PHARMACY & THERAPEUTICS COMMITTEE

Tuesday, June 11th, 2024
5:00pm – 7:00pm

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

Location: Microsoft Teams
Meeting ID: 213 313 432 781
Password: 7XjZ2F

IMPORTANT PUBLIC HEALTH AND SAFETY MESSAGE REGARDING PARTICIPATION AT ALAMEDA ALLIANCE FOR HEALTH COMMITTEE MEETINGS

STATE OR LOCAL OFFICIALS CONTINUE TO IMPOSE OR RECOMMEND MEASURES TO PROMOTE SOCIAL DISTANCING. AS A RESULT OF THE COVID-19 VIRUS, AND RESULTING ORDERS AND DIRECTION FROM THE PRESIDENT OF THE UNITED STATES, THE GOVERNOR OF THE STATE OF CALIFORNIA, AND THE ALAMEDA COUNTY HEALTH OFFICER, THE PUBLIC WILL NOT BE PERMITTED TO PHYSICALLY ATTEND THE ALAMEDA ALLIANCE FOR HEALTH MEETING TO WHICH THIS AGENDA APPLIES.
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 mhoy@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,,891789508#. IF YOU USE THE LINK AND PARTICIPATE VIA COMPUTER, YOU MAY, THROUGH THE USE OF THE CHAT FUNCTION, REQUEST AN OPPORTUNITY TO SPEAK ON ANY AGENDIZED ITEM, INCLUDING GENERAL PUBLIC COMMENT. YOUR REQUEST TO SPEAK MUST BE RECEIVED BEFORE THE ITEM IS CALLED ON THE AGENDA. IF YOU PARTICIPATE BY TELEPHONE, YOU MAY SUBMIT ANY COMMENTS VIA THE E-COMMENT EMAIL ADDRESS DESCRIBED ABOVE OR PROVIDE COMMENT DURING THE MEETING AT THE END OF EACH TOPIC.

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

AGENDA

ITEM	DESCRIPTION	TIME	VOTE
I)	**Call to order** *Donna Carey, MD, Interim Chief Medical Officer – Alameda Alliance* • Agenda Overview	2 min	-
II)	**Informational Updates** *Donna Carey, MD, Interim Chief Medical Officer – Alameda Alliance* *Helen Lee, PharmD, MBA, Senior Pharmacy Director – Alameda Alliance* • CalAIM Updates (ECM, CS, TCS, LTC, ICF-DD, BH/ABA) • DHCS Audit • DSNP Readiness • New P&T Member – Dr. Betsy Yuan • Medi-Cal Rx MCDAC Drugs (See Next Page)	15 min	-
III)	**Pharmacy Utilization Reports (Quarter 1, 2024)** *Helen Lee, PharmD MBA, Senior Pharmacy Director – Alameda Alliance* • Top 50 Drugs by Cost • Top 50 PA Reviewed Drugs	2 min	-

MCDAC Drug	Indication	CDL Status	Recommendation Based on - Safety, Efficacy, Essential Need, Misuse Potential, etc.
Opvee®(nalmefene) 2.7mg/0.1ml Nasal Spray	Emergency treatment of known or suspected overdose induced by natural or synthetic opioids in adults and pediatric patients aged 12 years and older.	F-PA	Keep F-PA
Tyenne®(tocilizumab-aazg)	Rheumatoid Arthritis, Giant Cell Arteritis, Polyarticular Juvenile Idiopathic Arthritis, and Systemic Juvenile Idiopathic Arthritis.	F-PA	Keep F-PA

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

Discussion will Concern: *Review and Recommendations to changes to the AAH Formulary and utilization management for selected drug classes*
Estimated Date of Public Disclosure: 6/11/2024 *(formulary changes only; no trade secrets will be disclosed)*

IV) E-Voting Material/Consent Agenda

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

Helen Lee, PharmD, MBA, 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 closedsession.)

Monographs/Class Reviews	Changes
Opioid Use Disorder Agents Class Review (with PA criteria)	• No changes
Phosphate Binders Class Review (with PA criteria)	• No changes
Benign Prostatic Hyperplasia (BPH) Class Review	• No changes
Contraceptives foams, devices Class	• No changes
Gaucher Disease Class Review	• No changes
Ridaura Monograph	• No changes
Medication Request Guidelines	**Changes**
Opioid Use Disorder (OUD) Agents	• No changes
Phosphate Binders	• No changes
Formulary, step therapy required *For drugs without specific criteria	• No changes
Non-formulary and prior authorization required oral liquid formulations	• No changes

10 min EV

Cholinesterase Inhibitors	• No changes
febuxostat (Uloric)	• No changes
Lamotrigine ER	• No changes
Levalbuterol (Xopenex/Xopenex HFA)	• No changes
Lidocaine Patch	• Remove Gen7T and Synera as they have been
Potassium-removing agents	• No changes
Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	• Minor wording change for clarity
Fenofibrates	• Remove generic Antara as it has been discontinued
Nutritional formulas, infant formulas (STC C5F C5C)	• Remove STC information, as this refers to FDB
Lipotropics	• No changes
Long acting opioids	• No changes
Serotonin Receptor Agonists (Triptans)	• No changes
Pregabalin (Lyrica and Lyrica CR)	• No changes
Rufinamide (Banzel)	• No changes
vigabatrin (Sabril)	• Corrected minor grammar error to be consistent with package insert
Sedative Hypnotics	• Remove Zolpimist as it has been discontinued
Epidiolex (cannabidiol)	• No changes
Tiagabine (Gabitril)	• No changes
Topiramate (Topamax) sprinkles	• No changes
Hepatitis C Medications	• Change to treatment summary in recommended regimens for patients who have failed Mavyret treatment and require Vosevi
Short acting opioid containing	• No changes
Hemlibra (emicizumab-kxwh)	• No changes
Aptiom (eslicarbazepine)	• No changes
Alprazolam (Xanax)	• No changes
Rectiv (nitroglycerin) ointment	• No changes
Diuretics	• No changes
Sleep Disorder Therapy	• No changes
Palforzia	• No changes

Gonadotropin Releasing Hormone	• Streamlining language and abbreviations
Lupkynis	• Update diagnostic requirement wording for simplicity
Radicava ORS (edaravone)	• No changes
Daybue (trofinetide)	• No changes
Filspari	• No changes
Joenja	• No changes
Skyclarys (omaveloxolone)	• No changes
Physician Administered Drug (PAD) Guidelines	**Changes**
Leqembi	• Update coverage duration language for clarity
B-Cell Maturation Antigen (BCMA) Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy	• No changes
Naglazyme	• No changes
Radicava (edaravone)	• No changes
Interim Formulary Updates	
• See p. 154 in packet	
Summary of Physician Administered Drug (PAD) Updates	
• None	
Pharmacy Policy & Procedure Updates	
• RX-012 - DU Policies - Pharmacy Portal DU Access	• Cleaned and updated document to reflect current policy post Magellan to Prime transition.
• RX-013 -Physician Facility-Administered Drugs	• Updated policy for clarity (e.g., COC).
ED Oversight	
• None	
90 Day Maintenance List updates	
• Annual review – no additions	
P&T Meeting Minutes	
• P&T Meeting Minutes Q1 March 19, 2024	

New Business

Iryna Makukh, PharmD, Pharmacist – PerformRx

New PADs

- Amtagvi
- Lenmeldy

New MRGs

- Filsuvez
- Complement Inhibitors for the Treatment of Myasthenia Gravis Agents
- Eohilia
- Wegovy

45 min V

Class Reviews, Monographs, and Recommendations

Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Rezdiffra monograph
   a. New MRG: Rezdiffra
2. Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists Class Review

Medication Request Guidelines

Rahel Negash, PharmD, Pharmacist – Alameda Alliance

1. Hepatitis B Drugs
2. Transthyretin-mediated Amyloidosis Agents
3. Medications for Attention Deficit Hyperactivity Disorder (ADHD) and Narcolepsy
4. Roflumilast (Daliresp)
5. Injectable Atypical Antipsychotic Medications
6. Hereditary Angioedema (HAE)
7. Adenosine Triphosphate-Citrate Lyase (ACL) inhibitors
8. Xolair for Asthma and Urticaria
9. Anti-Obesity Medications

Physician Administered Drug (PAD) Policies

Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Aduhelm
2. Anti-CD19 CAR-T Immunotherapies
3. SMN2 Splicing Modifiers for the Treatment of Spinal Muscular Atrophy (SMA)
4. Generalized Pustular Psoriasis (GPP) Agents
5. Vyjuvek

10 min V

Informational Updates on New Developments in Pharmacy

Iryna Makukh, PharmD, Pharmacist – PerformRx

- New Product Review

2 min -

Old Business

Iryna Makukh, PharmD, Pharmacist – PerformRx

- None

2 min -

RECONVENE IN OPEN SESSION

Public Comment

Adjournment

ACTION / FOLLOW-UP ITEMS		
ITEM	**DUE DATE**	**RESPONSIBLE**

FUTURE P&T MEETINGS	
NEXT MEETING	**2024 P&T MEETINGS**
September 24, 2024	December 17, 2024

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 Helen Lee at 510-747- 6241 or hlee@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 1st Quarter 2024

- The top 50 drugs accounted for **1,076 claims** for **590 members** and cost **$1,357,202,** which is an increase of $237,924 in spend from the previous quarter.
- Biktarvy remains at number one, claims have gone up by 5, and there is one additional member since the previous quarter.
- Zejula is up to number 2 with 3 claims for 1 member. This medication is managed via the Oral and Injectable Oncology Medications MRG.
- Vemlidy is down to number 3 with 47 claims for 19 members. This medication is managed via the Hepatitis B MRG, which was loosened during Q4 2022 P&T to require trial and failure of, or reason not to use, entecavir (previously generic Viread and entecavir).
- Ozempic is at numbers 4, 6 and 11, with 181 total claims for 89 members. There was an increase of 40 claims and of 17 members from the previous quarter.
- Tagrisso is at number 5 with 4 claims for one member. There was an increase of one claim for one member from the previous quarter. This medication is managed via the Oncology MRG.

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
1	201625	Biktarvy Oral Tablet 50-200-25 MG	30	10	$114,527.83
2	223302	Zejula Oral Tablet 100 MG	3	1	$106,178.85
3	195609	Vemlidy Oral Tablet 25 MG	47	19	$71,263.97
4	209911	Ozempic (1 MG/DOSE) Subcutaneous Solution Pen-injector 4 MG/3ML	74	33	$68,914.76
5	190947	Tagrisso Oral Tablet 80 MG	4	1	$64,083.03
6	221271	Ozempic (0.25 or 0.5 MG/DOSE) Subcutaneous Solution Pen-injector 2 MG/3ML	68	39	$63,303.67
7	214809	Skyrizi Pen Subcutaneous Solution Auto-injector 150 MG/ML	3	2	$60,736.01
8	202548	Humira Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	4	1	$53,770.28
9	170343	Jakafi Oral Tablet 5 MG	3	1	$49,964.40
10	199757	Verzenio Oral Tablet 50 MG	3	1	$44,323.50
11	218338	Ozempic (2 MG/DOSE) Subcutaneous Solution Pen-injector 8 MG/3ML	39	17	$36,356.03
12	207961	Rybelsus Oral Tablet 7 MG	33	16	$30,759.38

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
13	120505	Sprycel Oral Tablet 20 MG	2	1	$29,855.32
14	139308	Promacta Oral Tablet 25 MG	4	1	$28,105.29
15	193034	Ocaliva Oral Tablet 5 MG	3	1	$26,752.65
16	122702	Januvia Oral Tablet 100 MG	50	20	$26,460.46
17	185810	Trulicity Subcutaneous Solution Pen-injector 0.75 MG/0.5ML	28	11	$26,383.85
18	177191	Eliquis Oral Tablet 5 MG	45	22	$25,384.25
19	197146	Cosentyx Sensoready (300 MG) Subcutaneous Solution Auto-injector 150 MG/ML	3	1	$21,349.31
20	201117	Steglatro Oral Tablet 15 MG	64	24	$21,308.94
21	219135	Skyrizi Subcutaneous Solution Cartridge 360 MG/2.4ML	1	1	$20,666.08
22	192429	Taltz Subcutaneous Solution Auto-injector 80 MG/ML	3	1	$20,494.68
23	201116	Steglatro Oral Tablet 5 MG	54	25	$20,439.23
24	212379	Cabenuva Intramuscular Suspension Extended Release 600 & 900 MG/3ML	3	2	$18,140.79
25	219459	Paxlovid (300/100) Oral Tablet Therapy Pack 20 x 150 MG & 10 x 100MG	31	31	$17,628.99
26	176358	Xeljanz Oral Tablet 5 MG	3	1	$17,133.30
27	182488	Glatiramer Acetate Subcutaneous Solution Prefilled Syringe 40 MG/ML	3	1	$16,013.49
28	217445	Tarpeyo Oral Capsule Delayed Release 4 MG	1	1	$15,968.13
29	204204	Shingrix Intramuscular Suspension Reconstituted 50 MCG/0.5ML	75	72	$15,619.17
30	190802	Genvoya Oral Tablet 150-150-200-10 MG	4	2	$15,602.35
31	207962	Rybelsus Oral Tablet 14 MG	16	8	$14,925.17

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
32	197463	Dupixent Subcutaneous Solution Prefilled Syringe 300 MG/2ML	4	1	$14,877.54
33	182336	Farxiga Oral Tablet 10 MG	25	10	$13,788.29
34	184849	Jardiance Oral Tablet 25 MG	23	11	$13,366.49
35	207960	Rybelsus Oral Tablet 3 MG	14	12	$13,036.55
36	197908	Tymlos Subcutaneous Solution Pen-injector 3120 MCG/1.56ML	5	2	$12,886.85
37	170142	Xarelto Oral Tablet 20 MG	22	9	$12,589.92
38	185813	Trulicity Subcutaneous Solution Pen-injector 1.5 MG/0.5ML	13	8	$12,235.04
39	217440	Apretude Intramuscular Suspension Extended Release 600 MG/3ML	3	2	$11,393.25
40	93533	Entecavir Oral Tablet 0.5 MG	37	17	$10,907.14
41	192096	Odefsey Oral Tablet 200-25-25 MG	3	1	$10,666.74
42	127437	FreeStyle Lite Test In Vitro Strip	137	91	$10,288.41
43	223763	Arexvy Intramuscular Suspension Reconstituted 120 MCG/0.5ML	28	28	$7,947.07
44	176224	Linzess Oral Capsule 145 MCG	15	7	$7,692.84
45	211382	Dupixent Subcutaneous Solution Pen-injector 300 MG/2ML	2	1	$7,545.98
46	193670	Xiidra Ophthalmic Solution 5 %	11	6	$7,434.46
47	17581	Premarin Vaginal Cream 0.625 MG/GM	18	12	$7,334.63
48	205122	Actemra ACTPen Subcutaneous Solution Auto-injector 162 MG/0.9ML	2	1	$7,159.82
49	181560	Actemra Subcutaneous Solution Prefilled Syringe 162 MG/0.9ML	3	1	$7,075.03
50	212085	Trulicity Subcutaneous Solution Pen-injector 4.5 MG/0.5ML	7	3	$6,562.92
TOTAL			**1076**	**590**	**$1,357,202.13**

Medi-Cal Top 50 Drugs by Cost for 1st Quarter 2024

- The top 50 drugs accounted for **36,007 claims** for **30,640 members** and cost **$48,416,394.87,** which is an increase of $6,868,129.68 in spend from the previous quarter.
- Biktarvy remains at the number 1 spot with 850 claims for 653 members. An increase of 174 claims from last quarter.
- Ozempic has risen from number 3 to number 2, with 1,877 claims for 1,521 members. This is an increase of 403 claims from last quarter.
- Humira has also risen from the number 4 from the number 3 spot with 129 claims for 106 members. This is an increase of 20 claims since last quarter.
- Jardiance 10mg has moved up to the number 4 spot from number 6, with 1,647 claims for 1,485 members. This is an increase of 496 claims from last quarter.
- Jardiance 25mg remains at the number 5 spot with 1,536 claims for 1,435 members. This is an increase of 139 claims from last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	44426	BIKTARVY 50-200-25 MG TABLET	850	653	$5,548,080.07
2	53536	OZEMPIC 0.25-0.5 MG/DOSE PEN	1877	1521	$2,657,616.71
3	43506	HUMIRA(CF) PEN 40 MG/0.4 ML	129	106	$2,197,550.20
4	36716	JARDIANCE 10 MG TABLET	1647	1485	$2,105,275.80
5	36723	JARDIANCE 25 MG TABLET	1536	1435	$2,076,795.96
6	49591	SKYRIZI 150 MG/ML PEN	89	77	$2,026,513.32
7	48208	OZEMPIC 1 MG/DOSE (4 MG/3 ML)	979	831	$1,748,337.33
8	28159	STELARA 90 MG/ML SYRINGE	39	36	$1,381,033.53
9	48277	DUPIXENT 300 MG/2 ML PEN	159	127	$1,265,564.77
10	97400	JANUVIA 100 MG TABLET	892	822	$1,238,488.78
11	42624	VEMLIDY 25 MG TABLET	402	338	$1,122,050.37
12	27418	INVEGA SUSTENNA 234 MG/1.5 ML	168	130	$1,057,629.43
13	33935	ELIQUIS 5 MG TABLET	972	774	$1,020,423.13

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
14	49099	CABENUVA ER 600 MG-900 MG SUSP	129	114	$1,006,041.49
15	52125	OZEMPIC 2 MG/DOSE (8 MG/3 ML)	531	435	$1,005,470.64
16	97724	ENBREL 50 MG/ML SURECLICK	72	61	$938,145.35
17	25200	FREESTYLE LITE TEST STRIP	4775	4442	$930,732.53
18	46965	RYBELSUS 7 MG TABLET	431	395	$876,333.58
19	40133	TAGRISSO 80 MG TABLET	30	21	$791,975.96
20	34394	FARXIGA 10 MG TABLET	595	519	$783,981.59
21	98637	BASAGLAR 100 UNIT/ML KWIKPEN	1569	1306	$766,193.52
22	40953	DESCOVY 200-25 MG TABLET	220	171	$745,144.64
23	43968	SYMTUZA 800-150-200-10 MG TAB	100	78	$734,223.71
24	47136	TRIKAFTA 100-50-75 MG/150 MG	11	10	$713,191.16
25	46966	RYBELSUS 14 MG TABLET	313	288	$679,085.28
26	22913	ALBUTEROL HFA 90 MCG INHALER	14230	11733	$677,822.15
27	44014	HUMIRA(CF) PEN 80 MG/0.8 ML	19	18	$672,623.45
28	49754	WEGOVY 2.4 MG/0.75 ML PEN	306	228	$652,025.87
29	37169	TRULICITY 0.75 MG/0.5 ML PEN	443	361	$634,961.50
30	43699	MAVYRET 100-40 MG TABLET	40	40	$632,910.89
31	40092	GENVOYA TABLET	87	71	$628,990.63
32	37789	COSENTYX SNRDY 300MG DOSE-2PEN	41	30	$613,379.15
33	37682	ABILIFY MAINTENA ER 400 MG SYR	119	90	$579,092.46
34	47426	VYONDYS-53 100 MG/2 ML VIAL	2	2	$556,879.20

