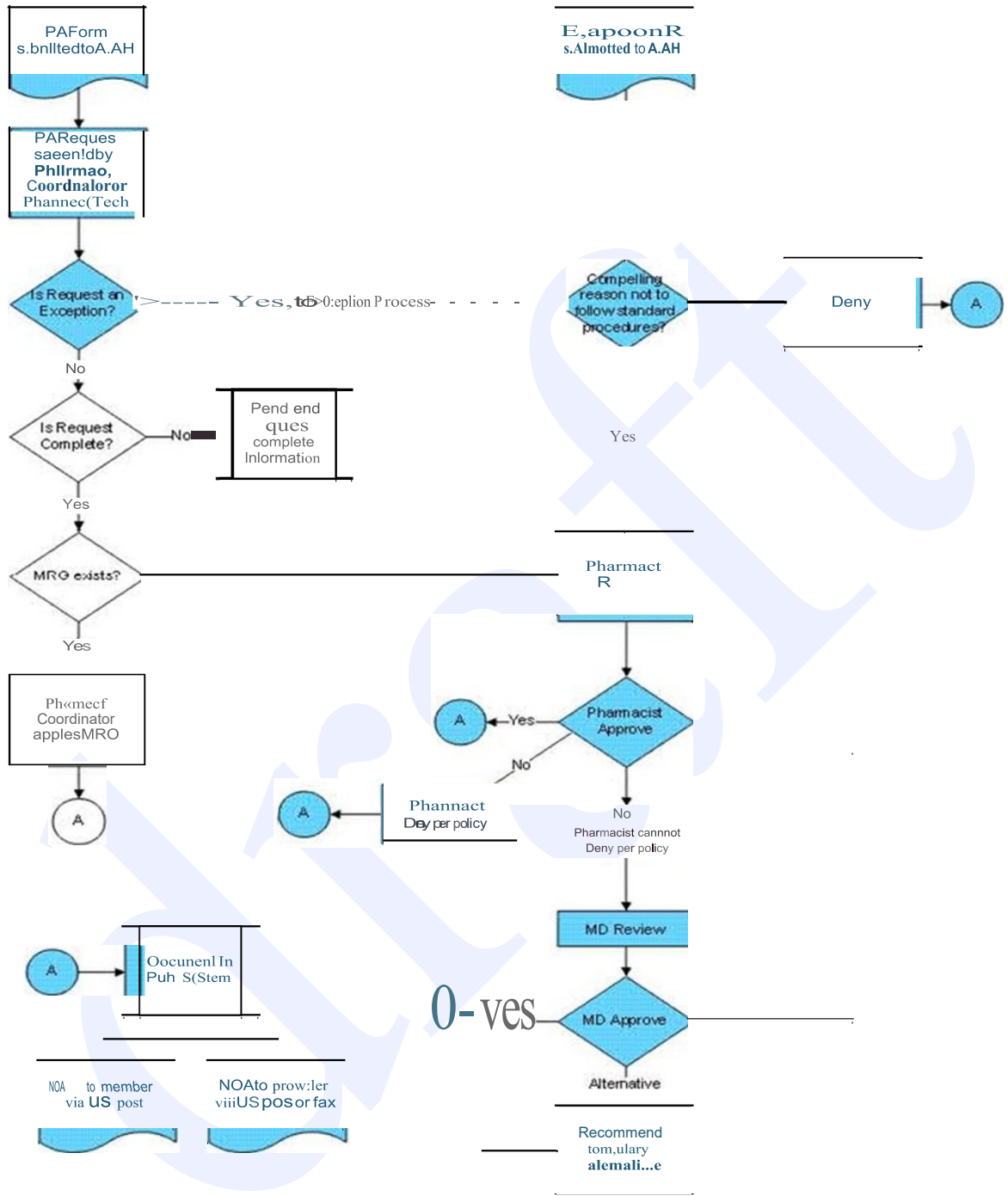
Table 2. Pharmacy Benefit Determination Turnaround Timetable of Different Regulatory Bodies

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)





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	IHSS
Effective Date	6/16/2020
Administrative Oversight Committee Approval Date	5/21/2025

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) One vacation override per drug 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.

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

Attachment 1 – Exception Review Process Flow Chart

REVISION APPROVAL 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, 5/21/2025, 9/2025

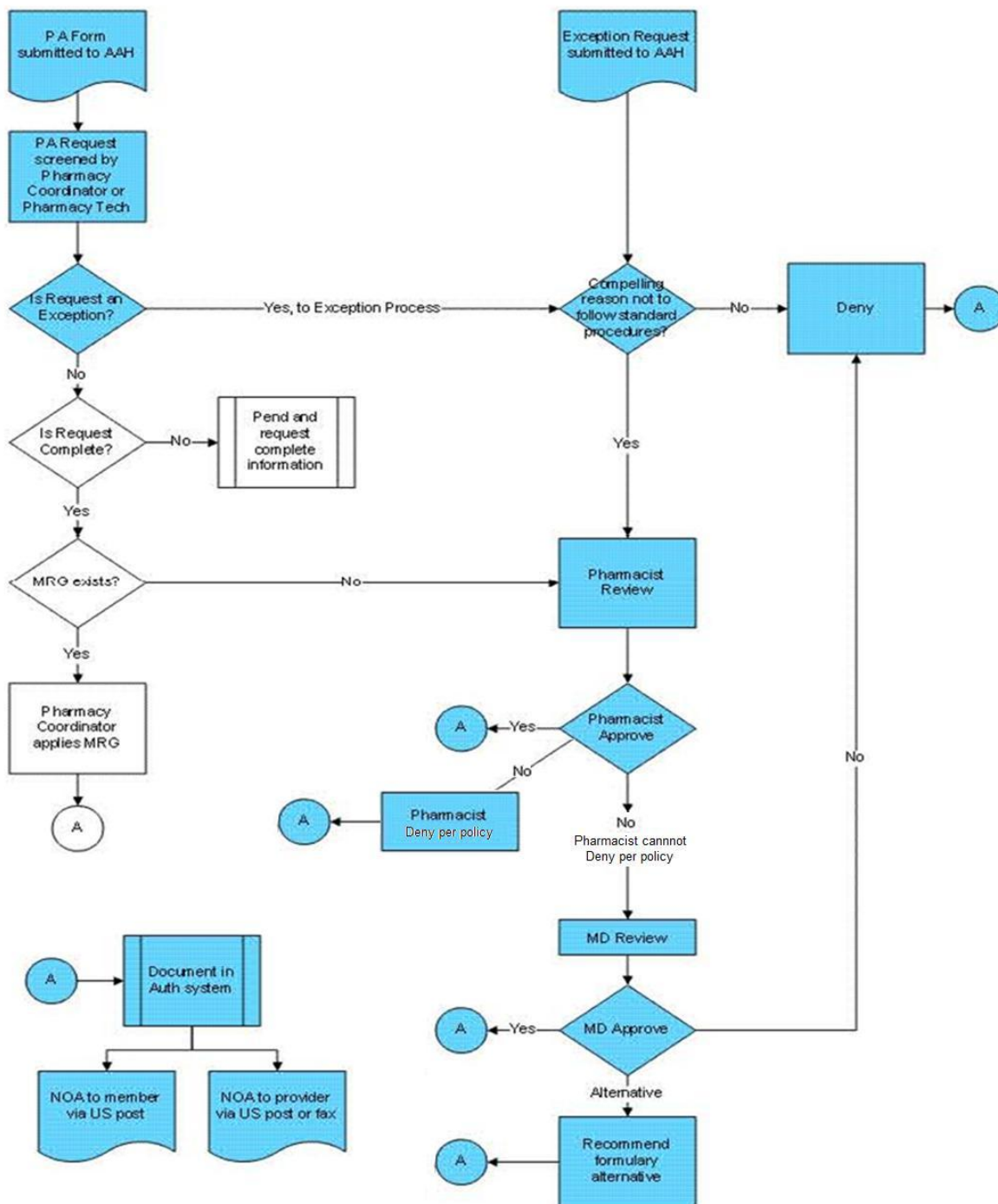
REFERENCES

- 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.

Pharmaceutical Management Procedures (Prior Authorization and Exception Process)





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

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
Administrative Oversight Committee Approval Date	~~5/21/2025~~ <u>3/3/2026</u>

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 Prior Authorization Review Process and/or RX-0002b3, Prior Authorization and Exception Review 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 recent (5 years or less) 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 public website.
- ~~8.9.~~ Alliance will mail the formulary and is available to Alliance Providers, Pharmacies, and Members upon request.
- ~~9-10.~~ 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.
- ~~10-11.~~ 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 single-source antiretroviral medications (including PrEP) without prior authorization/step therapy requirement. Mandatory generic requirements apply.

12.

13.~~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 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~~
 - a. ~~treatment outcome systems~~ to optimize the quality of the pharmacy services
 - b. Review the formulary on an annual ~~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 members and its PP providers about formulary additions, deletions, and modifications to policies and procedures ~~and~~ after each quarterly P&T Committee meeting, or more frequently as needed.
2. ~~Alliance posts a Providers are notified through the Quarterly Formulary Update Summary provider bulletin to the public website updates.~~
3. Alliance will mail the Quarterly Formulary Update Summary upon request.
- 1.4. ~~I Quarterly Formulary Update Summary nformation~~ 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~~ and changes to preferred/nonpreferred status/formularies
 - c. Prior authorization criteria and guideline updates
 - 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
- e.5. Members and providers impacted by negative changes are notified by mail at least 30 days prior to effective date of such changes. Negative changes include: change of a drug to more expensive drug tier, addition of Prior Authorization, Step Therapy, or Quantity Limits to a drug, or any other change which would otherwise reduce or restrict a member's benefit access.
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~~

3.6. Member Services Department is also notified of formulary changes. A copy of the Quarterly Summary of Formulary Update Summaries 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 of Member Services on an as-needed basis.

- 4.7. 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 formulary change requests ~~for change to the formulary~~ on a quarterly basis. ~~basis.~~

D. Content Management of Formulary Changes

The Alliance regularly updates publicly available formulary materials ~~s-available-online-to Providers and Members~~. The Alliance synchronizes resource updates ~~the dates that different information resources are updated to~~ to ensure consistency. Upon completion, the following content is updated:

1. Quarterly Formulary Update Summary
2. PBM updates the online Formulary Search Tool to reflect changes
3. PBM prepares printed formulary after quarterly P&T Committee approved changes have been implemented.
4. Printed formulary will be posted to Alliance website within 45 days of the P&T Committee meeting.

1. —

- a. ~~Alliance Provider website:~~
- i. ~~Document of Summary of Formulary Updates document uploaded~~
- b. ~~Online Drug Formulary Search Tools: Current PBM updates the On-line Search tool to reflect the changes.~~
- e. ~~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

RELATED POLICIES AND PROCEDURES

RX-002 Prior Authorization Review Process

RX-005 P&T Committee Roles and Scope

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

~~Attachment 1: Request for Formulary Review~~

P&T Charter

REVISION APPROVAL 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, 5/21/2025, 3/3/2026

REFERENCES

~~• NCQA UM 12, Element A, B, D~~

• NCQA UM 10, Elements 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.



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
Administrative Oversight Committee Approval Date	5/21/2025

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).

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's request 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

RX-002 Prior Authorization Review Process
 RX-004 Formulary Management

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENT

REVISION APPROVAL HISTORY

11/13/2020, 3/16/2021, 6/21/2022, 3/28/2023, 6/20/2023, 4/10/2024, 9/24/2024, 5/21/2025

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
Administrative Oversight Committee Approval Date	5/21/2025

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 or she 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 APPROVAL 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, 5/21/2025

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

RX-006 Pharmacy Services Staff Description

MONITORING

This policy will be reviewed annually to ensure effectiveness.



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

POLICY AND PROCEDURE

Policy Number	RX-007
Policy Name	Pharmaceutical Patient Safety, <u>Drug Recalls, Quality Assurance</u>
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	<u>Medi-Cal, D-SNP, IHSS</u>
Effective Date	05/01/2012
Administrative Oversight Committee Approval Date	<u>5/21/2025</u> <u>3/4/2026</u>

POLICY STATEMENT

This policy documents Alameda Alliance for Health (Alliance) Pharmacy Department patient safety procedures and functions.

The Alliance 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:

"A medication error 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 health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use."

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.”~~

Collaboration

PROCEDURE

Pharmacy Benefit Drug Recalls and Withdrawals Procedure

- 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: dangerous or defective products that may cause serious health problems or even death
 2. Class II: less dangerous products than Class I, that may cause only temporary health problems
 3. Class III: products for which use or exposure is not likely to cause adverse health consequences
- B. Market withdrawal or voluntary recall is a removal 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. Alliance's PBM checks FDA drug recall notifications and generates member impact reports using claims data. The reports contain the member and prescriber mailing information, describe the withdrawal, recommend contacts for further information, and instruct how to dispose of remaining recalled product.
- D. Drug recall notifications are sent to impacted members and prescribers. Alliance will notify members within 48 hours for Class I and within 30 days for Class II recalls/withdrawals. Class III recalls are not acted upon. The Alliance will not act on limited FDA withdrawal impacting specific lots of products. The PBM does not collect product lot numbers and it is not possible to identify utilization by members.
- E. The process for market withdrawal involves the following formulary management actions:
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. Product is terminated from Alliance formularies.
 3. Product is terminated from all applicable drug management programs.
 4. Prior Authorizations for affected product are terminated.
-

Medical Benefit Drug Recalls and Withdrawals Procedure

- A. Pharmacy Technicians check shared email inbox < D4@alamedaalliance.org> for FDA Recall Alerts.
1. Lot specific recalls are not acted upon. The Alliance does not have access to which members and providers may have encountered a specific lot.
 2. Class III recalls are not acted upon.
- B. The Pharmacy Department works with the Analytics Department to identify members and prescribing providers impacted for recalls classified as Class I, Class II and Market Withdrawals recall.
- Impacted members are those who have a medical claim for the recalled
- i. physician administered drug within 180 days prior to the recall.
 - ii. Impacted prescribing providers are those who submitted a medical claim for the recalled physician administered drug within 180 days prior to the recall on a medical claim.
- C. Using the results from the Analytics Department, the Pharmacy Department sends the impacted member and prescriber lists to Provider Services and Communications & Outreach to ensure impacted members and providers will be notified by letter. The letter will contain the summary details of the recall, including drug name, strength, manufacturer, NDC number(s), whom to contact with further concerns, and how to dispose of remaining recalled product (if applicable).
- a. For Class I recalls, Alliance will notify impacted members and prescribers by letter within 15 business days or less of the FDA notice.
 - b. For Class II recalls or Market Withdrawals, Alliance will notify impacted members and prescribers by letter within 30 days or less of the FDA notice.

Communicating Drug Recalls and Withdrawals

- A. ~~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 plan website. The content can be located under “Safety Resources” within the “Pharmacy & Drug Benefits” section.
-
-
- B. The Pharmacy Department will forward recall notices and impact reports to Alliance departments such Provider Services, Member Services, Utilization Management and Claims Department.
-

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.
-

Annual Patient Part D Safety Reports

CMS releases Annual Patient Safety Reports on the Acumen Patient Safety Analysis Web Portal. Alameda Medicare Operations will designate Pharmacy Department users of the Acumen Patient Safety Analysis Web Portal.-

The report is updated monthly and contains an annual set of Patient Safety measures. These measure packages include a summary contract-level report for each measure and additional beneficiary-level files.

- Alliance downloads and reviews measure packages to compare performance to benchmark averages and monitor progress in improving measure rates.
- Alliance will identify members and prescribers needing outreach using the Patient Safety reports and internal analytics.
- Alliance will transmit Patient Safety reports to PBM for further review, analysis and Case Management, as specific in the *CMS Part D DMP Guidance* manual.

All measures are calculated based on Pharmacy Quality Alliance (PQA) measure specifications and Value Sets, which include NDCs. The PQA updates their Value Sets biannually, usually in February and July. The April year of service (YOS) reports use the most recent updated PQA NDC lists and the ICD-10 diagnoses codes for both current and prior year data. Between NDC list updates, Alliance may observe differences between their internal monitoring reports and the Patient Safety reports, especially if applying more real-time NDC changes or capturing PDE data not yet submitted to or processed by CMS.

The Patient Safety Analysis Web Portal facilitates communication between CMS, Part D plan sponsors, and Acumen, LLC. Alliance can view “at-a-glance” Rate Summary and Performance Graphs for each measure and respond directly to outlier notices. Alliance may review their underlying measure data in the reports and alert CMS if potential errors or anomalies are identified in the rate calculations per the measure specifications. For questions regarding rate calculations, diagnosis codes, exclusions, or underlying data, Alliance may contact PatientSafety@AcumenLLC.com.

Overutilization Monitoring System / Drug Management Program **Policy Statement on Drug Management Programs (DMPs):**

In accordance with CMS regulations and the *CMS 2026 Part D DMP Guidance*, Alliance implements a Drug Management Program to identify and manage beneficiaries at risk for misuse or abuse of frequently abused drugs (FADs), specifically opioids and benzodiazepines. Alliance will utilize CMS’s Overutilization Monitoring System (OMS) criteria to identify Potential At-Risk Beneficiaries (PARBs) and, through the delegated PBM, conduct thorough case management to determine At-Risk Beneficiaries (ARBs). Case management will include clinical outreach to prescribers, verification of risk, and documentation of prescriber agreement when applicable. Beneficiaries identified as ARBs may be subject to coverage limitations, including point-of-sale (POS) claim edits, prescriber limitations, and/or pharmacy limitations, with consideration for beneficiary preferences and reasonable access.

Operational Requirements and Compliance:

Alliance or its delegated PBM will ensure that all DMP activities are supported by written policies and procedures, approved by the appropriate clinical oversight committee, and executed by licensed clinical staff. The plan will comply with all notification requirements, including timely issuance of Initial and Second Notices, and will provide beneficiaries with appeal rights as outlined in 42 CFR § 423.580. Exempted beneficiaries—such as those receiving hospice care, cancer-related pain treatment, or residing in long-term care facilities—will be excluded from DMPs upon reliable identification. The plan will report all relevant data to CMS via OMS and MARx systems within required timeframes and will coordinate with other sponsors to ensure continuity of care for beneficiaries transitioning between plans.

PARB Identification Criteria

Minimum OMS Criteria

- Opioid use >90 MME/day from multiple prescribers/pharmacies.
- History of opioid-related overdose + recent opioid prescription.

Supplemental OMS Criteria

- Use of opioids from ≥7 prescribers or pharmacies, regardless of MME.
- _____

Exemptions

Beneficiaries are **exempt** from DMPs if they:

- Are treated for cancer-related pain.
- Receive hospice or palliative care.
- Reside in LTC facilities with single-pharmacy contracts.
- Have sickle cell disease.
- _____

Case Management Requirements

- Clinical staff must contact prescribers to verify risk and discuss limitations.
- Sponsors must document outreach and prescriber responses.
- If prescribers are unresponsive after 3 attempts in 10 business days, sponsors may proceed with POS edits.
- _____

Beneficiary Notices

1. **Initial Notice:** Sent after case management, outlines intended limitations.
2. **Second Notice:** Sent if limitation is implemented.
- Alternate Second Notice:** Sent if no limitation is imposed or beneficiary is exempt.
3. _____

Coverage Limitations

Sponsors may impose:

1. **POS Claim Edits:** Limit drug types or dosages.
2. **Prescriber Limitations:** Restrict to selected prescribers.
- Pharmacy Limitations:** Restrict to selected pharmacies.
3. _____

Prescriber/Pharmacy Selection

- Beneficiary preferences are prioritized unless they conflict with network policies or risk mitigation.
- Sponsors must ensure **reasonable access** based on geography, health needs, and usage patterns.

•

Appeals and Extensions

- Beneficiaries may appeal within 60 days of the Second Notice.
- Coverage limitations may be extended for up to 2 years with clinical justification and prescriber agreement.
- Alliance's PBM is delegated for ARB Appeals

•

Data Reporting

- Sponsors must report case management and coverage decisions to CMS via OMS and MARx.
- Timely data sharing between sponsors is required when beneficiaries change plans.

•

Recalls and Withdrawals

- OMS
Within 30 days of receiving an OMS report, Alliance will report case management status for:
 - Each PARB 1 identified through OMS to the sponsor
 - Each PARB 1 that the sponsor identifies
 - Each PARB 2 or ARB 2 for which a gaining sponsor received a transaction reply code of TRC 376 (New Enrollee CARA Status Notification) from the DTRR
- MARx
No later than 7 days from the action date, Alliance will provide the following information in MARx:
 - The date of an Initial Notice to a PARB (Notification start-date)
 - The date of a Second Notice to an ARB any time a Second Notice is required
 - The date of an Alternate Second Notice when a sponsor terminates an "active CARA status"
- Sponsor-to-Sponsor Information Transfer
- A. ~~Alliance will provide case management information to the receiving plan no later than 2 weeks from the receiving plan's request when an PARB or ARB member disenrolls from Alliance. 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.~~

~~I. ——— 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.~~

~~II. ——— 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

ARBs (At-Risk Beneficiaries): Confirmed through case management and subject to coverage limitations.

CMS: Centers for Medicare and Medicaid Services

DMP: Drug Management Program

FAD(s): Frequently Abused Drugs

FDA: Food and Drug Administration

MARx: Medicare Advantage and Prescription Drug system used by the Centers for Medicare & Medicaid Services (CMS)

MME: Morphine Milligram Equivalents

NCC MERP: National Coordinating Council for Medication Error Reporting and Prevention.

NCQA: National Committee on Quality Assurance

NDC: National Drug Code

NDDF: National Drug Data File

OMS: Overutilization Monitoring System

PARBs (Potential At-Risk Beneficiaries): Identified via CMS's Overutilization Monitoring System (OMS) or prior plan data.

PBM: Pharmacy Benefit Manager (Currently, PerformRx)

POS: Point of Service

URAC: Utilization Review Accreditation Commission

- 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-~~(PerformR~~
~~*)~~ Provider Relations
 Quality Improvement
 Member Services
[Analytics](#)
[Communications & Outreach](#)

RELATED POLICIES AND PROCEDURES

~~None~~[P&T Charter](#)

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[P&T Charter](#)

REVISION APPROVAL 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, 5/21/2025, [9/3/2025](#), [3/4/2026](#)

REFERENCES

- [CMS Part D Manual, Chapter 7 – Prescription Drug Benefit Manual, section 20.5 – Medication Error Identification and Reduction \(MEIR\)](#)
- [CMS Part D Drug Management Program \(DMP\) Guidance \(Part D Drug Management Program Policy Guidance\)](#)
- ~~PerformRx Policy, DRUM-1-02 - Internal Medication Error Identification and Reduction Systems~~
- ~~NCQA [2026](#), UMA [4](#), ~~12~~ Element [1C](#)~~
- ~~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~~
- [Food and Drug Administration \(FDA\) Recalls, Corrections and Removals](#)
- <https://www.cms.gov/files/document/2025-patient-safety-memo-202504.pdf>
- [42 CFR§ 423.153\(f\)\(2\) - requirements for case management, clinical contact, and prescriber verification for the purposes of DMPs](#)
-

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
Administrative Oversight Committee Approval Date	5/21/2025

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

- CORE 1-08
Pharmacy System Us

- DRUM 1-05 UM
System Controls - 03

-

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None

REVISION APPROVAL HISTORY

12/11/2018, 06/25/2019, 3/16/2021, 6/28/2022, 6/20/2023, 4/10/2024, 5/21/2025

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.



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
Administrative Oversight Committee Approval Date	5/21/2025

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 APPROVAL HISTORY

3/17/20, 03/16/21, 6/21/2022, 3/28/2023, 4/10/2024, 5/21/2025

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.



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
Administrative Oversight Committee Approval Date	5/21/2025

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 and Senior Director, Pharmacy Services or designee and reported to the UM Committee and Board of Governors (BOG).
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 APPROVAL 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, 5/21/2025

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.



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
Administrative Oversight Committee Approval Date	5/21/2025

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)).