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
35	38702	INVEGA TRINZA 819 MG/2.63 ML	51	51	$549,081.65
36	97005	HUMIRA PEN 40 MG/0.8 ML	46	36	$517,866.36
37	43505	HUMIRA(CF) 40 MG/0.4 ML SYRING	23	20	$502,306.85
38	30819	XARELTO 20 MG TABLET	427	371	$486,744.28
39	43222	DUPIXENT 300 MG/2 ML SYRINGE	59	51	$469,790.87
40	43148	ILARIS 150 MG/ML VIAL	9	7	$466,725.17
41	44495	ZTLIDO 1.8% TOPICAL SYSTEM	926	815	$460,727.51
42	49055	TAKHZYRO 300 MG/2 ML SYRINGE	3	2	$460,583.31
43	49487	APRETUDE ER 600 MG/3 ML VIAL	98	89	$459,949.41
44	37633	ODEFSEY TABLET	75	58	$455,281.15
45	36999	TRIUMEQ 600-50-300 MG TABLET	75	61	$446,450.64
46	45169	EPIDIOLEX 100 MG/ML SOLUTION	70	49	$426,481.87
47	44106	HEMLIBRA 105 MG/0.7 ML VIAL	4	3	$421,804.40
48	48574	TRULICITY 3 MG/0.5 ML PEN	227	198	$413,815.70
49	39858	STRENSIQ 80 MG/0.8 ML VIAL	1	1	$411,879.60
50	28530	XIFAXAN 550 MG TABLET	111	80	$402,341.95
TOTAL			**36,007**	**30,640**	**$48,416,394.87**

636 IHSS Top 50 Prior Authorization Requests by Volume for 1st Quarter 2024

- Top 50 PA requests = 200. There were 258 total PA requests for quarter 1.
  - 69 requests (35%) were approved. This approval rate is lower, by 13%, than what was observed last quarter.
  - 131 requests (65%) were denied or partially approved.
- Wegovy is up at numbers 1, 10, 13, 23, and 24 with 39 total requests and 5 approvals (13%).
  - Wegovy requires a diagnosis of obesity or BMI ≥27 and at least one weight-related comorbidity (diabetes, hypertension, hyperlipidemia) or history of heart attack, despite diet and exercise, and trial and failure or inability to use Qsymia and Contrave.
- Jardiance is at numbers 2 & 8 with 21 total requests and 6 approvals (29%).
  - The formulary alternative is Steglatro, with trial and failure of metformin.
  - During the Q1 Alameda P&T meeting the SGLT2 Inhibitors and Combinations criteria were updated to include a 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.
- Lidocaine 5% patch and Ozempic 0.25-0.5 mg/dose is at number 3 and 4 with 12 requests and 1 approval (8%) for each drug.
  - Lidocaine requires a diagnosis of neuropathic pain and a trial and failure of gabapentin or pregabalin and one other formulary alternative used for neuropathic pain or morphine MME ≤ 50 for 3 months.
  - Ozempic requires a trial and failure of metformin.
- Vemlidy 25 mg is down to number 5 and had a total of 11 requests, from which there were 7 approvals (64%).
  - Vemlidy requires a diagnosis of Hepatitis B, and trial and failure of, intolerance to, or inability to use entecavir tablets.
- Xiidra is at number 6 with 10 requests and 2 approvals (20%).
  - Xiidra requires trial and failure or inability to use artificial tears and cyclosporine (Restasis) 0.05% dropperette.

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
1	Wegovy Subcutaneous Solution Auto-injector 0.25 MG/0.5ML	22	4	18.18%	17	77.27%	1	4.55%
2	Jardiance Oral Tablet 10 MG	13	3	23.08%	9	69.23%	1	7.69%
3	Lidocaine External Patch 5 %	12	1	8.33%	11	91.67%	0	0.0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
4	Ozempic (0.25 or 0.5 MG/DOSE) Subcutaneous Solution Pen-injector 2 MG/3ML	12	1	8.33%	10	83.33%	1	8.33%
5	Vemlidy Oral Tablet 25 MG	11	7	63.64%	3	27.27%	1	9.09%
6	Xiidra Ophthalmic Solution 5 %	10	2	20.0%	6	60.0%	2	20.0%
7	Entecavir Oral Tablet 0.5 MG	9	8	88.89%	0	0.0%	1	11.11%
8	Jardiance Oral Tablet 25 MG	8	3	37.5%	5	62.5%	0	0.0%
9	Contrave Oral Tablet Extended Release 12 Hour 8-90 MG	6	3	50.0%	3	50.0%	0	0.0%
10	Wegovy Subcutaneous Solution Auto-injector 0.5 MG/0.5ML	6	1	16.67%	4	66.67%	1	16.67%
11	Zepbound Subcutaneous Solution Auto-injector 2.5 MG/0.5ML	6	1	16.67%	3	50.0%	2	33.33%
12	Tretinoin External Cream 0.025 %	5	1	20.0%	4	80.0%	0	0.0%
13	Wegovy Subcutaneous Solution Auto-injector 1 MG/0.5ML	5	0	0.0%	5	100.0%	0	0.0%
14	cycloSPORINE Ophthalmic Emulsion 0.05 %	4	3	75.0%	1	25.0%	0	0.0%
15	Saxenda Subcutaneous Solution Pen-injector 18 MG/3ML	4	1	25.0%	3	75.0%	0	0.0%
16	Tretinoin External Cream 0.05 %	4	3	75.0%	1	25.0%	0	0.0%
17	Dupixent Subcutaneous Solution Pen-injector 300 MG/2ML	3	2	66.67%	0	0.0%	1	33.33%
18	Febuxostat Oral Tablet 40 MG	3	1	33.33%	2	66.67%	0	0.0%
19	Otezla Oral Tablet 30 MG	3	1	33.33%	2	66.67%	0	0.0%
20	Rybelsus Oral Tablet 3 MG	3	2	66.67%	1	33.33%	0	0.0%
21	Rybelsus Oral Tablet 7 MG	3	0	0.0%	1	33.33%	2	66.67%
22	Tranexamic Acid Oral Tablet 650 MG	3	1	33.33%	1	33.33%	1	33.33%
23	Wegovy Subcutaneous Solution Auto-injector 1.7 MG/0.75ML	3	0	0.0%	3	100.0%	0	0.0%
24	Wegovy Subcutaneous Solution Auto-injector 2.4 MG/0.75ML	3	0	0.0%	2	66.67%	1	33.33%
25	Buprenorphine HCl-Naloxone HCl Sublingual Film 8-2 MG	2	2	100.0%	0	0.0%	0	0.0%
26	Ezetimibe Oral Tablet 10 MG	2	0	0.0%	2	100.0%	0	0.0%
27	Farxiga Oral Tablet 10 MG	2	1	50.0%	1	50.0%	0	0.0%
28	Farxiga Oral Tablet 5 MG	2	1	50.0%	0	0.0%	1	50.0%
29	Jublia External Solution 10 %	2	0	0.0%	2	100.0%	0	0.0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
30	Linzess Oral Capsule 290 MCG	2	1	50.0%	1	50.0%	0	0.0%
31	Lubiprostone Oral Capsule 24 MCG	2	1	50.0%	1	50.0%	0	0.0%
32	Miebo Ophthalmic Solution 1.338 GM/ML	2	0	0.0%	2	100.0%	0	0.0%
33	Morphine Sulfate ER Oral Tablet Extended Release 15 MG	2	2	100.0%	0	0.0%	0	0.0%
34	Phentermine HCl Oral Tablet 37.5 MG	2	2	100.0%	0	0.0%	0	0.0%
35	Tacrolimus External Ointment 0.1 %	2	1	50.0%	0	0.0%	1	50.0%
36	Tadalafil Oral Tablet 20 MG	2	0	0.0%	2	100.0%	0	0.0%
37	Trelegy Ellipta Inhalation Aerosol Powder Breath Activated 100-62.5-25 MCG/ACT	2	0	0.0%	2	100.0%	0	0.0%
38	Acetylcysteine Inhalation Solution 20 %	1	1	100.0%	0	0.0%	0	0.0%
39	Actemra ACTPen Subcutaneous Solution Auto-injector 162 MG/0.9ML	1	1	100.0%	0	0.0%	0	0.0%
40	Actemra Subcutaneous Solution Prefilled Syringe 162 MG/0.9ML	1	1	100.0%	0	0.0%	0	0.0%
41	Acyclovir External Cream 5 %	1	0	0.0%	1	100.0%	0	0.0%
42	Adapalene External Gel 0.3 %	1	1	100.0%	0	0.0%	0	0.0%
43	Admelog SoloStar Subcutaneous Solution Pen-injector 100 UNIT/ML	1	0	0.0%	1	100.0%	0	0.0%
44	Ajovy Subcutaneous Solution Auto-injector 225 MG/1.5ML	1	0	0.0%	1	100.0%	0	0.0%
45	ALPRAZolam Oral Tablet 1 MG	1	1	100.0%	0	0.0%	0	0.0%
46	Atovaquone Oral Suspension 750 MG/5ML	1	1	100.0%	0	0.0%	0	0.0%
47	Azelaic Acid External Gel 15 %	1	1	100.0%	0	0.0%	0	0.0%
48	Basaglar KwikPen Subcutaneous Solution Pen-injector 100 UNIT/ML	1	1	100.0%	0	0.0%	0	0.0%
49	Breztri Aerosphere Inhalation Aerosol 160-9-4.8 MCG/ACT	1	0	0.0%	1	100.0%	0	0.0%
50	Calcipotriene External Solution 0.005 %	1	1	100.0%	0	0.0%	0	0.0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
TOTAL		**200**	**69**	**35%**	**114**	**57%**	**17**	**8%**

Medi-Cal Top 50 Prior Authorization Requests by Volume for 1st Quarter 2024

- The top 50 drugs accounted for **208,531 claims** for **187,022 members** and cost **$4,636,174.09.**
- Albuterol remains at the number 1 spot with 14,230 claims for 11,733 members. An increase of 684 claims from last quarter.
- Ibuprofen remains at the number 2 spot with 9,506 claims for 8,516 members. This is an increase of 1,661 claims from last quarter.
- Aspirin also remains at the sam spot with 9144 claims for 8,444 members. This is an increase of 1,305 claims from last quarter.
- Fluticasone remains at number 4 with 8,636 claims for 8,028 members. There was an increase of 1,252 claims from last quarter.
- Loratadine has risen from the number 6 spot to number 5 with 6,680 claims for 5,985 members. This is an increase of 1,496 claims from last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	22913	ALBUTEROL HFA 90 MCG INHALER	14230	11733	$677,822.15
2	35742	IBUPROFEN 600 MG TABLET	9506	8516	$137,448.93
3	00161	ASPIRIN EC 81 MG TABLET	9144	8444	$101,965.19
4	62263	FLUTICASONE PROP 50 MCG SPRAY	8636	8028	$184,181.02
5	60563	LORATADINE 10 MG TABLET	6680	5985	$110,685.91
6	45680	DICLOFENAC SODIUM 1% GEL	6462	5684	$198,884.82
7	49291	CETIRIZINE HCL 10 MG TABLET	5797	5340	$94,128.71
8	16965	ACETAMINOPHEN 500 MG CAPLET	5688	5143	$79,413.41
9	43722	ATORVASTATIN 40 MG TABLET	5455	5016	$80,846.30
10	02683	AMLODIPINE BESYLATE 5 MG TAB	5308	4800	$73,826.97
11	02682	AMLODIPINE BESYLATE 10 MG TAB	5061	4553	$72,477.95
12	25200	FREESTYLE LITE TEST STRIP	4775	4442	$930,732.53
13	10857	METFORMIN HCL 1,000 MG TABLET	4684	4342	$77,439.59

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
14	04348	OMEPRAZOLE DR 20 MG CAPSULE	4332	3735	$68,949.89
15	43721	ATORVASTATIN 20 MG TABLET	4277	3988	$60,829.44
16	10810	METFORMIN HCL 500 MG TABLET	4260	3750	$67,101.80
17	86212	POLYETHYLENE GLYCOL 3350 POWD	4236	3910	$108,339.06
18	46430	FAMOTIDINE 20 MG TABLET	4221	3693	$61,726.68
19	00781	GABAPENTIN 300 MG CAPSULE	4211	3462	$75,222.63
20	94422	VITAMIN D2 1.25MG(50,000 UNIT)	4073	3765	$59,499.94
21	94444	MONTELUKAST SOD 10 MG TABLET	3937	3640	$57,726.99
22	29840	BENZONATATE 100 MG CAPSULE	3528	3228	$51,292.82
23	43720	ATORVASTATIN 10 MG TABLET	3505	3271	$48,560.13
24	40120	PANTOPRAZOLE SOD DR 40 MG TAB	3491	2920	$55,701.10
25	12486	HYDROCODONE-ACETAMIN 5-325 MG	3477	2606	$52,223.19
26	09101	DOCUSATE SODIUM 100 MG SOFTGEL	3434	3052	$45,953.11
27	00223	VITAMIN D3 25 MCG TABLET	3393	3201	$42,058.99
28	16965	ACETAMINOPHEN 500 MG TABLET	3334	3010	$33,216.69
29	99882	VITAMIN D3 50 MCG SOFTGEL	3276	3146	$41,067.80
30	39661	AMOXICILLIN 500 MG CAPSULE	3241	3049	$44,841.75
31	20045	ONDANSETRON ODT 4 MG TABLET	3131	2860	$48,602.82
32	04695	FEROSUL 325 MG TABLET	3022	2734	$42,017.46
33	94781	FOLIC ACID 1 MG TABLET	2946	2506	$49,576.91

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
34	35793	NAPROXEN 500 MG TABLET	2854	2512	$48,066.71
35	14851	LOSARTAN POTASSIUM 50 MG TAB	2832	2564	$40,633.56
36	94200	FREESTYLE 28G LANCETS	2772	2661	$55,039.12
37	48191	TAMSULOSIN HCL 0.4 MG CAPSULE	2705	2320	$45,943.15
38	35744	IBUPROFEN 800 MG TABLET	2676	2325	$44,023.28
39	35930	CHILDREN IBUPROFEN 100 MG/5 ML	2672	2488	$50,787.32
40	35930	IBUPROFEN 100 MG/5 ML SUSP	2667	2472	$45,504.57
41	16391	TRAZODONE 50 MG TABLET	2641	2051	$43,180.55
42	16964	ACETAMINOPHEN 325 MG TABLET	2529	2376	$25,785.90
43	34824	HYDROCHLOROTHIAZIDE 25 MG TAB	2520	2284	$36,096.23
44	67076	AMOX-CLAV 875-125 MG TABLET	2494	2330	$42,893.63
45	93375	AMOXICILLIN 400 MG/5 ML SUSP	2479	2368	$44,785.89
46	14850	LOSARTAN POTASSIUM 25 MG TAB	2452	2215	$34,066.84
47	39802	CEPHALEXIN 500 MG CAPSULE	2431	2278	$36,796.92
48	35741	IBUPROFEN 400 MG TABLET	2429	2314	$34,292.06
49	13943	HYDROXYZINE HCL 25 MG TABLET	2372	1851	$37,969.33
50	14853	LOSARTAN POTASSIUM 100 MG TAB	2255	2061	$35,946.35
TOTAL			**208,531**	**187,022**	**$4,636,174.09**

Opioid Use Disorder

Therapeutic Class Review

CLASS OVERVIEW

Opioid use disorder (OUD) involves use of illicitly obtained heroin, misuse of prescribed opioid medications, or use of diverted opioid medications. OUD is a chronic, relapsing illness, associated with morbidity and mortality. In patients who have undergone withdrawal from opioids, maintenance treatment is used to prevent relapse. Pharmacotherapy options for long-term maintenance treatment include opioid agonists (methadone or buprenorphine), opioid antagonists (naltrexone), or opioid partial agonist combinations (buprenorphine/naloxone). Buprenorphine is generally associated with less sedation and risk of respiratory depression compared with methadone, and buprenorphine-based products may be prescribed in an outpatient setting with additional training, whereas methadone prescribing is limited only to licensed opioid treatment programs (OTPs). Due to better toxicity profile and ease of use, buprenorphine products are now available in several formulations, ranging from sublingual tablets to long-acting injections. Nationwide, there has been a movement among health plans to remove restrictions from medication assisted treatment in order to combat the opioid abuse epidemic.

Opioid overdoses have also been a leading cause of injury-related death over the last decade. Professional societies recommend prescription of naloxone to third parties (bystanders) as part of a harm reduction program. Bystander-administered naloxone by the intramuscular and intranasal routes can be used successfully to resuscitate opioid overdose patients. Providing opioid users, family members, and friends with naloxone, accompanied by teaching them how to recognize opioid toxicity, may reduce overdose mortality. Over the last few years, the FDA has approved several new formations of naloxone (Kloxxado®, Zimhi™) with higher potency. Opvee® (nalmefene) is an alternative to naloxone with a longer duration of action that was approved in 2023. Additionally, in 2023, the FDA made a landmark decision in approving an over-the-counter (OTC) version of Narcan®, making naloxone more accessible. OTC availability of naloxone ensures that patients and caregivers will be able to purchase it from retailers that do not have a pharmacy (e.g., grocery stores, convenience stores).

UTILIZATION FINDINGS

There were 30 claims for 20 members, for a total cost of $2,165 and an average cost per claim of $72. The most highly utilized medication was Naloxone 4 mg nasal spray, with 11 claims, followed by Buprenorphine/naloxone 2 mg-0.5 mg, 8 mg-2 mg sublingual tablets with 7 claims. There were 2 prior authorizations with 2 approvals (100%).

RECOMMENDATIONS

- No changes

CLINICAL SUMMARY

Opioid use disorder (OUD) involves use of illicitly obtained heroin, misuse of prescribed opioid medications, or use of diverted opioid medications. OUD is a chronic, relapsing illness, associated with significant morbidity and mortality. The incidence of OUD and overdose deaths involving opioids has been increasing since the 1990s and has reached epidemic proportions. In the U.S., 5.7 million people were estimated in 2019 to have used heroin at some point in their lives, while 3.8 million people reported past month misuse of a prescription pain medication. The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines opioid use disorder as presence of two out of eleven outlined symptoms, including withdrawal, tolerance, interference in activities of daily living, and presence of opioid seeking behaviors. Severity of the condition is based on the number of symptoms present at the time of diagnosis. Disease trajectory typically consists of time periods with remission and relapse. Many patients are capable of sustaining periods of abstinence; however, they tend to be at a significantly greater risk of mortality associated with the disease, when compared to unaffected populations.

Treatment of OUD is centered on reducing opioid use and improving the patient's psychosocial status by empowering individuals with the ability to self-manage and seek changes for themselves. Opioid detoxification and supervised withdrawal during acute symptoms may help facilitate taking next steps towards chronic maintenance, but acute intervention alone has not demonstrated chronic benefit in addiction treatment. Integrating pharmacologic therapy along with psychotherapy can help ensure that treatment is effective and medication diversion is prevented. Pharmaceutical treatment options for opioid dependence include opioid agonist therapy (e.g., buprenorphine, buprenorphine/naloxone, methadone), and opioid antagonist (e.g., naltrexone) therapy. Choice of agent depends on patient characteristics, resources available to the patient and level of motivation.

For patients who have access to a well-structured addiction program, methadone is considered a viable option. Methadone is a long-acting opioid agonist that reduces cravings for opioids and maintains high levels of opioid tolerance to reduce the euphoric effects of subsequent illicit opioid use. Only licensed OTPs or licensed inpatient hospital units in the United States are permitted to order and dispense methadone for opioid dependence.

For most individuals buprenorphine is preferred, especially if they are unable or unwilling to reach an addiction clinic. Buprenorphine is a partial opioid agonist that is commonly taken sublingually and often administered in a combination preparation with naloxone to discourage intravenous buprenorphine abuse. Buprenorphine is generally associated with less sedation and risk of respiratory depression compared with methadone. Due to a better toxicity profile and ease of use, buprenorphine products are also now available in several different formulations. Newer sublingual formulations (Zubsolv®) provide greater bioavailability, which means a lower therapeutic dose of buprenorphine is required, thereby possibly reducing side effects such as constipation. Longer-acting injectable formulations of buprenorphine (Sublocade™, Brixadi®) have also been developed to treat patients with limited adherence, or those who misuse or divert transmucosal buprenorphine. Sublocade™ is administered once a month, while Brixadi® is given once weekly. Buprenorphine was also available as long-acting implants (Probuphine®); however, they were discontinued in 2020.

For patients who are highly motivated and have access to addiction counseling and therapy, naltrexone-based treatment may be an alternative. Naltrexone is an opioid antagonist that blocks the effects of opioids if they are used, thus preventing the user from experiencing opioid intoxication or physiologic dependence with subsequent use and therefore reinforces abstinence. Naltrexone is not recommended to be used prior to the completion of detoxification as it can cause immediate withdrawal symptoms. Oral naltrexone for the treatment of OUD is often adversely affected by poor medication adherence and is not recommended except under very limited circumstances. Instead, the once monthly long-acting naltrexone formulation (Vivitrol®) is preferred, especially among patients with difficulty adhering to daily medication.

Opioid overdose continues to be a significant public health issue in the U.S., with more than 103,000 reported fatal overdoses occurring in 2022, primarily driven by synthetic opioids such as illicit fentanyl. Professional societies

recommend prescription of naloxone to third parties (bystanders) as part of a harm reduction program. Bystander-administered naloxone by the intramuscular and intranasal routes can be used successfully to resuscitate patients who have overdosed on opioids. Providing opioid users, family members, and friends with naloxone, accompanied by teaching them how to recognize opioid toxicity, may reduce overdose mortality. Preventive intervention includes teaching people how to identify individuals most likely to overdose, to recognize clinical signs of opioid overdose, and how to intervene including how to perform cardiopulmonary resuscitation and how to administer naloxone. The usual adult dose of lay-administered naloxone in the event of opioid overdose is 0.4 injected intravenously, intramuscularly, or subcutaneously. Intranasal naloxone (Narcan®) delivers a pre-measured 4 mg dose. Repeated doses are typically necessary if respiratory depression continues or recurs prior to arrival of emergency personnel.

Due to the relative potency of many synthetic opioids, some have theorized that higher doses of naloxone, or use of more potent and longer-acting opioid antagonists may be required to effectively reverse overdoses. Over the last few years, the FDA has approved several new formations of naloxone (Kloxxado®, Zimhi™) with higher potency. Kloxxado® is a nasal spray that delivers a pre-measured 8 mg dose, while Zimhi™ is 5 mg injection that can be administered subcutaneously or intramuscularly. Opvee® (nalmefene) is an alternative to naloxone with a longer duration of action that was approved in 2023. Opvee® delivers a pre-measured dose of 2.7 mg intranasally, however, there is some concern that the longer duration of action of nalmefene may be a disadvantage as it may mean that longer monitoring and/or management of precipitated withdrawal may be required.

Additionally, in 2023, the FDA made a landmark decision in approving an OTC version of Narcan®, making naloxone more accessible. This was followed by a second OTC naloxone nasal spray approved later in the year called RiVive™. RiVive™ provides a slightly smaller pre-measured dose of 3 mg and launched in early 2024. OTC availability of naloxone will make it more readily available to families and friends of those with OUD and ensures that patients and caregivers will be able to purchase it from retailers that do not have a pharmacy (e.g., grocery stores, convenience stores).

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INDICATIONS, DOSING, and ADMINISTRATION

Medication	Indications	Dosing
Opioid Antagonists		
Naltrexone oral tablets	Opioid use disorder Alcohol use disorder	25 mg orally once daily for 1 to 3 days, and if tolerated, increase the dose to 50 mg/day orally
Vivitrol® (naltrexone ER) intramuscular injection		Inject 380 mg intramuscularly once every 4 weeks
Naloxone syringe, vials	Opioid overdose	Administer subcutaneously, intramuscularly, intranasally (with a mucosal atomization device), or intravenously at initial doses of 0.4 mg to 2 mg with repeated administration every 3 minutes if no response For complete or partial opioid reversal after post-operative opioid administration, initiate with doses of 0.05 to 0.2mg administered every 2 to 3 minutes to obtain the desired response
Naloxone (Narcan®) nasal spray		4 mg (contents of 1 nasal spray) as a single dose in one nostril; may repeat every 2 to 3 minutes in alternating nostrils until medical assistance becomes available
Kloxxado® (naloxone) nasal spray		8 mg (contents of 1 nasal spray) as a single dose in one nostril; may repeat every 2 to 3 minutes in alternating nostrils until medical assistance becomes available
RiVive™ (naloxone) nasal spray		3 mg (contents of 1 nasal spray) as a single dose in one nostril; may repeat every 2 to 3 minutes in alternating nostrils until medical assistance becomes available
Zimhi™ (naloxone) syringe		5 mg (contents of 1 syringe) as a single dose; may repeat every 2 to 3 minutes until emergency medical assistance becomes available
Nalmefene vial		Administer subcutaneously, intramuscularly, or intravenously at an initial dose of 0.5 mg; a second dose of 1 mg may be administered 2 to 5 minutes later if needed; if there is no clinical response following a total dose of 1.5 mg, it is unlikely that continued administration of nalmefene will be beneficial
Opvee® (nalmefene) nasal spray		2.7 mg (contents of 1 nasal spray) as a single dose in one nostril; may repeat every 2 to 5 minutes in alternating nostrils until medical assistance becomes available
Partial Opioid Agonists		
Buprenorphine sublingual tablets	Opioid use disorder	Initial: Start with 2 to 4 mg sublingually; if no signs of precipitated withdrawal after 1 to 2 hours and dose is tolerated, may increase dose in increments of 2 to 4 mg to a dose that is clinically effective and provides 24 hours of stabilization

Medication	Indications	Dosing
		Maintenance: After the first day of treatment, maintain total daily dose from day 1 and adjust dose in increments of 4 mg to a level that maintains treatment and suppresses opioid withdrawal symptoms; doses ≥16 mg/day have been associated with greater efficacy; limited evidence exists for doses >24 mg/day
Sublocade® (buprenorphine ER) subcutaneous injection	Treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine product and used it for at least 7 days	300 mg subcutaneously once per month for 2 months, followed by 100 mg monthly for maintenance; if 100 mg is tolerated, but not effective, increase to 300 mg per month
Brixadi® (buprenorphine ER) subcutaneous injection	Treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with buprenorphine	Initial: 16 mg subcutaneously, followed by an additional 8 mg dose within 3 days of the initial dose for a total recommended weekly dose of 24 mg; may administer an additional 8 mg dose after at least 24 hours after the previous dose, for a total weekly dose of 32 mg Maintenance dose: 16 to 32 mg subcutaneously once weekly; titrate at weekly intervals as needed up to a maximum of 32 mg once weekly
Partial Opioid Agonist & Opioid Antagonist Combinations		
Buprenorphine/naloxone (Suboxone®) sublingual tablets and films	Opioid use disorder	Initial: - Day 1: Start with 2 mg/0.5 mg or 4 mg/1 mg sublingually; may titrate dose, based on control of acute withdrawal symptoms, in increments of 2 mg/0.5 mg to 4 mg/1 mg every 2 hours up to a maximum dose of 8 mg/2 mg - Day 2: A single dose of up to 16 mg/2 mg sublingually may be given Maintenance: - 16 mg/2 mg sublingually once daily, dose should be adjusted in increments or decrements of 2 mg/ 0.5 mg or 4 mg/1 mg to a level that maintains treatment and suppresses opioid withdrawal symptom; max effective dose is 24 mg/6 mg per day

Medication	Indications	Dosing
Zubsolv® (buprenorphine/naloxone) sublingual tablets		Induction: - Day 1: Start with 1.4 mg/0.36 mg sublingually; based on control of acute withdrawal symptoms, may administer additional doses in increments of 1 to 2 tablets of 1.4 mg/0.36 mg every 1.5 to 2 hours to achieve total daily dose of 5.7 mg/1.4 mg - Day 2: A single dose of 11.4 mg/2.9 mg sublingually may be given Maintenance: - 11.4 mg/2.9 mg sublingually once daily, dose should be adjusted in increments or decrements of 2.9 mg/0.71 mg or lower to a level that maintains treatment and suppresses opioid withdrawal symptoms; max effective dose is 17.2 mg/4.2 mg per day

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Buprenorphine (Sublocade®, Brixadi®)	**Risk of serious harm or death** (Sublocade™ and Brixadi® only): Serious harm or death could result if subcutaneous injection is administered intravenously. The injection forms a solid mass upon contact with body fluids and may cause occlusion, local tissue damage, and thromboembolic events, including life-threatening pulmonary emboli if administered intravenously.	None
Buprenorphine/naloxone (Suboxone®, Zubsolv®)	None	
Naltrexone (Vivitrol®)	None	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
Naloxone (Narcan®, RiVive™, Kloxxado®, Zimhi™)		None
Nalmefene (Opvee®)		

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
All products with buprenorphine – Buprenorphine tablets, Buprenorphine/naloxone films and tablets, Sublocade®, Brixadi®, and Zubsolv®	Concerns related to adverse effects: - Accidental opioid overdose: Patients who had been treated with buprenorphine may respond to lower opioid doses than previously used; this could result in potentially life-threatening opioid intoxication - May cause central nervous system (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) - Hepatitis has been reported; hepatic events ranged from transient, asymptomatic transaminase elevations to hepatic failure; in many cases, patients had preexisting hepatic impairment - Hypersensitivity, including bronchospasm, angioneurotic edema, and anaphylactic shock, have been reported - May cause severe hypotension (including orthostatic hypotension and syncope) - QT prolongation: Buprenorphine has been observed to cause QTc prolongation; avoid using in patients with a personal or family history of long QT syndrome or in patients taking concurrent class IA or III antiarrhythmics or other medications that prolong the QT interval - Respiratory depression (Injection only): Carbon dioxide retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids Disease-related concerns: - May obscure diagnosis or clinical course of patients with acute abdominal conditions - Use with caution in patients with adrenal insufficiency, including Addison disease - Use with caution in patients with biliary tract dysfunction, including acute pancreatitis; opioids may cause constriction of sphincter of Oddi - Use with caution in patients with a history of ileus or bowel obstruction - Avoid use in patients with impaired consciousness or coma because these patients are susceptible to intracranial effects of CO2 retention - Use with caution in patients with delirium tremens - Use with extreme caution in patients with head injury, intracranial lesions, or elevated intracranial pressure (ICP); exaggerated elevation of ICP may occur - Use sublingual tablet with caution in patients with moderate hepatic impairment; dosage adjustment recommended in severe hepatic impairment; patients with preexisting moderate or severe hepatic impairment are not candidates for the ER injection; if moderate or severe hepatic impairment develops during treatment with the ER injection, continue with caution and monitor for toxicity for several months - Use with caution in patients who are morbidly obese - Use with caution in patients with prostatic hyperplasia and/or urinary stricture - Use with caution in patients with toxic psychosis - Use with caution in patients with renal impairment - Use with caution in patients with a history of seizure disorders; may cause or exacerbate preexisting seizures. - Use with caution in patients with sleep-related disorders, including sleep apnea, due to increased risk for respiratory and CNS depression. - Use with caution in patients with thyroid dysfunction. Concurrent drug therapy issues: - Benzodiazepines and other CNS depressants: Concomitant use may result in respiratory depression and sedation, which may be fatal Dosage form specific issues: - Injection: Injection-site reactions (e.g., pain, erythema, pruritus), some resulting in abscess, ulceration, or necrosis, have been reported

Medication	Warnings/Precautions
	- Some products may contain latex Other warnings/precautions: - Acute pain: When using buprenorphine for treatment of opioid use disorder, treat acute pain with nonopioid analgesics whenever possible - Discontinuation of therapy: There is no maximum recommended duration for maintenance treatment of opioid use disorder; patients may require treatment indefinitely - Naloxone access: Health care providers should consider offering naloxone to patients prescribed medications to treat OUD - Partial opioid agonist and mixed opioid agonist/antagonist overdose: Reversal of partial opioid agonists or mixed opioid agonist/antagonists (e.g., buprenorphine, pentazocine) may be incomplete and higher than normal doses and repeated administration of naloxone may be required
All products containing naloxone – Buprenorphine/naloxone films and tablets, Zubsolv®, naloxone injection, naloxone nasal spray, RiVive™, Kloxxado®, and Zimhi™	Concerns related to adverse effects: - Acute opioid withdrawal: Administration of naloxone causes the release of catecholamines, which may precipitate acute withdrawal or unmask pain in those who regularly take opioids - Combativeness: Some patients may be agitated or combative when resuscitated with naloxone; there is greater risk of combativeness in patients using fentanyl Disease-related concerns: - Use with caution in patients with cardiovascular disease or in patients receiving medications with potential adverse cardiovascular effects (e.g., hypotension, pulmonary edema or arrhythmias); pulmonary edema and cardiovascular instability, including ventricular fibrillation, have been reported in association with abrupt reversal when using opioid antagonists - Use caution in patients with history of seizures; avoid use in the treatment of meperidine-induced seizures Other warnings/precautions: - Opioid overdose symptom recurrence: Recurrence of respiratory and/or CNS depression is possible if the opioid involved is long-acting; continuously observe patients until there is no further risk of recurrent respiratory or CNS depression - Partial opioid agonist and mixed opioid agonist/antagonist overdose: Reversal of partial opioid agonists or mixed opioid agonist/antagonists (e.g., buprenorphine, pentazocine) may be incomplete and larger or repeat doses of naloxone may be required - Substance use disorder involving opioid use: To prevent overdose deaths, there are initiatives to dispense naloxone for self- or buddy-administration to patients at risk of opioid overdose (e.g., recipients of high-dose opioids, suspected or confirmed history of illicit opioid use) and individuals likely to be present in an overdose situation (e.g., family members of illicit drug users)
All products containing nalmefene – Nalmefene injection and Opvee ®	Disease-related concerns: - Use with caution in patients with cardiovascular disease or in patients receiving medications with potential adverse cardiovascular effects (e.g., hypotension, pulmonary edema, arrhythmias); pulmonary edema and cardiovascular instability, including ventricular fibrillation, have been reported in association with abrupt reversal when using opioid antagonists Other warnings/precautions:

Medication	Warnings/Precautions
	- Opioid overdose: When compared to naloxone, nalmefene has a longer duration of action at fully reversing doses; however, prolonged or recurrent respiratory depression is possible if the opioid involved is long-acting (e.g., methadone, levo-alpha-acetylmethadol); recurrence of respiratory depression may occur even with an adequate initial response to nalmefene; continuously observe patients until there is no further risk of recurrent respiratory depression - Substance use disorder involving opioid use: To prevent overdose deaths, there are initiatives to dispense an opioid antagonist for self- or buddy-administration to patients at risk of opioid overdose (e.g., recipients of high-dose opioids, suspected or confirmed history of illicit opioid use) and individuals likely to be present in an overdose situation (e.g., family members of illicit drug users) - Partial opioid agonist and mixed opioid agonist/antagonist overdose: Reversal of respiratory depression secondary to a partial opioid agonist (e.g., buprenorphine) may be incomplete; larger or repeat doses of nalmefene may be required
All naltrexone products – Naltrexone oral tablets and Vivitrol®	Concerns related to adverse effects: - Suicidal thoughts, attempted suicide, and depression have been reported postmarketing Disease-related concerns: - Bleeding disorders: 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 - Use is not recommended in acute hepatitis or hepatic failure - Use with caution in patients with moderate to severe renal impairment (has not been studied(Dosage form specific issues: - Vehicle used in the injectable naltrexone IM 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: - Discontinuation of therapy: There is no maximum recommended duration for maintenance treatment of opioid use disorder; patients may require treatment indefinitely - Patients should be opioid-free (including tramadol) for a minimum of 7 to 10 days; patients transitioning from buprenorphine or methadone may be vulnerable to precipitation of withdrawal symptoms for as long as 2 weeks; use of naltrexone does not eliminate or diminish withdrawal symptoms; oral naltrexone tablets have not been shown to be more effective than placebo for opioid use disorder due to poor patient adherence - Naloxone access: Patients being treated for an opioid use disorder have the potential for relapse and are at risk for opioid overdose; this risk may be increased in patients treated with naltrexone near the end of the naltrexone dosing interval (particularly if using naltrexone injection), if a dose of naltrexone is missed, or when naltrexone treatment is discontinued.

PRACTICE GUIDELINES

The American Society of Addiction Medicine (ASAM) National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 focused update. J Addict Med. 2020;14(2S Suppl 1):1-91.