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 APPROVAL HISTORY

10/12/2017, 12/11/2018, 3/16/2021, 3/15/2022, 3/28/2023, 4/10/2024,
5/21/2025

REFERENCES

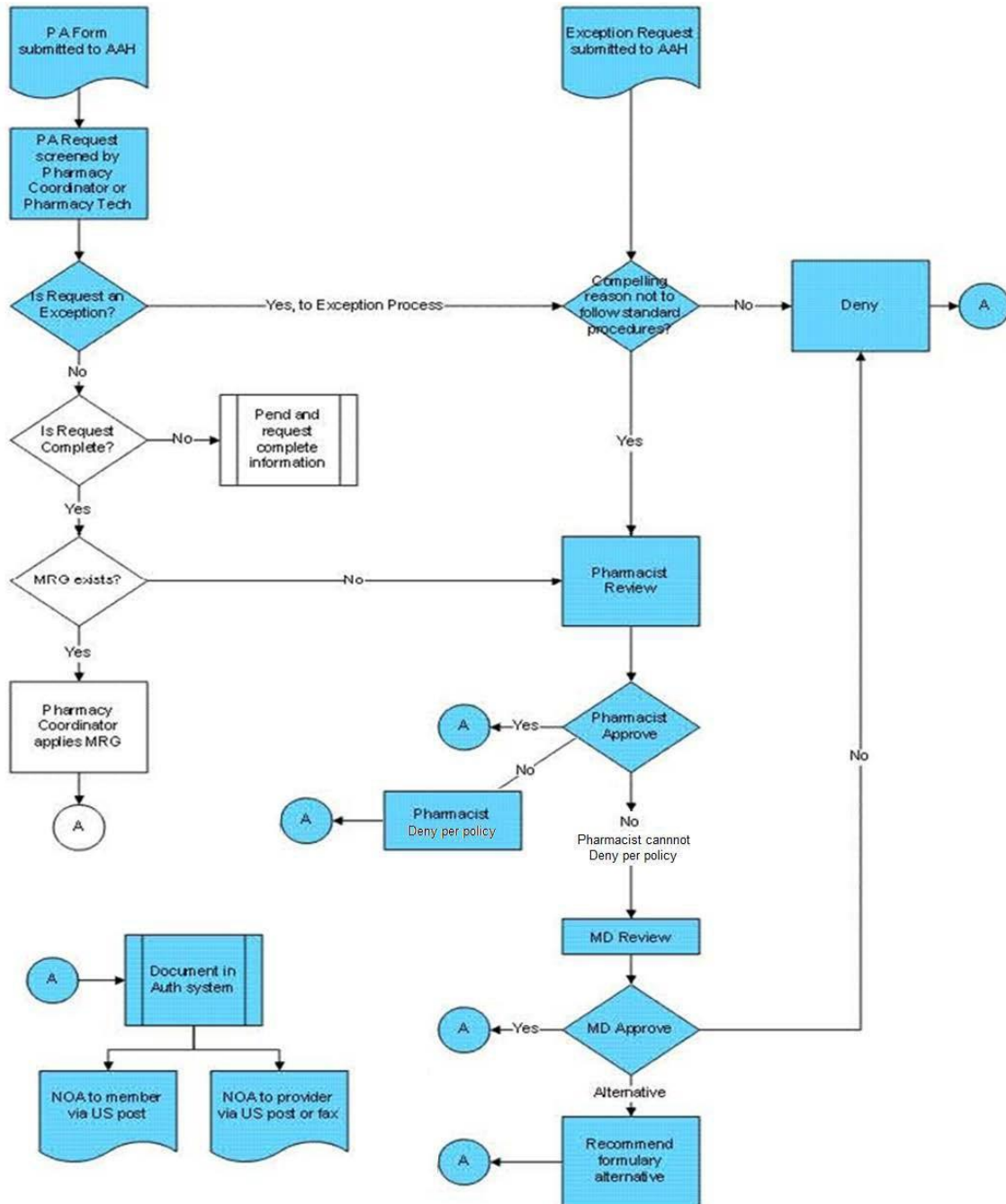
- California Code of Regulations (CCR), Health & Safety Code, §§1367.01,1367.21, 1367.22, 1367.24 and 1373.96
- CCR, Welfare & Institutions Code, §14185
- CCR, Title 22, §§51003, 51014.1, 51014.2, 53854 and 53894
- CCR Title 28 §1300.67.24
- MMCD Policy Letter 08-013
- NCQA, 2016 HP Standards & Guidelines, 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)





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

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
Administrative Oversight Committee Approval Date	5/21/2025

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 Rx secure 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 OktaSM 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 Managed



Medi-Cal Rx

Care Plan MeetandGreet



MCP CL



DHCS-6520-Medi-C

Preseal MCP Designated

REVISION APPROVAL HISTORY

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

Blue = Material 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, D-SNP
Effective Date	7/17/2023
Administrative Oversight Committee Approval Date	12/29/2025

POLICY STATEMENT

The Alameda Alliance for Health (the “Alliance”) has an established process for reviewing and processing physician-administered drugs (PAD) authorization requests when requested under medical benefit for medical necessity. 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. The Alliance ensures parity in coverage of pharmaceuticals used to treat medical/surgical, mental health, gender dysphoria and substance abuse disorders.

PROCEDURE

- I. The Alliance is responsible for reviewing physician-administered drugs (PAD) or medical drugs when billed as medical claims. Drug classes “carved out” to Medi-Cal Fee-For-Service (FFS) in the Medi-Cal manual will not be reviewed. “Carved out” drugs shall be referred to Medi-Cal FFS for review.
- II. The Alliance is responsible for reviewing Medicare Part B drugs, in accordance with Medicare coverage criteria. See Appendix II for definitions of Part B drugs.
- III. **Prior Authorization Process Guidelines**
Prior Authorization review and approval criteria or PAD Medication Review Guidelines are utilized and required for medical drug authorizations.
The Alliance utilizes evidence-based prior authorization criteria approved by the P&T Committee. Prior authorization criteria are developed and reviewed annually. Sources used to create criteria may include (in no particular order):
 - A. Medi-Cal guidelines (for Medi-Cal line of business)
 - B. Medicare National Coverage Determinations (NCD) or Local Coverage Determinations (LCD)
 - C. Food and Drug Administration (FDA) Package Insert labeling
 - D. Peer-reviewed scientific literature
 - E. Professional medical society treatment Standards of Care including but not limited to:
 - a) Infectious Disease Society of America (IDSA)
 - b) American Medical Association (AMA)

- c) American Academy of Orthopedic Surgeons (AAOS)
- d) American Academy of Pediatrics (AAP)
- e) American Psychiatric Association (APA)
- f) American College of Rheumatology (ACR)
- g) American Diabetes Association (ADA)
- h) American Academy of Dermatology (AAD)
- i) American Academy of Ophthalmology (AAO)
- j) American Association of Clinical Endocrinologists (AACE)
- k) American College of Cardiology (ACC)
- F. Pharmaceutical care compendia including but not limited to:
 - a) American Hospital Formulary Services (AHFS)
 - b) Truven Health Analytics
 - c) Micromedex DrugDeX (DrugDex)
 - d) Elsevier/Gold Standard Clinical Pharmacology
 - e) Wolters Kluwer Lexi-Drugs (Lexicomp®, Facts & Comparisons®, and UpToDate®)
- G. Milliman Care Guidelines
- H. National Comprehensive Cancer Network (NCCN)
- I. National Institutes of Health (NIH)

IV. 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.

V. **Prior Authorization Procedures**

All providers are required to submit prior authorization for PAD drugs billed on medical claim.

- A. 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
- B. Prior authorization requests may be submitted electronically, phone or by fax to the Alliance UM Department.

- C. Pre-Service/Post-Service Review Pharmacist Reviewer(PR)
 - A. Pharmacist reviews the authorization request using criteria established by Pharmacy & Therapeutics (P&T) Committee. If authorization criteria does not exist, reviewer will perform a medical necessity review using clinical evidence from sources referenced in III. Prior Authorization Process Guidelines.
 - B. The Pharmacist Reviewer determination decision will be entered into the care decision platform database and will be communicated to the member and prescriber.
 - C. Requests which cannot be approved by the reviewing Pharmacist will be sent for Medical Director review.

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. Retro requests will be reviewed for medical necessity as per UM-057. 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.

VI. 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

VII. 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

VIII. 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.

IX. 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.

- X. 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.

Pharmacy Services will comply with appropriate UM policies as they relate to pharmacy supported authorizations, NOA letters and regulatory requirements (see RX-011 Decision and Notification Requirements).

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

RX-011 Decision and Notification Requirements
UM-001 Utilization Management
UM-057 Authorization Service Request

REVISION APPROVAL HISTORY

6/20/2023, 12/19/2023, **8/21/2024**, 5/21/2025, **12/29/2025**

Blue = Material 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, 1374.72
 - 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
 - 42 CFR section 438.900 et seq
 - CMS Medicare Prescription Drug Benefit Manual, Chapter 6 – Part D Drugs and Formulary Requirements
-
-

APPENDIX II Medicare Part B Drugs

- For determination of Medicare Part B drugs, please refer to CMS Medicare Prescription Drug Benefit Manual, Chapter 6 – Part D Drugs and Formulary Requirements, Appendices B & C.



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

POLICY AND PROCEDURE

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
Administrative Oversight Committee Approval Date	<u>5/21/2025</u> <u>3/4/2026</u>

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 drugs pharmaceutical 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~~
- e. ~~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~~
 - e. ~~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.B. 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 APPROVAL HISTORY

New Policy: 8/21/2024

Updates Approved: 5/21/2025, 3/4/2026

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~~

RX-014 Physician/Facility-Administered Drugs PAD PA List Management

MONITORING

Draft

This policy will be reviewed annually to ensure effectiveness.

Draft



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	MCAL, IHSS
Effective Date	5/21/2025
Administrative Oversight Committee Approval Date	5/21/2025

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-administration 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

None

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None

REVISION APPROVAL HISTORY

New Policy: 5/21/2025

REFERENCES

None

MONITORING

Reviewed annually for updates



Alameda Alliance for Health

1240 South Loop Road

Alameda, CA 94502

Phone Number: **1.510.747.4567**

Toll-Free: **1.877.932.2738**

If you cannot hear or speak well (CRS/TTY):

711/1.800.735.2929

www.alamedaalliance.org

90-Day Supply on Maintenance Medications

Medications are available for Alameda Alliance for Health (Alliance) Group Care members through their choice of in-network retail pharmacies or the 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 the 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
Minoxidil
Nadolol
Niacin
Nicardipine
Nifedipine
Nitroglycerin
Olmesartan

Blood Pressure & Heart Health (cont.)

Pentoxifylline
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
Pioglitazone

Diabetes (cont.)

Pioglitazone/Metformin
Rosiglitazone
Rosiglitazone/Metformin
Tolazamide
Tolbutamide

Gastrointestinal Health

Balsalazide
Sulfasalazine
Ursodiol

Gout

Allopurinol
Probenecid

High Cholesterol

Atorvastatin
Cholestyramine/Aspartame
Colestipol
Docosahexaenoic Acid/EPA
Ezetimibe/Simvastatin
Fenofibrate
Fenofibrate, nanocrystallized
Fluvastatin
Gemfibrozil
Lovastatin
Omega-3 Fatty Acids/Fish Oil
Omega-3 Fatty Acids/Vitamin E
Simvastatin

Human Immunodeficiency Virus (HIV)

Emtricitabine-Tenofovir
Descovy

Liver Disease

Adefovir
Baraclude solution
Entecavir
Lamivudine
Tenofovir 300 mg tablets
Vemlidy
Viread

Men's Health

Alfuzosin
Doxazosin
Finasteride
Tamsulosin
Terazosin

Mental Health

Bupropion
Duloxetine
Escitalopram
Fluoxetine
Mirtazapine
Paroxetine
Sertraline
Trazodone

Miscellaneous

Cabergoline
Fludrocortisone

Miscellaneous (cont.)

Hydroxychloroquine
Hydroxyurea
Leflunomide
Methazolamide
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

Seizures & Epilepsy (cont.)

Ezogabine
Gabapentin
Levetiracetam
Levetiracetam NaCl
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
Oxybutynin

Vitamins & Nutritional Health

B Complex with Vitamin C
Calcitriol
Calcium Acetate 667 mg
Calcium Carbonate
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



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	DENOGEST & 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Alliance計畫成員服務處，電話：**1.510.747.4567**。

P&T Committee Meeting
Minutes
December 16, 2025



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

PHARMACY & THERAPEUTICS COMMITTEE
Record of Committee Meeting Minutes
Tuesday, December 16, 2025 | 5:00pm – 7:00pm

Status	Voting Committee Members	Organization	Initials	Officer / Notes
P	Donna Carey, MD	Chief Medical Officer-Alliance	DC	Chairman
P	Luke Lim, R.Ph.	Senior Director of Pharmacy Services – Alliance	LL	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
P	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: 5:00PM	
II) Informational Updates	D. Carey L. Lim	Informational Update •DSNP go-live 2026 - Partnering with clinics The organization has begun its DSNP (Dual Special Needs Plan) implementation by starting small work with only one clinic from each CHCN entity and initially expecting to serve about 1,500 members, currently there are about 185 enrolled. To support the rollout, extensive training is underway for both internal staff and providers, including mandatory Model of Care training for anyone interacting with DSNP members. The team is focused on understanding the specific requirements that differentiate DSNP from the existing medical line of business. With DSNP, the organization now manages three lines of business: Group Care, Medical, and DSNP. This new line introduces changes to pharmacy operations, including updated turnaround expectations and new performance measures to ensure compliance and maintain a high-quality plan. - 365-day operations, TATs, & STAR measures The pharmacy team has been developing several new programs to support the organization's transition to Medicare. One of the most significant operational changes is the move to a 365-day pharmacy operation to meet Medicare's strict 24-hour turnaround requirements, including weekends and holidays. New workflows have been introduced for Part B services, with ongoing monitoring and adjustments. Pharmacists have also been focusing on Medicare Part D Stars measures, particularly those involving medication adherence and member engagement. Additional initiatives include the Medicare Prescription Payment Plan, which allows members to spread out their medication costs over the year, and the Drug Management Program (MTM), which emphasizes safe and appropriate opioid use. •Formulary [CMS selected drug list change d/t generic availability (Part D program) - Stelara, Xarelto, Entresto] There is an increased formulary oversight exercised by CMS and the PBM, which influences drug selection, utilization management, and other aspects of the Part D benefit. A recent board item focused on three medications—Stelara, Xarelto, and Entresto, which CMS had previously included in the Medicaid Manufacturer Discount Program. Due to market shifts such as the introduction of generics or biosimilars, these drugs are expected to leave the Medicare Discount Program beginning in the 2027 plan year. This example highlights the growing complexity of formulary decision-making under Medicare, a process in which PerformRx will provide support. Questions: PB: Xarelto and Entresto are also on the Medicare fair price drug list LL: That's right, yes.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
III) Pharmacy Utilization Reports (Quarter 3, 2025)	L. Lim	(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.) Top 50 Drugs by Cost (IHSS) - The top 50 drugs accounted for 1,341 claims for 688 members and cost \$1,685,511, which is an increase of \$61,035 in spend from the previous quarter. - Biktarvy remains at number one with 39 claims for 15 members. There was an increase of 4 claims since the previous quarter. - Ozempic is at numbers 2, 3, and 5, with 267 total claims for 123 members. There was a decrease of 11 claims and 8 members from the previous quarter. - Vemlidy is down to number 4 with 52 claims for 24 members. There was a decrease of 3 claims for 24 members in the previous quarter. This medication is managed via the Hepatitis B MRG, which requires trial and failure of, intolerance to, or reason not to use, entecavir. - Skyrizi is up at number 6 with 3 claims for 3 members. There was an increase of 1 claim and one additional member from the previous quarter. The medication is managed via the Specialty Biologic Agents MRG. Top 50 Drugs by Cost (Medi-Cal) - The top 50 drugs accounted for 31,791 claims for 27,189 members and cost \$66,059,008 which is an increase of \$3,108,517 spend and 1721 members (25,468) from 2Q2025. - MCAL membership April 404,947 vs July 405,754 - Compare 31,791 claims vs 29,741 claims in 2Q2025 - Biktarvy roughly stable utilization 907 vs 928 claims 2Q2025. - Jardiance both strengths also roughly stable. - Large increase in Skyrizi utilization from 119/110 to 143/131 over 2Q2025 - Wegovy with 17% increase from 1183 to 1383 claims since 2Q2025 - GLP1 for weight loss will be discontinued by Medi-Cal Rx starting 1/1/2026 - Impact will be Wegovy, Zepbound, Saxenda: 5401 members in 100 days ending 11/25/2025 - Dupixent from 221 claims to 286 (29% increase) Top 50 PA Reviewed Drugs by Volume (IHSS) - Top 50 PA requests = 278. There were 399 total PA requests for quarter 3. - o 71 requests (26%) were approved. This approval rate is the same as it was observed last quarter. - o 207 requests (74%) were denied or partially approved. - Wegovy is at numbers 1, 6, 8, 10 and 12 with 59 total requests and 13 approvals (22%). - o Wegovy to reduce excess body weight requires a diagnosis of class III/severe obesity (BMI $\geq$40) and trial and failure or inability to use Qsymia and Contrave. - o Wegovy to reduce the risk of major adverse cardiovascular events requires a documentation that the patient is obese or has BMI $\geq$27, has an established cardiovascular disease (prior myocardial		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		infarction, stroke or symptomatic peripheral arterial disease), patient is on standard of care treatment for CVD and does not have diabetes. - Zepbound is at numbers 2, 9, 15 & 35 with 40 total requests and 8 approvals (20%). - o Zepbound to reduce excess body weight requires a diagnosis of class III/severe obesity (BMI ≥ 40) and trial and failure or inability to use Qsymia and Contrave. - o Zepbound for moderate to severe obstructive sleep apnea requires trial and failure regarding lifestyle changes and behavioral modifications to reach BMI < 30 kg/m² and trial and failure or inability to use PAP therapy. - Lidocaine 5% patch is at number 3 with 25 requests and 4 approvals (16%). - o 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. - Jardiance is at numbers 4 & 5 with 31 total requests and 8 approvals (26%). - o 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 AND documentation of trial and failure, intolerance, contraindication or inability to use one preferred formulary step therapy medication. - Mounjaro is at number 7 with 8 requests. There were 4 approvals (50%). - o Mounjaro requires trial and failure of a metformin containing product. Top 50 PA Reviewed Drugs by Volume (Medi-Cal) - The top 50 PA requests = 3,173 - #1 most requested item is Freestyle Libre CGM - #3 Dexcom G7 Sensor is also CGM item - #4 Opzelura is a surprise; reformulation of oral Jakafi (ruxolitinib) for atopic dermatitis - Wegovy, Zepbound, and Ozempic are in top 10 – I predict volume will shift to Ozempic bc it does not have weight-loss indication - Sildenafil – ED indication, obviously very low 1.4% approval rate - Tadalafil – PAH indication so approval rate is higher at 10.4% - Estradiol valerate, Xcopri, Dupixent Pen, Sacubitril/valsartan have top 4 approval rates - Ozempic has third-lowest approval rate at 24.1%		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes																																														
IV) E-Voting Material/Consent Agenda	L. Lim B. Ochoa	E-Voting Material/Consent Agenda The following items have been sent to the voting committee for review via E-voting <i>Luke Lim, R.Ph., Senior Pharmacy Director – Alameda Alliance</i> <i>Benita Ochoa, CPhT, Lead Pharmacy Technician – Alameda Alliance</i> <i>(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.)</i> <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>Multivitamins Drug List Review</td><td> - No changes </td></tr><tr><td>Topical Antivirals 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>Butorphanol (Stadol NS)</td><td> - No changes </td></tr><tr><td>Endari</td><td> - Change naming convention to reflect generic availability of Endari </td></tr><tr><td>Diclofenac sodium (Solaraze) 3% gel</td><td> - No changes </td></tr><tr><td>Growth Hormone</td><td> - Remove Saizen as it has been discontinued </td></tr><tr><td>Rapid-Acting Insulin</td><td> - No changes </td></tr><tr><td>Long-Acting Basal Insulin</td><td> - Remove Levemir as it has been discontinued </td></tr><tr><td>Gonadotropin Releasing Hormone (GNRH) Agonists</td><td> - No changes </td></tr><tr><td>Ophthalmic Anti-Inflammatory Agents</td><td> - No changes </td></tr><tr><td>Fentanyl Citrate</td><td> - Remove Lazanda and Subsys as they have been discontinued </td></tr><tr><td>Proton Pump Inhibitors (PPIs)</td><td> - Change naming convention to reflect generic availability of Nexium oral granules packet </td></tr><tr><td>Ranolazine (Ranexa, Aspruzyo)</td><td> - No changes </td></tr><tr><td>Injectable Methotrexate</td><td> - Remove Otrexup as it has been discontinued </td></tr><tr><td>Temazepam (Restoril)</td><td> - No changes </td></tr></table>	Monographs/Class Reviews	Changes	Blood Glucose Test Strips Class Review	No changes	Multivitamins Drug List Review	No changes	Topical Antivirals Class Review	No changes	Urinary Tract Antispasmodics Class Review	No changes	Medication Request Guidelines	Changes	Oral and Injectable Oncology Medications	No changes	Non-Formulary/Prior Authorization Required Medications	No changes	Step Therapy Exception	No changes	Prior Authorization Exception	No changes	Butorphanol (Stadol NS)	No changes	Endari	Change naming convention to reflect generic availability of Endari	Diclofenac sodium (Solaraze) 3% gel	No changes	Growth Hormone	Remove Saizen as it has been discontinued	Rapid-Acting Insulin	No changes	Long-Acting Basal Insulin	Remove Levemir as it has been discontinued	Gonadotropin Releasing Hormone (GNRH) Agonists	No changes	Ophthalmic Anti-Inflammatory Agents	No changes	Fentanyl Citrate	Remove Lazanda and Subsys as they have been discontinued	Proton Pump Inhibitors (PPIs)	Change naming convention to reflect generic availability of Nexium oral granules packet	Ranolazine (Ranexa, Aspruzyo)	No changes	Injectable Methotrexate	Remove Otrexup as it has been discontinued	Temazepam (Restoril)	No changes	Approved via e-voting: Yes: 7 No: 0 Abstained: 0	
Monographs/Class Reviews	Changes																																																	
Blood Glucose Test Strips Class Review	No changes																																																	
Multivitamins Drug List Review	No changes																																																	
Topical Antivirals Class Review	No changes																																																	
Urinary Tract Antispasmodics Class Review	No changes																																																	
Medication Request Guidelines	Changes																																																	
Oral and Injectable Oncology Medications	No changes																																																	
Non-Formulary/Prior Authorization Required Medications	No changes																																																	
Step Therapy Exception	No changes																																																	
Prior Authorization Exception	No changes																																																	
Butorphanol (Stadol NS)	No changes																																																	
Endari	Change naming convention to reflect generic availability of Endari																																																	
Diclofenac sodium (Solaraze) 3% gel	No changes																																																	
Growth Hormone	Remove Saizen as it has been discontinued																																																	
Rapid-Acting Insulin	No changes																																																	
Long-Acting Basal Insulin	Remove Levemir as it has been discontinued																																																	
Gonadotropin Releasing Hormone (GNRH) Agonists	No changes																																																	
Ophthalmic Anti-Inflammatory Agents	No changes																																																	
Fentanyl Citrate	Remove Lazanda and Subsys as they have been discontinued																																																	
Proton Pump Inhibitors (PPIs)	Change naming convention to reflect generic availability of Nexium oral granules packet																																																	
Ranolazine (Ranexa, Aspruzyo)	No changes																																																	
Injectable Methotrexate	Remove Otrexup as it has been discontinued																																																	
Temazepam (Restoril)	No changes																																																	

Agenda Item	Discussion Leader	Discussion Summary		Action	Notes
		Testosterone Agents	• Remove Androderm as it has been discontinued		
		Thalomid (thalidomide)	• No changes		
		Topical Diclofenac	• No changes		
		Oral Anti-Fungals	• No changes		
		Gattex (teduglutide)	• No changes		
		Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors	• No changes		
		Otezla (apremilast) for Behcet Disease	• No policy changes, add Otezla XR formulation for completeness		
		Royaldee (calcifediol ER)	• No changes		
		Korlym (mifepristone)	• No changes		
		Tetracycline Antibiotics	• No changes		
		Botulinum Toxins A&B	• 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		
		HIF-PH Inhibitors (Hypoxia-inducible Factor Prolyl Hydroxylase Inhibitors) for CKD Anemia	• No changes		
		Lodoco	• No changes		
		Nemluvio	• No changes		
		Yorvipath	• No changes		
		Cobenfy	• No changes		
		Specialty Biologic Agents	• Add new Actemra biosimilar Avtozma to step 2 agents and new Tysabri biosimilar Tyruko to step 3		
		Thrombocytopenia Agents	• Switch brand to generic Promacta tablet listed preference and add new Wayrilz to NF section		
		Complement Inhibitors for the Treatment of Myasthenia Gravis	• Add new Maavy to list of drugs not to be used with Zibrysq		
		Ileal bile acid transporter inhibitors (IBATs)	• Add trial agents based on recent guidelines		
		Sohonos	• Expand coverage duration to 12 months to mirror primary endpoint in trials		
		Isotretinoin	• Add Accutane to F-PA coding to match criteria		

Agenda Item	Discussion Leader	Discussion Summary		Action	Notes
		Physician Administered Drug (PAD) Guidelines Injectable/Specialty Medications Oral and Injectable Oncology Medications Viltepso Neuromyelitis Optica Spectrum Disorder Botulinum Toxins A&B Veopoz Lantidra Gene Therapy for Sickle Cell Disease Tecelra Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) Agents	Changes - No changes - No changes - No changes, minor grammatical correction - No changes - No changes - No changes - No changes - Change naming convention to reflect generic availability of Endari - No changes - No changes		
		Interim Formulary Updates See p. 150 in packet			
		Summary of Physician Administered Drug (PAD) Updates See p. 152 in packet			
		Policy & Procedure Update RX-013 Physician Facility-Administered Drugs (PAD) Prior Authorization Review Process			
		DSNP Pharmacy Policy & Procedure (NEW) - RX-D-033 Medicare TrOOP, FIR and Nx Transactions - RX-D-035 Member Symptom Management Process			
		ED Oversight No changes			
		90 Day Maintenance List updates No changes			
		P&T Meeting Minutes P&T Meeting Minutes Q3 September 16,2025			

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes																
		Questions: PB: Can you clarify it was non-formular or formulary with PA for higher intensity insulins. RN: We can make an amendment to add the Tresiba and the Toujeo to formulary PA status and that would have the same criteria as the non-formulary. But the flag would be on our formulary. Messaging at point of sale would be formulary. RN: The amendment would be to make Toujeo and Tresiba formulary PA with the same nonformulary criteria. So basically, switching it from non-formulary to formulary PA. PB: 1st motion to approve amendment. AB: 2nd motion to approve amendment. Interim Formulary Changes These changes have been made to the Alliance’s formulary recently. The changes were necessary to enhance the formulary. <table><tr><th>Medication</th><th>Formulary Change</th></tr><tr><td>Prezcobix Oral Tablet 675-150 MG</td><td>NF to F</td></tr><tr><td>Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 100 MCG/ACT</td><td>NF to F</td></tr><tr><td>Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 50 MCG/ACT</td><td>NF to F</td></tr><tr><td>Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 200 MCG/ACT</td><td>NF to F</td></tr><tr><td>Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 100 MCG/ACT</td><td>F to NF</td></tr><tr><td>Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 50 MCG/ACT</td><td>F to NF</td></tr><tr><td>Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 200 MCG/ACT</td><td>F to NF</td></tr></table>	Medication	Formulary Change	Prezcobix Oral Tablet 675-150 MG	NF to F	Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 100 MCG/ACT	NF to F	Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 50 MCG/ACT	NF to F	Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 200 MCG/ACT	NF to F	Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 100 MCG/ACT	F to NF	Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 50 MCG/ACT	F to NF	Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 200 MCG/ACT	F to NF		
Medication	Formulary Change																			
Prezcobix Oral Tablet 675-150 MG	NF to F																			
Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 100 MCG/ACT	NF to F																			
Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 50 MCG/ACT	NF to F																			
Fluticasone Furoate Ellipta Inhalation Aerosol Powder Breath Activated 200 MCG/ACT	NF to F																			
Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 100 MCG/ACT	F to NF																			
Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 50 MCG/ACT	F to NF																			
Arnuity Ellipta Inhalation Aerosol Powder Breath Activated 200 MCG/ACT	F to NF																			