Treatment Options

- All FDA approved medications for the treatment of opioid use disorder should be available to all patients. Clinicians should consider the patient's preferences, past treatment history, current state of illness, and treatment setting when deciding between the use of methadone, buprenorphine, and naltrexone.
- There is no recommended time limit for pharmacological treatment.
- The venue in which treatment is provided should be carefully considered. Methadone can only be provided in OTPs and acute care settings (under limited circumstances). Buprenorphine can be prescribed by waivered clinicians in any setting, including OTPs and office based opioid treatment (OBOT) in accordance with the Federal law. Naltrexone can be prescribed in any setting by any clinician with the authority to prescribe medication. Clinicians should consider a patient's psychosocial situation, co-occurring disorders, and risk of diversion when determining which treatment setting is most appropriate.
- Methadone is recommended for patients who may benefit from daily dosing and supervision in an OTP, or for patients for whom buprenorphine for the treatment of opioid use disorder has been used unsuccessfully in an OTP or OBOT setting.
- Oral naltrexone for the treatment of opioid use disorder is often adversely affected by poor medication adherence and should not be used except under very limited circumstances. Clinicians should reserve its use for patients who would be able to comply with special techniques to enhance their adherence, for example, observed dosing. Extended-release injectable naltrexone reduces, but does not eliminate, issues with medication adherence.
- Naloxone, for the reversal of opioid overdose, should be provided to patients being treated for, or with a history of, opioid use disorder. Patients and family members/significant others should be trained in the use of naloxone in overdose.

Treating Opioid Withdrawal

- Using methadone or buprenorphine for opioid withdrawal management is recommended over abrupt cessation of opioids. Abrupt cessation of opioids may lead to strong cravings, and/or acute withdrawal syndrome which can put the patient at risk for relapse, overdose, and overdose death.
- Opioid withdrawal management (i.e., detoxification) on its own, without ongoing treatment for opioid use disorder, is not a treatment method for opioid use disorder and is not recommended. Patients should be advised about the risk of relapse and other safety concerns, including increased risk of overdose and overdose death. Ongoing maintenance medication, in combination with psychosocial treatment appropriate for the patient's needs, is the standard of care for treating opioid use disorder.
- By regulation, opioid withdrawal management with methadone must be done in an OTP or an acute care setting (under limited circumstances). For patients withdrawing from short acting opioids the initial dose should typically be 20-30 mg per day and the patient may be tapered off in approximately 6-10 days.
- Opioid withdrawal management with buprenorphine should not be initiated until there are objective signs of opioid withdrawal. Once signs of withdrawal have been objectively confirmed, a dose of buprenorphine sufficient to suppress withdrawal symptoms is given (an initial dose of 2-4 mg titrated up as needed to suppress withdrawal symptoms).
- Alpha-2 adrenergic agonists (e.g., FDA-approved lofexidine and off-label clonidine) are safe and effective for management of opioid withdrawal. However, methadone and buprenorphine are more effective in reducing the symptoms of opioid withdrawal, in retaining patients in withdrawal management, and in supporting the completion of withdrawal management.

- Opioid withdrawal management using ultra-rapid opioid detoxification (UROD) is not recommended due to high risk for adverse events or death. Naltrexone-facilitated opioid withdrawal management can be safe and effective but should be used only by clinicians experienced with this clinical method, and in cases in which anesthesia or conscious sedation are not employed.

Methadone

- The recommended initial dose of methadone ranges from 10 to 30 mg, with reassessment as clinically indicated (typically in 2 to 4 hours). Use a lower-than-usual initial dose (2.5 to 10 mg) in individuals with no or low opioid tolerance.
- Following initial withdrawal stabilization, the usual daily dose of methadone ranges from 60 to 120 mg. Some patients may respond to lower doses and some may need higher doses. Methadone titration should be individualized based on careful assessment of the patient's response and generally should not be increased every day. Typically, methadone can be increased by no more than 10 mg approximately every 5 days based on the patient's symptoms of opioid withdrawal or sedation.
- Patients transitioning from methadone to buprenorphine in the treatment of opioid use disorder should ideally be on low doses of methadone before making the transition. Patients on low doses of methadone (30–40 mg per day or less) generally tolerate transition to buprenorphine with minimal discomfort, whereas patients on higher doses of methadone may experience significant discomfort in transitioning medications.
- Patients transitioning from methadone to naltrexone must be completely withdrawn from methadone and other opioids, before they can receive naltrexone. The only exception would apply when an experienced clinician receives consent from the patient to embark on a plan of naltrexone-facilitated opioid withdrawal management.

Buprenorphine

- For patients who are currently opioid dependent, buprenorphine should not be initiated until there are objective signs of opioid withdrawal to reduce the risk of precipitated withdrawal.
- Once objective signs of withdrawal are observed, initiation of buprenorphine should start with a dose of 2–4 mg. Dosages may be increased in increments of 2–8 mg.
- Following initiation, buprenorphine dose should be titrated to alleviate symptoms. To be effective, buprenorphine dose should be sufficient to enable patients to discontinue illicit opioid use. Evidence suggests that 16 mg per day or more may be more effective than lower doses. There is limited evidence regarding the relative efficacy of doses higher than 24 mg per day, and the use of higher doses may increase the risk of diversion.
- The FDA recently approved several new buprenorphine formulations for treatment of opioid use disorder. As data regarding the effectiveness of these products are currently limited, clinicians should use these products as indicated and be mindful of emerging evidence as it becomes available.
- When considering a transition from buprenorphine to naltrexone, providers should note that 7–14 days should typically elapse between the last dose of buprenorphine and the start of naltrexone to ensure that the patient is not physically dependent on opioids before starting naltrexone.
- When considering a transition from buprenorphine to methadone, there is no required time delay because the transition to a full opioid agonist from a partial agonist does not typically result in an adverse reaction.
- Buprenorphine taper and discontinuation is a slow process and close monitoring is recommended. Buprenorphine tapering is generally accomplished over several months. Patients should be encouraged to remain in treatment for ongoing monitoring past the point of discontinuation.

Naltrexone

- Extended-release injectable naltrexone should generally be administered every 4 weeks by deep IM injection in the gluteal muscle at the set dosage of 380 mg per injection. Some patients, including those dosing as frequently as every 3 weeks.
- Oral naltrexone is not recommended except under limited circumstances.

- Transitioning from naltrexone to methadone or buprenorphine should be planned, considered, and monitored. Transitioning from an antagonist such as naltrexone to a full agonist (methadone) or a partial agonist (buprenorphine) is generally less complicated than transitioning from a full or partial agonist to an antagonist because there is no physical dependence associated with antagonist treatment and thus no possibility of precipitated withdrawal. Patients being transitioned from naltrexone to buprenorphine or methadone will not have physical dependence on opioids and thus the initial doses of methadone or buprenorphine should be low. Patients should not be transitioned until a significant amount of the naltrexone is no longer in their system, about 1 day for oral naltrexone or 28 days for extended-release injectable naltrexone.

Naloxone

- Naloxone should be administered in the event of a suspected opioid overdose.
- Naloxone may be administered to pregnant women in cases of overdose to save the mother's life.

Special Populations

- Treatment with methadone or buprenorphine is recommended and should be initiated as early as possible during pregnancy.
- Pregnant women who are physically dependent on opioids should receive treatment using methadone or buprenorphine rather than withdrawal management or psychosocial treatment alone.
- For patients with pain who have an active opioid use disorder but are not in treatment, methadone or buprenorphine should be considered. The patient's opioid use disorder and pain should be stabilized and managed concurrently.
- Opioid agonists (methadone and buprenorphine) and antagonists (naltrexone) may be considered for treatment of opioid use disorder in adolescents. Federal laws and FDA approvals should be considered when recommending pharmacotherapy for adolescent patients.

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

Stabilization and Withdrawal

- For patients with opioid use disorder, we recommend against withdrawal management, without planned ongoing pharmacotherapy treatment, due to high risk of relapse and overdose (Strong against; Not reviewed, Amended).
- For patients with opioid use disorder for whom opioid withdrawal management is indicated, we suggest using (Weak for; Reviewed, New-replaced):
    - Buprenorphine/naloxone (in any setting); or
    - Methadone or buprenorphine/naloxone (in inpatient or accredited OTPs)
- For patients with opioid use disorder for whom withdrawal management is indicated and for whom methadone and buprenorphine are contraindicated, unacceptable, or unavailable, we suggest offering clonidine or lofexidine as a second-line agent for opioid withdrawal management (Weak for; Reviewed, New-replaced).

Pharmacotherapy

- For patients with opioid use disorder, we recommend one of the following strategies (Strong for; Reviewed, Amended):
    - Buprenorphine/naloxone in any setting; or
    - Methadone or buprenorphine/naloxone provided through an accredited OTP
- For patients with opioid use disorder, we suggest offering extended-release naltrexone (IM) (Weak for; Reviewed, New-replaced).
- There is insufficient evidence to recommend any one of the different FDA-approved formulations or routes of delivery of buprenorphine over another (Neither for nor against; Reviewed, New-added).

- There is insufficient evidence to recommend for or against oral naltrexone for the treatment of opioid use disorder (Neither for nor against; Reviewed, Not changed).

Psychosocial Interventions

- For patients receiving medication treatment for opioid use disorder, there is insufficient evidence to recommend for or against any specific psychosocial interventions in addition to addiction-focused medical management (Neither for nor against; Reviewed, Amended).
- For patients with opioid use disorder for whom opioid use disorder pharmacotherapy is contraindicated, unacceptable, or unavailable, there is insufficient evidence to recommend for or against any specific psychosocial interventions (Neither for nor against; Not reviewed, Amended).

Recommendation Definitions

Strength of Recommendation	General Corresponding Text	Definition
Strong for/Strong against	We recommend…/We recommend against…	The Work Group is highly confident that desirable outcomes outweigh undesirable outcomes and vice-versa
Weak for/Weak against	We suggest…/We suggest against…	The Work Group is less confident of the balance between desirable and undesirable outcomes
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 previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted
Not Reviewed	Not changed	Recommendation from previous CPG was carried forward but not changed
	Amended	Recommendation from previous CPG was carried forward with a nominal change
	Deleted	Recommendation from previous CPG was deleted

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Degenhardt L, Clark B, Macpherson G, et al. Buprenorphine versus methadone for the treatment of opioid dependence: a systematic review and meta-analysis of randomised and observational studies. Lancet Psychiatry. 2023;10(6):386-402.	Systematic review and network meta-analysis conducted by searching Embase, MEDLINE, CENTRAL, and PsycINFO for relevant studies up to August 1, 2022. Studies included were all randomized controlled trials and observational studies of adults with opioid dependence comparing treatment with buprenorphine or methadone. A total of 83 randomized controlled trials and 193 observational studies were included.	• Primary endpoints: Retention in treatment at 1, 3, 6, 12, and 24 months, treatment adherence (measured through doses taken as prescribed, dosing visits attended, and biological measures), or extra-medical opioid use (measured by urinalysis and self-report) • Secondary endpoints: Use of benzodiazepines, cannabis, cocaine, amphetamines, and alcohol; withdrawal; craving; criminal activity and engagement with the criminal justice system; overdose; mental and physical health; sleep; pain; global functioning; suicidality and self-harm; and adverse events
Results: At timepoints beyond 1 month, retention was better for methadone than for buprenorphine: for example, at 6 months, the pooled effect favored methadone in randomized controlled trials (risk ratio [RR], 0.76; 95% confidence interval [CI], 0.67 to 0.85; I=74.2%; 16 studies, N=3,151) and in observational studies (RR, 0.77; 95% CI, 0.68 to 0.86; I=98.5%; 21 studies, N=155, 111). Retention was generally higher in randomized controlled trials than observational studies. There was no evidence suggesting that adherence to treatment differed with buprenorphine compared with methadone. There was some evidence that extra-medical opioid use was lower in those receiving buprenorphine in randomized controlled trials that measured this outcome by urinalysis and reported proportion of positive urine samples (over various time frames; standardized mean difference, 0.20; 95% CI, -0.29 to -0.11; I=0·0%; 3 studies, N=841), but no differences were found when using other measures. Some statistically significant differences were found between buprenorphine and methadone among secondary outcomes. There was evidence of reduced cocaine use, cravings, anxiety, and cardiac dysfunction, as well as increased treatment satisfaction among people receiving buprenorphine compared with methadone; and evidence of reduced hospitalization and alcohol use in people receiving methadone. These differences in secondary outcomes were based on small numbers of studies (maximum five) and were often not consistent across study types or different measures of the same constructs (e.g., cocaine use). **Conclusion**: Evidence from trials and observational studies suggest that treatment retention is better for methadone than for sublingual buprenorphine. Comparative evidence on other outcomes examined showed few statistically significant differences and was generally based on small numbers of studies. These findings highlight the imperative for interventions to improve retention, consideration of client-centered factors (such as client preference) when selecting between methadone and buprenorphine, and harmonization of data collection and reporting to strengthen future syntheses.		
Citation	**Design**	**Endpoints**
Lim J, Farhat I, Douros A, Panagiotoglou D. Relative effectiveness of medications for opioid-related disorders: A systematic review and network meta-analysis of randomized controlled trials. PLoS One. 2022;17(3):e0266142.	Systematic review and network meta-analysis conducted by searching Medline, EMBASE, PsycINFO, CENTRAL, and ClinicalTrials.gov for relevant studies up to February 12, 2022 comparing medications for OUD among people with opioid-related disorders. Studies included were randomized controlled clinical trials with adult patients with problematic opioid or heroin use who were receiving pharmacotherapy, including buprenorphine, methadone, naltrexone, and slow-release oral morphine (SROM). A total of 79 studies were included.	• Primary endpoint: Treatment retention • Secondary endpoint: Opioid use measured by urinalysis

Results: Methadone was the highest ranked intervention (Surface Under the Cumulative Ranking [SUCRA]=0.901) in the network with control being the lowest (SUCRA=0.000). Methadone was superior to buprenorphine for treatment retention (RR, 1.22; 95% credible interval [CrI], 1.06 to 1.40) and buprenorphine superior to naltrexone (RR, 1.39; 95% CrI, 1.10 to 1.80). However, due to a limited number of high-quality trials, confidence in the network estimates of other treatment pairs involving naltrexone and SROM remains low. **Conclusion**: All treatments had higher retention than the non-pharmacotherapeutic control group. However, additional high-quality randomized controlled trials are needed to estimate more accurately the extent of efficacy of naltrexone and SROM relative to other medications. For pharmacotherapies with established efficacy profiles, assessment of their long-term comparative effectiveness may be warranted.		
Citation	**Design**	**Endpoints**
Haight BR, Learned SM, Laffont CM, et al. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2019;393(10173):778-790.	This study was a randomized, placebo controlled, double blinded study with intervention group receiving injectable buprenorphine extended release. Patients either received buprenorphine 300 mg each month, buprenorphine 100 mg (300 mg for first 2 months followed by 100mg dose), or volume-matched placebo. Randomization occurred in a 4:4:1:1 ratio, where the higher ratios belonged to intervention groups and the lower ratios belong to the placebo groups. Included participants were treatment-seeking adults aged 18-65 years who had moderate or severe opioid use disorder and had entered an open-label run-in phase of up to 2 weeks' treatment with buprenorphine-naloxone sublingual film. All patients received weekly individual drug counseling.	• Primary endpoint: Participants' percentage abstinence from opioid use, defined as the percentage of each participant's negative urine samples and self-reports of illicit opioid use from week 5 to week 24
Results: Mean participants' percentage abstinence was 41.3% for buprenorphine extended release 300 mg and 42.7% for buprenorphine 100 mg, compared with 5.0% for placebo ($p<0.0001$ for both buprenorphine regimens). No compensatory non-opioid drug use was observed during buprenorphine treatment. The most common adverse events were headache, constipation, and injection-site pruritis. The safety profile of buprenorphine was consistent with other buprenorphine products for treatment of opioid use disorder, except for injection-site reactions, which were reported in more than 5% of all participants who received extended release buprenorphine, but were mostly mild and not treatment-limiting. **Conclusion**: Participants' percentage abstinence was significantly higher in both extended-release buprenorphine groups than in the placebo group. Treatment with buprenorphine was also well tolerated. The availability of this monthly formulation, delivered by health-care providers, represents an advance in treatment for opioid use disorder that enhances the benefits of buprenorphine by delivering sustained, optimal exposure, while reducing risks of current buprenorphine products.		
Citation	**Design**	**Endpoints**
Lofwall MR, Walsh SL, Nunes EV, et al. Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder: A Randomized Clinical Trial. JAMA Intern Med. 2018;178(6):764-773.	This study was a randomized, double blinded, double-dummy clinical trial conducted at 35 sites in the United States from December 29, 2015, through October 19, 2016. Participants were treatment-seeking adults with moderate-to-severe opioid use disorder. The objective of this study was to determine whether treatment involving novel weekly and monthly subcutaneous buprenorphine depot formulations is noninferior to a daily sublingual combination of buprenorphine hydrochloride and naloxone hydrochloride in the treatment of opioid use disorder. A total of 428 participants were included in this trial.	• Primary endpoints: Response rate and the mean proportion of opioid-negative urine samples for 24 weeks (responder status was defined as having no evidence of illicit opioid use for at least 8 of 10 prespecified points during weeks 9 to 24) • Secondary endpoints: Mean proportion of samples with no evidence of illicit opioid use (weeks 4-24) evaluated by a cumulative distribution function (CDF)

Results: The response rates were 14.4% for the sublingual buprenorphine/naloxone group and 17.4% for the subcutaneous buprenorphine group, a 3.0% difference (95% CI, −4.0 to 9.9; p<0001). The proportion of opioid-negative urine samples was 28.4% for the sublingual buprenorphine/naloxone group and 35.1% for the subcutaneous buprenorphine group, a 6.7% difference (95% CI, −0.1 to 13.6; p<0.001). The CDF for the subcutaneous buprenorphine group (26.7%) was statistically superior to the CDF for the sublingual buprenorphine/naloxone group (0; p=0.004).
Conclusion: Compared with SL buprenorphine, depot buprenorphine did not result in an inferior likelihood of being a responder or having urine test results negative for opioids and produced superior results on the CDF of no illicit opioid use. These data suggest that depot buprenorphine is efficacious and may have advantages.

Citation	Design	Endpoints
Krupitsky E, Nunes EV, Ling W, et al. Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled. Lancet. 2011 Apr 30; 377(9776):1506-13.	This study was randomized, placebo controlled, double blinded study with intervention group receiving injectable extended-release naltrexone 380 mg every 4 weeks. Patients had just been discharged from inpatients opioid use disorder treatment, i.e., an inpatient detoxification program. The study was 24 weeks long. Patients were randomized in both arms in 1:1 ratio in a permuted block method, and both groups were stratified by gender and site. All patients received psychological counseling throughout the duration of the trial.	• Primary endpoint: Response to treatment, which was assessed based on patient responses as well as drug urine screen • Secondary endpoints: Self-reported opioid free days, opioid craving scores, number of days of retention, and relapse to physiological opioid dependence.

Results: Patients in the naltrexone arm were abstinent from opioid use 90% of the time (95% CI, 69.9 to 92.4), compared to the placebo group, which was abstinent only 35% of the time (95% CI, 11.4 to 63.8). Patients in the naltrexone group self-reported a median of 99.2% (range 89.1 to 99.4) opioid-free days compared with 60.4% (46.2 to 94.0) for the placebo group (p=0.0004). The mean change in craving was –10.1 (95% CI, –12.3 to –7.8) in the naltrexone group compared with 0.7 (95% CI, –3.1 to 4.4) in the placebo group (p<0.0001). Median retention was over 168 days in the naltrexone group compared with 96 days (95% CI, 63 to 165) in the placebo group (p=0.0042). Naloxone challenge confirmed relapse to physiological opioid dependence in 17 patients in the placebo group compared with one in the naltrexone group (p<0.0001). Naltrexone was well tolerated. Two patients in each group discontinued owing to adverse events. No naltrexone-treated patients died, overdosed, or discontinued owing to severe adverse events.
Conclusion: For patients who have undergone detoxification and sustained periods of opioid free use, naltrexone extended-release injection is a viable option to prevent relapse, especially those who may lack motivation and might be non-adherent.

Citation	Design	Endpoints
Minozzi S, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A. Oral naltrexone maintenance treatment for opioid dependence. Cochrane Database Syst Rev. 2011;(4):CD001333.	Systematic review conducted by searching Cochrane Central Register of Controlled Trials (CENTRAL - The Cochrane Library), PubMed, and CINAHL to evaluate the effects of naltrexone maintenance treatment versus placebo or other treatments in preventing relapse in opioid addicts after detoxification. Studies included were randomized controlled clinical trials which focus on the use of naltrexone maintenance treatment versus placebo, or other treatments to reach sustained abstinence from opiate drugs. A total of 13 studies were included, involving 1,158 patients.	• Primary endpoint: Sustained abstinence from opiate drugs

Results: Comparing naltrexone versus placebo or no pharmacological treatments, no statistically significant difference were noted for all the primary outcomes considered. The only outcome statistically significant in favor of naltrexone is re incarceration (RR, 0.47; 95% CI, 0.26 to 0.84), but results come only from two studies. Considering only studies where patients were forced to adherence, a statistically significant difference in favor of naltrexone was found for retention and abstinence (RR, 2.93; 95% CI, 1.66 to 5.18). Comparing naltrexone versus psychotherapy, in the two considered outcomes, no statistically significant difference was found in the single study considered. Naltrexone was not superior to benzodiazepines and to buprenorphine for retention and abstinence and side effects.
Conclusion: The findings of this review suggest that oral naltrexone did not perform better than treatment with placebo or no pharmacological agent with respect to the number of participants re-incarcerated during the study period. If oral naltrexone is compared with other pharmacological treatments such as benzodiazepine and buprenorphine, no

statistically significant difference was found. The percentage of people retained in treatment in the included studies is however low (28%). The conclusion of this review is that the studies conducted have not allowed an adequate evaluation of oral naltrexone treatment in the field of opioid dependence. Consequently, maintenance therapy with naltrexone cannot yet be considered a treatment which has been scientifically proved to be superior to other kinds of treatment.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (01-01-2024 to 03-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Opioid Antagonists								
Naltrexone 50 mg oral tablet	6	3	$144.08	$24.01	0	0 (0%)	F	No change
Vivitrol® (naltrexone ER) 380 mg intramuscular injection	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Naloxone 0.4 mg/ml, 1 mg/ml injection syringe	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Naloxone 0.4 mg/ml injection solution	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Naloxone (Narcan®) 4 mg nasal spray	11	11	$751.61	$68.33	0	0 (0%)	F	No change
Kloxxado® (naloxone) 8 mg nasal spray	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Zimhi™ (naloxone) 5 mg/0.5 ml syringe	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Nalmefene 1 mg/mL injection solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Opvee® (nalmefene) 2.7 mg nasal spray	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Partial Opioid Agonists								
Buprenorphine 2 mg, 8 mg sublingual tablets	0	0	$0.00	$0.00	0	0 (0%)	F-QL 2mg (180/30) 8mg (90/30)	No change
Sublocade® (buprenorphine ER) 100 mg/0.5 mL, 300 mg/1.5 mL subcutaneous syringe	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Brixadi® (buprenorphine ER) 8 mg/0.16 ml, 16 mg/0.32 ml, 24 mg/0.48 ml, 32 mg/0.64 ml, 64 mg/0.18 ml, 96 mg/0.27 ml, 128 mg/0.36 ml subcutaneous syringe	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Partial Opioid Agonist & Opioid Antagonist Combinations								
Buprenorphine/naloxone 2 mg-0.5 mg, 8 mg-2 mg sublingual tablets	7	4	$400.05	$57.15	0	0 (0%)	F-QL 2mg-0.5mg (180/30) 8mg-2mg (90/30)	No change
Buprenorphine/naloxone (Suboxone®) 2 mg-0.5 mg, 4 mg-1 mg, 8 mg-2 mg, 12 mg-3 mg sublingual films	6	2	$869.59	$144.93	2	2 (100%)	F-PA	No change
Zubsolv® (buprenorphine/naloxone) 0.7 mg-0.18 mg, 1.4 mg-0.36 mg, 2.9 mg-0.71 mg, 5.7 mg-1.4 mg, 8.6 mg-2.1 mg, 11 mg-2.9 mg sublingual tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
TOTAL	30	20	$2,165.33	$72.18	2	2 (100%)		

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

PRIOR AUTHORIZATION CRITERIA

Opioid Use Disorder (OUD) Agents	
Therapeutic Classes (AHFS)	Opiate Partial Agonists
Medications	Formulary (with quantity limit) Buprenorphine (Subutex) sublingual tablet Buprenorphine/naloxone (Suboxone) sublingual tablet Formulary, PA required: Buprenorphine/naloxone (Suboxone) film Zubsolv (buprenorphine/naloxone) sublingual tablet Non-formulary, PA required: Sublocade (buprenorphine) subcutaneous injection Brixadi (buprenorphine) Weekly or Monthly subcutaneous injection Any other newly marketed agent for opioid use disorder
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 conditions are met, the request will be approved for up to 12 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	**INTIAL CRITERIA** **Buprenorphine/naloxone (Suboxone) film or Zubsolv (buprenorphine/naloxone) sublingual tablet** • Patient has a diagnosis of opioid use disorder • Dosing maximum of 24mg/day of buprenorphine or equivalent is requested (Dosing above 24mg/day may be approved on a case by case basis Documented trial and failure, contraindication, or intolerance to one of the following medications: buprenorphine (Subutex) tablet OR buprenorphine/naloxone (Suboxone) tablet is required **Sublocade:** • Patient has a diagnosis of moderate to severe opioid use disorder • Documented trial and failure, contraindication, or intolerance to one of the following medications: buprenorphine (Subutex) tablet OR buprenorphine/naloxone (Suboxone) tablet is required • Patient has initiated treatment with an oral or transmucosal buprenorphine containing product at a daily dose of 8-24 mg buprenorphine for at least 7 days prior to initiating treatment • Patient will not be receiving supplemental oral, sublingual, or transmucosal buprenorphine. **Brixadi:** • Patient has a diagnosis of moderate to severe opioid use disorder • Documented trial and failure, contraindication, or intolerance to one of the following medications: buprenorphine (Subutex) tablet OR buprenorphine/naloxone (Suboxone) tablet is required

	• Patient has initiated treatment with a single dose of at least 4mg of a transmucosal buprenorphine product or are already being treated with buprenorphine **RENEWAL CRITERIA** • Patient has a diagnosis of opioid use disorder • For buprenorphine/naloxone (Suboxone) film or Zubsolv (buprenorphine/naloxone) sublingual tablet, documentation must be provided for renewals after the first year that indicated prescriber has reevaluated the patient on an annual basis for a dosage lower than 24mg/day 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	Sublocade (buprenorphine) subcutaneous injection, Brixadi (buprenorphine) Weekly or Monthly subcutaneous injection, Zubsolv, and buprenorphine/naloxone (Suboxone) film are reserved for members who have used (or cannot use) buprenorphine (Subutex) tablets or buprenorphine/naloxone (Suboxone) tablets.
Last P&T Review Date	~~9/2023~~6/2024

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PERFORMRx℠

Phosphate Binders

Executive Summary

CLASS OVERVIEW

The following review encompasses oral pharmacotherapeutic agents for use in reduction of serum phosphate levels in patients with either chronic kidney disease (CKD) or end-stage renal disease (ESRD). Two main treatment approaches exist for reduction of serum phosphate levels in these patients; dietary phosphate restriction and use of phosphate binders.

Phosphate binders reduce levels by binding dietary phosphorous in the gastrointestinal (GI) tract, blocking absorption. They are either classified as calcium containing or non-calcium containing, and the choice of agent is dependent on cost, patient tolerance for the particular agent used, and other considerations such as whether the patient also has high serum calcium levels or those taking vitamin-D analogs. For those patients with high calcium levels, use of a non-calcium containing phosphate binder is the appropriate choice. Calcium-containing agents may also have adverse effects such as vascular calcification, hypercalcemia, adynamic bone disease, and some studies have shown increased mortality with their use compared to non-calcium containing phosphate binders in both dialysis and non-dialysis CKD patients. Consequently, non-calcium containing agents are typically preferred clinically but are more expensive. Both types lower serum phosphate to a similar degree. High phosphate levels have been shown to be associated with increased mortality in patients with CKD, but dietary restrictions and phosphate binders have not been shown to improve clinically important outcomes in patients with CKD not on dialysis. Some evidence alludes to decreased mortality in dialysis patients with the use of phosphate binders, but further study via randomized trials is warranted.

The most recent treatment guidelines from Kidney Disease Improving Global Outcomes (KDIGO) were released in July 2017. Overall, recommendations are similar to the prior (2009) KDIGO guideline. Relating to phosphate-lowering therapy, recommendations were re-worded to emphasize treating persistently elevated values and not preventatively, and treating towards normal range of serum phosphate rather than strict control to the normal range. Evidence now indicates calcium-based phosphate binders should be dose-restricted for all patients (not just based on hypercalcemia or arterial calcification), however the committee did not feel there was enough evidence to conclusively recommend against calcium-containing agents altogether. They also recognized there may be some settings where non-calcium containing agents are not available.

When the choice is made to initiate phosphate binder therapy, the lowest effective dose should be used. In patients where a calcium-containing phosphate binder is appropriate, it is suggested that elemental calcium doses (dietary and via pharmacologic agents) not exceed 2,000 mg per day, and the phosphate binder elemental calcium dose should not exceed 1,500 mg per day.

Ibsrela® (tenapanor), an agent already approved for treatment of irritable bowel syndrome with constipation and a novel mechanism of action (inhibition of intestinal sodium/hydrogen exchanger 3), was recently approved for treatment of hyperphosphatemia in CKD patients on dialysis. The product will be marketed for hyperphosphatemia under the trade name Xphozah®. The drug was approved by the FDA specifically as a second line therapy after failure or intolerance to phosphate binders. There are no other known phosphate binder agents near term in the development pipeline.

UTILIZATION FINDINGS

There were 16 claims for 7 members, for a total cost of $2,020 and an average cost per claim of $126. The most highly utilized medication was Sevelamer carbonate 800 mg tablets, with 7 claims, followed by Calcium acetate 667 mg capsules with 4 claims. There were no prior authorization requests.

RECOMMENDATIONS

- No changes

CLINICAL SUMMARY

CKD is defined as the presence of kidney damage (usually detected as urinary albumin excretion of ≥30 mg/day or equivalent) or decreased kidney function (defined as estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2) for three or more months, irrespective of the cause. The persistence of the damage or decreased function for at least three months is necessary to distinguish CKD from acute kidney disease/injury (AKI). As CKD progresses, patients gradually become more symptomatic. Once renal failure is advanced, some of the different signs and symptoms which may be observed include volume overload, hyperkalemia, metabolic acidosis, hypertension, anemia, and mineral and bone disorders (MBDs). Eventually, patients progress to ESRD and require hemodialysis to prevent death from uremia.

KDIGO classifies stages or categories of CKD according to their cause, the GFR category, and degree of albuminuria. Relative risk of prognosis of CKD is directly relational between the degree of GFR impairment and degree of albuminuria.

GFR categories in CKD

GFR category	GFR (ml/min/1.73 m^2)	Terms
G1	≥90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Albuminuria categories in CKD

Category	AER (mg/24 hours)	ACR (approximate equivalent) (mg/mmol)	ACR (approximate equivalent) (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.
*Relative to young adult level.
**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 hours [ACR >2220 mg/g; >220 mg/mmol]).

Over time the kidney becomes less efficient at filtering phosphate progressively leading to hyperphosphatemia and eventually to hyperparathyroidism and MBDs. Thus, the use of dietary restriction, phosphate binder medications, or both, are commonplace in treatment as CKD progresses. Vascular calcification is another complication as a result of the imbalance of bone mineralization and metabolism experienced by patients with CKD and puts patients at greater risk of mortality.

In non-dialysis CKD patients, a typical and guideline-recommended approach is to reduce serum phosphate levels only via dietary measures if the elevation is minor, adding a phosphate binder only if serum phosphate level remains persistently elevated (>5.5 mg/dL). For patients on dialysis, most often a dual approach of dietary measures and phosphate binders are initial treatment for elevated serum phosphate levels. For patients whom dietary restriction and phosphate binder use has failed, prolonged or daily dialysis can help to reduce levels, but is not standard practice for many reasons, and usually reserved for patients with very advanced disease (those in kidney failure).

INDICATIONS, DOSING and ADMINISTRATION

<table>
<tr><th>Medication</th><th>Indications</th><th>Dosing/Administration</th></tr>
<tr><td>Auryxia® (ferric citrate)</td><td>• The control of serum phosphorus levels in patients with chronic kidney disease (CKD) on dialysis
• The treatment of iron deficiency anemia in adult patients with chronic kidney disease not on dialysis</td><td>Hyperphosphatemia in CKD on dialysis:
• Initial dose: 2 tablets orally 3 times per day with meals
• Serum phosphorus levels should be monitored and the dose titrated by 1 to 2 tablets per day as needed to maintain serum phosphorus at target levels, max dose = 12 tablets daily
• Dose can be titrated at 1-week or longer intervals
Iron deficiency Anemia in CKD not on dialysis:
• Initial dose: 1 tablet orally 3 times per day with meals
• Adjust dose as needed to achieve and maintain hemoglobin goal, up to a maximum of 12 tablets daily</td></tr>
<tr><td>Lanthanum carbonate (Fosrenol®)</td><td>To reduce serum phosphate in patients with ESRD</td><td>• Initial dose: 1500 mg daily in divided doses with meals
• Titrate the dose every 2-3 weeks until an acceptable serum phosphate level is reached; maximum evaluated dose = 4500 mg daily
• Chewable tablets should not be swallowed whole.
• For oral powder: sprinkle powder on a small quantity of applesauce or other similar food and consume immediately; cannot be dissolved in liquid</td></tr>
<tr><td>Sevelamer HCl (Renagel®)</td><td>The control of serum phosphorus in patients with CKD on dialysis</td><td>Patients not taking a phosphate binder:
• Recommended starting dose is 800 to 1600 mg three times per day with meals
• Adjust by one tablet per meal in two week intervals as needed to obtain serum phosphorus target

Patients switching from calcium acetate:
• Similar reduction in serum phosphorus was seen with equivalent doses of Renagel® and calcium acetate.
• Recommended starting doses are as follows:
<table>
<tr><th>Calcium Acetate 667 mg (Tablets per meal)</th><th>Renagel® 800 mg (Tablets per meal)</th></tr>
<tr><td>1 tablet</td><td>1 tablet</td></tr>
<tr><td>2 tablets</td><td>2 tablets</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Medication</th><th>Indications</th><th>Dosing/Administration</th></tr>
<tr><td></td><td></td><td><table><tr><td>3 tablets</td><td>3 tablets</td></tr></table>
Tablets should be swallowed whole.</td></tr>
<tr><td>Sevelamer carbonate (Renvela®)</td><td>The control of serum phosphorus in adults and children 6 years of age and older with CKD on dialysis</td><td>Adult patients not taking a phosphate binder:
• Recommended starting dose of Renvela® is 0.8 to 1.6 g taken orally 3 times per day with meals based on serum phosphorus level
• Titrate dose by 0.8 g three times per day with meals at two-week intervals as necessary to achieve target serum phosphorus levels

Starting dose for pediatric patients not taking a phosphate binder:
• Starting dose for pediatric patients 6 years of age and older is 0.8 g to 1.6 g taken three times per day with meals based on the patient's Body Surface Area (BSA) category. Titrate as needed to achieve target levels at two-week intervals for 6 weeks and then every 4 weeks as needed to obtain serum phosphorus target.

Switching from sevelamer: use the same dose in grams

Switching from calcium acetate:<table><tr><th>Calcium Acetate 667 mg (Tablets per meal)</th><th>Renvela®</th></tr><tr><td>1 tablet</td><td>0.8 g</td></tr><tr><td>2 tablets</td><td>1.6 g</td></tr><tr><td>3 tablets</td><td>2.4 g</td></tr></table>• Tablets should be swallowed whole. Powder packets should be mixed in water or a small amount of food or beverage and consumed within 30 minutes.</td></tr>
<tr><td>Velphoro® (sucroferric oxyhydroxide)</td><td>The control of serum phosphorus levels in patients with CKD on dialysis</td><td>• Recommended starting dose is 3 tablets (1,500 mg) per day, administered as 1 tablet (500 mg) 3 times daily with meals
• Tablets must be chewed and not swallowed whole
• Monitor serum phosphorus levels and adjust the dose by 500 mg (1 tablet) per day as needed until an acceptable serum</td></tr>
</table>

Medication	Indications	Dosing/Administration
		phosphorus level is reached-titrate as often as weekly.
Calcium acetate (PhosLo®)	To reduce serum phosphorus in patients with ESRD	• Initial dose: 2 tablets (1334 mg) with each meal • Increase the dose gradually to reduce serum phosphorus levels to the target range, as long as hypercalcemia does not develop • Most patients require 3-4 tablets with each meal
Xphozah® (tenapanor HCl)	To reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.	Recommended dosage: 30 mg orally twice daily before the morning and evening meals
MagneBind 300® (calcium carbonate/magnesium carbonate)	Dietary supplement that reduces the absorption of dietary phosphate	1-3 tablets with meals, or as directed
MagneBind 400 Rx® (calcium carbonate/magnesium carbonate/folic acid)	Indicated as a prescription folic acid supplement with additional nutrients for kidney dialysis patients	1-3 tablets with 3 times a day with meals

BOXED WARNINGS and CONTRAINDICATIONS

	Auryxia® (ferric citrate)	Velphoro® (sucroferric oxyhydroxide)	Lanthanum carbonate (Fosrenol®)	Sevelamer (Renagel®, Renvela®)	Calcium acetate (PhosLo®)	Xphozah® (tenapanor HCl)	MagneBind 300® (Ca carbonate/Mg carbonate)	MagneBind 400 Rx® (Ca carbonate/Mg carbonate/FA)
Boxed Warnings								
None	✓	✓	✓	✓	✓	✓	✓	✓
Contraindications								
Hypersensitivity to active ingredient/formulation component				✓	✓			
Iron overload syndromes (e.g., hemochromatosis)	✓							
Bowel obstruction			✓	✓		✓		
Hypercalcemia, renal calculi					✓			
Hypermagnesemia								✓
Patients who have impaired renal function not on dialysis								✓
Not for use in patients under 6 years (diarrhea/severe dehydration)						✓		
None listed		✓					✓	

WARNINGS/PRECAUTIONS

	Auryxia® (ferric citrate)	Velphoro® (sucroferric oxyhydroxide)	Lanthanum carbonate (Fosrenol®)	Sevelamer (Renagel®, Renvela®)	Calcium acetate (PhosLo®)	Xphozah® (tenapanor HCl)	MagneBind 300® (Ca carbonate/Mg carbonate)	MagneBind 400 Rx® (Ca carbonate/Mg /carbonate/FA)
Iron toxicity: May increase serum iron, ferritin, and transferrin saturation (TSAT) and excessive elevations in iron stores	✓							
Stool discoloration: May cause discolored (dark) stools	✓							
Iron supplements: Patients receiving parenteral iron supplementation may require a dose reduction or discontinuation	✓							
Accidental overdose of iron-containing products causes fatal poisoning in children	✓							
Use in patients with significant GI disorders or post major GI surgery; hemochromatosis or other conditions associated with iron accumulation; hepatic disease; peritonitis during peritoneal dialysis has not be studied	✓							
Serious cases of GI obstruction, ileus, subileus, GI perforation and fecal impaction have been reported in patients; chewable tablets must be chewed completely to avoid GI events			✓					
May give appearance of an imaging agent during X-ray procedures due to radio-opaque properties			✓					
Cases of GI events (dysphagia, bowel obstruction, severe GI motility disorders, etc.) have been reported				✓				
Monitor bicarbonate, chloride; vitamins D, E, K; folic acid				✓				
Patients with ESRD may develop hypercalcemia					✓			
May aggravate digitalis toxicity					✓			
Diarrhea: discontinue in patients with severe diarrhea						✓		
None listed							✓	✓

PRACTICE GUIDELINES

Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl. 2017;7:1–59.