Agenda Item	Discussion Leader	Discussion Summary		Action	Notes
		Anusol-HC Rectal Suppository 25 MG	F to NF		
		Hemmorex-HC Rectal Suppository 25 MG	F to NF		
		Hemmorex-HC Rectal Suppository 30 MG	F to NF		
		Anucort-HC Rectal Suppository 25 MG	F to NF		
		Comirnaty 5-11 Years Intramuscular Suspension 10 MCG/0.3ML	NF to F		
		Comirnaty 5-11 Years Intramuscular Suspension 10 MCG/0.3ML	NF to F		
		Nuvaxovid COVID-19 Vaccine Intramuscular Suspension Prefilled Syringe 5 MCG/0.5ML	NF to F		
		Nuvaxovid COVID-19 Vaccine Intramuscular Suspension Prefilled Syringe 5 MCG/0.5ML	NF to F		
		Sacubitril-Valsartan Oral Tablet 24-26 MG	NF to F-QL (60/30)		
		Sacubitril-Valsartan Oral Tablet 49-51 MG	NF to F-QL (60/30)		
		Sacubitril-Valsartan Oral Tablet 97-103 MG	NF to F-QL (60/30)		
		Entresto Oral Tablet 24-26 MG	F-QL to NF		
		Entresto Oral Tablet 49-51 MG	F-QL to NF		
		Entresto Oral Tablet 97-103 MG	F-QL to NF		



Agenda Item	Discussion Leader	Discussion Summary		Action	Notes
		Eliquis Oral Capsule Sprinkle 0.15 MG	NF to F-QL (74/30)		
		Eliquis (2 MG Pack) Oral Tablet Soluble 4 x 0.5 MG	NF to F		
		Eliquis Oral Tablet Soluble 0.5 MG	NF to F		
		Eliquis (1.5 MG Pack) Oral Tablet Soluble 3 x 0.5 MG	NF to F		
		Otufi Subcutaneous Solution 45 MG/0.5ML	NF to F-PA		
		Otezla/Otezla XR Initiation Pk Oral Tablet Therapy Pack 10&20&30&(ER)75 MG	NF to F-PA-QL (41/30)		
		Otezla XR Oral Tablet Extended Release 24 Hour 75 MG	NF to F-PA-QL (30/30)		
		Doptelet Oral Capsule Sprinkle 10 MG	NF to F-PA		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes																																																
		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>J3389</td><td>PRADEMAGENE ZAMIKERACEL (ZEVASKYN)</td><td>Add</td></tr><tr><td>J9256</td><td>NIPOCALIMAB-AAHU (IMAAVY)</td><td>Add</td></tr><tr><td>J9326</td><td>ELISOTUZUMAB VEDOTIN- TLLV (EMRELIS)</td><td>Add</td></tr><tr><td>J3387</td><td>ELIVALDOGENE AUTOTEMCEL (SKYSONA)</td><td>Add</td></tr><tr><td>J0013</td><td>ESKETAMINE (SPRAVATO)</td><td>Add</td></tr><tr><td>Q5160</td><td>BEVACIZUMAB-NWGD (JOBEVNE), BIOSIMILAR</td><td>Add</td></tr><tr><td>Q5139</td><td>ECULIZUMAB-AEEB (BKEMV)</td><td>Remove</td></tr><tr><td>J9037</td><td>BELANTAMAB MAFODOTIN-BLMF (BLENREP)</td><td>Remove</td></tr><tr><td>J9371</td><td>VINCRIStINE SULFATE LIPOSOME (MARQIB)</td><td>Remove</td></tr><tr><td>J9259</td><td>PACLITAXEL PROTEIN- BOUND PARTICLES (AMERICAN REGENT)</td><td>Remove</td></tr><tr><td>J2503</td><td>PEGAPTANIB SODIUM (MACUGEN)</td><td>Remove</td></tr><tr><td>J2796</td><td>ROMIPLOSTIM (NPLATE)</td><td>Remove</td></tr><tr><td>J9037</td><td>BELANTAMAB MAFODONTIN-BLMF (BLENREP)</td><td>Remove</td></tr><tr><td>J9258</td><td>PACLITAXEL PROTEIN- BOUND PARTICLES (TEVA)</td><td>Remove</td></tr><tr><td>S0013</td><td>ESKETAMINE (SPRAVATO)</td><td>Remove</td></tr></table>	HCPCS Code	HCPCS Description	Action	J3389	PRADEMAGENE ZAMIKERACEL (ZEVASKYN)	Add	J9256	NIPOCALIMAB-AAHU (IMAAVY)	Add	J9326	ELISOTUZUMAB VEDOTIN- TLLV (EMRELIS)	Add	J3387	ELIVALDOGENE AUTOTEMCEL (SKYSONA)	Add	J0013	ESKETAMINE (SPRAVATO)	Add	Q5160	BEVACIZUMAB-NWGD (JOBEVNE), BIOSIMILAR	Add	Q5139	ECULIZUMAB-AEEB (BKEMV)	Remove	J9037	BELANTAMAB MAFODOTIN-BLMF (BLENREP)	Remove	J9371	VINCRIStINE SULFATE LIPOSOME (MARQIB)	Remove	J9259	PACLITAXEL PROTEIN- BOUND PARTICLES (AMERICAN REGENT)	Remove	J2503	PEGAPTANIB SODIUM (MACUGEN)	Remove	J2796	ROMIPLOSTIM (NPLATE)	Remove	J9037	BELANTAMAB MAFODONTIN-BLMF (BLENREP)	Remove	J9258	PACLITAXEL PROTEIN- BOUND PARTICLES (TEVA)	Remove	S0013	ESKETAMINE (SPRAVATO)	Remove		
HCPCS Code	HCPCS Description	Action																																																		
J3389	PRADEMAGENE ZAMIKERACEL (ZEVASKYN)	Add																																																		
J9256	NIPOCALIMAB-AAHU (IMAAVY)	Add																																																		
J9326	ELISOTUZUMAB VEDOTIN- TLLV (EMRELIS)	Add																																																		
J3387	ELIVALDOGENE AUTOTEMCEL (SKYSONA)	Add																																																		
J0013	ESKETAMINE (SPRAVATO)	Add																																																		
Q5160	BEVACIZUMAB-NWGD (JOBEVNE), BIOSIMILAR	Add																																																		
Q5139	ECULIZUMAB-AEEB (BKEMV)	Remove																																																		
J9037	BELANTAMAB MAFODOTIN-BLMF (BLENREP)	Remove																																																		
J9371	VINCRIStINE SULFATE LIPOSOME (MARQIB)	Remove																																																		
J9259	PACLITAXEL PROTEIN- BOUND PARTICLES (AMERICAN REGENT)	Remove																																																		
J2503	PEGAPTANIB SODIUM (MACUGEN)	Remove																																																		
J2796	ROMIPLOSTIM (NPLATE)	Remove																																																		
J9037	BELANTAMAB MAFODONTIN-BLMF (BLENREP)	Remove																																																		
J9258	PACLITAXEL PROTEIN- BOUND PARTICLES (TEVA)	Remove																																																		
S0013	ESKETAMINE (SPRAVATO)	Remove																																																		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
V) New Business	Iryna Makukh	<u>QL recommendations</u> - Quantity limits for several other plans and compared them to Alameda and came up with this list of drugs of quantity limit recommendations in order to optimize dosing and better control plan spend. So, here's a list of quantity limit recommendations. They're based on Companion dosing as well as dosing optimization. - In the interest of time, I will not go through all of them, but a couple of high-impact examples include Cabenuva, Ofev, Descovy, Linzess and Tradgenta. Recommendations are based on achieving the recommended daily dosing with the fewest units of medication. - Also, since the document was included in the packet, we had some discussions with the plan, and it was agreed to have quantity limits for Ajoyv and Cabenuva per 28 days instead of 30. That's because of some claims that were per 28 days, and some claims were per 30. So just to be more lenient. We decreased the QL per 28 days, so same QL per 28 days and I will pause now in case you have any questions about this. <u>Questions/Comments:</u> PB: Cabenuva, don't we get that every two months? IM: Yes, it can be monthly dosing, or it can be every two-month dosing schedule. The two, so, so the monthly dosing you, yeah, so but first you must do initiation injection 600 per 900 and then 400 per six per 600 every month. And every two months it is 600 per 900 for the like the first two injections, there are two initiation injections actually and then it goes 600 per 900 every two months. PB: How are we going to manage that when you're setting a 30-day limit? IM: So, they can get two for 30 days and that includes the initiation injection as well. Also, they can get like plus -7 days early or later if they are, you know, cannot do it on the exact same day. So, we would like to be more lenient. In order to make sure patients can get it. LR: The quantity limit is going to be calculated per day. So, the member will be able to get a two-month supply because it's just the per day dosing, if that makes sense. DC: Note on page 218 on the Cabenuva, it still says there's 30 days for the quantity limit. It's going to be 28 days, not 30 days. IM: Yes, thank you. <u>New MRG</u> <u>Anzupgo</u> - Moving on to the MRG criteria, new MRG criteria, it's on page 222. - The first criteria are for Anzupgo. Anzupgo is indicated for the treatment of moderate to severe chronic hand eczema. It's indicated for adults who have had an inadequate response to or for whom topical corticosteroids are not advisable. Anzupgo is a Jak inhibitor inhibiting the activity of Jak-123 and tyrosine kinase. - And it is the first product specifically indicated for CHE or chronic hand eczema. The price is \$3972 per month. That's based on WACC and recommended dosage of twice daily application to hands and wrists. And for the criteria, you should be excluded if patients currently use Opzelura. - Systemic jak inhibitors or potent immunosuppressants, and this is per limitations of use in the that says the use of Anzupgo in combination with other JAK inhibitors or potent immunosuppressants is	Move to approve: New MRG 1st: BD 2nd: AB Move to approve: New PAD 1st: BD 2nd: PB	

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		not recommended for coverage duration. The initial request will be approved for six months, and reauthorization request will be approved for 12. - Months. Trials were 16 weeks for safety and efficacy, therefore a standard six-month initial approval would be appropriate and for initial authorization medications prescribed at an FDA approved dose. Patients have diagnosis of moderate to severe chronic hand eczema per labeled indication. - We ask for documentation of hand eczema persisting for more than at least three months or occurring at least two times within 12-month time frame. And this is a definition of chronic hand eczema per the guidelines. - Also, we ask for trial and failure or contraindication to at least two formularies moderate to high potency topical corticosteroids, and this is per labeled indication and treatment algorithms for CHE that includes high potency topical corticosteroids. - TCI's but only a steroid sparing treatment option or oral corticosteroids and then resumption of topical steroids as first line. So Anzupgo would be considered as second line alternative treatment and for reauthorization we ask for documentation of provider attestation of positive clinical response such. - Such as significant clearing of the skin, reduction in itching and that medication is prescribed at an FDA approved dose. And that's all I have for these new criteria. Any questions on this one? <u>Brinsupri</u> - Next page 223, we have a new emerging criteria for Brinsupri and Brinsupri is a newly approved agent indicated for the treatment of non-cystic fibrosis bronchiectasis in adult and pediatric patients 12 years of age and older. - Bronchiectasis is a common respiratory condition characterized by recurrent or persistent productive cough, excessive sputum production, recurrent pulmonary infections and airway inflammation. In patients that are not diagnosed with cystic fibrosis, this condition is known as non-cystic fibrosis bronchiectasis. - Brinsupri is the first approved treatment for NCFB. It's the first DPP1 inhibitor approved and is an oral formulation designed to inhibit the activation of enzymes in neutrophils that are key drivers of chronic airway inflammation in NCFB. - The price is \$7333 per month. As for criteria, we require that medication is prescribed by or in consultation with a pulmonologist for coverage duration. The initial and reauthorization request will be approved for 12 months as primary endpoint was measured at 52 weeks. - For initial authorization, our required diagnosis of bronchiectasis confirmed by chest CT scan because diagnosis is based on combination of clinical history and radiologic evidence from a CT scan. Next, we ask for the documentation that patients do not have cystic fibrosis as per indication. - And at least two of the two patients in the past 12 months require an antibiotic prescription, urgent care or emergency room visit or hospitalization. And this was part of inclusion criteria in clinical trials and is a clinical feature used for diagnosis. - Lastly, medication is prescribed at an FDA approved dose. And for reauthorization, we ask for documentation of positive clinical response such as decrease in cough, sputum production, exacerbations and that medication is prescribed at an FDA approved dose.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		<u>Phenylalanine Hydroxylase Activators</u> - Next on page 224 and that's a new emergency criteria for phenylalanine hydroxylase activators. So, this new criteria includes phenylalanine hydroxylase activators, sapropterin, which is generic for Kuvan and newly approved agent Sephience. - Which are used for the treatment of PKU or phenylketonuria, which is a rare inherited metabolic disorder that prevents the body from breaking down the amino acid phenylalanine and without treatment phenylalanine or PHE builds up to toxic levels. - Blood and brain and that can lead to severe intellectual disability, seizures and developmental delays and a lifelong low phenylalanine diet is the primary treatment of PKU. Both agents are PAH activators. They are used in conjunction with a PHE restricted diet. - Both are oral pH activators with similar labels. However, Sephience is newer and significantly more expensive. The price of Sephience is 63,000 dollars, \$63,750 per month for a 70-kilogram adult and the price of Sapropterin, which is a generic. - It is \$12,240 per month for a 70-kilogram adult. As for criteria, drugs should be prescribed by a specialist experienced in treating PKU. It is recommended to confirm responsiveness with therapy continued only if effect if effectiveness is observed through a reduction of phenylalanine levels in blood in the first four weeks of escalating doses. So, for initial the request will be approved for a duration of one month. - For initial authorization, we require documentation of a confirmed diagnosis of PKU documentation of patient's baseline PHE level since it will be used to assess efficacy. Also, documentation that the patient is currently utilizing PHE restricted diet. - We ask for documentation of patient's current weight, again dosing based on weight and documentation of at least two separate blood PHD level results after initiation of therapy. - For initial authorization, we require documentation of a confirmed diagnosis of PKU documentation of patient's baseline PHE level since it will be used to assess efficacy. Also, documentation that the patient is currently utilizing PHE restricted diet. Since this is mainstay of treatment and both drugs should be used in conjunction with this diet, requests for Sephience also require a documented trial and failure, intolerance, or contraindication to Sapropterin in combination with PHU restricted diet. - Also, documentation of the patient's current weight since it's weight-based dosing and medication is being prescribed at an FDA approved dose. Dose for reauthorization. We ask for documentation of patient's current weight, again dosing based on weight and documentation of at least two separate blood PHD level results after initiation of therapy. And this is to make sure the patient responds to treatment and at PHD levels are below the baseline after. - The initiation of therapy and lastly medication is prescribed at an FDA approved dosage, and we also have similar language as in coverage duration that for SAP Sapropterin patients that were dosed at 20 milligram per kilogram per day which is the Max. - If they did not have the decrease in PHE from baseline, they are considered non-responders, and no additional treatment will be authorized and the similar language for sentence as well. And that is all I have for these criteria.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		<u>Nitisinone Products</u> - The next emerging criteria for Nitisinone products and Nitisinone medications. They are used to treat rare genetic disorders such as hereditary tyrosinemia type one or HT1 and alkaptonuria AKU. - They are available as both brand name and generic formulation. They work as HPPD inhibitors, which prevents the accumulation of toxic intermediate byproducts in the body that can cause severe liver, kidney, and neurological damage. - Harliku is a newly approved brand product from the list of these products, and it is indicated for the reduction of urine homogentisic acid in adult patients with AKU and there are no meaningful differences in Nitisinone products except that neither is available in higher strengths. - The price of Harliku is \$44,553 per month and the price of Nitisinone generic is \$2,190 per month. - With dosing for AKU, so a significant difference in price and for the criteria prescriber must be a specialist in the diagnosis submitted. - For coverage duration, initial requests will be approved for six months, and reauthorization requests will be approved for 12 months. - For initial authorization for AKU diagnosis of AKU confirmed by one of the following urinary HGA excretion of at least 0.4 grams per 24 hours. - The drug is prescribed at an FDA approved dose and for reauthorization we require at the station that member is achieving a clinical benefit from treatment and that medication is prescribed at an FDA approved dose. <u>New PAD</u> <u>Skysona</u> - Skysona is an autologous hematopoietic stem cell-based gene therapy indicated to slow the progression of neurologic dysfunction in boys 4 to 17. - Years of age with early active cerebral adrenal leukodystrophy or CALD without an available human leukocyte antigen matched donor for allogeneic hematopoietic stem cell transplant. So, CALD is a severe progressive and rare genetic disorder that affects the brain and adrenal glands. - Due to a defect in the ABCD1 gene, symptoms include behavioral changes, learning difficulties, problems with speech and coordination, and without treatment, the condition can lead to rapid disability. So Skysona is a novel gene therapy that adds functional copies of the ABCD1 gene into patient's hematopoietic stem cells, and this leads to bone marrow being able to produce cells capable of producing functional proteins that can participate in the degradation of the VLCFA phase. - That is at the heart of the pathophysiology for this disease. The price is \$3,000,000 for one-time treatment and for the criteria prescriber must be a specialist in the disease being treated. - For exclusion, patients with CALD secondary to head trauma should not get Skysona per the limitations of use in the PI since it has not been studied in this population. Also, patients positive for HIV were not studied in the trial and by labeling HIV positive patients' material would not be accepted.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- Also, female patients are excluded as this drop is indicated for boys 4 to 17 years of age. For coverage duration, the request will be approved for one time treatment since there is no data on repeated treatments. - And for initial authorization, members have a diagnosis of early active CALD per labeled indication and defined as all the following. So elevated very long chain of fatty acid levels. This was the clinical trial inclusion criteria. - Confirm mutations in the ABCD1 gene. This is to confirm known genetic cause of the disease. Patients are asymptomatic or widely symptomatic with neurologic function score of less than or equal to one and gadolinium enhancement on brain MRI of demyelinating lesions and loss scores of. - From 0.5 to 9. These are per the indication in the package insert and there is the definition of early active CALD. Next medication is prescribed at 98 approved doses. Members have not had a prior allogeneic hematopoietic stem cell transplant. - This was the exclusion criteria in the trial. And lastly, members have no HLA matched sibling donor for HSCT or a reason it is not appropriate. So, this is a current standard of care. - HSCT and reauthorizations are not permitted as members are limited to one-time treatment since safety and efficacy of repeat administration have not been evaluated. And that is all I have for this criteria. Any questions? <u>Spravato</u> - This PAD criteria are needed because Spravato should be administered under the supervision of a healthcare provider. There were no new clinical updates. So, this PAD criteria are based on already existing MRG policy that we have already discussed. So, there were no new clinical updates. - Clinical updates. This PAD criteria are the same as the MRG policy, and all the points are clinically appropriate and have not changed from last review. So please let me know if you want me to go over anything or if you have any questions about this criteria. <u>Questions/Comments:</u>		
VI) Class Reviews, Monographs, and Recommendations-	Iryna Makukh	1. <u>Hereditary Angioedema Agents Class Review</u> - The first-class review is for hereditary angioedema agents. Hereditary angioedema is a rare genetic disorder characterized by unpredictable episodes of severe swelling in various parts of the body, including face, throat, abdomen and limbs. - HAE is caused by a deficiency or dysfunction of a protein called C1 esterase inhibitor, and this protein in general helps regulate the immune system and prevents excessive inflammation. Agents that are available for HAE are available to both treat and prevent HAE attacks. - Prophylaxis may be used for the long term or short term in anticipation of procedures or stressful life events, and let's look at utilization on page 248. - There were no claims and no prior authorization requests. All products are non-formulary except for Orladeyo, which is the only oral agent for HAE prophylaxis and it's the most cost-effective agent for HAE prophylaxis. We do not recommend any formulary changes since there's no utilization.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- And there were several new products recently approved, and we need to update the criteria with these new products and PA criteria is on the next page 249. - So here we recommend adding three new agents, Ekterly and Andembry and Dawnzera, to non-preferred agents since they are more costly and there is no preference of one agent over another for treatment guidelines. And the only other change to the criteria is on the next page. - And we're just adding a statement for prophylaxis agents that if the request is for a non-preferred agent that the member has documented trial and failure or inability to use preferred agent. And this is for cost containment, and these are all changes recommended for this class review.		
		2. <u>PCSK9 Inhibitors Class Review</u> - This review covers PCSK 9 inhibitors and values to treat dyslipidemia as you all know and guidelines generally recommend PS PCSK 9 inhibitors and the later line agents after adequate LDL lowering has not been achieved with statins and with ezetimibe and there were some recent label expansions for Leqvio and Repatha labeling. They are now supporting. their use as monotherapy instead of as an add-on therapy with traditional statins or other agents to lower LDLC. - Also, Repatha and Praluent were also given approval for primary prevention of major cardiovascular events, and let's look at the utilization on page 285. - There were 20 claims for seven members for a total cost of \$10,562 and an average cost per claim of \$528. The most highly utilized medication was a Repatha SureClick subcutaneous pen injector with 14 claims. - Followed by Prevalent subcutaneous pen injectors with four claims. There were three prior authorization requests with one approval at 33% and both Prevalent and Repatha are one formulary with PA and they are similarly priced. - Repatha subcutaneous syringe has a lower average per RX cost here, but that's just because out of two claims, one was for one unit per 14 days, and the other claim was for two units per 28 days with a price of \$520. This is an average price per month with a regular. - Dose every two weeks. Um, also, lack failure is more costly and uh non-formulary and we do not recommend any changes to formulary coverage. And as mentioned earlier, Repatha and Praluent received label expansions and they are now indicated for primary prevention of major adverse cardiovascular. - Due to uncontrolled LDLC and not just for patients with established cardiovascular disease or high risk. We recommend streamlining PA criteria requirements based on those expanded indications and PA criteria is on the next page 286. - For the criteria we're requiring that provider indicates members LDLC is above goal or genetic tests submitted with a request for the diagnosis of familial hypercholesterolemia. All other criteria remain the same trial and failure of statin therapy and is that in combination. - with highest tolerated intensity statin. Also, we need to remove preferred NDCs from PA criteria and add all active NDCs to formulary since we only included preferred pricing NDCs previously and when I checked pricing on all NDCs that are missing from formulary. - They were all the same price as the NDCS that are currently on formulary. The recommendation is to add all NDCs formulary and since we only remove the preferred and lastly on the next page 287 next page.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- We are removing these sections for the diagnosis of FH since it's already covered above and no need to keep the primary and secondary prevention sections since now the drugs are indicated for primary prevention of major adverse cardiovascular events. - And these are all changes recommended for PCSK 9 inhibitor class review. Questions/Comments: PB: Why not just put 80mg? IM: We are keeping it as an option depending on what the patient can tolerate.		
VII) Medication Request Guidelines	Rahel Negash	The committee has reviewed and discussed the following updates and additions to the Medication Review Guidelines (MRG) Guideline (Changes): 1. Pulmonary Hypertension (PH) Agents - Our first policy here for the medication request guideline updates is our pulmonary hypertension policy. And so here the changes highlighted are for the new products Yutrepia. It will be on par with Tyvaso. - It is a new agent or new formulation that allows more uniform particle dispersion. - There are reports of fewer therapies. - Discontinuation with this product due to cough in comparison to Tyvaso. - The cost is comparable as well. - We are adding it on par with Tyvaso to provide options for both with the same criteria. - And there's no other changes with this policy. Comments: Guideline (Changes): 2. Agents for Primary Biliary Cholangitis - And this is agents for primary biliary cholangitis. - The first change you can see there in the medication section is that we're removing Ocaliva since it's no longer available on the market. It's been removed due to safety concerns. As it relates to the liver. - We are removing it from our formulary and from our policy. - And that removal is scattered throughout the policy. - The next change we have here relates to the confirmation of diagnosis. - In the PA review criteria section, we are requesting that the patients try to or have two out of 3 confirmed parameters instead of two out of two. So, in essence we're adding. - The first option would be positive AMA tests or other presence of PBC specific auto bodies and then also they could have confirmation of elevated serum alkaline phosphatase or ALP. - And then also we want to look at Histology, evidence of primary biliary cholangitis from a liver biopsy. So, two of the three would suffice to confirm diagnosis here. - And there's no other changes to this policy that we're not already mentioned. Comments: Guideline (Changes): 3. Ohtuvayre - Here we're adding a prescriber restriction to include pulmonologist when utilizing this product.	Move to approve: 1st: AB 2nd: PB	