- In patients with CKD G3a–G5D, treatments of CKD-MBD should be based on serial assessments of phosphate, calcium, and PTH levels, considered together (Not Graded).
- In patients with CKD G3a–G5D, we suggest lowering elevated phosphate levels toward the normal range (2C).
- In adult patients with CKD G3a–G5D, we suggest avoiding hypercalcemia (2C). In children with CKD G3a–G5D, we suggest maintaining serum calcium in the age-appropriate normal range (2C).
- In patients with CKD G5D, we suggest using a dialysate calcium concentration between 1.25 and 1.50 mmol/l (2.5 and 3.0 mEq/l) (2C).
- In patients with CKD G3a-G5D, decisions about phosphate-lowering treatment should be based on progressively or persistently elevated serum phosphate (Not Graded).
- In adult patients with CKD G3a–G5D receiving phosphate-lowering treatment, we suggest restricting the dose of calcium-based phosphate binders (2B). In children with CKD G3a–G5D, it is reasonable to base the choice of phosphate-lowering treatment on serum calcium levels (Not Graded).
- In patients with CKD G3a-G5D, we recommend avoiding the long-term use of aluminum-containing phosphate binders and, in patients with CKD G5D, avoiding dialysate aluminum contamination to prevent aluminum intoxication (1C).
- In patients with CKD G3a–G5D, we suggest limiting dietary phosphate intake in the treatment of hyperphosphatemia alone or in combination with other treatments (2D). It is reasonable to consider phosphate source (e.g., animal, vegetable, additives) in making dietary recommendations (Not Graded).
- In patients with CKD G5D, we suggest increasing dialytic phosphate removal in the treatment of persistent hyperphosphatemia (2C).

Recommendation Definitions

Level	Clinician Implications	Policy Implications
1 (recommend)	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure.
2 (suggest)	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

Quality of Evidence

Class/Level	Meaning
A (High)	We are confident that the true effect lies close to that of the estimate of the effect.
B (Moderate)	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C (Low)	The true effect may be substantially different from the estimate of the effect.
D (Very low)	The estimate of effect is very uncertain, and often will be far from the truth.

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
A Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy of Tenapanor as Adjunctive Therapy to Phosphate Binder Therapy in End-Stage Renal Disease (ESRD) Subjects With Hyperphosphatemia. **NCT03824587** **Xphozah Prescribing Information**	An interventional, randomized, parallel assignment, triple blind, randomized, phase 3 trial. Subjects were adult patients with chronic kidney disease, dialysis dependent and with hyperphosphatemia (≥5.5 and ≤10.0 mg/dL) despite current use of phosphate binder therapy. 236 patients were randomized 1:1 to placebo or tenapanor for 4 weeks in addition to their phosphate binder therapies.	• Primary: change from baseline in serum phosphorus levels at week four
Results: **Primary:** During the 4-week period, the serum phosphorus decreased by 0.7 mg/dL (95% CI: (0.3, 1.0), p=0.0004) in the add-on Xphozah group as compared to the add-on placebo group. **Conclusion**: Tenapanor significantly reduced serum phosphorus levels in patients on dialysis using phosphate binder therapy.		
Citation	**Design**	**Endpoints**
Ruospo M, Palmer SC, Natale P, et al. **Phosphate binders for preventing and treating chronic kidney disease-mineral and bone disorder (CKD-MBD).** Cochrane Database Syst Rev. 2018 Aug 22;8:CD006023. doi: 10.1002/14651858.CD006023.pub3.	A Cochrane systematic review update to the 2011 version. Studies up to July 12, 2018 were included, including RCTs of quasi RCTs of adults with CKD (of any GFR category) comparing a phosphate binder to another phosphate binder, placebo or usual care to lower serum phosphate. 104 studies were included with 13,744 adults. Sixty-nine new studies were included from the 2011 review to the 2018 update.	Assess benefits and harms of phosphate binders in terms of endpoints including: • all-cause and cardiovascular death • myocardial infarction • stroke • adverse events • vascular calcification and bone fracture • surrogates for such outcomes including serum phosphate, parathyroid hormone (PTH), and FGF23
Results: In CKD G2 to G5, compared with placebo or usual care, sevelamer, lanthanum, iron and calcium-based phosphate binders had uncertain or inestimable effects on death (all causes), cardiovascular death, myocardial infarction, stroke, fracture, or coronary artery calcification. Sevelamer may lead to constipation and lanthanum and iron-based binders probably increased constipation compared with placebo or usual care. Lanthanum may result in vomiting. Iron-based binders probably result in diarrhea, while the risks of other adverse events for all binders were uncertain. In CKD G5D sevelamer may lead to lower death (all causes) (RR 0.53, CI 0.30 to 0.91, low certainty) and induce less hypercalcemia (RR 0.30, CI 0.20 to 0.43, low certainty) when compared with calcium-based binders, and has uncertain or inestimable effects on cardiovascular death, myocardial infarction, stroke, fracture, or coronary artery calcification. The finding of lower death with sevelamer compared with calcium was present when the analysis was restricted to studies at low risk of bias (RR 0.50, CI 0.32 to 0.77). In absolute terms, sevelamer may lower risk of death (all causes) from 210 per 1000 to 105 per 1000 over a follow-up of up to 36 months, compared to calcium-based binders. Compared with calcium-based binders, lanthanum had uncertain effects with respect to all-cause or cardiovascular death, myocardial infarction, stroke, fracture, or coronary artery calcification and probably had reduced risks of treatment-related hypercalcemia (RR 0.16, CI 0.06 to 0.43, low certainty). There were no head-to-head studies of iron-based binders compared with calcium. The paucity of placebo-controlled studies in CKD G5D has led to uncertainty about the effects of phosphate binders on patient-important outcomes compared with placebo. It is uncertain whether the effects of binders on clinically-relevant outcomes were different for patients who were and were not treated with dialysis in subgroup analyses.		

Conclusion: Sevelamer may lower death (all causes) compared to calcium-based binders and incur less treatment-related hypercalcemia in G5D dialysis patients, while no clinically important benefits of any phosphate binder were found in relation to cardiovascular death, myocardial infarction, stroke, fracture or coronary artery calcification. When comparing to placebo, the effects of binders on patient-important outcomes are not certain. In patients with CKD G2 to G5, the effects of sevelamer, lanthanum, and iron-based phosphate binders on cardiovascular, vascular calcification, and bone outcomes compared to placebo or usual care, are also uncertain and they may incur constipation, while iron-based binders may lead to diarrhea.

Citation	Design	Endpoints
Wang F, et al. **Effect of Lanthanum Carbonate on All-Cause Mortality in Patients Receiving Maintenance Hemodialysis: a Meta-Analysis of Randomized Controlled Trials.** Kidney Blood Press Res. 2018; 43(2): 536-44.	This was a meta-analysis of 9 RCTs; 2,813 patients examining lanthanum carbonate with other phosphate binders in adult dialysis patients (other binders included calcium carbonate, calcium acetate, and sevelamer). Used Cochrane Risk of Bias tool for assessment.	Primary: All-cause mortality Secondary: • Major CV events • Serum phosphate, calcium, iPTH levels

Results:

Primary:

- All-cause mortality was significantly lower in lanthanum versus control in 6 of 9 studies (odds ratio: 0.45, 95% CI 0.32-0.63, P<0.00001)

Secondary:

- Meta-analysis of 4 studies that reported CV events found no significant difference between lanthanum and other phosphate binders (P = 0.07); heterogeneity was significant (I2 = 64%, P = 0.04)
- Serum calcium levels were significantly lower with lanthanum versus others (WMD -0.53, 95% CI -0.67 to -0.38, P<0.00001), but serum iPTH was significantly higher (WMD 68.94, 95% CI 34.55-103.33, p<0.0001); heterogeneity was not significant for these outcomes

Conclusion: Meta-analysis found reduced mortality risk with lanthanum versus other phosphate binders, primarily CCPBs. However, there was no difference in CV events. However, the meta-analysis included a small number of studies, patient populations in each study were small, and methodology was variable.

Citation	Design	Endpoints
Habbous S, Przech S, Acedillo R, Sarma S, Garg AX, Martin J. **The efficacy and safety of sevelamer and lanthanum versus calcium-containing and iron-based binders in treating hyperphosphatemia in patients with chronic kidney disease: a systematic review and meta-analysis.** Nephrol Dial Transplant. 2017 Jan 1;32(1):111-125. doi: 10.1093/ndt/gfw312.	A systematic review and meta-analysis of 51 trials (8829 patients) was performed. Eligible studies were randomized trials on adults (>18 years of age) published in peer-reviewed journals (i.e. not abstracts) that compared sevelamer, lanthanum or iron-based binders with any other phosphate binder (excluding studies where only a nonactive placebo control was used or where a combination of active controls was used). Studies were not restricted by language, year of publication or study size.	• Primary: all-cause mortality • Secondary: major cardiovascular events, bone-related events, calciphylaxis and biochemical events, loss to follow-up, hospitalization rates.

Results: Compared with calcium-based binders, all-cause mortality was nonsignificantly lower with sevelamer {risk ratio [RR] 0.62 [95% confidence interval (CI) 0.35-1.08]} and lanthanum [RR 0.73 (95% CI 0.18-3.00)], but risk of bias was concerning. Compared with calcium-based binders, sevelamer reduced the risk of hypercalcemia [RR 0.27 (95% CI 0.17-0.42)], as did lanthanum [RR 0.12 (95% CI 0.05-0.32)]. Sevelamer reduced hospitalizations [RR 0.50 (95% CI 0.31-0.81)], but not lanthanum [RR 0.80 (95% CI 0.34-

1.93)]. The presence/absence of other clinically relevant outcomes was infrequently reported. Compared with calcium-based binders, sevelamer reduced serum calcium, low-density lipoprotein and coronary artery calcification, but increased intact parathyroid hormone. The clinical relevance of these changes is unknown since corresponding clinical outcomes were not reported. Lanthanum had less favorable impact on biochemical parameters. Sevelamer hydrochloride and sevelamer carbonate were similar in three studies. Sevelamer was similar to lanthanum (three studies) and iron-based binders (three studies).
Conclusion: Sevelamer was associated with a nonsignificant reduction in mortality and significantly lower hospitalization rates and hypercalcemia compared with calcium-based binders. However, differences in important outcomes, such as cardiac events, fractures, calciphylaxis, hyperchloremic acidosis and health-related quality of life remain understudied. Lanthanum and iron-based binders did not show superiority for any clinically relevant outcomes. Future studies that fail to measure clinically important outcomes (the reason why phosphate binders are prescribed in the first place) will be wasteful.

Citation	Design	Endpoints
Patel L, Bernard LM, Elder GJ. **Sevelamer Versus Calcium-Based Binders for Treatment of Hyperphosphatemia in CKD: A Meta-Analysis of Randomized Controlled Trials.** Clin J Am Soc Nephrol. 2016 Feb 5;11(2):232-44. doi: 10.2215/CJN.06800615.	Researchers performed an update to the sevelamer versus calcium-based binder (CBB) component of the 2011 Cochrane systematic review and meta-analysis, comparing efficacy of sevelamer versus CBBs (Ca salts, Ca acetate, Ca carbonate, and Ca ketoglutarate) on patient level, intermediate, and biochemical end points. Twenty-five studies to March 31, 2015 with 4770 participants (88% on hemodialysis) were included. Cochrane methods and quality of reporting guidelines were followed. Eligible studies were published randomized, controlled trials (RCTs) and quasi-RCTs (using predictable methods for treatment allocation) >8 weeks in duration enrolling adults with CKD stages 3–5 and on dialysis (eGFR≤59 ml/min per 1.73 m^2 or on dialysis). In RCTs, the first phase was included where possible. Post-transplantation studies were excluded along with single-arm or observational studies and abstracts.	• Patient-level: all-cause and CV mortality, CV events, hospitalization, fracture at any site, calciphylaxis, treatment–related adverse effects. • Biochemical outcomes: values of serum Ca, phosphorus (P), and Ca × P product, PTH, differences in total cholesterol, LDL-cholesterol (LDL-C) and HDL-cholesterol (HDL-C), incidence of hypercalcemia.

Results: Patients receiving sevelamer had lower all-cause mortality (risk ratio [RR], 0.54; 95% confidence interval [95% CI], 0.32 to 0.93), no statistically significant difference in cardiovascular mortality (n=2712; RR, 0.33; 95% CI, 0.07 to 1.64), and an increase in combined GI events of borderline statistical significance (n=384; RR, 1.42; 95% CI, 0.97 to 2.08). For biochemical outcomes, patients receiving sevelamer had lower total serum cholesterol (mean difference [MD], -20.2 mg/dl; 95% CI, -25.9 to -14.5 mg/dl), LDL-cholesterol (MD, -21.6 mg/dl; 95% CI, -27.9 to -15.4 mg/dl), and calcium (MD, -0.4 mg/dl; 95% CI, -0.6 to -0.2 mg/dl) and a reduced risk of hypercalcemia (RR, 0.30; 95% CI, 0.19 to 0.48). End of treatment intact parathyroid hormone was significantly higher for sevelamer (MD, 32.9 pg/ml; 95% CI, 0.1 to 65.7 pg/ml). Serum phosphate values showed no significant differences.
Conclusion: Patients with CKD stages 3-5D using sevelamer have lower all-cause mortality compared with those using CBBs. Because of a lack of placebo-controlled studies, questions remain regarding phosphate binder benefits for patients with CKD stages 3-5 and not on dialysis.

Citation	Design	Endpoints
Rodby RA, Umanath K, Niecestro R, et al. **Ferric Citrate, an Iron-Based Phosphate Binder, Reduces Health Care Costs in Patients on Dialysis Based on Randomized Clinical Trial Data**. *Drugs in R&D*. 2015;15(3):271-279. doi:10.1007/s40268-015-0103-y.	This study used results data from a 52-week phase III clinical trial (NCT01191255) and attempted to generalize this to the US ESRD population to calculate the potential impact of the use of ferric citrate (FC) on ESRD cost/patient/year. 441 adult subjects with ESRD who received FC or active control (AC) of sevelamer carbonate and/or calcium acetate were included. Differences in erythropoiesis-stimulating agents (ESAs) and IV iron usage between the treatment groups were modeled over time using generalized linear mixed models and zero-inflated Poisson models. Trends were modeled via logarithmic curves, and utilization patterns were applied to the general dialysis population to estimate expected resource savings.	Costs saved/patient/year using FC versus AC

Results: The model suggests an annual decrease of 129,106 U of ESAs and 1960 mg of IV iron per patient in the second year after a switch from AC to FC. Applying 2013 Medicare pricing, this would save $1585 in ESAs and $516 in IV iron: a total of $2101/patient/year; these savings would be expected to double for managed care plans. **Conclusion:** Phosphate binding with FC reduces IV iron and ESA usage. Given the high cost burden of ESRD, the researchers' model demonstrates significant potential cost savings.		
Citation	**Design**	**Endpoints**
Cannata-Andía JB, Fernández-Martín JL, Locatelli F et al. **Use of phosphate-binding agents is associated with a lower risk of mortality.** *Kidney Int*. 2013 Nov;84(5):998-1008. doi: 10.1038/ki.2013.185. Epub 2013 Jul 03.	This analysis sought to determine the association between the use of single and combined phosphate-binding agents and survival in 6797 patients of the COSMOS study: a 3-year follow-up, multicenter, open-cohort, observational prospective study carried out in 227 dialysis centers from 20 European countries. Patient phosphate-binding agent prescriptions (time-varying) and the case-mix-adjusted facility percentage of phosphate-binding agent prescriptions (instrumental variable) were used as predictors of the relative all-cause and cardiovascular mortality using Cox proportional hazard regression models. Three different multivariate models that included up to 24 variables were used for adjustments.	All-cause mortality, cardiovascular mortality
Results: After multivariate analysis, patients prescribed phosphate-binding agents showed a 29% and 22% lower all-cause and cardiovascular mortality risk, respectively. The survival advantage of phosphate-binding agent prescription remained statistically significant after propensity score matching analysis. A decrease of 8% in the relative risk of mortality was found for every 10% increase in the case-mix-adjusted facility prescription of phosphate-binding agents. **Conclusion**: All single and combined therapies with phosphate-binding agents, except aluminum salts, showed a beneficial association with survival.		
Citation	**Design**	**Endpoints**
Jamal SA, Vandermeer B, Raggi P, et al. **Effect of calcium-based versus non-calcium-based phosphate binders on mortality in patients with chronic kidney disease: an updated systematic review and meta-analysis.** *Lancet*. 2013;382(9900):1268.	A systematic review of articles published after August 1, 2008 until October 22, 2012 searching Medline, Embase, IPA, Cochrane Central Register, and Cumulative Index to Nursing and Allied Health Literature was performed. Investigators included all randomized and non-randomized trials that compared outcomes between patients with CKD taking calcium-based and non-calcium-based binders. Eighteen studies met inclusion criteria, but 11 of these trials reported on mortality.	Effect of calcium-based versus non-calcium-based phosphate binders on mortality in patients with chronic kidney disease
Results: Analysis of 11 randomized trials (4622 patients) that reported an outcome of mortality showed that patients assigned to non-calcium-based binders had a 22% reduction in all-cause mortality compared with those assigned to calcium-based phosphate binders (risk ratio 0.78, 95% CI 0.61-0.98). **Conclusion**: Non-calcium-based phosphate binders are associated with a decreased risk of all-cause mortality compared with calcium-based phosphate binders in patients with chronic kidney disease. Further studies are needed to identify causes of mortality and to assess whether mortality differs by type of non-calcium-based phosphate binder. The analysis did not evaluate CV mortality.		
Citation	**Design**	**Endpoints**
Navaneethan SD, Palmer SC, Vecchio M et al. **Phosphate binders for preventing and treating bone disease in chronic kidney disease patients.** *Cochrane Database Syst Rev* 2011: CD006023	MEDLINE, EMBASE, the Cochrane Renal Groups' Specialized Register and CENTRAL searched in 2010 for relevant studies and included 60 RCTs or quasi-RCTs (7631 participants) that assessed effects of various phosphate binders in adults with CKD. Studies of phosphate binders, alone or in combination with other (non-randomized) co-interventions (for example vitamin D compounds) were included. The first phase of randomized cross-over studies was included.	All-cause mortality, cardiovascular mortality, cardiovascular events, hospitalization, fracture, treatment-related adverse events, hypercalcemia, hyperphosphatemia, serum phosphorus.

Results: There was no significant reduction in all-cause mortality or serum calcium by phosphorus product with sevelamer hydrochloride compared to calcium-based agents. There was a significant reduction in serum phosphorus (16 studies, 3126 participants: MD 0.23 mg/dL, 95% CI 0.04 to 0.42) and parathyroid hormone (PTH) (12 studies, 2551 participants; MD 56 pg/mL, 95% CI 26 to 84) but a significant increase in the risk of hypercalcemia (12 studies, 1144 participants: RR 0.45, 95% CI 0.35 to 0.59) with calcium-based agents compared to sevelamer hydrochloride. There was a significant increase in the risk of adverse GI events with sevelamer hydrochloride in comparison to calcium salts (5 studies, 498 participants: RR 1.58, 95% CI 1.11 to 2.25). Compared with calcium-based agents, lanthanum significantly reduced serum calcium (2 studies, 122 participants: MD -0.30 mg/dL, 95% CI -0.64 to -0.25) and the Ca x P product, but not serum phosphorus levels. The effects of calcium acetate on biochemical end-points were similar to those of calcium carbonate. The phosphorus lowering effects of novel agents such as ferric citrate, colestilan and niacinamide were only reported in a few studies.
Conclusion: The authors concluded that all available phosphate-binders reduced serum phosphate concentrations in comparison to placebo but that data to date do not support superiority of novel non-calcium binding agents for patient-level outcomes such as all-cause mortality and cardiovascular end points in CKD.

Citation	Design	Endpoints
Kovesdy CP, Kuchmak O, Lu JL, Kalantar-Zadeh K. **Outcomes associated with phosphorus binders in men with non-dialysis-dependent CKD.** *Am J Kidney Dis*. 2010;56(5):842. doi: 10.1053/j.ajkd.2010.06.011.	This was a historical cohort study that looked at 1,188 men with moderate and advanced non-dialysis dependent CKD at a single medical center. Investigators examined associations of any phosphorus-binder administration (calcium containing or non-calcium containing, with sevelamer being the only non-calcium containing binder found) with all-cause mortality and the slopes of estimated glomerular filtration rate using time-varying Cox models and mixed-effects models. Associations also were examined in intention-to-treat analyses and in 133 patient-pairs matched according to propensity scores.	All-cause mortality, estimated GFR

Results: 344 patients were treated with a phosphorus binder; 658 patients died (mortality rate, 141 deaths/1,000 patient-years; 95% CI, 131-153) during a median follow-up of 3.1 years. Treatment with phosphorus binders (most patients were on calcium-containing binders) was associated with significantly lower mortality (adjusted HR, 0.61; 95% CI, 0.45-0.81; P<0.001). Results were similar when exposure was modeled in intention-to-treat analyses and examining propensity-matched patients. Phosphorus-binder use was not associated with significant changes in kidney function loss.
Conclusion: Administration of phosphorus binders is associated with lower mortality in men with moderate and advanced non-dialysis-dependent CKD.

Citation	Design	Endpoints
Isakova T, Gutiérrez OM, Chang Y, Shah A, Tamez H, Smith K, Thadhani R, Wolf M. **Phosphorus binders and survival on hemodialysis**. *J Am Soc Nephrol*. 2009;20(2):388. doi: 10.1681/ASN.2008060609.	A prospective cohort study of 10,044 hemodialysis patients using Cox proportional hazards analyses compared 1 year all-cause mortality among patients who were or were not treated with phosphate binders. Intention-to-treat analyses were performed to compare patients who began treatment with phosphorus binders during the first 90 days after initiating hemodialysis (n = 3555) with those who remained untreated during that period (n = 5055). As-treated analyses modeled phosphorus binder treatment as a time-dependent exposure.	All-cause mortality

Results: One-year mortality was 191 deaths/1000 patient-years at risk. The phosphorus binder–treated group had a significantly lower mortality rate than the untreated group in the unmatched cohort (136 *versus* 235 deaths/1000 patient-years at risk).
Conclusion: Treatment with phosphorus binders was independently associated with decreased mortality compared with no treatment in the intention-to-treat, as-treated, and matched analyses.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (01-01-2024 to 03-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Phosphate Binders								
calcium acetate (PhosLo®) 667 mg capsules	4	2	$309.84	$77.46	0	0 (0%)	F	No change
calcium acetate (PhosLo®) 667 mg tablets	2	1	$119.51	$59.76	0	0 (0%)	F	No change
lanthanum carbonate (Fosrenol®) 500, 750, 1000 mg chewable tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Fosrenol® (lanthanum carbonate) 750, 1000 mg powder packets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
sevelamer HCl (Renagel®) 400 mg, 800 mg tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
sevelamer carbonate (Renvela®) 0.8, 2.4 g powder packets	3	1	$1,011.45	$337.15	0	0 (0%)	F-PA	No change
sevelamer carbonate (Renvela®) 800 mg tablets	7	3	$579.11	$82.73	0	0 (0%)	F	No change
Velphoro® (sucroferric oxyhydroxide) 500 mg chewable tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Auryxia® (ferric citrate) 210mg tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
MagneBind 300® (calcium carbonate/magnesium carbonate) 250-300 mg tablets (OTC)	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
MagneBind 400 Rx® (calcium carbonate/magnesium carbonate/folic acid) 80-115-1 mg tablets	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Xphozah® (tenapanor) 20 mg, 30 mg tablets	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	16	7	$2,019.91	$126.24	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

Medication Request Guidelines

Recommendation: No changes

Phosphate Binders	
Therapeutic Classes (AHFS)	Phosphate-removing agents
Medications	**Formulary** Calcium acetate Sevelamer carbonate (Renvela) 800 mg tablet **Formulary, PA required** sevelamer hcl (Renagel) tablet **- PREFERRED** Lanthanum carbonate (Fosrenol) tablets **- PREFERRED** Sevelamer carbonate (Renvela) powder pack Fosrenol (lanthanum carbonate) powder pack Auryxia (ferric citrate) tablets Velphoro (sucroferric oxyhydroxide) chewable 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	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	Sevelamer HCL (Renagel) tablet and lanthanum carbonate (Fosrenol) tablet are approved when the following criteria are met: • Documentation of a trial and failure, contraindication, or intolerance sevelamer carbonate (Renvela) tablet Sevelamer carbonate (Renvela) powder packets, Fosrenol (lanthanum carbonate) powder packets, Auryxia tablets, and Velphoro tablets are approved when the following criteria are met: • Documentation of a trial and failure, contraindication, or intolerance to sevelamer carbonate (Renvela) tablet • Documentation of a trial and failure, contraindication, or intolerance to Sevelamer HCL (Renagel) tablet OR lanthanum carbonate (Fosrenol) tablet
Criteria Statement	Sevelamer hcl (Renagel) tablets and lanthanum carbonate (Fosrenol) tablets are reserved for members who have used (or cannot/should not use) sevelamer carbonate (Renvela) tablets. Sevelamer carbonate (Renvela) powder packets, Fosrenol (lanthanum carbonate) powder packets, Auryxia tablets, and Velphoro tablets are reserved for members who have used (or cannot/should not use) sevelamer carbonate (Renvela) tablet AND sevelamer hcl (Renagel) tablets or lanthanum carbonate (Fosrenol) tablets.
Last P&T Review Date	6/2024~~6/2023~~

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Benign Prostatic Hyperplasia

Executive Summary

CLASS OVERVIEW

Benign prostatic hyperplasia (BPH) a histological diagnosis that is increasingly prevalent with male age. Prevalence increases starting at age 40-45 years to reach 60% at age 60 and 80% at age 80. BPH can be asymptomatic, or it may cause lower urinary tract symptoms (LUTS) such as frequent urination, nocturia, hesitancy, urgency, and weak urinary stream. Lifestyle and behavioral interventions are considered first-line management for all patients. The drug therapy management of symptomatic patients is reviewed herein; however, even without medical therapy approximately a third of men will stabilize and another third will have symptom regression. Complicated cases may require specialist evaluation and surgical intervention.

There are three classes of drugs used for medical management: alpha-1-adrenergic antagonists (α-blockers), 5-alpha reductase inhibitors (5-ARIs), and phosphodiesterase-5 (PDE-5) inhibitors. Alpha-blockers are typically used first line as their effects are immediate; 5-ARIs require continuous administration for 6-12 months to be efficacious and as so are usually reserved for patients intolerant to the hypotensive effects of α-blockers. PDE-5 inhibitors are reserved for patients with comorbid erectile dysfunction due to limited efficacy data. Additionally, combination therapy is available. Combination options consist of an α-blocker plus a 5-ARI (Jalyn®), or a 5-ARI plus a PDE-5 inhibitor (Entadfi™). Entadfi is the newest treatment option for BPH with approval in December 2021.

The 2021 American Urological Association (AUA) published guidelines related to the management of benign prostatic hyperplasia are summarized in this review.

UTILIZATION FINDINGS

There were 119 claims for 98 members totaling $1,319.64 for an average cost per claim of $11.09. The most highly utilized medication was tamsulosin (Flomax) 0.4 mg oral capsule with 72 claims, followed by finasteride (Proscar) 5 mg oral tablet, with 17 claims. There were no prior authorization requests.

RECOMMENDATIONS

- No changes

CLINICAL SUMMARY

Benign prostatic hyperplasia (BPH) a histological diagnosis that is increasingly prevalent with male age. Prevalence increases starting at age 40-45 years to reach 60% at age 60 and 80% at age 80. BPH may be asymptomatic, or it may cause lower urinary tract symptoms (LUTS) such as frequent urination, nocturia, hesitancy, urgency, and weak urinary stream. Lifestyle and behavioral interventions are considered first-line management for all patients. The drug therapy management of symptomatic patients is reviewed herein; however, even without medical therapy approximately a third of men will stabilize and another third will have symptom regression. Complicated cases may require specialist evaluation and surgical intervention.

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The 2021 American Urological Association (AUA) published guidelines related to the management of benign prostatic hyperplasia are summarized in this review. Nymozarfex (fexapotide), an injectable treatment option, is in the pipeline as a potential new approach for BPH treatment for patients who are unable to tolerate oral therapy. Nymozarfex originally had an anticipated approval for March 2023, however, the FDA issued a refusal to file letter after identifying an outstanding issue of longer-term safety data. Nymox Pharmaceutical is preparing the required documentation for resubmission.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Doxazosin (Cardura®)	Treatment of signs and symptoms of BPH	1 mg once daily; titrate at 1- to 2-week intervals up to 8 mg once daily based on response and tolerability
Cardura® XR (doxazosin)		4 mg once daily; titrate at 3- to 4- weeks intervals up to 8 mg once daily based on response and tolerability Conversion from immediate release (IR): Omit final evening dose of IR product prior to starting 4 mg morning dosing with XR product
Terazosin		1 mg at bedtime; titrate over several weeks up to 10 mg once daily based on response and tolerability; if no response after 4 to 6 weeks of 10 mg/day, may increase to 20 mg/day
Tamsulosin (Flomax®)		0.4 mg once daily; if response is inadequate after 2 to 4 weeks, may increase to 0.8 mg once daily
Silodosin (Rapaflo®)		8 mg once daily with a meal
Alfuzosin (Uroxatral®)		10 mg once daily
Dutasteride (Avodart®)	Treatment of symptomatic BPH [to improve symptoms, reduce the risk of acute urinary retention (AUR), and to reduce the risk of need for BPH-related surgery] alone or in combination therapy with tamsulosin	0.5 mg once daily
Finasteride (Proscar®)	Treatment of symptomatic BPH (to improve symptoms, reduce the risk of AUR, and to reduce the risk of need for BPH-related surgery); alone or in combination with an α-blocker to reduce the risk of symptomatic progression	5 mg once daily
Dutasteride/tamsulosin (Jalyn®)	Treatment of symptomatic BPH in men with an enlarged prostate	One capsule (0.5 mg dutasteride/0.4 mg tamsulosin) once daily ~30 minutes after the same meal each day
Tadalafil (Cialis®)	Treatment of the signs and symptoms of BPH	5 mg once daily (when used with finasteride to initiate BPH therapy, the recommended duration of therapy is ≤26 weeks)
Entadfi™ (finasteride/tadalafil)	Treatment of signs and symptoms of BPH in men with an enlarged prostate	One capsule (5mg finasteride/5mg tadalafil) daily (the recommended duration of therapy is up to 26 weeks)

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Doxazosin (Cardura®)	None	Hypersensitivity to the active ingredient, other quinazolines, or any component of the formulation
Cardura® XR (doxazosin)		
Terazosin		
Tamsulosin (Flomax®)		
Silodosin (Rapaflo®)		Hypersensitivity to silodosin or any component of the formulation; concurrent use with strong CYP3A4 inhibitors; severe renal or hepatic impairment
Alfuzosin (Uroxatral®)		Hypersensitivity to alfuzosin or any component of the formulation; concurrent use with potent CYP3A4 inhibitors; moderate or severe hepatic impairment
Dutasteride (Avodart®)	None	Hypersensitivity to the active ingredient, other 5-ARIs, or any component of the formulation; use in pediatric patients; pregnancy or women of childbearing potential
Finasteride (Proscar®)		
Dutasteride/tamsulosin (Jalyn®)	None	Hypersensitivity to dutasteride, tamsulosin, other 5-ARIs, or any component of the formulation; use in pediatric patients; pregnancy or women of childbearing potential
Tadalafil (Cialis®)	None	Hypersensitivity to tadalafil or any component of the formulation; concurrent use of organic nitrate (regularly and/or intermittently) or guanylate cyclase stimulators (e.g. riociguat)
Entadfi™ (finasteride/tadalafil)	None	Concurrent use of organic nitrate (regularly and/or intermittently) or guanylate cyclase stimulators (e.g. riociguat), hypersensitivity to Entadfi or any of its components, prengancy

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Doxazosin (Cardura®) Cardura® XR (doxazosin)	Concerns related to adverse effects (AEs): allergic reactions, CNS depression, floppy iris syndrome, decreases in white blood cells and neutrophil count, orthostatic hypotension/syncope, priapism Disease related concerns: use caution in patients with heart failure, angina, recent myocardial infarction, mild to moderate hepatic impairment; rule out prostatic carcinoma
Terazosin	Concerns related to AEs: CNS depression, floppy iris syndrome, orthostatic hypotension/syncope, priapism Disease related concerns: may exacerbate underlying myocardial dysfunction
Tamsulosin (Flomax®)	Concerns related to AEs: floppy iris syndrome, orthostatic hypotension/syncope, priapism, patients with a sulfa allergy may rarely develop allergy to tamsulosin, angina Disease related concerns: it is recommended to rule out prostatic carcinoma before beginning therapy, may exacerbate underlying myocardial dysfunction
Silodosin (Rapaflo®)	Concerns related to AEs: floppy iris syndrome, orthostatic hypotension/syncope Disease related concerns: use caution in patients with mild-moderate hepatic impairment, moderate renal impairment
Alfuzosin (Uroxatral®)	Concerns related to AEs: floppy iris syndrome, orthostatic hypotension/syncope, priapism, angina, CNS depression Disease related concerns: use caution in patients with history of tachyarrythmia, mild hepatic impairment, known QT prolongation, severe renal impairment, rule out prostatic carcinoma
Dutasteride (Avodart®)	Disease related concerns: diminished urinary flow, use caution in patients with hepatic impairment, increase in the incidence of high-grade prostate cancers has been observed Concurrent drug therapy concerns: use caution with concurrent use of CYP3A4 inhibitors
Finasteride (Proscar®)	Disease related concerns: diminished urinary flow, use caution in patients with hepatic impairment, increase in the incidence of high-grade prostate cancers has been observed
Dutasteride/tamsulosin (Jalyn®)	Concerns related to AEs: floppy iris syndrome, orthostatic hypotension/syncope, priapism, patients with a sulfa allergy may rarely develop allergy to tamsulosin Disease related concerns: diminished urinary flow, use caution in patients with hepatic impairment, increase in the incidence of high-grade prostate cancers has been observed, use caution in patients with ESRD
Tadalafil (Cialis®)	Concerns related to AEs: angina chest pain, use caution in patients with retinitis pigmentosa, sudden decrease or loss of hearing, hypotension/syncope, priapism, rare vision loss as a sign of nonarteritic anterior ischemic optic neuropathy Disease related concerns: use caution in patients with anatomical penis deformation, bleeding disorders, cardiovascular disease, hepatic impairment, peptic ulcer disease, pulmonary veno-occlusive disease, renal impairment; use is not recommended in patients with hypotension
Entadfi™ (finasteride/tadalafil)	Concerns related to AEs: decreased libido, decreased volume of ejaculate, breast enlargement, breast tenderness, rash, headache, dyspepsia, back pain, myalgia, flushing, limb pain, nasal congestion Disease related concerns: cardiovascular risk, sudden hearing loss, effects on bleeding, limit expose to pregnant females, ocular adverse reactions, use with caution in patients with predisposed priapism, use with caution in patients with other urological conditions, evaluate for prostate cancer

PRACTICE GUIDELINES

Sandhu JS, Bixler BR, Dahm P, et al. Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia (BPH): AUA Guideline Amendment 2023. J Urol. 2023;10.