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- And then also, we're changing the PA review criteria to match the recommendations based on our guidelines. In short, we're removing the requirement of an inhaled corticosteroid, and we'd only want to see them use a long-acting beta 2 agonist or a long-acting muscarinic antagonist. - Those would be the two preferred agents prior to approval of the Ohtuvayre. - There are no other changes to this policy. <u>Comments:</u> Guideline (Changes): 4. Complement Inhibitors for the Treatment of PNH - This is for a complement inhibitor for the treatment of PNH. - And here we can see there's a few changes. - The first is just in the title. So, because there is a new indication for Fabhalta for C3G we are including it here for review. - We are also adding the prescriber for a nephrologist to be included in the restrictions. This will be handled in nephrology. - In the PA review criteria section, we can see that we're separating the policy by disease state and indications. So, the first would be PNH and so here we're also aligning the confirmation of diagnosis with the symptoms as opposed to just the hemoglobin alone. And so, you can see that that's struck since that's specific to Fabhalta based on some of the pivotal trials. - We want to see confirmation of at least one of the following symptoms. - It includes fatigue and hemoglobinuria, abdominal pain, shortness of breath and such. - If we move to the next page, we see the next disease state. - For IgA nephropathy and that has its own policy. - So, we are just referencing that for clarity and then we are including the C3G for Fabhalta indication. - The requirements would be the appropriate diagnosis, confirmed by renal biopsy. And then we want to see that the patient's CRC3 level is reduced as well looking for UPCR that is at least one. - And we also want to see eGFR is at least thirty and we want to see that they have tried and failed the maximally recommended ACE or ARB for at least 90 days and this is based on the initial trials for approval of the on the therapy. - And then we also want to see trial and failure of mycophenolate and glucocorticoid or a reason they can't use it. - And then we want to see that the patient does not have recurrent C3G post kidney transplant. - The only other change here relating to the criteria is the reauthorization. - So, we also are just including that improvement in UPCR since that was one of the endpoints for Fabhalta in treating C3G. - And there are no other changes here. <u>Comments:</u> Guideline (Changes): 5. Injectable/Infusible Bone-Modifying Agents for Oncology Indications - Here we are highlighting the introduction of new biosimilars for Xgeva and Prolia. - We can see in the medication section, we are separating it by the available biosimilars for each. - So Xgeva has the Bilprevda the Wyost, Bomynta, Osenvelt, Xbryk		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- And then Prolia has the biosimilars available there as well. - Under the PA Review Criteria section, we do have preferred agents based on cost, efficacy and those are the ones that will be preferred. - For Xgeva, it's Bilprevda. And then for Prolia it is Bidlyos. - We would prefer Bidlyos. - Throughout the policy, we are also referencing the biosimilar language, so that the appropriate products are being referenced and reviewed. - But there are no other changes here, just more availability of biosimilars, which is great. <u>Comments:</u> Guideline (Changes): 6. Injectable/Infusible Agents for Osteoporosis and Paget's Disease - Our next policy, which is on page 300 for injectable and fusible agents for osteoporosis and Paget's disease. - And this is similar to the previous policy we are updating based on availability of biosimilars, so. - For Prolia, we are listing the preferred biosimilars that are available and then language in the medication section. - And then also the PA Review criteria section to show which of these biosimilars are most cost effective. Bidlyos is preferred here. - There are no other changes to review of requests on this policy, just referencing the shift from. <u>Comments:</u> Guideline (Changes): 7. Wegovy - The next policy we have is for Wegovy. - So initially this policy was created to reference the new indication for Wegovy. But as we move forward with new research, there are more indications for our GLP one. - We are combining in one policy for all the non-weight loss indications for these products. And so we are including Zepbound here. - Also, Wegovy has a new indication for MASH, so we are including that. - And we can see that exclusion criteria section is being updated to reference or to address all the medications that apply. - So, we are taking out type one and two diabetes as an exclusion criterion since that is specific to Wegovy. And we are also making changes in the age restriction section. - So just making it more specific for Wegovy and cardiovascular risk reduction, we want to see that Members are at least 45 since that was what was studied in the initial trials. And then we want to see all FDA approved indications. - Prescriber restrictions are also specific to the indication. We want to see that for Wegovy and Mash, for example, would be a hepatologist, GI endocrinology or some specialists in the treatment of liver disease for Wegovy and CVD risk reduction we're not restricting that to any specific prescribers and then Zepbound for OSA. We want to see a specialist in sleep disorders. - Similar to previous policies were separated by indications.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- So, when we get requests for, we Wegovy for instance and we have the condition for risk reduction or major adverse cardiovascular events in adults with established CVD. We will look at this section. - And the change here we can see that in the prescriber restrictions we are including the Type 1 and type 2 diabetes here instead of in the above section since it is specific to Wegovy and then we are also including mash since we have that new indication. - We want to see appropriate diagnosis of mash for moderate to advanced liver fibrosis. We want to see that they have F2 or F35 fibrosis confirmed by biopsy or by noninvasive tests and then. - Attestation of appropriate lifestyle, counseling or nutrition and exercise and then avoid alcohol intake. - Next, we see that Zepbound listed here. - We did have a policy for this, but we are including it here for OSA. And so, we want to see that the BMI is 30 or more, that they have moderate to severe OSA. - And that they have tried lifestyle changes, behavioral modifications like healthy diet and exercise. - And then we want to see that they have at least one of the following, which would be a sleep test showing that their AHI, which is their apnea hypopnea index, is at least 15 while they're on PAP therapy. - They can also have that sleep test showing that they have an AHI of 15 and previous trial and failure of PAP therapy, or a reason they cannot use PAP therapy. - And then we are also going to exclude patients for whom are pregnant for this disease state. - Reauthorization criteria are specific for condition, so we see for Wegovy and the risk reduction for major adverse cardiovascular events in adults with CVD disease. We do want to see that they have appropriate fill rates to make sure they are getting the maximum benefit from therapy. - And then for mash, the same thing at least 80% and we want to see that they have appropriate dosing and their fibrosis score is not worsening so it is less than 3. - For Zepbound requests we want to see that the dose is appropriate. - Also, they have had positive clinical responses, and they have 80% full rate as well. Comments: PB: For MASH, it should be fine to you to make sure you insist on hepatologist or GI. Our access is ok and it is not hard to get the elastograms thus far. What is challenging is consulting with a sleep medicine specialist. RN: Ok so there is an issue with access. We can make an amendment to the policy to remove the restriction for a sleep disorder specialist. Guideline (Changes): 8. Zepbound for Moderate to Severe Obstructive Sleep Apnea - The next policy is for Zepbound. - So, it relates to that OSA, and it's on page 306. - This is just getting retired since it was included in the previous policy as it combined. Guideline (Changes): 9. Anti-Obesity Medications - Here you can see in the medication section we're making updates based on what we previously discussed. - So just referencing MASH and OSA and the new non weight loss indications criteria just to be thorough.		

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		- We are driving the correct review when we get these medication requests. - And then in the PA Review criteria section, we do have some updates for our non GLP ones we are proposing to revert to BMI over 30 or 27. - Or plus comorbidity if it's at 27 to allow more access to non-GOP agents for weight loss. - So that's structured throughout the policy for Phentermine, Alli, Qsymia along with Contrave. - If we move to the next page, we can see the next change and it's under Qsymia. - So here to just be clearer, we're adding reference to state that we want to see clinic notes and paid claims for trial and failure or Phentermine and topiramate agents, just to confirm appropriate review. - And so, you see that note listed for Contrave and for our GLP 1 - And the last change can be found under Saxenda, Wegovy and Zepbound. - So here we're just adding language to state if a GLP one agonist is already approved and the prescriber wants to switch to another GLP one for the same indication. Then we wouldn't require that they go through all the preferred agents again, so that they can switch to a different GLP 1 agonist. - No other changes in this policy. Guideline (Changes): 10. Rezdifra - The first change we have is in the exclusion criteria section so we're removing thyroid disease based on new evidence and FDA review that this is no longer significant. - We just want to update, so we make sure we have appropriate review and then the prescriber restriction, we're including an endocrinologist, this is more lenient here when we get requests. - And then PA review criteria here. Since we have Wegovy that's now available, we're adding that as a preferred option based on cost efficacy. - No other changes in this policy. <u>Comments:</u> 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. Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS) - The first policy with updates is for HCP administered IV disease modifying therapies for multiple sclerosis. And here we're adding Ocrevus Zunovo, which is Ocrelizumab with hyaluronidase days given as a subcutaneous injection by HCP. We're adding it for completion for completeness as it has been missing from the policy and pricing is a parity with Ocrevus and another change is that we're adding Tyruko. - Which is a new Tysabri biosimilar and cost of Tyruko is about 20% discount from brand and we have language in the criteria on using the biosimilar or providing a medical reason why it's not possible before the brand product. - And here recommendation is just to streamline language on immunizations requirement. We recommend broader language to get at the attestation that provider is following administration guidelines for live and non-live immunizations in accordance with products prescribing information and immunization guidelines. - Or has documented medical reasons for patients not receiving recommended immunizations. So just wanted to make language a bit more generic so that it applies to all drugs in this section and those are all changes to this criteria. Comments: Guideline (Changes): 2. Complement Inhibitors - Similarly to the MRG policy, we're updating PNH initial authorization on the next page. - And just like an MRG, we want to require the presence of a sign or symptom of PNH instead of just relying on hemoglobin value. And this is better aligned with guidelines. And the only other recommendation here is to add trial and failure of the soliris biosimilar epysqli for cost containment only applicable to adults since biosimilar epysqli is not approved in pediatric patients. - And these are all changes to this policy, no other changes Comments: Guideline (Changes): 3. Myasthenia Gravis Agents - Here we are updating the drug list section to include Imaavy, which is the new neonatal FC receptor blocker. - Indicated for the treatment of generalized myasthenia gravis in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor or anti-mask antibody positive. Also, we're updating age restrictions with Imaavy since it is indicated in 12-year-old patients and. - Older and there are some references in the initial authorization section on the next page 318 here just change language a bit for no concurrent use of these therapies. - Included Zilbrysq since it was missing from the list. And lastly, we're adding trial and failure of Vyvgart, Vyvgart Hytrulo or Rystiggo before other more costly agents in adults for cost containment. - As there are no recent guidelines to direct which class should come first and current 2021 guidelines reserve complement inhibitors for severe and refractory myasthenia gravis. And these are all changes to this criteria.	Approved 1 st : BD 2 nd : AB	

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
		<u>Comments:</u> Guideline (Changes): 4. Injectable/Infusible Agents for Osteoporosis and Paget's Disease - Here recommendations are like the MRGS. So here we're just adding newly released Prolia biosimilars to the drug list and adding trial and failure of the biosimilar before Prolia reference product. <u>Comments:</u>		
IX) Informational Updates on New Developments in Pharmacy	Iryna Makukh	<u>New Product Review</u> • New Products discussed.		

			BRAND NAME	GENERIC NAME/DOSAGE FORM	RECOMMENDATION			
			Andembry	garadacimab-gxii subcutaneous solution auto-injector 200 mg/1.2 mL	Non-formulary (see updated MRG criteria)			
			Ekterly	Sebetralstat 300mg oral tablet	Non-formulary (see updated MRG criteria)			
			Kerendia	finerenone oral tablet 40 mg	Non-formulary			
			Penmenvy	meningococcal groups A, B, C, W, and Y vaccine, intramuscular suspension reconstituted	F-QL-AL (Already added via CRF; QL: 2 fills/lifetime, AL: 10-25 years of age)			
			Orlynvah	sulopenem etzadroxil-probenecid oral tablet 500-500 mg	Non-formulary			
			Orquidea	norethindrone oral tablet 0.35 mg	Non-formulary			
			Omnipod 5 Libre2Plus G6 Intro Kit (Gen 5)	omnipod 5 libre2plus g6 intro kit (gen 5)	Non-formulary			
			Tyfast Flu A/B Covid-19 Multip In Vitro Kit	tyfast flu A/B covid-19 multip in vitro kit	Non-formulary			
			Gonal-f RFF	follitripin alfa rediject subcutaneous solution pen-injector 300 unit/0.48 mL, 450 unit/0.72 mL	Non-formulary			

			Egrifta WR	tesamorelin acetate subcutaneous kit 11.6 mg	Non-formulary			
			Dicyclomine	dicyclomine hcl oral tablet 40 mg	Non-formulary			
			Avgemsi	gemcitabine intravenous Solution 1 gm/26.3 mL, 2 gm/52.6 mL	Non-formulary			
			MiCort HC#	hydrocortisone acetate external cream 2.5%	Non-formulary			
			Spevigo	spesolimab-sbzo subcutaneous solution prefilled syringe 300 mg/2 mL	Non-formulary			
			Anzupgo	delgocitinib external cream 20 mg/gm	Non-formulary (see new MRG criteria)			
			Sephience	sepiapterin oral packet 250 mg, 1000 mg	Non-formulary (see new MRG criteria)			
			Tepadina	thiotepa & sodium chloride intravenous solution reconstituted 200 mg/200 mL	Non-formulary			
			Fluorouracil#	fluorouracil external cream 0.5 %	Non-formulary			
			Triamcinolone Acetonide#	triamcinolone acetonide injection suspension 10 mg/mL	Non-formulary			

			Pyzchiva	ustekinumab-ttwe subcutaneous solution auto-injector 45 mg/0.5 mL, 90 mg/mL	Non-formulary			
			Vizz	aceclidine hcl ophthalmic solution 1.44 %	Non-formulary			
			MODD1	MODD1 patient welcome kit, supply kit	Non-formulary			
			Analpram HC#	hydrocortisone-pramoxine external lotion 2.5-1 %	Non-formulary			
			Hydrocortisone acetate	hydrocortisone acetate external cream 2.5 %	Non-formulary			
			Hernexeos	zongertinib oral tablet 60 mg	Non-formulary			
			Brynovin	sitagliptin oral solution 25 mg/mL	Non-formulary			
			TNKase	tenecteplase intravenous kit 25 mg	Non-formulary			
			Prezcobix	cobicistat-darunavir ethanolate oral tablet 675-150 mg	F-QL (Already added via CRF)			
			Remodulin	treprostinil injection solution 8 mg/20 mL	Non-formulary			
			Modeyso	dordaviprone oral capsule 125 mg	Non-formulary			

			Brinsupri	brensocatib oral tablet 10 mg, 25 mg	Non-formulary (see new MRG criteria)			
			Butalbital-APAP-Caffeine#	butalbital-APAP-caffeine oral solution 50-325-40 mg/15 mL	Non-formulary			
			Jaythari	deflazacort oral tablet 6 mg, 18 mg, 30 mg, 36 mg	Non-formulary			
			Brukinsa	zanubrutinib oral tablet 160 mg	Non-formulary			
			Kirsty	insulin aspart-xjhz 100 unit/mL vial, pen injector	Non-formulary			
			Jobevne	bevacizumab-nwgd intravenous solution 100 mg/4 mL, 400 mg/16 mL	Non-formulary			
			Kyxata	carboplatin intravenous solution 80 mg/8 mL, 500 mg/50 mL	Non-formulary			
			Bosentan	bosentan oral tablet soluble 32 mg	Non-formulary			
			Dawnzera	donidalorsen subcutaneous solution auto-injector 80 mg/0.8 mL	Non-formulary (see updated MRG criteria)			
			Unloxcyt	cosibelimab-ipdl intravenous solution 300 mg/5 mL	Non-formulary			
			Papzimeos	zopapogene imadenovec-drba subcutaneous suspension	Non-formulary			

				500000000000 pu/mL				
			Dexcom G7	dexcom 15-day sensor miscellaneous	Non-formulary			
			Pen Needle	pen needle/5-bevel tip miscellaneous 31g X 8 mm	Non-formulary			
			Wayrilz	rilzabrutinib oral tablet 400 mg	Non-formulary (see updated MRG criteria)			
			Leqembi Iqlik	lecanemab-irmb subcutaneous solution auto-injector 360 mg/1.8 mL	Non-formulary			
			Liomny	liothyronine oral tablet 5 mcg, 25 mcg, 50 mcg	Non-formulary			
			Clemsza	clemastine oral tablet 2.68 mg	Non-formulary			
			Lurbiro	flurbiprofen oral tablet 100 mg	Non-formulary			
			Pro Comfort Pen Needles	pen needle miscellaneous 32 g X 8 mm	Non-formulary			
			Blujepa	gepotidacin oral tablet 750 mg	Non-formulary			
			Zurnai	nalmefene injection solution auto-injector 1.5 mg/0.5 mL	Non-formulary			

			Brekiya	dihydroergotamine s ubcutaneous solution auto-injector 1 mg/mL	Non-formulary			
			Fibryga	fibrinogen intravenous solution reconstituted 2 gm	Non-formulary			
			Adalimumab-ryvk	adalimumab-ryvk (1 pen) subcutaneous auto-injector kit 80 mg/0.8 mL	Non-formulary			
			Luizza	norethindrone acetate-ethinyl estradiol 1.5/30 oral tablet 1.5-30 mg- mcg, 1-20 mg-mcg	Non-formulary			
			Zelvysia	sapropterin oral packet 100 mg, 500 mg	Non-formulary (see new MRG criteria)			
			Pyquvi	deflazacort oral suspension 22.75 mg/mL	Non-formulary			
			Oxytocin +RFID	oxytocin +RFID injection solution 10 unit/ mL	Non-formulary			
			Eliquis	apixaban oral capsule sprinkle 0.15 mg, oral tablet soluble 0.5 mg, (2 mg pack) oral tablet soluble 4 x 0.5 mg, (1.5 mg pack) oral tablet soluble 3 x 0.5 mg	F (Already added via CRF)			
			Inlexzo	gemcitabine intravesical device 225 mg	Non-formulary			

			Otulf	ustekinumab-aaaz subcutaneous solution 45 mg/0.5mL	F-PA-QL (Already added via CRF)			
			Avtozma	tocilizumab-anoh intravenous solution 80 mg/4mL, 200 mg/10mL, 400 mg/20mL	Add to F-PA (see updated MRG criteria)			
			Skytrofa	lonapegsomatropin- tcgd subcutaneous cartridge 0.7 mg, 1.4 mg, 1.8 mg, 2.1 mg, 2.5 mg	Non-formulary			
			Bildyos	donosumab-nxxp subcutaneous solution prefilled syringe 60 mg/mL	Add to F-PA (see updated MRG and PAD criteria)			
			Bilprevda	denosumab-nxxp subcutaneous solution 120 mg/1.7mL	Add to F-PA (see updated MRG criteria)			
			Phyrago	dasatinib oral tablet 20 mg, 50 mg, 70 mg, 100 mg, 140 mg	Non-formulary			
			Injectafer	ferric carboxymaltose intravenous solution 1000 mg/20 mL	Non-formulary			
			Exxua	gepirone oral tablet extended release 24- hour 18.2 mg, 36.3 mg, 54.5 mg, 72.6 mg, titration pack oral tablet extended release 24-hour 18.2 mg	Non-formulary			
			Escitalopram	escitalopram oxalate oral capsule 15 mg	Non-formulary			

Agenda Item	Discussion Leader	Discussion Summary					Action	Notes
			Otezla & Otezla XR	apremilast oral tablet extended release 24-hour 75 mg, initiation pk oral tablet therapy pack 10 mg, 20mg, 30 mg; (ER) 75 mg	F-PA-QL (Already added via CRF)			
			Tyruko	natalizumab-sztn intravenous concentrate 300 mg/15 mL	Non-formulary (see updated PAD and MRG criteria)			
			Doptelet	avatrombopag oral capsule sprinkle 10 mg	F-PA (Already added via CRF)			
			Zanaflex	tizanidine oral capsule 8 mg	Non-formulary			
			Krystexxa	pegloticase intravenous solution 8 mg/50 mL	Non-formulary			
			Tremfya	guselkumab CD/UC induction subcutaneous solution auto-injector 200 mg/ 2mL	Non-formulary			
			Phyrago	dasatanib oral tablet 80 mg	Non-formulary			
			MiloPhene	clomiphene oral tablet 50 mg	Non-formulary			
			Harliku	nitisinone oral tablet 2 mg	Non-formulary (see new MRG criteria)			
X) Old Business		- MRG criteria update Topical Antibiotics						
		Comments:						



Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
XI) Public Comment	D. Carey	No comment		
Adjournment	D. Carey	Meeting adjourned at 6:34PM	None	

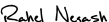
P&T Committee Meeting Minutes
December 16, 2025



Signed by:

D19D528C0085408
Luke Lim, R.Ph.
Senior Director, Pharmacy Services
Alameda Alliance for Health

01/27/2026 | 5:28 PM PST
Date

DocuSigned by:

B271482055A85403
Rahel Negash, PharmD
Supervisor, Pharmacy Services
Alameda Alliance for Health

01/27/2026 | 5:20 PM PST
Date

DocuSigned by:

B37F13824FC5570D
Donna Carey, MD
Chief Medical Officer
Alameda Alliance for Health

01/28/2026 | 11:41 AM PST
Date

P&T Committee Meeting Minutes
December 16, 2025



Page 35 of 35

New

Forzinity	
Therapeutic Classes (AHFS)	Other Miscellaneous Therapeutic Agents
Medications	Forzinity (elamipretide)
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	Prescribed by a cardiologist, endocrinologist, hematologist, geneticist, neurologist, or other provider specializing in the treatment of Barth Syndrome
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months, 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	<u>Initial Authorization:</u> • Diagnosis of Barth Syndrome confirmed via identification of mutations in the TAZ gene per genetic testing • Patient’s current weight is provided with the request and is ≥ 30 kg • Pediatrics: patient does not have renal impairment • Adults: patient is not on dialysis • Requested dose is within FDA approved dosing guidelines <u>Re-Authorization:</u> • Patient has not experienced a serious hypersensitivity reaction to Forzinity • Documentation or provider attestation of clinical benefit (i.e. 6-minute walk test, Total Fatigue Score on the Barth syndrome Symptom Assessment, muscle strength, cardiac function, etc.)
Criteria Statement	Forzinity is reserved for members with a diagnosis of Barth Syndrome, who have a current weight of at least 30kg. It is reserved for pediatric patients without renal impairment and for adults who are not on dialysis.
Last P&T Review Date	3/2026

New

Rhapsido	
Therapeutic Classes (AHFS)	Neutrophil Serine Protease (NSP) Inhibitors
Medications	Rhapsido (remibrutinib)
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	According to package insert
Prescriber Restrictions	Prescribed by, or in consultation with, an allergist, immunologist, or dermatologist
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months, 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	<u>Initial Authorization:</u> • Medication is prescribed at an FDA approved dose • Diagnosis of chronic spontaneous urticaria for at least 6 weeks with uncontrolled symptoms • Patient has had at least a 2-week trial and failure of, or has a contraindication to, at least two different H1 antihistamines (e.g. cetirizine, levocetirizine, loratadine, desloratadine, fexofenadine) at four times the standard FDA-approved dose • Patient has had at least a 2-month trial of, or has a contraindication to, Xolair (omalizumab) <u>Re-Authorization:</u> • Documentation or provider attestation of positive clinical response (i.e. change from baseline in weekly itch severity score, etc.) • Medication is prescribed at an FDA approved dose
Criteria Statement	Rhapsido is reserved for members with a diagnosis of chronic spontaneous urticaria for at least 6 weeks with uncontrolled symptoms, who tried or were unable to use two different H1 antihistamines and Xolair.
Last P&T Review Date	3/2026

New

Papzimeos	
Medications	Papzimeos (zopapogene imadenovec)
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	None
Required Clinical Information	See "Other Criteria" below
Age Restrictions	According to package insert Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescribed by, or in consultation with a pulmonologist, otolaryngologist, oncologist, or other specialist in the treatment of recurrent respiratory papillomatosis
Coverage Duration	If all criteria are met, the request will be approved for up to a 12-week course of therapy. Renewal requests or requests for more than a one-time course of therapy will not be approved.
Maximum Billable Units	Variable
Other Criteria	<u>Initial Authorization</u> • Member has a diagnosis of recurrent respiratory papillomatosis • Documentation is provided confirming human papilloma type 6 or 11 • Member has a history of voice or airway symptoms which have required 3 or more clinically indicated interventions (surgical resection or laser ablation of disease) in the previous 12 months ***Renewal requests or requests for more than a one-time course of therapy 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	3/2026

Gene Therapies for Spinal Muscular Atrophy	
Medications	Zolgensma (onasemnogene abeparvovec-xioi) Itvisma (onasemnogene abeparvovec-brve)
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	• Patient has previously received Zolgensma or Itvisma • Advanced spinal muscular atrophy (SMA) (e.g., complete paralysis of limbs, permanent ventilator-dependence) • Administration to premature neonates before reaching full-term gestational age
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Zolgensma: Patient must be less than 2 years of age Itvisma: Patient must be 2 to less than 18 years of age Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescribed by a neurologist
Coverage Duration	Authorization will be placed for 1 dose
Maximum Billable Units	Variable
Other Criteria	Patient must meet all of the following criteria: For Zolgensma: • Diagnosis of Spinal Muscular Atrophy (SMA) • Bi-allelic mutations in the survival motor neuron 1 (SMN1) gene • Baseline anti-AAV9 antibody titers of ≤1:50 measured using an enzyme-linked immunosorbent assay (ELISA) • Patient's body weight is provided • Dosing is consistent with FDA approved labeling For Itvisma: • Diagnosis of Spinal Muscular Atrophy (SMA) • Confirmed mutation in the survival motor neuron 1 (SMN1) gene • Onset of clinical signs and symptoms at ≥ 6 months of age • Patient is able to sit independently, but has never had the ability to walk independently • Baseline anti-AAV9 antibody titers of ≤1:50 measured using an enzyme-linked immunosorbent assay (ELISA) • Dosing is consistent with FDA approved labeling • For any patients currently using Spinraza or Evrysdi, continued use after Itvisma therapy will not be authorized. The safety and effectiveness of repeat administration of Zolgensma or Itvisma 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	3/2026

Insulins

Executive Summary

Class Overview

Insulin products are FDA-approved to improve glycemic control in patients with diabetes mellitus (DM). DM is a group of metabolic disorders that includes type 1, type 2, and gestational diabetes. This commonly presents as hyperglycemia, with etiologies varying based on type but including reduced insulin secretion, increased glucose production, or decreased glucose utilization. Secondary pathophysiological changes also occur in these patients due to the dysregulation involved with diabetes, including renal disease, neuropathy, visual impairment, hearing loss, and cardiac complications.

Insulin is a key component of diabetes management by providing glycemic control and preventing irreversible pathophysiological complications. There are many insulin products, and they are grouped by type: ultra-long acting, long-acting, intermediate, rapid-acting, short-acting, premixed, and biosimilars. Although all insulin products have a similar mechanism of action, their roles in therapy differ due to their various time to onset, peak time, and duration of action. Insulin therapy is commonly administered by subcutaneous injections, which allows for prolonged absorption.

According to the 2025 American Diabetes Association Clinical Guidelines, individuals with type 1 diabetes (T1DM) require insulin treatment as first-line therapy. This is an essential part of therapy for T1DM due to the hallmark pathophysiology of the disorder, which is complete absence or near-absence of beta cell function. Without insulin therapy, the patient's blood glucose could cause irreparable and even fatal consequences. Insulin replacement regimens often consist of basal and prandial insulin. Basal insulin – intermediate or long-acting insulin, is used to maintain blood sugar levels steady throughout meals and overnight. While prandial insulin – short or rapid-acting insulin, is often taken at or before meals to control blood sugar levels. For individuals with type 2 diabetes (T2DM), there is still some level of beta cell functioning and some degree of insulin production, so insulin therapy is not a first-line recommendation. Even so, the guidelines recommend early addition of basal insulin to oral therapy to extend the time to treatment failure. For both conditions, treatment is patient-centered and depends on multiple external factors.

Utilization Findings

There were 184 claims for 114 members, for a total cost of \$32,094.05, and an average cost per claim of \$174.42. The most highly utilized medication was insulin lispro subcutaneous pen-injector with 54 claims, followed by Lantus Solostar subcutaneous pen with 44 claims. There were 6 prior authorization requests with 1 approval (17%).

Recommendations

- Add Insulin Glargine Solostar Subcutaneous Solution Pen-injector 300 UNIT/ML to F-PA and remove Toujeo SoloStar® 300 unit/mL subcutaneous pen from formulary for cost containment
- Add Insulin Glargine Max SoloStar Subcutaneous Solution Pen-injector 300 UNIT/ML to F-PA and remove Toujeo Max SoloStar Subcutaneous Solution Pen-injector 300 UNIT/ML from formulary for cost containment
- Add NovoLOG Mix 70/30 Subcutaneous Suspension (70-30) 100 UNIT/ML to F-QL (30mL/30 days) due to generic insulin aspart mix discontinuation and current shortages

- Add NovoLOG Mix 70/30 FlexPen Subcutaneous Suspension Pen-injector (70-30) 100 UNIT/ML to F-QL (30mL/30 days) due to generic insulin aspart mix discontinuation and current shortages
- Change naming convention to show generic availability of Toujeo Solostar in PA criteria
- Add Kirsty (insulin aspart-xjhz) and Merilog (insulin aspart-szjj) to the drug list in PA criteria

Clinical Summary

Insulin products are FDA-approved to improve glycemic control in patients with diabetes mellitus (DM). DM is a group of chronic metabolic disorders that predominantly are known as type 1 (T1DM) or type 2 (T2DM). Diabetes is prevalent in approximately 37 million adults in the USA, and 1 in 5 people are undiagnosed. When uncontrolled, it leads to hyperglycemia, which is defined as blood glucose greater than 125 mg/dL while fasting and greater than 180 mg/dL 2 hours postprandial. This commonly presents as blurred vision, fatigue, polydipsia, polyuria, and polyphagia. The etiologies for diabetes vary depending on type. T1DM is an autoimmune reaction that completely halts the body's ability to produce insulin. These individuals are diagnosed in early childhood and account for 5-10% of diabetes diagnoses. On the other hand, T2DM can be triggered by a variety of processes, including insulin resistance, genetic markers, and lifestyle factors. These individuals are usually diagnosed later in life and account for 90-95% of all diabetes diagnoses. Secondary pathophysiological changes associated with diabetes occur in these patients including renal disease, neuropathy, visual impairment, hearing loss, and cardiac complications. Diabetes is the leading cause of kidney failure, lower-limb amputations, and adult blindness, if left untreated.

According to the 2025 American Diabetes Association (ADA) Clinical Guidelines, pharmacologic therapy should be guided by patient-centered treatment factors, including comorbidities and treatment goals. Insulin is a key component of diabetes management for both type 1 and 2 diabetes, by providing glycemic control and preventing irreversible pathophysiological complications. Insulin is the first-line therapy for patients with T1D and should be initiated immediately upon diagnosis. Pharmacologic therapy in T2D should be initiated after the consideration of healthy lifestyle habits, diabetes self-management, education, and social determinants of the person. Pharmacologic approaches including combination therapy with agents such as metformin, glucagon-like peptide 1 receptor agonists, sodium-glucose cotransporter 2 inhibitors and other agents should be considered prior. Insulin should be considered as part of any combination regimen when hyperglycemia is severe. Common practice is to initiate insulin therapy for people who present with blood glucose levels ≥ 300 mg/dL or A1C $> 10\%$ or if the individual has symptoms of hyperglycemia (i.e., polyuria or polydipsia) or evidence of catabolism (weight loss). There are many insulin products, and they are grouped by type: ultra-long acting, long-acting, intermediate, rapid-acting, short-acting, premixed, and biosimilar. Although all insulin products have a similar mechanism of action, their roles in therapy vary due to time to onset, peak time, and duration of action.

There are two broad categories that these types of insulin fall under: basal insulin and prandial insulin. Basal insulin provides a constant level of insulin that is absorbed slowly and works to allow the body to use it throughout the day whenever needed, similarly to the way an individual's pancreas would produce insulin. This term refers to three types of insulin: intermediate, long-acting, and ultra-long-acting. Intermediate insulin, such as NPH, has an onset of 1-2 hours, a peak effect around 4-12 hours, and ultimately lasts over 12 hours of the day. Long-acting insulins, such as glargine, has an onset of 1 ½ - 2 hours and then exhibits a stable plateau effect that lasts 24 hours. Ultra-long-acting insulin, such as degludec begins to work in 1-6 hours and then can last 36 hours or more. The main role in therapy for basal insulin is to control blood sugar overnight, while fasting, and between meals. Prandial insulin, also known as meal-time insulin, acts rapidly within the body to manage the elevation of glucose that occurs following meals. It is commonly taken three

times a day with breakfast, lunch, and dinner. This term refers to two types of insulin: short-acting and rapid-acting. Short-acting insulin, such as regular human, has an onset of 30-60 minutes, a peak effect around 2-3 hours, and works for an additional 3-6 hours after that. Rapid-acting insulin, such as aspart and lispro, has an onset of about 3-20 minutes, a peak of about 1-3 hours, and will last for 5 hours. The main role in therapy for prandial insulin is to control the blood glucose spikes that occur after meals, as well as to correct any unintentional spikes that occur between meals or during the night.

Additional insulin options include pre-mixed combination insulins and biosimilars. Combination insulins are formulated with rapid or short-acting insulin plus intermediate or long-acting insulin. Their pharmacokinetics favor both 24-hour efficacy and patient convenience. Their primary role in therapy is to provide a simple insulin treatment plan by combining basal and prandial insulin. This is preferred for patients who may need ease of therapy and convenience such as senior citizens or those with disabilities. Furthermore, biosimilars are biological products that are very similar to products already approved by the FDA, with no true meaningful differences outside of the way they are produced. They offer the same safety and effectiveness at potentially lower costs. The first two insulin biosimilar products to be approved were Semglee® (insulin glargine-yfgn) and Rezvoglar™ (insulin glargine-aglr). Semglee® came to market in 2021 at a 65% discount from Lantus® as the first interchangeable biological product. Rezvoglar™ came to market in 2023 with a 78% discount to Lantus®. In February 2025, Merilog® (insulin aspart-szjj) was approved as the first biosimilar to reference Novolog. Shortly after, in July 2025, Kirsty® (insulin aspart-xjhz) was approved as the second insulin aspart biosimilar. One major difference between Merilog® and Kirsty® is that Kirsty® has interchangeability status with Novolog, while Merilog® does not.

With regards to future advancements, there are multiple insulin biosimilars and in the Pipeline. Gan & Lee Pharmaceuticals has a few insulin biosimilars in the Pipeline including insulin glargine, aspart and lispro products. These biosimilars have anticipated approval dates before the end of 2025. Amphastar is seeking approval of an insulin aspart biosimilar, AMP-004, with anticipated approval by March 2026. Additionally, there is a non-biosimilar product in the Pipeline, Awiqli (insulin icodec), which is being reviewed for the second time. Novo Nordisk received a Complete Response Letter in July 2024 citing issues related to the manufacturing process of Awiqli. Novo resubmitted the BLA in September 2025 and Awiqli has an anticipated approval date of March 2026. If approved, Awiqli would become the first once-weekly basal insulin available in the United States, providing an alternative to daily basal insulin injections for adults living with type 2 diabetes.

Practice Guidelines

American Diabetes Association, 9. Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes-2025. Diabetes Care 1 January 2025.

- Pharmacologic Therapy for Adults with Type 1 Diabetes
 - Treat most adults with type 1 diabetes with continuous subcutaneous insulin infusion or multiple daily doses of prandial (injected or inhaled) and basal insulin. **A**
 - For most adults with type 1 diabetes, insulin analogs (or inhaled insulin) are preferred over injectable human insulins to minimize hypoglycemia risk. **A**
 - Early use of continuous glucose monitoring is recommended for adults with type 1 diabetes to improve glycemic outcomes and quality of life and to minimize hypoglycemia. **B**
 - Automated insulin delivery systems should be offered to all adults with type 1 diabetes. **A**
 - To improve glycemic outcomes and quality of life and to minimize hypoglycemia risk, most adults with type 1 diabetes should receive education on how to match mealtime insulin doses to carbohydrate intake and fat and protein intake. They should also be taught how to modify the insulin dose (correction dose) based on concurrent glycemia, glycemic trends (if available), sick-day management, and anticipated physical activity. **B**
 - Insulin treatment plan and insulin-taking behavior should be reevaluated at regular intervals (e.g., every 3–6 months) and adjusted to incorporate specific factors that impact choice of treatment and ensure achievement of individualized glycemic goals. **E**
- Pharmacologic Therapy for Adults with Type 2 Diabetes
 - Healthy behaviors, diabetes self-management education and support, avoidance of therapeutic inertia, and social determinants of health should be included in the glucose-lowering management of type 2 diabetes. **A**
 - A person-centered shared decision-making approach should guide the choice of glucose-lowering medications for adults with type 2 diabetes. Use medications that provide sufficient effectiveness to achieve and maintain intended treatment goals with consideration of the effects on cardiovascular, kidney, weight, and other relevant comorbidities; hypoglycemia risk; cost and access; risk for adverse reactions and tolerability; and individual preferences. **E**
 - Combination therapy can be considered in adults with type 2 diabetes at treatment initiation to shorten time to attainment of individualized treatment goals. **A**
 - In adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease, the treatment plan should include medications with demonstrated benefits to reduce cardiovascular events (e.g., glucagon-like peptide 1 receptor agonist [GLP-1 RA] and/or sodium–glucose cotransporter 2 [SGLT2] inhibitor) for glycemic management and comprehensive cardiovascular risk reduction (irrespective of A1C). **A**
 - In adults with type 2 diabetes who have heart failure (HF) (with either reduced or preserved ejection fraction), an SGLT2 inhibitor is recommended for both glycemic management and prevention of HF hospitalizations (irrespective of A1C). **A**
 - In adults with type 2 diabetes and symptomatic heart failure with preserved ejection fraction (HFpEF) and obesity, a GLP-1 RA with demonstrated benefits for both glycemic management and reduction of HF-related symptoms (irrespective of A1C) is recommended. **A**
 - In adults with type 2 diabetes who have CKD (with confirmed estimated glomerular filtration rate [eGFR] 20–60 mL/min/1.73 m² and/or albuminuria), an SGLT2 inhibitor or GLP-1 RA with demonstrated benefit in this population should be used for both glycemic management (irrespective of A1C) and for slowing

progression of CKD and reduction in cardiovascular events. The glycemic benefits of SGLT2 inhibitors are reduced at eGFR <45 mL/min/1.73 m². **A**

- In adults with type 2 diabetes and advanced CKD (eGFR <30 mL/min/1.73 m²), a GLP-1 RA is preferred for glycemic management due to lower risk of hypoglycemia and for cardiovascular event reduction. **B**
- In adults with type 2 diabetes, metabolic dysfunction–associated steatotic liver disease (MASLD), and overweight or obesity, consider using a GLP-1 RA or a dual glucose-dependent insulintropic polypeptide (GIP) and GLP-1 RA with potential benefits in metabolic dysfunction–associated steatohepatitis (MASH) for glycemic management and as an adjunctive to healthy interventions for weight loss. **B**
- In adults with type 2 diabetes and biopsy-proven MASH or those at high risk for liver fibrosis (based on noninvasive tests), pioglitazone, a GLP-1 RA, or a dual GIP and GLP-1 RA is preferred for glycemic management due to potential beneficial effects on MASH. **B**
- Combination therapy with pioglitazone plus a GLP-1 RA can be considered for the treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven MASH or those at high risk of liver fibrosis (identified with noninvasive tests) due to potential beneficial effects on MASH. **B**
- Medication plan and medication-taking behavior should be reevaluated at regular intervals (e.g., every 3–6 months) and adjusted as needed to incorporate specific factors that impact choice of treatment. **E**
- Treatment modification (intensification or deintensification) for adults not meeting individualized treatment goals should not be delayed. **A**
- Choice of glucose-lowering therapy modification should take into consideration individualized glycemic and weight goals, presence of comorbidities (cardiovascular, kidney, liver, and other metabolic comorbidities), and the risk of hypoglycemia. **A**
- When initiating a new glucose-lowering medication, reassess the need for and/or dose of medications with higher hypoglycemia risk (i.e., sulfonylureas, meglitinides, and insulin) to minimize the risk of hypoglycemia and treatment burden. **A**
- Concurrent use of dipeptidyl peptidase 4 (DPP-4) inhibitors with a GLP-1 RA or a dual GIP and GLP-1 RA is not recommended due to lack of additional glucose lowering beyond that of a GLP-1 RA alone. **B**
- In adults with type 2 diabetes who have not achieved their individualized weight goals, additional weight management interventions (e.g., intensification of lifestyle modifications, structured weight management programs, pharmacologic agents, or metabolic surgery, as appropriate) are recommended. **A**
- In adults with type 2 diabetes, initiation of insulin should be considered regardless of background glucose-lowering therapy or disease stage if symptoms of hyperglycemia are present or when A1C or blood glucose levels are very high (i.e., A1C >10% [>86 mmol/mol] or blood glucose ≥300 mg/dL [≥16.7 mmol/L]). **E**
- In adults with type 2 diabetes and no evidence of insulin deficiency, a GLP-1 RA, including a dual GIP and GLP-1 RA, is preferred to insulin. **A**
- If insulin is used, combination therapy with a GLP-1 RA, including a dual GIP and GLP-1 RA, is recommended for greater glycemic effectiveness as well as beneficial effects on weight and hypoglycemia risk for adults with type 2 diabetes. Insulin dosing should be reassessed upon addition or dose escalation of a GLP-1 RA or dual GIP and GLP-1 RA. **A**
- In adults with type 2 diabetes who are initiating insulin therapy, continue glucose-lowering agents (unless contraindicated or not tolerated) for ongoing glycemic and metabolic benefits (i.e., weight, cardiometabolic, or kidney benefits). **A**

- Additional Recommendations for All Individuals with Diabetes

- Monitor for signs of overbasalization during insulin therapy, such as significant bedtime-to-morning or postprandial-to-preprandial glucose differential, occurrences of hypoglycemia (aware or unaware), and high glycemic variability. When overbasalization is suspected, a thorough reevaluation should occur promptly to further tailor therapy to the individual's needs. **E**
- Glucagon should be prescribed for all individuals requiring intensive insulin therapy or at high risk for hypoglycemia. Family, caregivers, school personnel, and others providing support to these individuals should know its location and be educated on how to administer it. Glucagon preparations that do not require reconstitution are preferred. **B**
- Routinely assess all people with diabetes for financial obstacles that could impede their diabetes management. Clinicians, members of the diabetes care team, and social services professionals should work collaboratively, as appropriate and feasible, to support these individuals by implementing strategies to reduce costs, thereby improving their access to evidence-based care. **E**
- In adults with diabetes and cost-related barriers, consider use of lower-cost medications for glycemic management (i.e., metformin, sulfonylureas, thiazolidinediones, and human insulin) within the context of their risks for hypoglycemia, weight gain, cardiovascular and kidney events, and other adverse effects. **E**

Recommendation Definitions

Class/Level	Definition
A	• Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including ○ Evidence from a well-conducted multicenter trial ○ Evidence from a meta-analysis that incorporated quality ratings in the analysis • Compelling nonexperimental evidence • Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including ○ Evidence from a well-conducted trial at one or more institutions ○ Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	• Supportive evidence from well-conducted cohort studies ○ Evidence from a well-conducted prospective cohort study or registry ○ Evidence from a well-conducted meta-analysis of cohort studies • Supportive evidence from a well-conducted case-control study
C	• Supportive evidence from poorly controlled or uncontrolled studies ○ Evidence from randomized clinical trials with one or more major OR three or more minor methodological flaws that could invalidate the results ○ Evidence from observational studies with high potential for bias (case series with comparison with historical controls) ○ Evidence from case series or case reports • Conflicting evidence with the weight of evidence supporting the recommendation
E	• Expert consensus or clinical experience

Formulary Placement, Utilization and Cost Experience (10-01-2025 to 12-31-2025)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Long-Acting Insulins								
Basaglar Kwikpen®, Basaglar Tempo Pen®, Lantus Solostar® (insulin glargine) 100 unit/mL subcutaneous pen	44	32	\$3,907.17	\$88.80	0	0 (0%)	F-QL(30/30)	No change
Rezvoglar KwikPen™ (insulin glargine-aglr) 100 unit/mL subcutaneous pen	0	0	\$0.00	\$0.00	0	0 (0%)	F-QL(30/30)	No change
Insulin glargine-yfgn (Semglee® (yfgn)) 100 unit/mL subcutaneous pen	32	20	\$2,396.78	\$74.90	1	0 (0%)	F-QL(30/30)	No change
Insulin glargine-yfgn (Semglee® (yfgn)) 100 unit/mL subcutaneous solution vial	2	1	\$211.56	\$105.78	0	0 (0%)	F-QL(30/30)	No change
Lantus® (insulin glargine) subcutaneous solution vial	5	3	\$437.10	\$87.42	0	0 (0%)	F-QL(30/30)	No change
Insulin glargine (Toujeo SoloStar®, Toujeo Max SoloStar®) 300 unit/mL subcutaneous pen	4	2	\$2,059.52	\$514.88	0	0 (0%)	F-PA	→Switch to generic insulin glargine 300 u/mL on F-PA
Insulin degludec U-100 (Tresiba FlexTouch®) 100 unit/mL subcutaneous pen	1	1	\$128.12	\$128.12	0	0 (0%)	NF	No change
insulin degludec (Tresiba®) 100 unit/mL subcutaneous solution vial	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Insulin degludec U-200 (Tresiba FlexTouch®) 200 unit/mL subcutaneous pen	4	3	\$733.31	\$183.33	3	0 (0%)	F-PA	No change
Rapid-Acting Insulins								
Afrezza® (insulin oral inhalation) 4, 8, 12 unit cartridge, 4-8 unit cartridge, 4-8-12 unit cartridge, 8-12 unit cartridge	0	0	\$0.00	\$0.00	1	0 (0%)	NF	No change
Apidra® (insulin glulisine)100 unit/mL subcutaneous solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Apidra® SoloStar (insulin glulisine) 100 unit/mL subcutaneous pen	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Insulin aspart (Novolog®, Fiasp®, Novolog® ReliOn) 100 unit/mL injection solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Insulin aspart (Novolog® PenFill, Fiasp® PenFill, Fiasp® PumpCart) 100 unit/mL subcutaneous cartridge solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Insulin aspart (Novolog® FlexPen, Fiasp® FlexTouch, Novolog® FlexPen ReliOn,) 100 unit/mL subcutaneous pen-injector solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Kirsty® (insulin aspart-xjhz) 100 unit/mL subcutaneous pen-injector solution, injection solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Merilog® (insulin aspart-szjj) SoloStar 100 unit/mL subcutaneous pen-injector solution, Merilog® injection solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Lyumjev™ KwikPen (insulin lispro-aabc) 100 unit/mL, 200 unit/mL, Lyumjev™ Tempo Pen 100 unit/mL subcutaneous pen-injector solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Lyumjev™ (insulin lispro-aabc) 100 unit/mL subcutaneous injection solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Insulin lispro (Admelog® SoloStar, Humalog® Junior KwikPen, Humalog® KwikPen, Humalog® Tempo Pen) 100 unit/mL subcutaneous pen-injector solution	54	33	\$8,634.51	\$159.90	0	0 (0%)	F-QL(30/30)	No change

Insulin lispro (Humalog® Junior KwikPen) 100 unit/mL subcutaneous solution pen-injector	0	0	\$0.00	\$0.00	0	0 (0%)	F-QL(30/30)	No change
Humalog® KwikPen (Insulin lispro) 200 unit/mL subcutaneous pen-injector solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Humalog® (insulin lispro) 100 unit/mL subcutaneous cartridge solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Insulin lispro (Admelog®, Humalog®) 100 unit/mL injection solution	6	3	\$392.55	\$65.43	0	0 (0%)	F-QL(30/30)	No change
Short-Acting Insulins								
Novolin® R FlexPen, Novolin® R ReliOn FlexPen (insulin regular) 100 unit/mL subcutaneous pen	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Humulin® R, Novolin® R, Novolin® R ReliOn (insulin regular) 100 unit/mL vial	2	1	\$88.96	\$44.48	0	0 (0%)	F-QL(30/30)	No change
Humulin® R (insulin regular) 500 unit/mL KwikPen subcutaneous pen	7	4	\$9,953.17	\$1,421.88	1	1 (100%)	F-QL(15/30)	No change
Myxredlin® (insulin regular) 100 unit/100 mL IV solution	0	0	\$0.00	\$0.00	0	0 (0%)	NF	No change
Intermediate-Acting Insulins								
Humulin® N, Novolin® N, Nologin® N ReliOn (insulin NPH) 100 unit/mL subcutaneous vial	6	2	\$262.14	\$43.69	0	0 (0%)	F-QL(30/30)	No change
Humulin® N, Novolin® N, Novolin® N ReliOn (insulin NPH) 100 unit/mL subcutaneous pen	7	3	\$1,089.62	\$155.66	0	0 (0%)	F-QL(30/30)	No change
Combination Insulins								
Insulin aspart protamine and insulin aspart (Novolog® Mix, Novolog® Mix ReliOn) 70/30 100 unit/mL injection suspension	1	1	\$60.77	\$60.77	0	0 (0%)	F-QL(30/30)	→Add Novolog brand to F-QL
Insulin aspart protamine and insulin aspart (Novolog® Mix FlexPen, Novolog® Mix ReliOn FlexPen) 70/30 100 unit/mL subcutaneous pen	4	2	\$422.48	\$105.62	0	0 (0%)	F-QL(30/30)	→Add Novolog brand to F-QL
Humalog® Mix (insulin lispro protamine and insulin lispro) 75/25 100 unit/mL subcutaneous suspension	0	0	\$0.00	\$0.00	0	0 (0%)	F-QL(30/30)	No change
Humalog® Mix KwikPen (insulin lispro protamine and insulin lispro) 50/50 100 unit/mL subcutaneous pen-injector suspension	0	0	\$0.00	\$0.00	0	0 (0%)	F-QL(30/30)	No change
Insulin lispro protamine and insulin lispro (Humalog® Mix KwikPen) 75/25 100 unit/mL subcutaneous pen-injector suspension	3	2	\$668.30	\$222.77	0	0 (0%)	F-QL(30/30)	No change
Humulin®, Novolin®, Novolin® ReliOn (insulin NPH and insulin regular) 70/30 100 unit/mL injection suspension	0	0	\$0.00	\$0.00	0	0 (0%)	F-QL(30/30)	No change
Humulin® KwikPen, Novolin® FlexPen, Novolin® ReliOn FlexPen (insulin NPH and insulin regular) 70/30 100 unit/mL injection suspension	2	1	\$647.59	\$323.80	0	0 (0%)	F-QL(30/30)	No change
TOTAL	184	114	\$32,094.05	\$174.42	6	1 (17%)		

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: Change naming convention to show generic availability of Toujeo Solostar

Long-Acting Basal Insulin	
Therapeutic Classes (AHFS)	Insulins
Medications	<u>Formulary with quantity limit (30/30):</u> Insulin glargine-yfgn solution 100 unit/ml vial and pen injector PREFERRED Rezvoglar (insulin glargine-aglr) 100unit/ml KwikPen PREFERRED Lantus Solostar (insulin glargine) 100 unit/ml, Lantus (insulin glargine) 100 unit/ml vial PREFERRED <u>Formulary with PA:</u> insulin glargine (Toujeo Solostar) (insulin glargine) 300 unit/ml pen Tresiba (insulin degludec) 200 unit/ml pen <u>Non-formulary</u> Semglee (YFGN) (insulin glargine) 100 unit/ml vial and pen Insulin glargine (Winthrop) 100 unit/ml vial, Solostar Tresiba (insulin degludec) 100 unit/ml vial and pen Basaglar (insulin glargine) KwikPen 100 unit/ml 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	For requests for formulary with PA and non-formulary basal insulin, approve if: • Diagnosis of Type I or Type II Diabetes • Documentation of trial and failure, inability to use, intolerance, or contraindication to one formulary preferred long-acting insulin For requests above the quantity limit • 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.
Criteria Statement	Formulary with PA and non-formulary basal insulins are reserved for members with diabetes who have used (or cannot/should not use) one preferred formulary basal insulin: insulin glargine-yfgn solution 100 unit/ml vial / pen injector, Lantus Solostar/ vial, or Rezvoglar KwikPen.
Last P&T Review Date	4/2/2025/3/2026

Recommendation: Add Kirsty (insulin aspart-xjhz) and Merilog (insulin aspart-szjj) to the drug list

Rapid-Acting Insulin	
Therapeutic Classes (AHFS)	Insulins
Medications	<u>Formulary with quantity limits:</u> Admelog U-100 vial and Admelog Solostar Insulin Lispro 100 units/ml vial, pen <u>Non-formulary</u> Apidra 100 units/ml vial Apidra Solostar 100 units/ml Humalog KwikPen 100 units/ml, 200 units/ml Humalog 100 units/ml vial, cartridge Novolog 100 units/ml vial Novolog FlexPen 100 units/ml Fiasp vial, FlexTouch, penfill Lyumjev KwikPen (insulin lispro-aabc) 100units/ml, 200units/ml Insulin aspart 100 units/ml Kirsty (insulin aspart-xjhz) 100 unit/mL pen-injector Merilog (insulin aspart-szjj) SoloStar 100 unit/mL 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	For requests for non-formulary rapid acting insulin, approve if: • Diagnosis of Type I or Type II Diabetes • Documentation of trial and failure, inability to use, intolerance, or contraindication to one of the formulary rapid acting insulins. If request is for pen formulation, documentation of trial and failure, inability to use, intolerance, or contraindication to using Admelog Solostar or Insulin Lispro 100 units/ml vial or pen must be provided.
Criteria Statement	Non-formulary rapid acting insulins are reserved for members with diabetes who have used (or cannot/should not use) Admelog vial, Admelog Solostar, Insulin Lispro 100 units/ml vial or pen.
Last P&T Review Date	12/20253/2026

References

1. Lexicomp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on November 10, 2025.
2. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>. Accessed on November 10, 2025.
3. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: <http://www.fda.gov/>. Accessed on November 10, 2025.
4. American Diabetes Association Professional Practice Committee. "Standards of Care in Diabetes—2025." *Diabetes Care* 48, Supplement 1 (2025): S1–S364. DOI: 10.2337/dc25-S000
5. American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm – 2023 Update. Samson, Susan L. et al. *Endocrine Practice*, Volume 29, Issue 5, 305 – 340. [https://www.endocrinepractice.org/article/S1530-891X\(23\)00034-4/fulltext](https://www.endocrinepractice.org/article/S1530-891X(23)00034-4/fulltext)
6. Centers for Disease Control and Prevention. National Diabetes Statistics Report. May 15, 2024. <https://www.cdc.gov/diabetes/php/data-research/index.html>. Accessed on November 10, 2025.
7. Lingvay I, Asong M, Desouza C, et al. Once-Weekly Insulin Icodec vs Once-Daily Insulin Degludec in Adults With Insulin-Naive Type 2 Diabetes: The ONWARDS 3 Randomized Clinical Trial. *JAMA*. Published online June 24, 2023. doi:10.1001/jama.2023.11313

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 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 4 claims for 2 members, for a total cost of \$174.72, and an average cost per claim of \$43.68. The most highly utilized drug was teriflunomide tablets with 4 claims. There were no prior authorization requests.

Recommendations

- No formulary changes
- Change naming conventions to reflect generic availability of Mavenclad in PA criteria
- Add Ocrevus Zunovo (hyaluronidase facilitated subcutaneous product for HCP administration) and Tyruko (Tysabri biosimilar) to the policy and streamline language on immunizations requirement for all products

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 least 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 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, dimethyl fumarate (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. Dimethyl fumarate 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 dimethyl fumarate can affect adherence.

Fingolimod (Gilenya®) had been the only approved sphingosine-1-phosphate (S1P) modulator until recently and competes directly with dimethyl fumarate 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 fingolimod. Monitoring for Mayzent® and Ponvory® is required only for 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 teriflunomide (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 teriflunomide, 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-xiyy). 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. A biosimilar for Tysabri®, called Tyruko® (natalizumab-sztn), was approved in 2023 and became available in 2025. The price of Tyruko® is about 20% below that of Tysabri®. 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. It is currently available as a generic from a couple of manufacturers, with several additional generics in the pipeline. The addition of generics in the MS therapeutic space, specifically among oral therapies, has heavily influenced formulary management. In the past 5 years, generics for Tecfidera®, Aubagio®, and Gilenya® have launched, and as a result, more payers have moved to a “generic first” step requirement prior to approving other significantly more expensive MS treatments.

Several other drugs are in the pipeline for MS. Fenebrutinib, tolebrutinib, remibrutinib, masitinib, and orelabrutinib are all oral Bruton's tyrosine kinase (BTK) inhibitors that would represent a new class of therapies for MS. All are in Phase 3 trials, with potential approval coming over the next few years. The BTK inhibitors will likely be used following one or more generic products in the MS category. Tolebrutinib was expected to be approved in late 2025, however, the FDA issued complete response letter (CRL) citing a substantial and unusually high risk of severe drug-induced liver injury seen with tolebrutinib, including cases requiring liver transplant and one death. The FDA also noted that the manufacturer did not provide sufficiently robust, consistent evidence of benefit in any clearly defined MS population. Anti-CD 20 molecules in the pipeline include a high dose formulation of Ocrevus® as well as several ocrelizumab biosimilars. Frexalimab is a monoclonal antibody in Phase 3 trials that aims to block CD40/CD40L pathways, which help adaptive and innate immune cell activation. If approved, it would offer a novel mechanism of action compared to alternative injectable MS treatments. 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 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
Tyruko® (natalizumab-sztn)		
Briumvi® (ublituximab-xiyy)	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
Cladribine (Mavenclad®)	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.

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 natalizumab
Tyruko® (natalizumab-sztn)		
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)		Known hypersensitivity to dimethyl fumarate or any inactive ingredients
Dimethyl fumarate (Tecfidera®)		Known hypersensitivity to monomethyl fumarate, dimethyl fumarate or diroximel fumarate or any excipients
Bafiertam® (monomethyl fumarate)		Concurrent therapy with dimethyl fumarate or diroximel fumarate

Medication	Boxed Warnings	Contraindications
Vumerity® (diroximel fumarate)		Hypersensitivity (e.g., anaphylaxis, angioedema) to diroximel fumarate, dimethyl 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
Cladribine (Mavenclad®)	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

Medication	Boxed Warnings	Contraindications
		accompanied by primary adrenocortical insufficiency or adrenocortical hyperfunction, 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

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)	• Infusion reactions • Infections • PML • Reduced immunoglobulins • Malignancies • Immune-mediated colitis
Ocrevus Zunovo™ (ocrelizumab and hyaluronidase-ocs)	
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
Tyruko® (natalizumab-sztn)	
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 • Tumefactive 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 • Tumefactive 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
Cladribine (Mavenclad®)	• 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 IFNβ, glatiramer acetate, and natalizumab that overall contributed outcome data for 9881 participants (66%).	To estimate the relative efficacy and acceptability of interferon β-1b (IFNβ-1b) (Betaseron), interferon β-1a (IFNβ-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 IFNβ-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 IFNβ-1a (Avonex) (OR 0.28, 95% CI 0.22 to 0.36; OR 0.19, 95% CI 0.06 to 0.60, respectively). IFNβ-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 IFNβ-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), IFNβ-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 IFNβ-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 IFNβ-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 IFNβ-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 IFNβ-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 IFN β -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 IFN β -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. IFN β -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 IFN β -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 IFN β -1a (Rebif) or between azathioprine and IFN β -1a (Rebif) should be top priority on the research agenda and follow-up of the trial cohorts should be mandatory.

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 MEDLINE (via PubMed), EMBASE, and Cochrane Library. The Cochrane Collaboration tool to assess the risk of bias for RCTs was used.	To compare the safety profile of high-efficacy disease-modifying therapies (DMTs) natalizumab, fingolimod, alemtuzumab, cladribine, ocrelizumab, ofatumumab, ozanimod, as well as a 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.”

Formulary Placement, Utilization and Cost Experience (10-01-2025 to 12-31-2025)

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	0	0	\$0.00	\$0.00	0	0 (0%)	20mg F-PA; QL(30/30) 40mg F-PA; QL(12/30)	No change
Extavia® (interferon beta 1b) 0.3 mg subcutaneous vial kit	0	0	\$0.00	\$0.00	0	0 (0%)	NF	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-PA	No change
Avonex® (interferon beta 1a) 30 mcg/0.5 mL intramuscular pen kit	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 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	4	2	\$174.72	\$43.68	0	0 (0%)	F	No change
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	0	0	\$0.00	\$0.00	0	0 (0%)	F-PA; QL (120/30)	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
Cladribine (Mavenclad®) 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
Tyruko® (natalizumab-sztn) 300 mg/15 mL intravenous 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	4	2	\$174.72	\$43.68	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: Change naming conventions to reflect generic availability of Mavenclad

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) Non-preferred: fingolimod (GILENYA) 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) ~~cladribine (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) ~~cladribine (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 ~~cladribine (Mavenclad)~~ ~~(cladribine)~~. If all of the criteria for ~~cladribine (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, dimethyl fumarate (Tecfidera), or teriflunomide (Aubagio) approve.
- If the request is for a non-preferred agent, the member must have a documented trial of two preferred agents or have a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing two of these therapies (exception Gilenya, see bullet below)

AND

- If the request is for fingolimod (Gilenya), 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 is for fingolimod (Gilenya) 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, 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 two preferred agents, or have a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing two of these therapies (exception Gilenya, see bullet below)

AND

- If the request is for fingolimod (Gilenya), 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 is for fingolimod (Gilenya) and the member has “highly active” MS approve <u>WITHOUT</u> 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 <u>cladribine</u> (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. <u>Reauthorization</u> <u>CIS</u> • 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. <u>RRMS and SPMS</u> • 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 <u>cladribine</u> (Mavenclad) ~~(cladribine)~~ ○ Member’s current weight ○ **NO MORE THAN 2 COURSES IN TOTAL WILL BE APPROVED.** <u>Continuation of Therapy/Grandfathering Provision:</u> Members with history (within the past 90 days or past 12 months for <u>cladribine</u> [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), 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 preferred agents.
Last P&T Review Date	~~3/2025~~ 3/2026

Recommendation:

- Add Ocrevus Zunovo (hyaluronidase facilitated subcutaneous product for HCP administration) and Tyruko (Tysabri biosimilar) as they are missing from the policy
- Streamline language on immunizations requirement for all products

Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	
Therapeutic Classes (AHFS)	Immunomodulatory agents
Medications	Non-Preferred Ocrevus (ocrelizumab) <u>Ocrevus Zunovo (ocrelizumab and hyaluronidase-ocsq)</u> Rituxan (rituximab) Ruxience (rituximab-pvvr) - biosimilar Truxima (rituximab-abbs) - biosimilar Riabni (rituximab-arxx) - biosimilar Rituxan Hycela (rituximab/hyaluronidase) Lemtrada (alemtuzumab) Tysabri (natalizumab) <u>Tyruko (natalizumab-sztn) - biosimilar</u> Briumvi (ublituximab-xiyy) 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, <u>Tyruko</u> 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/<u>Tyruko</u> 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 two preferred agents or a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing two of these therapies.
 - Preferred agents: glatiramer, dimethyl fumarate (Tecfidera), and teriflunomide (Aubagio)

OR

- For members with “highly active” MS requesting Lemtrada (alemtuzumab), Tysabri (natalizumab), Tyruko, or rituximab, a trial with Gilenya (fingolimod) alone will be acceptable.
- If the request is for Ocrevus (ocrelizumab), Ocrevus Zunovo, Briumvi (ublituximab-xiyy), -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 provider is following administration guidelines for live and the member has received all non-live immunizations in accordance with product's prescribing information and immunization guidelines for rituximab according to immunization guidelines or has a documented medical reason for patient 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) or Tyruko (natalizumab-sztn), 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), Ocrevus Zunovo, or rituximab, documentation of the following has been submitted
 - Attestation that the member has been screened for and does not have active HBV
 - Attestation that provider is following administration guidelines for live and Member has received all non-live immunizations in accordance with product's prescribing information and immunization guidelines for rituximab, according to immunization guidelines or has a documented medical reason for patient 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. <u>Reauthorization</u> <u>CIS</u> ○ 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. <u>PPMS, RRMS, or SPMS</u> ○ 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) <u>or Tyruko (natalizumab-sztn)</u>, 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 <u>Continuation of Therapy Provision:</u> 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), <u>Ocrevus Zunovo</u>, rituximab, Briumvi (ublituximab-xiyy), Lemtrada (alemtuzumab), ~~and~~ Tysabri (natalizumab), <u>and Tyruko</u> are reserved for members with multiple sclerosis who have tried and failed or have a reason not to use two of the following agents: glatiramer, 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 two of the following agents: glatiramer, dimethyl fumarate (Tecfidera), or teriflunomide (Aubagio).
Last P&T Review Date	<u>3/2025</u> 3/2026

Recommendation: 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 $\leq$ 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	3/20253/2026

Recommendation: 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	~~3/2025~~ 3/2026

References

1. Loma I, Heyman R. Multiple Sclerosis: Pathogenesis and Treatment. *Current Neuropharmacology*. 2011;9(3):409-416. doi:10.2174/157015911796557911.
2. Olek MJ. Clinical presentation, course, and prognosis of multiple sclerosis in adults. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>. Accessed on January 6, 2025.
3. Olek MJ. Initial disease-modifying treatment of relapsing-remitting multiple sclerosis in adults. UpToDate. Waltham, MA: UpToDate Inc. <http://www.uptodate.com>. Accessed on January 6, 2025.
4. 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.
5. Multiple Sclerosis Coalition. The Use Of Disease-Modifying Therapies In Multiple Sclerosis: Principles and Current Evidence. A Consensus Paper by the Multiple Sclerosis Coalition (2019 update). Available at http://ms-coalition.org/wp-content/uploads/2019/06/MSCDMTPaper_062019.pdf.
6. 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.
7. 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.
8. 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.
9. 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.
10. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: <https://clinicaltrials.gov/>. Accessed on January 6, 2025.
11. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: <https://www.ncbi.nlm.nih.gov/pubmed>. Accessed on January 6, 2025.
12. Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on January 6, 2025.
13. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: <http://www.fda.gov/>. Accessed on January 6, 2025.
14. IPD Analytics. Bay Harbor Islands, Florida: IPD Analytics, LLC. <http://www.ipdanalytics.com>. Accessed on January 6, 2026.

Alameda MRGs for review Q1 2026 P&T Changes

Recommendation:

- Add Exdensus—new pulmonary biologic indicated for add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype in adult and pediatric patients aged 12 years and older
- Update documented baseline FEV₁<90% in pediatric population as it applies to all agents, except Cinqair that is only indicated for adults
- Add criteria for Exdensus based on inclusion criteria in clinical trial
- Add Nucala to COPD section as it received a new indication for use in COPD
- Update EoE indication for Dupixent as it was updated to include pediatric patients weighing at least 15 kg
- Add criteria for new indications for Dupixent: 1) chronic spontaneous urticaria (CSU) in adult and pediatric patients 12 years and older who remain symptomatic despite H1 antihistamine treatment; 2) for the treatment of adult patients with bullous pemphigoid (BP)
- Add clinical benefit endpoints used in pivotal trials for CSU and bullous pemphigoid indications

Pulmonary Biologics for Respiratory and Eosinophilic Conditions	
Therapeutic Classes (AHFS)	Interleukin antagonists
Medications	Nucala (mepolizumab) Fasenra (benralizumab) Cinqair (reslizumab) Dupixent (dupilumab) Tezspire (tezepelumab) <u>Exdensus (depemokimab)</u> 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 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 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	<u>Initial Authorization:</u> <u>Asthma:</u> • Confirmed diagnosis of one of the following: ○ Nucala, Fasenra, <u>and</u> Cinqair, <u>and</u> Exdensus: 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, and Exdensus~~: ≥ 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 FEV₁ < 80% of predicted with evidence of reversibility by bronchodilator response.
 - ~~Tezspire ONLY~~: If age is < 18 years, the member has a documented baseline FEV₁ < 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
 - ~~Exdensus: ≥ 2 exacerbations in the past 12 months requiring systemic corticosteroids~~
 - 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 and Nucala only):
- Confirmed diagnosis of COPD
 - Documentation has been provided of blood eosinophil count within one of the following ranges:
 - ~~Dupixent: ≥ 300 cells/mcL (within the past 12 months)~~
 - ~~Nucala: ≥ 150 cells/mcL (within 6 weeks of request) OR ≥ 300 cells/mcL (within the past 12 months)~~
 - The member has a documented post-bronchodilator FEV₁/FVC ratio < 0.7 and post-bronchodilator FEV₁ of ~~320% to 780%~~ 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.

Formatted: Bulleted + Level: 2 + Aligned at: 0.5" + Indent at: 0.75", Tab stops: Not at 0.5"

- 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
- 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 4015 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

Chronic Spontaneous Urticaria (CSU) (Dupixent only):

- Confirmed diagnosis of CSU
- Documented history of urticaria for at least 6 weeks
- Member remains symptomatic despite a minimum two-week trial of a second generation H1 antihistamine at the maximum tolerated dose; or has a medical reason for not utilizing a second-generation antihistamine
- The prescribed dose is within FDA approved dosing guidelines

Formatted: Space After: 0 pt

Formatted: Space After: 0 pt, Bulleted + Level: 1 + Aligned at: 0.25" + Indent at: 0.5", Tab stops: Not at 0.5"

Bullous Pemphigoid (Dupixent only):

- Confirmed diagnosis of bullous pemphigoid
- Member has a Bullous Pemphigoid Disease Area Index (BPDAI) activity score ≥ 24
- Member has a Peak Pruritus Numeric Rating Scale (NRS) score ≥ 4
- Documented trial and failure, intolerance, or contraindication to at least three of the following:
 - High potency topical corticosteroids
 - Oral corticosteroids
 - Doxycycline
 - Immunosuppressive therapies (ex. azathioprine, mycophenolate, methotrexate, etc.).

Formatted: Space After: 0 pt

Formatted: Space After: 0 pt, Bulleted + Level: 1 + Aligned at: 0.25" + Indent at: 0.5", Tab stops: Not at 0.5"

Formatted: Underline, Font color: Black, Ligatures: None

	• <u>The prescribed dose is within FDA approved dosing guidelines</u> <u>Eosinophilic granulomatosis with polyangiitis (EGPA) (Nucala & Fasenra only):</u> • 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 <u>Hypereosinophilic Syndrome (HES) (Nucala only):</u> • Confirmed diagnosis of FIP1 like 1-platelet derived growth factor receptor alpha (FIP1L1-PDGFRα)-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) <u>Criteria for re-authorization:</u> • Documentation 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; <u>CSU: decrease in severe itching or urticaria activity; Bullous Pemphigoid: sustained remission, improvement in Peak Pruritus NRS score</u>). • The prescribed dose is within FDA approved dosing guidelines	Formatted: Font: (Default) Arial, 10 pt Formatted: Underline, Font color: Black, Ligatures: None Formatted: Bulleted + Level: 1 + Aligned at: 0.25" + Indent at: 0.5", Tab stops: Not at 0.5" Formatted: List Paragraph, Bullets, Indent: Left: 1.04", Right: -0.01"
Criteria Statement	For asthma, Nucala, Dupixent, Fasenra, Cinqair, ~~and~~ Tezspire, ~~and~~ Exdensus 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 ~~and Nucala are~~ reserved for members with a diagnosis of COPD, eosinophil count <u>in the treatment range per package insert ≥ 300 cells/mcL</u>, 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 ~~40~~15kg. 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. <u>For Chronic Spontaneous Urticaria (CSU), Dupixent is reserved for members with a diagnosis of CSU with history of urticaria for at least 6 weeks, who remain symptomatic despite trial of second generation H1 antihistamine.</u> <u>For Bullous Pemphigoid, Dupixent is reserved for members with a diagnosis of bullous pemphigoid with BPDAl activity score of at least 24 and NRS score of at least 4, who had trial and failure or were unable to use at least three of the following: high potency topical corticosteroids, oral corticosteroids, doxycycline, immunosuppressive therapies.</u> For eosinophilic granulomatosis with polyangiitis (EGPA), Nucala and Fasenra are 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	<u>3/29/253/2026</u>

Recommendation: Retire criteria as Symlin was discontinued

Symlin (pramlintide)	
Therapeutic Classes (AHFS)	Amylinomimetics
Medications	<u>Formulary, PA required</u> 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 $\leq 9\%$
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	3/2025

Recommendation:

- Add Tezspire to criteria as it received a new indication for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP)
- Update age restriction to encompass all products

Biologic Agents for Nasal Polyposis	
Therapeutic Classes (AHFS)	SKIN AND MUCOUS MEMBRANE AGENTS, MISC.; RESPIRATORY TRACT AGENTS, MISCELLANEOUS
Medications	<u>Formulary, PA required</u> Dupixent (dupilumab) Xolair (omalizumab) Nucala (mepolizumab) Tezspire (tezepelumab)
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, <u>Tezspire</u> or Xolair concomitantly or with another pulmonary biologic (e.g. Fasenra, Cinqair)
Required Clinical Information	See “ PA Review Criteria ” below
Age Restrictions	<u>Per Package Insert Patients must be 18 years age or older</u> 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, urticaria, and food allergy, please refer to the “Xolair (omalizumab) for Asthma, 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 Respiratory and Eosinophilic Conditions” policy** **Nucala & Tezspire: For asthma or other eosinophilic conditions, please refer to the “Pulmonary Biologics for Respiratory and Eosinophilic Conditions” policy** <u>Initial Authorization:</u> • 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

	<u>Re-authorization:</u> • 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, <u>Tezsprie</u> 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	<u>3/2025</u> 3/2026

Recommendation: Remove the exclusion of concomitantly used long-acting nitrates since it is not expressly contraindicated in the labeling and per guidelines both may be recommended in certain situations.

Verquvo	
Therapeutic Classes (AHFS)	VASODILATING AGENTS, MISCELLANEOUS
Medications	<u>Formulary, PA required</u> 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	<u>3/2025</u> 3/2026

Recommendation: Add Vizz (aceclidine) ophthalmic solution to criteria. It's a cholinergic muscarinic receptor agonist indicated for the treatment of presbyopia in adults, priced comparably with the other two agents.

Presbyopia Agents	
Therapeutic Classes (AHFS)	Miotics
Medications	Vuity (pilocarpine HCl ophthalmic solution) Qlosi (pilocarpine HCl ophthalmic solution) Vizz (aceclidine 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 Vizz: 45-75 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, Vizz 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	3/20253/2026

Recommendation:

- Add new agent Jascayd to formulary with PA and to the criteria. Jascayd is a new phosphodiesterase 4 (PDE4) inhibitor approved for the treatment of idiopathic pulmonary fibrosis (IPF) in adult patients.
- Update Initial criteria for all diagnoses since non-smoking status does not apply to Jascayd per the package insert.
- Revise FVC requirement to $\geq 45\%$ as this was the cutoff used in the pivotal clinical trial for Jascayd.
- Add trial and failure of pirfenidone before more costly brand products for the diagnosis of IPF.

Antifibrotic Respiratory Tract Agents	
Therapeutic Classes (AHFS)	Antifibrotic Agents
Medications	<u>Formulary, PA required</u> Ofev (nintedanib) pirfenidone (Esbriet) <u>Jascayd (nerandomilast)</u>
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	<u>INITIAL CRITERIA FOR ALL DIAGNOSES:</u> • Patient is 18 years of age or older • Documentation has been provided that the patient does not smoke (<u>Ofev and pirfenidone only</u>) <u>INITIAL CRITERIA FOR IDIOPATHIC PULMONARY FIBROSIS:</u> • 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 <u>5045%</u> within 30 days of request • <u>For Ofev or Jascayd, patient must also have a trial and failure, intolerance, or contraindication to pirfenidone</u> <u>INITIAL CRITERIA FOR SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (ILD) (SSc-ILD):</u> • The request is for Ofev (nintedanib). • Confirmed diagnosis of SSc-ILD attested to by prescriber • FVC $\geq 40\%$ within 30 days of request • Trial and failure of mycophenolate mofetil (MMF), cyclophosphamide or azathioprine. <u>INITIAL CRITERIA FOR CHRONIC FIBROSING INTERSTITIAL LUNG DISEASE (ILDs) WITH A PROGRESSIVE PHENOTYPE:</u> • 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 <u>(Ofev and pirfenidone only)</u>
Criteria Statement	Ofev, <u>Jascayd</u>, and pirfenidone are reserved for members with a diagnosis of pulmonary fibrosis have pulmonary function tests with FVC over <u>5045%</u>, and have documentation of non-smoking status <u>(for Ofev and pirfenidone only)</u>. <u>Additionally, for Ofev or Jascayd, patient must also have a trial and failure, intolerance, or contraindication to pirfenidone.</u> 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	<u>9/20253/2026</u>

Formatted: Font: (Default) Arial, 10 pt

Recommendation:

- Add Adalimumab-bwwd (unbranded Hadlima), Starjemza (ustekinumab-hmny), and Ustekinumab-aauz (unbranded Otulfi) to Formulary with QL and to the drug list as Step 1 preferred agents as they are cost-effective biosimilars.
- Adalimumab-bwwd Subcutaneous Solution Auto-injector/syringe 40 MG/0.4ML QL: Loading Dose: 3.2mL; Maintenance: 1.6 ML per 28 day(s)
- Starjemza Subcutaneous Solution Prefilled Syringe 90 MG/ML QL: Initial: 2 syringes (2mL); Maintenance: 1 syringe (1mL)/56 days
Starjemza Subcutaneous Solution Prefilled Syringe 45 MG/0.5ML QL: Initial: 2 syringes (1mL); Maintenance: 1 syringe (0.5mL)/84 days
Starjemza Subcutaneous Solution 45 MG/0.5ML QL: Initial: 2 vials (1mL); Maintenance: 1 vial (0.5mL)/84 days
- Ustekinumab-aauz Subcutaneous Solution Prefilled Syringe 90 MG/ML QL: Initial: 2 syringes (2mL); Maintenance: 1 syringe (1mL)/56 days
Ustekinumab-aauz Subcutaneous Solution Prefilled Syringe 45 MG/0.5ML QL: Initial: 2 syringes (1mL); Maintenance: 1 syringe (0.5mL)/84 days.

Specialty Biologic Agents	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	<u>Step 1: Preferred (pays at point-of-sale)</u> Hadlima (adalimumab-bwwd) Adalimumab-fkjp (Hulio) Adalimumab-aaty (Yuflyma)-- 80mg/0.8mL dose formulation available Simlandi (adalimumab-ryvk) Adalimumab-bwwd (unbranded Hadlima) Starjemza (ustekinumab-hmny) Ustekinumab-aauz (unbranded Otulfi)
	<u>Step 2: Preferred (PA required)</u> Enbrel (etanercept) Simponi, Simponi Aria (golimumab) Infliximab Inflectra (infliximab-dyyb) Avsola (infliximab-axxq) Renflexis (infliximab-abda) Orencia (abatacept) Xeljanz, Xeljanz XR (tofacitinib) Kineret (anakinra) Otezla (Apremilast) Siliq (brodalumab) Kevzara (sarilumab) Avtozma (tocilizumab-anoh) Tyenne (tocilizumab-aazg) Tofidence (tocilizumab-bavi) Olumiant (baricitinib) Entyvio (vedolizumab) Otulfi (ustekinumab-aauz) Yesintek (ustekinumab-kfce) Imuldosa (ustekinumab-srlf)

	<u>Step 3: Non-Preferred (PA required)</u> Humira (adalimumab) Stelara (ustekinumab) Skyrizi (risankizumab) Actemra (tocilizumab) Arcalyst (rilonacept) Ilaris (canakinumab) Tremfya (guselkumab) Remicade (infliximab) Cosentyx (secukinumab) Zeposia (ozanimod) Taltz (ixekizumab) Tysabri (natalizumab) Tyruko (natalizumab-sztn) Cimzia (certolizumab) Rinvoq (upadacitinib) Ilumya (tildrakizumab-asmn) Sotyktu (deucravacitinib) Bimzelx (bimekizumab) OmvoH (mirikizumab) Zymfentra (infliximab) All adalimumab biosimilar agents not listed in step 1 (ex. Amjevita, Cyltezo, Hyrimoz, Yuflyma, etc.) Litfulo (ritlectinib) All Stelara biosimilars not listed in step 2 (ex. Steqeyma, Selarsdi, etc.) 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. ** Non-FDA approved (i.e. off-label) uses; refer to the “Off-Label Use” policy**
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 a specialist in the field to treat the member’s respective medical condition
Coverage Duration	If all of the conditions are met, requests will be approved for 12 months.
PA Review Criteria	Initial Authorization: - The drug is being requested for an appropriate use (per the references outlined in “Covered Uses”) - The dose requested is appropriate for the requested use (per the references outlined in “Covered Uses”) - If the request is for a preferred Step 2 agent, documentation has been provided that the member has tried and failed or has a medical reason why (e.g. intolerance, contraindication) they cannot use a preferred Step 1 agent appropriate for the requested use (per the references outlined in “Covered Uses”) - If the request is for a non-preferred Step 3 agent, documentation has been provided that the member has tried and failed or has a medical reason why (e.g. intolerance, contraindication) they cannot use one preferred step 1 agent and one preferred step 2 agent appropriate for the requested use (per the references outlined in covered uses) AND: - If the request is for a reference biologic drug with a biosimilar or interchangeable

	biologic drug (ex. Humira, Remicade, Stelara), documentation of one of the following: - The provider has verbally, or in writing, submitted a member-specific reason why the reference biologic is required based on the member's condition or treatment history; AND if the member had side effects or a reaction to the biosimilar or interchangeable biologic, the provider has completed and submitted an FDA MedWatch form to justify the member's need to avoid these drugs. MedWatch form must also be included with the prior authorization request. Form FDA 3500 – Voluntary Reporting - 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 *NOTE: - Requests for 80mg/0.8mL dose presentations of Humira or non-preferred biosimilar adalimumab agents, preferred biosimilar adalimumab-aaty 80mg/0.8mL should be used - Requests for Humira 10 mg/0.1 mL in pediatric patients may be approved without a trial of a step 1 or step 2 agent, when requested for an appropriate use (per the references outlined in "Covered Uses") <u>Reauthorization:</u> - Documentation submitted indicates that the member has obtained clinical benefit from the medication. - The drug is being requested for an appropriate use and dose (per the references outlined in "Covered Uses")
Criteria Statement	Step 2 preferred prior authorization required medications are reserved for members with an appropriate indication and dose, who have used (or cannot/should not use) a preferred step 1 medication. Step 3 non-preferred prior authorization required medications are reserved for members with an appropriate indication and dose, who have used (or cannot/should not use) a preferred step 1 medication and a step 2 preferred prior authorization required medication.
Last P&T Review Date	~~12/2025~~ 3/2026

Recommendation:

- Change policy name to encompass all drugs in the criteria
- Add Redemplo--an apolipoprotein C-III (apoC-III)-directed small interfering ribonucleic acid (siRNA) indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome
- Add trial and failure, intolerance, or contraindication to Redemplo for Tryngolza requests for cost containment

Tryngolza/Familial Chylomicronemia Syndrome Agents	
Therapeutic Classes (AHFS)	Antilipemic Agents
Medications	Tryngolza (olezarsen), <u>Redemplo (plozasiran)</u>
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	According to package insert
Prescriber Restrictions	Prescriber must be an endocrinologist, lipidologist, or cardiologist experienced in, or in consultation with a specialist experienced in, familial chylomicronemia syndrome (FCS)
Coverage Duration	If all of the criteria are met, the request will be approved for 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: • The member's most recent triglyceride level is ≥ 880 mg/dL (10 mmol/L) • The member is refractory to standard triglyceride lowering therapies (e.g., statins, fibrates, omega-3 fatty acids, and niacin) • The member has undergone genetic testing to confirm a diagnosis of FCS with ONE of the following results: ◦ The member has a pathogenic gene mutation in FCS-causing genes (e.g., <i>LPL</i>, <i>GPIHBP1</i>, <i>APOA5</i>, <i>APOC2</i>, or <i>LMF1</i>) ◦ The member has inconclusive genetic results and has documentation supporting the diagnosis of FCS by ONE of the following: ▪ North America Familial Chylomicronemia Syndrome (NAFCS) score ≥ 45 ▪ FCS score ≥ 10 ▪ History of acute pancreatitis ▪ History of recurrent abdominal pain without other known causes • Medication is prescribed at an FDA approved dose • <u>The prescriber attests the member will follow a low-fat diet</u> • <u>If the request is for Tryngolza, member must also have a trial and failure, intolerance, or contraindication to Redemplo</u> Re-Authorization: • Documentation of a positive clinical benefit (e.g., reduction in fasting triglyceride level from baseline, fewer acute pancreatitis events) • Medication is prescribed at an FDA approved dose • The prescriber attests the member will continue to follow a low-fat diet
Criteria Statement	Tryngolza <u>and Redemplo</u> <u>is/are</u> reserved for members who have a diagnosis of FCS, triglyceride level of ≥ 880 mg/dL (10mmol/L), are refractory to standard triglyceride

Formatted: Highlight

	lowering therapies, and will follow a low-fat diet. <u>Additionally, for Tryngolza requests, member must also have trial and failure, intolerance, or contraindication to Redemplo.</u>
Last P&T Review Date	<u>6/20253/2026</u>

Recommendation:

- Add Voyxact-- an A Proliferation Inducing Ligand (APRIL) blocker, indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk for disease progression.
- Add SGLT2 inhibitors requirement for all initial requests as per newest 2025 KDIGO guidelines that recommend that patients who are at risk of progressive loss of kidney function with IgAN should be treated with an SGLT2 inhibitor.
- Update proteinuria definition to total urine protein $\geq 0.5\text{g/day}$ per the 2025 KDIGO guidelines
- Add trial and failure or inability to use Filspari for Fabhalta and Vanrafia requests based on updated guidelines that recommend patients who are at risk of progressive loss of kidney function with IgAN be treated with Filspari and for cost containment.
- Add trial and failure or inability to use Tarpeyo for Voyxact requests because Voyxact targets upstream immune pathways and is expected to compete with Tarpeyo and for cost containment.

Immunoglobulin A (IgA) Nephropathy Agents	
Therapeutic Classes (AHFS)	Endothelin Receptor Antagonists, Miscellaneous Therapeutic Agents
Medications	Fabhalta (iptacopan), Filspari (sparsentan), Tarpeyo (budesonide), Vanrafia (atrasentan), <u>Voyxact (sibeprenlimab-szsi)</u>
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	For Filspari and Vanrafia only: pregnancy
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	According to package insert
Prescriber Restrictions	Prescribed by or in consultation with a nephrologist
Coverage Duration	If all of the criteria are met, it will be approved as follows: • Initial requests: Fabhalta: 6 months; Filspari, Tarpeyo, Vanrafia, <u>Voyxact</u>: 9 months • Reauthorization: Fabhalta, Filspari, Vanrafia, <u>Voyxact</u>: 12 months; Reauthorization requests for Tarpeyo will not be allowed as the safety and efficacy of subsequent courses have not been established 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 primary IgA nephropathy verified by biopsy • <u>Member is on an ACE inhibitor or ARB at a maximally tolerated dose OR there is a medical reason that they cannot be on one</u> • <u>Member is on an SGLT2 inhibitor at a maximally tolerated dose OR there is a medical reason that they cannot be on one</u> • Member has proteinuria (defined as total urine protein $\geq 0.5\text{ g/day}$) • Member has an estimated glomerular filtration rate (eGFR) $\geq 30\text{ mL/min/1.73 m}^2$ • Medication is prescribed at an FDA approved dose • For Fabhalta: ○ Documentation patient complies with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria ○ <u>Member is at risk for disease progression as defined by a urine protein-to-creatinine ratio (UPCR) $\geq 1.5\text{ g/g}$</u> ○ <u>Documentation of trial and failure, intolerance, or contraindication to Filspari</u> • For Filspari:

	○ Documentation of baseline liver function ○ Attestation that member will discontinue use of renin-angiotensin-aldosterone system (RAAS) inhibitors, endothelin receptor antagonists, and/or aliskiren upon initiation of Filspari • For Vanrafia: ○ Member is at risk for disease progression as defined by a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g ○ <u>Documentation of trial and failure, intolerance, or contraindication to Filspari</u> • <u>For Voyxact:</u> ○ <u>Documentation of trial and failure, intolerance, or contraindication to Tarpeyo</u> <u>Re-Authorization:</u> • Documentation of positive clinical response (e.g. decrease in UPCR, stabilization of eGFR) • Medication is prescribed at an FDA approved dose • For Filspari: ○ Documentation of liver function ***Reauthorization requests for Tarpeyo will not be allowed as the safety and efficacy of subsequent courses have not been established***
Criteria Statement	Fabhalta, Filspari, Tarpeyo, and Vanrafia are reserved for members who have a diagnosis of IgA nephropathy, are on ACE inhibitor or ARB <u>and on SGLT2 inhibitor</u>, have proteinuria and eGFR ≥ 30 mL/min/1.73 m². Additionally, for Fabhalta and Vanrafia <u>requests</u>, members are at risk for disease progression, and <u>require trial and failure or inability to use Filspari</u>. <u>For Filspari, members will discontinue use of RAAS inhibitors/aliskiren upon initiation of Filspari and baseline liver function is provided. For Voyxact, members should have trial and failure, intolerance, or contraindication to Tarpeyo.</u>
Last P&T Review Date	<u>9/20253/2026</u>

Recommendation:

- Add new formulation of Wegovy tablets to the drug list and language regarding appropriate dose and formulation
- Add trial of Wegovy injectable before Wegovy tablet for utilization containment for risk reduction of major adverse cardiovascular events indication.

GLP1 Receptor Agonists (Wegovy/Zepbound) for Non-Weight Loss Indications	
Therapeutic Classes (AHFS)	Incretin Mimetics
Medications	Wegovy (semaglutide) injection, tablets Zepbound (tirzepatide) injection **Please Note: If the request is for Wegovy/Zepbound to reduce excess body weight and maintain weight reduction long term, refer to criteria for Anti-Obesity Medications**
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	• Requests for a diagnosis of weight reduction and maintenance for overweight or obesity • Concurrent use of any glucagon-like-peptide-1 receptor agonist • Personal or family history of medullary thyroid carcinoma • Multiple Endocrine Neoplasia syndrome type 2
Required Clinical Information	See "PA Review Criteria"
Age Restrictions	Wegovy for cardiovascular risk reduction: Member must be ≥ 45 years of age, all others per FDA approved labeling
Prescriber Restrictions	Provider is or treatment is in consultation with: •Wegovy for MASH: hepatologist, gastroenterologist, endocrinologist, or a specialist in the treatment of liver disease •Wegovy for CVD risk reduction: N/A •Zepbound for Obstructive Sleep Apnea: N/A
Coverage Duration	Initial Approval 6 months Later Approvals 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:

- All requests: Requested dose and formulation (injectable, tablet) is/are appropriate per labeling

Wegovy Requests:

For **risk reduction of major adverse cardiovascular events** in adults with established CV disease, the following must be met:

- Medication is prescribed for reducing the risk of adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with **established cardiovascular** disease. Documentation demonstrates patient has history of one or more of the following:
 - Prior myocardial infarction
 - Prior stroke
 - Symptomatic peripheral arterial disease, as evidenced by ≥1 of the following:
 - Intermittent claudication with ankle brachial index <0.85 (at rest)
 - Peripheral arterial revascularization procedure
 - Amputation due to atherosclerotic disease
- Documentation is provided that patient is overweight or obese, defined as a body mass index (BMI) ≥ 27 kg/m²
- Patient is receiving standard of care treatment of CVD, as appropriate/indicated, including an antiplatelet agent (ex. aspirin or P2Y₁₂ inhibitor), lipid-lowering drug (ex. statin, otherwise ezetimibe, fibrate, and/or PCSK-9 inhibitor), antihypertensive (ex. beta blocker, ACE-I, ARB)
- Patient does not have a personal history of type 1 or type 2 diabetes
- Documentation is provided patient's Hb A1c ≤ 6.5%
- For Wegovy tablets, please provide a medical reason for not using Wegovy injection

For the treatment of **noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH)**, with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults, all of the following must be met:

- Diagnosis of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced liver fibrosis
- Documentation of stage F2 to F3 fibrosis confirmed by biopsy or a noninvasive test (NIT)
- Prescriber attestation to providing lifestyle counseling on nutrition and exercise
- Prescriber attestation that member avoids excess alcohol intake

Zepbound Requests:

For treatment of **moderate to severe obstructive sleep apnea** in adults, the following must be met:

- Patient's body mass index (BMI) is provided and is 30 kg/m² or more
- 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/m²
- 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 <u>Re-Authorization:</u> <u>Wegovy Requests:</u> For risk reduction of major adverse cardiovascular events in adults with established CV disease, the following must be met: • Patient is receiving standard of care treatment of CVD, as appropriate/indicated, including an antiplatelet agent (ex. aspirin or P2Y12 inhibitor), lipid-lowering drug (ex. statin, otherwise ezetimibe, fibrate, and/or PCSK-9 inhibitor), antihypertensive (ex. beta blocker, ACE-I, ARB) • Patient continues to not have Type 1 or Type 2 diabetes • Patient is adherent to therapy, as evidenced by claims records demonstrating $\geq 80\%$ fill rate For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults, all of the following must be met: • Requested dose is appropriate per labeling • The member continues to have a fibrosis stage of ≤ 3 • Patient is adherent to therapy, as evidenced by claims records demonstrating $\geq 80\%$ fill rate <u>Zepbound Requests:</u> For treatment of moderate to severe obstructive sleep apnea in adults, the following must be met: • 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 $\geq 80\%$ fill rate
Criteria Statement	Wegovy is reserved for risk reduction of major adverse cardiovascular events for members who are overweight or obese, have an established cardiovascular disease, receive standard of care treatment for CVD, have Hb A1c $\leq 6.5\%$ and do not have diabetes. Additionally, Wegovy is reserved for members with a diagnosis of MASH with moderate to advanced liver fibrosis, who avoid excess alcohol intake. 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/m², 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	<u>12/2025</u> 3/2026

Recommendation: add new formulation of Wegovy tablets to the drug list and add trial of Wegovy injectable before Wegovy tablet for utilization containment.

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) Phentermine/topiramate (Qsymia) Contrave (naltrexone/bupropion) Saxenda (liraglutide) Wegovy (semaglutide) injection, tablets Zepbound (tirzepatide) Any other newly marketed agent **Please Note: If the request is for Wegovy to reduce the risk of major adverse cardiovascular events, MASH, or for Zepbound for OSA, please refer to the “GLP1 Receptor Agonists (Wegovy/Zepbound) for Non-Weight Loss Indications” 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
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 <u>Phentermine HCL (Adipex-P)</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 • For phentermine (Lomaira): trial and failure or medical reason for not using generic phentermine (Adipex-P) <u>Alli</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 <u>Phentermine/topiramate (Qsymia)</u> • 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 ◦ For pediatrics: BMI in the ≥95th percentile standardized for age and sex ▪ https://www.cdc.gov/healthyweight/bmi/calculator.html

	- Clinic notes and paid claims to confirm 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 - Clinic notes and paid claims to confirm trial and failure, contraindication, or intolerance to use phentermine/topiramate (Qsymia) <u>Saxenda, Wegovy, and Zepbound</u> - Diagnosis of class III/severe obesity (including documentation of BMI ≥ 40) - Clinic notes and paid claims to confirm trial and failure, contraindication, or intolerance to use phentermine/topiramate (Qsymia) AND Contrave - Members who have been established on a GLP-1 agonist are permitted to switch to a different GLP-1 agonist with appropriate indication without meeting requirements above <u>For Wegovy tablets, please provide a medical reason for not using Wegovy injection</u> <u>Xenical:</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 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
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. Phentermine/topiramate (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) phentermine/topiramate (Qsymia). Saxenda, Wegovy, and Zepbound are reserved for members who have a diagnosis of class III/severe obesity with a body mass index of ≥ 40 and who have used (or cannot/should not use) phentermine/topiramate (Qsymia) and Contrave. <u>Additionally, for Wegovy tablets, a medical reason should be provided for not using Wegovy injection.</u>

	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	~~12/2025~~ <u>3/2026</u>

Alameda PADs for review Q1 2026 P&T Changes

Recommendation:

- Add Yimmugo to policy—new IV immune globulin product indicated for the treatment of primary humoral immunodeficiency in patients 2 years of age or older.
- Update Kawasaki disease and chronic B-cell lymphocytic leukemia indications with newer guideline recommendations

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) <u>Yimmugo (IV) (Immune Globulin-dira)</u>
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 **are** met, approve for **up to two doses 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 **4500**mg/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 ~~isn~~ 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	3/20253/2026

Recommendation:

- Change policy name to encompass all drugs in the criteria
- Add Redempho--an apolipoprotein C-III (apoC-III)-directed small interfering ribonucleic acid (siRNA) indicated as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome
- Add trial and failure, intolerance, or contraindication to Redempho for Tryngolza requests for cost containment

Tryngolza/Familial Chylomicronemia Syndrome Agents	
Medications	Tryngolza (olezarsen), Redempho (plozasiran)
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	According to package insert
Prescriber Restrictions	Prescriber must be an endocrinologist, lipidologist, or cardiologist experienced in, or in consultation with a specialist experienced in, familial chylomicronemia syndrome (FCS)
Coverage Duration	If all the criteria are met, the request will be approved for 6 months for initial requests, and 12 months for renewal requests.
Maximum Billable Units	Variable
Other Criteria	Initial Authorization • The member's most recent triglyceride level is ≥ 880 mg/dL (10 mmol/L) • The member is refractory to standard triglyceride lowering therapies (e.g., statins, fibrates, omega-3 fatty acids, and niacin) • The member has undergone genetic testing to confirm a diagnosis of FCS with ONE of the following results: ◦ The member has a pathogenic gene mutation in FCS-causing genes (e.g., <i>LPL</i>, <i>GPIHBP1</i>, <i>APOA5</i>, <i>APOC2</i>, or <i>LMF1</i>) ◦ The member has inconclusive genetic results and has documentation supporting the diagnosis of FCS by ONE of the following: ▪ North American Familial Chylomicronemia Syndrome (NAFCS) score ≥ 45 ▪ FCS score ≥ 10 ▪ History of acute pancreatitis ▪ History of recurrent abdominal pain without other known causes • Medication is prescribed at an FDA approved dose • The prescriber attests the member will follow a low-fat diet • If the request is for Tryngolza, member must also have a trial and failure, intolerance, or contraindication to Redempho Re-Authorization: • Documentation of a positive clinical benefit (e.g., reduction in fasting triglyceride level from baseline, fewer acute pancreatitis events) • Medication is prescribed at an FDA approved dose • The prescriber attests the member will continue to follow a low-fat diet If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review

Formatted: Highlight

Last Review Date	<u>6/20253/2026</u>

Recommendation: Add Bosaya--new interchangeable biosimilar to Prolia to the drug list

Injectable/Infusible Agents for Osteoporosis and Paget's Disease	
Medications	ibandronate (Boniva) injection zoledronic acid (Reclast) Prolia (denosumab) Prolia biosimilars: Bilyos, Jubbonti, Connexence, Stoboclo, Ospomyv, Bosaya teriparatide (Forteo) Tymlos (abaloparatide) Evenity (romosozumab-aqqg) Pamidronate 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), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	N/A
Coverage Duration	If all conditions are met, the request will be approved for up to 12 months. ***FORTEO/TERIPARATIDE/TYMLOS REQUESTS WILL ONLY BE APPROVED FOR A TOTAL DURATION OF 24 MONTHS*** *** EVENITY WILL ONLY BE APPROVED FOR A TOTAL OF 12 MONTHS*** reauthorization requests will be approved for up to 12 months.
Maximum Billable Units	Variable
Other Criteria	CRITERIA FOR APPROVAL FOR ALL REQUESTS: • Dose is appropriate per label or supported by compendia/standard of care guidelines • The member is taking adequate calcium and vitamin D supplementation • The member has a documented (consistent with pharmacy claims) adequate trial of an oral bisphosphonate or has a medical reason (e.g. intolerance, hypersensitivity, contraindication, etc.) for not using an oral bisphosphonate • If the request is for Prolia (denosumab), the member has a documented trial and failure with the biosimilar product, or a medical reason (e.g. intolerance, contraindication, etc.) as to why the member is unable to use biosimilar is provided POSTMENOPAUSAL OR MALE OSTEOPOROSIS: • If the request is for very high risk postmenopausal osteoporosis or postmenopausal osteoporosis with prior fractures, a documented trial and failure of an oral bisphosphonate will not be required. ◦ Very high risk is defined as having one or more of the following: ▪ History of fracture in the past 12 months ▪ Multiple fractures ▪ Fractures while on drugs causing skeletal harm (e.g. long-term glucocorticoids) ▪ Very low T scores (< -3.0) ▪ High risk for falls ▪ History of injurious falls

- Very high fracture probability as determined by fracture risk assessment tool (FRAX) (e.g. major osteoporosis fracture >30%, hip fracture > 4.5%)
- Documentation was submitted indicating the member is a postmenopausal woman or a male over 50 years of age and one of the following:
 - A bone mineral density (BMD) value consistent with osteoporosis (i.e., T-scores equal to or less than -2.5)
 - Has had an osteoporotic fracture
 - A T-score between -1 and -2.5 at the femoral neck or spine and a 10 year hip fracture probability >3% or a 10 year major osteoporosis-related fracture probability >20% based on the US-adapted WHO absolute fracture risk model.
- If the request is for Forteo (teriparatide), Teriparatide, Evenity (romosozumab), or Tymlos (abaloparatide), one of the following applies to the member:
 - Documented trial and failure of ibandronate (Boniva) or zoledronic acid (Reclast) AND a denosumab product or has a medical reason (e.g. intolerance, contraindication, etc.) why these therapies are not suitable to be used
 - Has severe osteoporosis (T-Score -3.5 or below, or T-Score of -2.5 or below plus a fragility fracture)
- If the request is for Forteo or Evenity, a medical reason why member is unable to use Tymlos or teriparatide, if appropriate, based on the diagnosis.
 - Requests for brand Forteo (teriparatide) also require a medical reason why the member is unable to use Teriparatide
- If the request is for Evenity, the member does not have a history of a heart attack or stroke within the preceding year

GLUCOCORTICOID-INDUCED OSTEOPOROSIS THERAPY:

- For members ≥ 40 years of age on long-term glucocorticoid therapy:
 - Documentation that the member is currently utilizing glucocorticoid therapy for a minimum of 3 months
 - Dosage of the glucocorticoid therapy is greater than 2.5 mg of prednisone daily or its equivalent
 - Member has a moderate to very high risk of fracture based on ONE of the following:
 - History of osteoporotic fracture
 - BMD less than or equal to -1 at the hip or spine
 - FRAX 10-year probability of hip or combined major osteoporotic fracture of ≥1 and 10 percent (with glucocorticoid adjustment), respectively
- For adult members (all ages) receiving HIGH dose glucocorticoid therapy:
 - Member has a moderate to very high risk of fracture based on ONE of the following:
 - History of prior fracture
 - Glucocorticoid dose ≥ 30 mg/day or cumulative ≥ 5 grams/year of prednisone or its equivalent
 - Continuing glucocorticoid treatment ≥ 7.5 mg/day of prednisone or its equivalent for ≥ 6 months AND BMD Z score < -3 OR significant BMD loss (> least significant change of DXA)
- If the request is for Forteo (teriparatide), Teriparatide, or Tymlos (abaloparatide), the member has a documented trial and failure of zoledronic acid (Reclast) or a denosumab product or a medical reason (e.g. intolerance, contraindication, etc.) as to why the member is unable to use these medications is provided:

	○ Requests for brand Forteo (teriparatide) also require a medical reason why the member is unable to use Teriparatide PAGET'S DISEASE: • Documentation of a confirmed diagnosis of Paget's disease. • Documentation (from within 60 days of the request) that the member has a serum alkaline phosphatase level of $\geq$ two times the upper limit of normal OR the member is symptomatic OR the patient is at risk for complication from Paget's disease CRITERIA FOR REAPPROVAL: • The member has documentation of clinical benefit from the medication
Last Review Date	~~12/2025~~ 3/2026

Recommendation:

- Add exclusion criteria to restrict Spinraza and Evrysdi use if the patient has previously received Itivisma as it is not clinically supported at this time.
- Add additional measure of motor function test used in Evrysdi trials—Motor Function Measure 32 (MFM-32) to the initial approval and reauthorization sections.

SMN2 Splicing Modifiers for the Treatment of Spinal Muscular Atrophy (SMA)	
Medications	Spinraza (nusinersen) Evrysdi (risdiplam)
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	• Concomitant use of Evrysdi and Spinraza • Patient has previously received treatment with Itivisma
Required Clinical Information	For Evrysdi: Patient's body weight
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Neurologist
Coverage Duration	For Evrysdi: If all of the conditions are met, the request will be approved for 6 months for initial approval, followed by 12 months for reauthorization requests. For Spinraza: If all of the conditions are met, the request will be approved for 6 months for 5 doses (4 loading doses and 1st maintenance dose) for initial approval, and 12 months for 3 additional maintenance doses for reauthorization requests.
Maximum Billable Units	Variable
Other Criteria	For Initial Approval: • Member has confirmed diagnosis of spinal muscular atrophy (SMA) types I, II or III and the molecular genetic test with mutation analysis was submitted • For Spinraza: Documentation of genetic testing confirming either two or three copies of the SMN2 gene OR four copies of the SMN2 gene with symptomology of SMA • For Evrysdi: Documentation of genetic testing confirming two or three or four copies of the SMN2 gene • Baseline motor function or motor milestone achievement was submitted with request [e.g. CHOP Infant Test of Neuromuscular Disorders (CHOP-INTEND), or Hammersmith Functional Motor Scale Expanded Scores (HFMSE), or Hammersmith Infant Neurological Examination (HINE), or 6 minute walk test in subjects able to walk, <u>or Motor Function Measure 32 (MFM-32)</u>, or <u>Revised Upper Limb Module (RULM)</u> score] • The request is for an FDA approved dose Reauthorization: • Documentation of a positive clinical response was submitted with request (e.g. improvement, maintenance, or reduction in decline of motor function/motor milestone achievement scores using CHOP-INTEND, HFMSE, 6 minute walk test, <u>RULM</u> score, <u>MFM-32</u>, or HINE) • The 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 Review Date	6/2025/2026

Formatted: Font: (Default) Arial, 10 pt, Font color: Black, Ligatures: None

Formatted: Font: (Default) Arial, 10 pt, Font color: Black, Ligatures: None

Formatted: List Paragraph,Bullets, Indent: Left: -0", Bulleted + Level: 1 + Aligned at: 0.25" + Indent at: 0.5"

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Inluriyo	imlunestrant tosylate oral tablet 200 mg	Eli Lilly	Treatment of adults with ER-positive, HER2-negative, ESR1 mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy	\$24,107	Orserdu	Non-formulary
Keytruda Qlex	pembrolizumab and berahyaluronidase alfa-pmph subcutaneous solution 395-4800 mg -unt/2.4 mL, 790-9600 mg -unt/4.8 mL	Merck	Approved for most solid tumor indications for Keytruda; see package insert for details	\$12,031 every 3 weeks or \$24,063 every 6 weeks	Keytruda IV	Non-formulary
Rhapsido	remibrutinib oral tablet 25 mg	Novartis	For the treatment of chronic spontaneous urticaria (CSU) in adult patients who remain symptomatic despite H1 antihistamine treatment	\$4,521	Dupixent, Xolair	Non-formulary (see new MRG criteria)
Koselugo	selumetinib oral capsule sprinkle 5 mg, 7.5 mg	AstraZeneca	For the treatment of pediatric patients 1 year of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN)	\$70-\$105 per capsule (weight-based dosing)	Gomekli	Non-formulary
Jascayd	nerandomilast oral tablet 9 mg, 18 mg	Boehringer Ingelheim	For the treatment of idiopathic pulmonary fibrosis in adult patients	\$16,219	Ofev, Esbriet	Add to F-PA (see updated MRG criteria)

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Beizray	docetaxel intravenous solution 80 mg/4 mL & 25% (50 mL), 2 x 80 mg/4 mL & 25% (50 mL)	Zhuhai	- Breast Cancer (BC): single agent for locally advanced or metastatic BC after chemotherapy failure; and with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positive BC - Non-small Cell Lung Cancer (NSCLC): single agent for locally advanced or metastatic NSCLC after platinum therapy failure; and with cisplatin for unresectable, locally advanced or metastatic untreated NSCLC - Castration-Resistant Prostate Cancer (CRPC): with prednisone in metastatic castration-resistant prostate cancer - Gastric Adenocarcinoma (GC): with cisplatin and fluorouracil for untreated, advanced GC, including the gastroesophageal junction - Squamous Cell Carcinoma of the Head and Neck (SCCHN): with cisplatin and fluorouracil for induction treatment of locally advanced SCCHN	\$3,580-\$7,160 per unit	Indication dependent; oncology therapy	Non-formulary
Forzinity	elamipretide subcutaneous solution 280 mg/3.5 mL	Stealth Biotherapeutics	To improve muscle strength in adult and pediatric patients with Barth syndrome weighing at least 30 kg	\$61,044	None	Non-formulary (see new MRG criteria)
Ryoncil	remestemcel-l-rknd 100 kg to <112.5 kg intravenous kit 9 x 3.8 mL, 112.5 kg to <125 kg intravenous kit 10 x 3.8 mL, 125 kg to <137.5 kg intravenous kit 11 x 3.8 mL, 137.5 kg to <150 kg intravenous kit 12 x 3.8 mL	Mesoblast	For the treatment of steroid refractory acute graft versus host disease (SR-aGvHD) in pediatric patients 2 months of age and older	\$1,552,000 for an 8-dose course of therapy	Jakafi, mycophenolate, corticosteroids	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Zoryve	roflumilast external cream 0.05 %	Arcutis	• Zoryve cream, 0.3%, is indicated for the topical treatment of plaque psoriasis, including intertriginous areas, in adult and pediatric patients 6 years of age and older • Zoryve cream, 0.15%, is indicated for the topical treatment of mild to moderate atopic dermatitis in adult and pediatric patients 6 years of age and older • Zoryve cream, 0.05%, is indicated for the topical treatment of mild to moderate atopic dermatitis in pediatric patients 2 to 5 years of age	\$965 per 60 gm tube	Topical corticosteroids, topical calcineurin inhibitors	Non-formulary
Yimmugo	immune globulin intravenous, human – dira intravenous solution 5 gm/50 mL, 10 gm/100 mL, 20 gm/200 mL	Biotest AG	• For the treatment of primary humoral immunodeficiency (PI) in patients 2 years of age or older	\$14,232 (max dose every 3 weeks in a 70 kg patient)	Gammagard, Octagam	Non-formulary (see updated PAD criteria)
Palsonify	paltusotine oral tablet 20 mg, 30 mg	Crinetics	• For the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option	\$24,165	Injectable somatostatin analogs	Non-formulary
Enbumyst	bumetanide nasal solution 0.5 mg/0.1 mL	Corstasis	• For the treatment of edema associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome in adults	\$1,200 for a box of 12 single-use sprays	Oral diuretics (furosemide)	Non-formulary
Minimed Instinct	glucose sensor	Medtronic	• Diabetes	\$450	Dexcom, FreeStyle	Non-formulary
Valtva 1/35	ethynodiol diacetate and ethinyl estradiol 1-35 mcg oral tablet	Xiromed LLC	• For the prevention of pregnancy in women who elect to use oral contraceptives as a method of contraception	\$22	Other generic oral contraceptives	Add to F

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Cimzia	certolizumab pegol subcutaneous prefilled syringe kit 200 mg/mL	UCB Inc.	- Reducing signs and symptoms of Crohn’s disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy - Treatment of adults with moderately to severely active rheumatoid arthritis - Treatment of active polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years of age and older - Treatment of adult patients with active psoriatic arthritis - Treatment of adults with active ankylosing spondylitis - Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation - Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy	\$3,000 per 200 mg dose	Adalimumab, Enbrel	Non-formulary, add QL: Initial dose: 6 syringes/28 days; Maintenance: 4 syringes per 28 days.
Vabrinty	leuprolide acetate subcutaneous kit 30 mg, 45 mg	UroNova	For the treatment of advanced prostate cancer	\$18,400 per kit	Eligard	Non-formulary
Gabapentin (Once Daily)	gabapentin (once daily) oral tablet 450 mg, 750 mg, 900 mg	Zydus	For the management of postherpetic neuralgia	\$414 - \$827	Other generic gabapentin	Non-formulary
Medtronic MiniMed 780G	Medtronic MiniMed 780G kit	Medtronic	Diabetes	\$11,426	Other insulin pump systems	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Piperacillin-Tazobactam-NaCl	piperacillin-tazobactam-nacl intravenous solution reconstituted 4-0.5 gm/100 mL	B. Braun Medical	Treatment of: - Intra-abdominal infections in adult and pediatric patients 2 months of age and older - Nosocomial pneumonia in adult and pediatric patients 2 months of age and older - Skin and skin structure infections in adults - Female pelvic infections in adults - Community-acquired pneumonia in adults	\$28 per 100 mL bag	Other IV beta-lactam antibiotics, other generic piperacillin-tazobactam products	Non-formulary
Vyscoxa	celecoxib oral suspension 10 mg/mL	Carwin	In adults for: - Osteoarthritis (OA) - Rheumatoid Arthritis (RA) - Ankylosing Spondylitis (AS) In pediatric patients two years and older for - Juvenile Rheumatoid Arthritis (JRA)	\$3,672	NSAIDs, generic celecoxib capsules	Non-formulary
Selarsdi	ustekinumab-aekn subcutaneous solution 45 mg/0.5 mL	Teva	Adult patients with: - moderate to severe plaque psoriasis (PsO) 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)	\$2,088 per vial	Other Stelara biosimilars	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Ospomyv	denosumab-dssb subcutaneous solution prefilled syringe 60 mg/mL	Cordavis	Treatment of: • postmenopausal women with osteoporosis at high risk for fracture • to increase bone mass in men with osteoporosis at high risk for fracture • of glucocorticoid-induced osteoporosis in men and women at high risk for fracture • to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer • to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer	\$975 per dose	Other Prolia biosimilars	Non-formulary
Tyzavan	vancomycin intravenous solution 1000 mg/200 mL	Hikma	• Septicemia • Infective Endocarditis • Skin and Skin Structure Infections • Bone Infections • Lower Respiratory Tract Infections	\$18 per 1 gm dose	Generic vancomycin	Non-formulary
Starjemza	ustekinumab-hmny subcutaneous solution prefilled syringe 45 mg/0.5 mL and 90 mg/mL, 45 mg/0.5mL vial, intravenous solution 130 mg/26 mL	Bio-Thera Solutions	Adult patients with: • moderate to severe plaque psoriasis (PsO) 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)	\$430-\$550 per dose	Other Stelara biosimilars	Add to F-QL (see updated MRG criteria)
Blenrep	belantamab mafodotin-blmf intravenous solution reconstituted 70 mg	GlaxoSmithKline	• Indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least two prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent	\$72,000 every 3 weeks	Other chemotherapy agents	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Midazolam-Sodium Chloride	midazolam-nacl (PF) intravenous solution 50-0.8 mg/50mL-%, 100-0.8 mg/100 mL-%	B. Braun	Continuous intravenous infusion for sedation of intubated and mechanically ventilated adult, pediatric, and neonatal patients as a component of anesthesia or during treatment in a critical care setting	\$11-\$14 per unit	Midazolam-nacl 0.9%	Non-formulary
Lynkuet	elinzanetant oral capsule 60 mg	Bayer	For the treatment of moderate to severe vasomotor symptoms (VMS) due to menopause	\$625	Veozah, other hormonal therapies for VMS due to menopause (estradiol, micronized progesterone)	Non-formulary
Inlexzo	gemcitabine intravesical implant 225 mg	Janssen	For the treatment of adult patients with Bacillus Calmette-Guérin (BCG)-unresponsive, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ(CIS), with or without papillary tumors	\$69,000 every 3 weeks	Adstiladrin, Keytruda	Non-formulary
Tonmya	cyclobenzaprine tablet sublingual 2.8 mg	Tonix	For treatment of fibromyalgia in adults	\$1,860	Cyclobenzaprine tablets	Non-formulary
Auranofin	auranofin oral capsule 3 mg	Coral Way Pharma	Indicated in the management of adults with active classical or definite rheumatoid arthritis (ARA criteria) who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of full doses of one or more nonsteroidal anti-inflammatory drugs	\$1,550	Methotrexate, TNF inhibitors	Non-formulary
Transderm Scop	scopolamine transdermal patch 72 Hour 1 mg/3 days	Baxter	- Nausea and vomiting associated with motion sickness - Post-operative nausea and vomiting (PONV) associated with recovery from anesthesia and/or opiate analgesia and surgery	\$150	Generic scopolamine, oral Dramamine	Non-formulary
Pazopanib	pazopanib hcl oral tablet 400 mg	Torrent	- For the treatment of adults with advanced renal cell carcinoma - For the treatment of adults with advanced soft tissue sarcoma (STS) who have received prior chemotherapy	\$8,909	Other generic pazopanib (200 mg tablets)	F-PA (already added via CRF)

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Theophylline [#]	theophylline er oral tablet extended release 12-hour 100 mg, 200 mg	Brandywine	For the treatment of the symptoms and reversible airflow obstruction associated with chronic asthma and other chronic lung diseases, e.g., emphysema and chronic bronchitis	\$96-\$142 (for 100-200 mg per day dosing)	Theophylline oral liquid	Add to F
Ustekinumab-aauz	ustekinumab-aauz subcutaneous solution prefilled syringe 45 mg/0.5mL, 90 mg/mL	Fresenius Kabi	Adult patients with: - moderate to severe plaque psoriasis (PsO) 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)	\$575-\$985 per 90-day supply	Wezlana, Yesintek, Steqeyma, & other Stelara biosimilars	Add to F-QL (see updated MRG criteria)
Tacrolimus	tacrolimus intravenous solution 5 mg/mL	Nexus	Prophylaxis of organ rejection in kidney, liver, heart, or lung transplant	\$250 per vial	Mycophenolate injection	Non-formulary
Ketorolac	ketorolac tromethamine +RFID injection solution 30 mg/mL	Fresenius Kabi	For the short-term (≤5 days) management of moderately severe acute pain that requires analgesia at the opioid level, usually in a postoperative setting	\$4 per dose	Ketorolac tablets	Non-formulary
Tyvaso DPI	treprostinil institutional kit inhalation powder 80 mcg, maintenance kit inhalation powder 80 mcg	United Therapeutics	- Treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability - Treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability	\$44,296 per 28 days	Treprostinil IV/SC	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Subvenite	lamotrigine oral suspension 10 mg/mL	OWP	• Adjunctive therapy for the following seizure types in patients aged 2 years and older: ○ partial-onset seizures ○ primary generalized tonic-clonic (PGTC) seizures ○ generalized seizures of Lennox-Gastaut syndrome • Conversion to monotherapy in adults (aged 16 years and older) with partial-onset seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single antiepileptic drug (AED) • Maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in patients treated for acute mood episodes with standard therapy	\$720 per 8 oz bottle	Lamotrigine tabs, chewables, ODT	Non-formulary
Lasix ONYU	furosemide subcutaneous cartridge kit 80 mg/2.67 mL, reusable unit/charg miscellaneous	SQ Innovation	• For the treatment of edema in adult patients with chronic heart failure	\$475 per 80 dose unit, \$300 for device	Furosemide IV or oral tablets	Non-formulary
Hymovis One	hyaluronan intra-articular solution prefilled syringe 32 mg/4 mL	FIDIA	• For the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy or simple analgesics (e.g., acetaminophen)	\$667 per syringe	Synvisc, Hyalgan	Non-formulary
Kymbee	deflazacort oral tablet 6 mg, 18 mg, 30 mg, 36 mg	Upsher-Smith	• For the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older <i>Additional pediatric use information is approved for PTC Therapeutics, Inc.'s Emflaza® (deflazacort) tablets. However, due to PTC Therapeutics, Inc.'s marketing exclusivity rights, this drug product is not labeled with that information.</i>	\$16,577 (30 mg dose, variable based on weight)	Other generic deflazacort	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Piperacillin-Tazobactam-NaCl	piperacillin-tazobactam-nacl intravenous solution reconstituted3-0.375 gm/50mL	B. Braun Medical	Treatment of: - Intra-abdominal infections in adult and pediatric patients 2 months of age and older - Nosocomial pneumonia in adult and pediatric patients 2 months of age and older - Skin and skin structure infections in adults - Female pelvic infections in adults - Community-acquired pneumonia in adults	\$23 per 50 mL bag	Other IV beta-lactam antibiotics, other generic piperacillin-tazobactam products	Non-formulary
Famotidine	famotidine intravenous solution 20 mg/5 mL, 40 mg/10 mL, 200 mg/50 mL	Sagent	For use in hospitalized adults, or as an alternative to oral famotidine in adults, for the treatment of: - active duodenal ulcer (DU) - active gastric ulcer (GU) - symptomatic nonerosive gastroesophageal reflux disease (GERD) - erosive esophagitis due to GERD, diagnosed by endoscopy - treatment of pathological hypersecretory conditions (e.g., Zollinger-Ellison syndrome, multiple endocrine neoplasias) - reduction of the risk of duodenal ulcer recurrence Pediatric Patients 1 Year of Age and Older - Famotidine Injection is indicated in hospitalized pediatric patients 1 year of age and older, or as an alternative to oral famotidine in pediatric patients 1 year of age and older, for the treatment of peptic ulcer disease	\$5 per 5mL dose, \$10 per 10 mL dose, \$6,400 per 50 mL vial	Other generic famotidine	Non-formulary
Lymphir	denileukin diftitox-cxdl intravenous solution reconstituted 300 mcg	Citius	For the treatment of adult patients with relapsed or refractory Stage I-III cutaneous T-cell lymphoma (CTCL) after at least one prior systemic therapy	\$94,380	Poteligeo, Adcetris, bexarotene	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Tyvaso DPI	treprostinil DPI maintenance kit inhalation powder 112 x 32mcg & 112 x64mcg, 112 x 48mcg & 112 x64mcg	United Therapeutics	- Treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability - Treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability	\$44,296 per 28 days	Treprostinil IV/SC	Non-formulary
Desloratadine	desloratadine oral solution 0.5 mg/mL	INA	Seasonal Allergic Rhinitis - Desloratadine oral solution is indicated for the relief of the nasal and non-nasal symptoms of seasonal allergic rhinitis in patients 2 years of age and older Perennial Allergic Rhinitis - Desloratadine oral solution is indicated for the relief of the nasal and non-nasal symptoms of perennial allergic rhinitis in patients 6 months of age and older Chronic Idiopathic Urticaria - Desloratadine oral solution is indicated for the symptomatic relief of pruritus, reduction in the number of hives, and size of hives, in patients with chronic idiopathic urticaria 6 months of age and older	\$7,500	Loratadine oral solution	Non-formulary
Komzifti	ziftomenib oral capsule 200 mg	Kura Oncology	A menin inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible nucleophosmin 1 (NPM1) mutation who have no satisfactory alternative treatment options	\$48,500	Revuforj	Non-formulary
Javadin	clonidine oral solution 0.02 mg/mL	Arbor	Treatment of hypertension in adult patients, to lower blood pressure	\$480	Clonidine oral tablet, transdermal patch	Non-formulary
Imaavy	nipocalimab-aahu intravenous solution 300 mg/1.62 mL	Janssen Biotech	Treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive	\$24,960 (maintenance dose for ~70kg patient)	Vyvgart, Vyvgart Hytrulo, Rystiggo	Non-formulary

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Redempro	plozasiran subcutaneous solution prefilled syringe 25 mg/0.5 mL	Arrowhead	An adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS)	\$15,000 per dose (every 3 months)	Tryngolza	Non-formulary (see updated MRG and PAD criteria)
Tyzavan	vancomycin intravenous solution 750 mg/150 mL, 500 mg/100 mL, 1750 mg/350 mL, 2000 mg/400 mL, 1250 mg/250 mL, 1500 mg/300 mL	Hikma	- Septicemia - Infective Endocarditis - Skin and Skin Structure Infections - Bone Infections - Lower Respiratory Tract Infections	\$9-\$36	Generic vancomycin	Non-formulary
Hyrnuo	sevabertinib oral tablet 10 mg	Bayer	For the treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) whose tumors have <i>HER2 (ERBB2)</i> tyrosine kinase domain (TKD) activating mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy	\$24,000	Hernexeos	Non-formulary
Voyxact	sibeprenlimab-szsi subcutaneous solution prefilled syringe 400 mg/2 mL	Otsuka	To reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk for disease progression	\$30,000	Filspari, Vanrafia, Fabhalta	Non-formulary (see updated MRG criteria)
Midazolam	midazolam intramuscular solution auto-injector 10 mg/0.7 mL	Rafa	For the treatment of status epilepticus in adults	\$200 per dose	Intranasal midazolam	Non-formulary
Itvisma	onasemnogene abeparvec-brve intrathecal suspension 1200000000000000 vg/3 mL	Novartis	For the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients 2 years of age and older with confirmed mutation in <i>survival motor neuron 1 (SMN1)</i> gene	\$2.6 M	Spinraza, Evrysdi	Non-formulary (see new and updated PAD criteria)
Omlonti	omidenepag isopropyl ophthalmic solution 0.002 %	Ocuvex	For the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension	\$350	latanoprost	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Heparin	heparin sodium (porcine) +RFID injection solution 1000 unit/mL	Fresenius Kabi	• Prophylaxis and treatment of venous thrombosis and pulmonary embolism; • Prevention of postoperative deep venous thrombosis and pulmonary embolism in patients undergoing major abdominothoracic surgery or who, for other reasons, are at risk of developing thromboembolic disease; • Atrial fibrillation with embolization; • Treatment of acute and chronic consumptive coagulopathies (disseminated intravascular coagulation); • Prevention of clotting in arterial and cardiac surgery; • Prophylaxis and treatment of peripheral arterial embolism • Anticoagulant use in blood transfusions, extracorporeal circulation, and dialysis procedures	\$7 per vial	None	Non-formulary
OmvoH	mirikizumab subcutaneous solution prefilled syringe, auto- injector 200 mg/2 mL	Lilly	• Moderately to severely active ulcerative colitis in adults • Moderately to severely active Crohn's disease in adults	\$10,879	Adalimumab, ustekinumab	Non-formulary
Piperacillin- Tazobactam- NaCl	piperacillin-tazobactam- nacl intravenous solution reconstituted 2-0.25 gm/50 mL	B. Braun Medical	Treatment of: • Intra-abdominal infections in adult and pediatric patients 2 months of age and older • Nosocomial pneumonia in adult and pediatric patients 2 months of age and older • Skin and skin structure infections in adults • Female pelvic infections in adults • Community-acquired pneumonia in adults	\$18 per 50 mL bag	Other IV beta-lactam antibiotics, other generic piperacillin- tazobactam products	Non-formulary
Pokonza	potassium chloride oral packet 15 meq	Carwin	• For the treatment and prophylaxis of hypokalemia with or without metabolic alkalosis, in patients for whom dietary management with potassium-rich foods or diuretic dose reduction is insufficient)	\$1,291	Potassium chloride tablets	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Ranitidine [#]	ranitidine oral tablet 150 mg, 300 mg	Rising	• Short- term treatment of active duodenal ulcer. Most patients heal within 4 weeks. Studies available to date have not assessed the safety of Ranitidine in uncomplicated duodenal ulcer for periods of more than 8 weeks. • Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of acute ulcers. No placebo- controlled comparative studies have been carried out for periods of longer than 1 year. • The treatment of pathological hypersecretory conditions (e.g., Zollinger-Ellison syndrome and systemic mastocytosis). • Short-term treatment of active, benign gastric ulcers. Most patients heal within 6 weeks and the usefulness of further treatment has not been demonstrated. Studies available to date have not assessed the safety of ranitidine in uncomplicated, benign gastric ulcer for periods of more than 6 weeks. • Maintenance therapy for gastric ulcer patients at reduced dosage after healing of acute ulcers. Placebo- controlled studies have been carried out for 1 year. • Treatment of GERD. Symptomatic relief commonly occurs within 24 hours after starting therapy with Ranitidine Tablets USP, 150 mg twice daily. • Treatment of endoscopically diagnosed erosive esophagitis. Symptomatic relief of heartburn commonly occurs within 24 hours of therapy initiation with Ranitidine Tablets USP, 150 mg 4 times daily. • Maintenance of healing of erosive esophagitis. Placebo- controlled trials have been carried out for 48 weeks.	\$398-\$792	famotidine	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Adalimumab-bwwd	adalimumab-bwwd subcutaneous solution auto-injector, prefilled syringe, 40 mg/0.4mL	Cordavis	- Rheumatoid arthritis - Polyarticular juvenile idiopathic arthritis - Active psoriatic arthritis - Active ankylosing spondylitis - moderately to severely active Crohn’s disease - moderately to severely active ulcerative colitis - moderate to severe chronic plaque psoriasis - moderate to severe hidradenitis suppurativa - non-infectious intermediate, posterior, and panuveitis	\$450 per dose	Other biosimilar adalimumab products	Add to F-QL (see updated MRG criteria)
Perampanel	perampanel oral suspension 0.5 mg/mL	Novadoz	- Treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy 4 years of age and older - Adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients with epilepsy 12 years of age and older	\$3,175	Other anticonvuslants (ex. topiramate)	Non-formulary
Cryselle [#]	norgestrel-ethinyl estradiol oral tablet 0.3-30 mg-mcg	Teva	For use by females of reproductive potential to prevent pregnancy.	\$23	Yaz, Loestrin FE, Ortho Tri Cyclen	Add to F
Jaythari	deflazacort oral suspension 22.75 mg/mL	Zydus	- For the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older. <i>Additional pediatric use information is approved for PTC Therapeutics, Inc.'s Emflaza™ (deflazacort) tablets. However, due to PTC Therapeutics, Inc.'s marketing exclusivity rights, this drug product is not labeled with that information.</i>	\$14,000 (22.75 mg dose, variable based on weight)	Other generic deflazacort	Non-formulary
Wegovy	semaglutide oral tablet 1.5 mg, 4 mg, 9 mg, 25 mg	Novo Nordisk	- To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight. - To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition.	\$1,349	Wegovy injection, Zepbound	F-PA-QL (already added via CRF; QL: 30/30; see updated MRG criteria)

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Exdensur	depemokimab-ulaa subcutaneous solution prefilled syringe 100 mg/mL	GlaxoSmithKline	For add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype in adult and pediatric patients aged 12 years and older.	\$4,333	Nucala, Fasenra	Non-formulary (see updated MRG criteria)
Epioxa HD/ Epioxa	riboflavin 5-phosphate sodium ophthalmic prefilled syringe kit 0.239 & 0.177 %	Glaukos	Indicated in epithelium-on corneal collagen cross-linking for the treatment of keratoconus in adults and pediatric patients aged 13 years and older, in conjunction with the O2n System and the Boost Goggles.	\$78,000 for a kit	Photrex ^a , Photrex ^a Viscous	Non-formulary
Rybrevant Faspro	amivantamab and hyaluronidase-lpuj subcutaneous solution 1600-20000 mg-ut/10 mL, 2240-28000 mg- ut/14 mL	Janssen	- In combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test. - In combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor. - In combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test. - As a single agent for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA approved test, whose disease has progressed on or after platinum-based chemotherapy.	\$12,383 - \$17,336 per 10 mL, 14 mL unit; dosing variable per weight and indication	Rybrevant IV	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Vraylar	cariprazine oral capsule 0.5 mg, 0.75 mg	AbbVie	• Treatment of schizophrenia in adults and pediatric patients 13 years of age and older. • Acute treatment of manic or mixed episodes associated with bipolar I disorder in adults and pediatric patients 10 years of age and older. • Treatment of depressive episodes associated with bipolar I disorder in adults. • Adjunctive therapy to antidepressants for the treatment of major depressive disorder in adults.	\$1,519	Aripiprazole, quetiapine	Non-formulary
Potassium Chloride	potassium chloride oral packet 40 meq	IPG	• For the treatment and prophylaxis of hypokalemia with or without metabolic alkalosis, in patients for whom dietary management with potassium-rich foods or diuretic dose reduction is insufficient	\$2,582	Potassium chloride tablets	Non-formulary
Xpovio	selinexor (80 mg once weekly) oral tablet therapy pack 80 mg	Karyopharm	• In combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. • In combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody. • For the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).	\$34,722	Indication dependent, oncology therapy	Non-formulary
Cardamyst	etripamil nasal solution 2 x 70 mg/dose	Milestone	• For the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia to sinus rhythm in adults.	\$1,650 for a 2-dose package	None	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Beizray	docetaxel intravenous concentrate 20 mg/mL	Zhuhai	- Breast Cancer (BC): single agent for locally advanced or metastatic BC after chemotherapy failure; and with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positive BC - Non-small Cell Lung Cancer (NSCLC): single agent for locally advanced or metastatic NSCLC after platinum therapy failure; and with cisplatin for unresectable, locally advanced or metastatic untreated NSCLC - Castration-Resistant Prostate Cancer (CRPC): with prednisone in metastatic castration-resistant prostate cancer - Gastric Adenocarcinoma (GC): with cisplatin and fluorouracil for untreated, advanced GC, including the gastroesophageal junction - Squamous Cell Carcinoma of the Head and Neck (SCCHN): with cisplatin and fluorouracil for induction treatment of locally advanced SCCHN	\$895 per vial, dosing is BSA and indication dependent	Indication dependent, oncology therapy	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.
#	Re-activation of previously discontinued product (i.e., other available NDCs now inactive)