Alpha-adrenergic Blockers

- Clinicians should offer one of the following alpha blockers as a treatment option for patients with bothersome, moderate to severe LUTS/BPH: alfuzosin, doxazosin, silodosin, tamsulosin, or terazosin. (Moderate Recommendation; Evidence Level: Grade A)
- When prescribing an alpha blocker for the treatment of LUTS/BPH, the choice of alpha blocker should be based on patient age and comorbidities, and different adverse event profiles (e.g., ejaculatory dysfunction [EjD], changes in blood pressure). (Moderate Recommendation; Evidence Level: Grade A)
- When initiating alpha blocker therapy, patients with planned cataract surgery should be informed of the associated risks and be advised to discuss these risks with their ophthalmologists. (Expert Opinion)

5- Alpha Reductase Inhibitors

- For the purpose of symptom improvement, 5- ARI monotherapy should be used as a treatment option in patients with LUTS/BPH with prostatic enlargement as judged by a prostate volume of > 30g on imaging, a prostate specific antigen (PSA) > 1.5ng/dL, or palpable prostate enlargement on digital rectal exam (DRE). (Moderate Recommendation; Evidence Level: Grade B)
- 5-ARIs alone or in combination with alpha blockers are recommended as a treatment option to prevent progression of LUTS/BPH and/or reduce the risks of urinary retention and need for future prostate-related surgery. (Strong Recommendation; Evidence Level: Grade A)
- Before starting a 5-ARI, clinicians should inform patients of the risks of sexual side effects, certain uncommon physical side effects, and the low risk of prostate cancer. (Moderate Recommendation; Evidence Level: Grade C)
- Clinicians may consider 5-ARIs as a treatment option to reduce intraoperative bleeding and peri- or postoperative need for blood transfusion after transurethral resection of the prostate (TURP) or other surgical intervention for BPH. (Expert Opinion)

PDE-5 Inhibitors

- For patients with LUTS/BPH irrespective of comorbid erectile dysfunction (ED), 5mg daily tadalafil should be discussed as a treatment option. (Moderate Recommendation; Evidence Level: Grade B)

Combination Therapy

- 5-ARI in combination with an alpha blocker should be offered as a treatment option only to patients with LUTS associated with demonstrable prostatic enlargement as judged by a prostate volume of > 30g on imaging, a PSA >1.5ng/dL, or palpable prostate enlargement on DRE. (Strong Recommendation; Evidence Level: Grade A)
- Anticholinergic agents, alone or in combination with an alpha blocker, may be offered as a treatment option to patients with moderate to severe predominant storage LUTS. (Conditional Recommendation; Evidence Level: Grade C)
- Beta-3-agonists in combination with an alpha blocker may be offered as a treatment option to patients with moderate to severe predominate storage LUTS. (Conditional Recommendation; Evidence Level: Grade C)
- Clinicians may offer the combination of lowdose daily 5mg tadalafil with alpha blockers for the treatment of LUTS/BPH. (Conditional Recommendation; Evidence Level: Grade C)
- Clinicians may offer the combination of low dose daily tadalafil 5mg with finasteride for the treatment of LUTS/BPH. (Conditional Recommendation; Evidence Level: Grade C)

Recommendation Definitions

Strength of Evidence Category	GRADE Certainty Rating	Definition
A	High	• Very confident that the true effect lies close to that of the estimate of the effect
B	Moderate	• Moderately confident in the effect estimate • The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
C	Low Very Low	• Confidence in the effect estimate is limited • The true effect may be substantially different from the estimate of the effect • Very little confidence in the effect estimate • The true effect is likely to be substantially different from the estimate of effect

Evidence Grade	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is substantial -Applies to most patients in most circumstances and future research is unlikely to change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is substantial -Applies to most patients in most circumstances but better evidence could change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) appears substantial -Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is moderate -Applies to most patients in most circumstances and future research is unlikely to change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is moderate -Applies to most patients in most circumstances but better evidence could change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) appears moderate -Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (Net benefit or harm comparable to other options)	-Benefits = Risks/Burdens -Best action depends on individual patient circumstances -Future Research is unlikely to change confidence	-Benefits = Risks/Burdens -Best action appears to depend on individual patient circumstances -Better evidence could change confidence	-Balance between Benefits & Risks/Burdens unclear -Net benefit (or net harm) comparable to other options -Alternative strategies may be equally reasonable -Better evidence likely to change confidence
Clinical Principle	A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature		

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Dong Z, Wang Z, Yang K, Liu Y, Gao W, Chen W. Tamsulosin versus terazosin for benign prostatic hyperplasia: a systematic review. Syst Biol Reprod Med. 2009 Aug;55(4):129-36. doi: 10.3109/19396360902833235.	Meta-analysis of randomized controlled trials (RCTs) or quasi-RCTs evaluating tamsulosin versus terazosin in the treatment of BPH. Trials were identified by review of PubMed, Embase, the Cochrane Library, Chinese biomedicine literature database (CBM). 12 of 68 identified RCTs were included involving a total of 2,816 men.	• Weighted mean difference (WMD) of international prostate symptom score (IPSS), quality of life (QOL), maximum urinary flow rate (Q(max)), average urinary flow rate (Q(ave)), residual volume, prostate volume, and relative risk (RR) of AEs
Results: Tamsulosin was found to be better than terazosin when assessed by IPSS (WMD=-1.24 95% CI [- 1.98, -0.51]). There was no significant difference between the two groups in QOL (WMD=0.04 95% CI [-0.16, 0.24]), Qmax (WMD=-0.38 95% CI [-1.18, 0.41]), Q(ave) (WMD=-0.39 95% CI [- 0.84, 0.06]), residual volume (WMD=-4.32 95% CI [-10.96, 2.33]), and prostate volume (WMD=-0.28 95% CI [- 3.37, 2.81]). Fewer patients receiving tamsulosin experienced dizziness (RR -0.38 95% CI [0.30, 0.48]), severe hypotension (RR=0.16 95% CI [0.04, 0.68]), and dry mouth (RR=0.14 95% CI [0.03, 0.77]), compared with patients receiving terazosin. **Conclusion**: The authors concluded that "Many of the high quality RCTs showed beneficial effects of tamsulosin in terms of improving IPSS." However, a robust conclusion as to whether tamsulosin is more efficacious than terazosin could not be drawn due to various study limitations.		

Citation	Design	Endpoints
Shim SR, Kim JH, Chang IH, et al. Is Tamsulosin 0.2 mg Effective and Safe as a First-Line Treatment Compared with Other Alpha Blockers?: A Meta-Analysis and a Moderator Focused Study. Yonsei Med J. 2016 Mar;57(2):407-18. doi: 10.3349/ymj.2016.57.2.407	Meta-analysis of RCTs in MEDLINE, EMBASE, and Cochrane library from January 1980 to June 2013 to evaluate the efficacy of tamsulosin 0.2 mg. 10 of 2862 identified articles were included involving a total of 1418 subjects.	• Standardized mean differences (SMD) in IPSS, maximal urinary flow rate (Qmax), post-voided residual volume (PVR), quality of life (QoL) and AEs
Results: The pooled overall SMD in the mean change of IPSS from baseline for the tamsulosin group versus the control group was 0.02 [95% confidence interval (CI); -0.20, 0.25]. The pooled overall SMD in the mean change of QoL from baseline for the tamsulosin group versus the control group was 0.16 (95% CI; -0.16, 0.48). The regression analysis with the continuous variables revealed no significance in all outcomes. **Conclusion**: Tamsulosin 0.2 mg has similar efficacy and fewer adverse events, compared with silodosin and terazosin, as an initial treatment strategy for men with LUTS.		

Citation	Design	Endpoints
Dahm P, Brasure M, MacDonald R, et al. Comparative Effectiveness of Newer Medications for Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: A Systematic Review and Meta-analysis. Eur Urol. 2017 Apr;71(4):570-581. doi: 10.1016/j.eururo.2016.09.032.	Meta-analysis of RCTs and observational studies in Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, and Ovid Embase bibliographic databases through June 2016 to evaluate the efficacy of newer α-blockers, antimuscarinics, a beta-3 adrenoceptor agonist, PDE-5 inhibitors, or combination therapy with one of these medications as an active comparator. 43 RCTs and 5 observational studies were included. Studies were stratified by intervention type: 10 trials evaluated silodosin 8 mg versus tamsulosin 0.2-0.4 mg; 18 trials evaluated a urinary anticholinergic plus an α-blocker to an α-blocker alone; 1 trial evaluated mirabegron plus and α-blocker to an α-blocker alone; 6 trials evaluated tadalafil versus α_{1A}-blockers tamsulosin or alfuzosin; 3 trials evaluated sildenafil versus an α-blocker; 4 trials evaluated a PDE-5 inhibitor (tadalafil, sildenafil or vardenafil) plus an α-blocker to an α-blocker alone; 1 trial evaluated tadalafil plus a 5-ARI versus a 5-ARI alone; 1 trial evaluated tadalafil versus a 5-ARI/α-blocker combination.	• Mean change, reported as weighted mean difference (WMD), from baseline in IPSS score and IPSS QoL, RR of withdrawals • Each endpoint was assigned a strength of evidence: high, moderate, low or insufficient
Results: There was moderate strength of evidence supporting similar efficacy of silodosin and tamsulosin 0.2-0.4 mg and a greater withdrawal rate due to AEs with silodosin. There was low to moderate strength of evidence supporting similar efficacy of tadalafil 5 mg and tamsulosin 0.2-0.4 mg and moderate evidence suggesting a higher rate of AEs with tadalafil. There was low strength of evidence supporting improved efficacy of alfuzosin compared with tadalafil and insufficient evidence related to adverse effects of each. **Conclusion**: None of the drugs or drug combinations newly used to treat BPH demonstrated superiority to traditional α-blocker treatment. Taken together with the studies' short time-horizon and less assurance of the safety of the newer agents, their current value in treating BPH appears low.		

Citation	Design	Endpoints
Yuan JQ, Mao C, Wong SYS, et al. Comparative Effectiveness and Safety of Monodrug Therapies for Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia. Medicine (Baltimore). 2015 Jul; 94(27): e974. Published online 2015 Jul 13. doi: 10.1097/MD.0000000000000974.	Meta-analysis and network meta-analysis (NMA) of RCTs comparing α-blockers, 5-ARIs, muscarinic receptor antagonists (MRAs), PDE-5 inhibitors, or placebo for the treatment of BPH. 124 trials evaluating 58,548 participants were included.	• Mean difference (MD) in IPSS and peak urinary flow (PUF)
Results: When compared with placebo, α-blockers, 5-ARIs, and PDE-5 inhibitors reduced IPSS by −1.35 to −3.67 points and increased PUF by −0.02 to 1.95 mL/s, with doxazosin (IPSS: MD, −3.67[−4.33 to −3.02]; PUF: MD, 1.95[1.61 to 2.30]) and terazosin (IPSS: MD, −3.37 [−4.24 to −2.50]; PUF: MD, 1.21[0.74 to 1.66]) showing the greatest improvement. IPSS improvement scores were comparable among tamsulosin, alfuzosin, naftopidil, silodosin, dutasteride, sildenafil, vardenafil, and tadalafil. AEs and withdraws due to AEs were generally comparable among various agents. **Conclusion**: Doxazosin and terazosin appear to be the most effective agents to treat BPH, though evaluated α-blockers, 5-ARIs, and PDE-5 inhibitors are also effective. There are no major differences in the overall safety profile of the evaluated agents.		

Citation	Design	Endpoints
Wang X, Wang X, Li S, Meng Z, Liu T, Zhang X. Comparative effectiveness of oral drug therapies for lower urinary tract symptoms due to benign prostatic hyperplasia: a systematic review and network meta-analysis. PLoS One. 2014 Sep 12;9(9):e107593. doi: 10.1371/journal.pone.0107593. eCollection 2014.	NMA of RCTs in PubMed, Cochrane Library and Embase comparing different drug therapies for LUTS/BPH. 66 RCTs covering seven different therapies with 29,384 participants were included.	• MD in IPSS total score, storage subscore and voiding subscore; and maximum urinary flow rate (Qmax)
Results: α-blockers plus PDE-5 inhibitors ranked highest in the test of IPSS total score, storage subscore and voiding subscore. The combination therapy of α-blockers plus 5-ARIs was the best for increasing Qmax with a MD of 1.98 (95% CI, 1.12 to 2.86) as compared to placebo. α-blockers plus MRAs ranked secondly on the reduction of IPSS storage subscore, although monotherapies including MRAs showed no effect on this aspect. Additionally, PDE-5 inhibitors alone showed great effectiveness for LUTS/BPH except Qmax. **Conclusion**: Combination therapy with α-blockers plus PDE-5 inhibitors is recommended for short-term treatment for LUTS/BPH. There was also evidence that PDE-5 inhibitors used alone were efficacious except on Qmax. Caution is advised when using MRAs. Further clinical studies of longer duration that consider more treatment outcomes, such as disease progression, are required.		

Citation	Design	Endpoints
Wang XH, Wang X, Shi MJ, Li S, Liu T, Zhang XH. Systematic review and meta-analysis on phosphodiesterase 5 inhibitors and α-adrenoceptor antagonists used alone or combined for treatment of LUTS due to BPH. Asian J Androl. 2015 Nov-Dec;17(6):1022-32. doi: 10.4103/1008-682X.154990.	Pair-wised and network meta-analysis of RCTS in Cochrane Library (Issue 1, January 2014), PubMed (1966–January 2014) and Embase (1984–January 2014). 12 RCTs fully met inclusion criteria.	• MD in IPSS score, maximum flow rate, postvoided residual urine (PVR), QoL and erectile function (IIEF) score
Results: α-blockers trended toward improved efficacy compared to PDE-5 inhibitors in decreasing IPSS score and increasing maximum flow rate. α-blockers were significantly more effective in reduction of postvoided residual urine with a MD of 3.67 (95% CI 1.56 to 5.77, P = 0.0006) whereas PDE-5 inhibitors showed greater effect on increasing IIEF score with a MD of 9.82 (95% CI 3.80 to 15.85, P = 0.001). **Conclusion**: PDE-5 inhibitors plus α-blockers ranked the highest on the improvement of LUTS/BPH. PDE-5 inhibitor monotherapy was also effective except that it demonstrated less reduction of PVR than α-blockers. Both combined- or mono-therapy were found to be safe.		

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (01-01-2024 to 03-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
α-blockers								
doxazosin (Cardura®) 1 mg, 2 mg, 4 mg, 8 mg oral tablet	9	7	$95.34	$10.59	0	0 (0%)	F	No change
Cardura® XL (doxazosin) 4 mg, 8 mg ER oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
tamsulosin (Flomax®) 0.4 mg oral capsule	72	62	$761.28	$10.57	0	0 (0%)	F	No change
terazosin 1 mg, 2 mg, 5 mg, 10 mg oral capsule	6	6	$81.41	$13.57	0	0 (0%)	F	No change
silodosin (Rapaflo®) 4 mg, 8 mg oral capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
alfuzosin (Uroxatral®) 10 mg ER oral tablet	1	1	$28.34	$28.34	0	0 (0%)	F-QL (30 per 30 days)	No change
5-α Reductase Inhibitors								
finasteride (Proscar®) 5 mg oral tablet	17	16	$213.54	$12.56	0	0 (0%)	F	No change
dutasteride (Avodart®) 0.5 mg oral capsule	14	6	$139.73	$9.98	0	0 (0%)	F	No change
Combination Products (α-blockers/5-α-reductase Inhibitors)								
dutasteride/tamsulosin (Jalyn®) 0.5-0.4 mg oral capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Combination Products (5-α Reductase Inhibitors/Phosphodiesterase Type 5 Inhibitors)								
Entadfi™ (finasteride/tadalafil) 5-5mg oral capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Phosphodiesterase Type 5 Inhibitors								
tadalafil (Cialis®) 2.5 mg, 5 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Total	119	98	$1,319.64	$11.09	0	0 (0%)		

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1. Sandhu JS, Bixler BR, Dahm P, et al. Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia (BPH): AUA Guideline amendment 2023. J Urol. 2023;10.1097/JU.0000000000003698. https://doi.org/10.1097/JU.0000000000003698. Accessed on February 14, 2024.
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14. Uroxatral (alfuzosin) [prescribing information]. St. Michael, Barbados: Concordia Pharmaceuticals Inc; May 2020.
15. Flomax (tamsulosin) [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals; January 2019.
16. Cardura (doxazosin) [prescribing information]. New York, NY: Pfizer; January 2022.
17. Cardura XL (doxazosin) [prescribing information]. New York, New York: Pfizer; April 2022.
18. Jalyn (dutasteride/tamsulosin) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2020.
19. Rapaflo (silodosin) [prescribing information]. Parsippany, NJ: Actavis; December 2020.
20. Terazosin hydrochloride [prescribing information]. East Brunswick, NJ: Avert Pharmaceuticals Inc; August 2021.
21. Proscar (finasteride) [prescribing information]. Jersey City, NJ: Organon LLC; June 2021.
22. Avodart (dutasteride) [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; September 2020.
23. Cialis (tadalafil) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; April 2023.
24. Entadfi (finasteride/tadalafil) [prescribing information]. Miami, FL: Very Inc; December 2021.

Contraceptives – Foams and Devices

Executive Summary

CLASS OVERVIEW

This review covers contraceptive foams, films, gels, jellies, sponges and other devices including condoms and diaphragms. Phexxi™ (lactic acid, citric acid monohydrate, and postassium bitartrate) and all diaphragms are prescription-only products. The remaining products are available over-the-counter. All products reviewed herein are used to prevent pregnancy. Some (e.g. latex condoms) are also indicated to prevent the transmission of sexually transmitted infections.

UTILIZATION FINDINGS

There were no claims and no prior authorization requests.

RECOMMENDATIONS

- No Changes

PRACTICE GUIDELINES

Centers for Disease Control and Prevention. (2016). US Selected Practice Recommendations (US SPR) for Contraceptive Use, 2016. https://www.cdc.gov/reproductivehealth/contraception/mmwr/spr/summary.html. Accessed on December 30, 2022.

The Centers for Disease Control and Prevention (CDC) published contraceptive guidance for healthcare providers in 2016. This guidance is referred to as the "US Medical Eligibility Criteria for Contraceptive Use (US MEC)" and comprises recommendations for the use of specific contraceptive methods by women and men who have certain characteristics or medical conditions. The choice of contraceptive agent (both hormonal and non-hormonal) should be made on a patient-specific basis. Please refer to CDC guidelines for more information.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (01-01-2024 to 03-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Diaphragms/Cervical Caps (Prescription-only)								
Caya® Contoured Diaphragm 60 mm - 85 mm vaginal insert	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Femcap™ Cervical Cap 22, 26, 30 mm vaginal insert	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Wide-Seal Diaphragm 60, 65, 70, 75, 80, 85, 90, 95 mm vaginal insert	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Omniflex Diaphragm 65 mm vaginal insert	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Condoms (Over-the-counter)								
Condoms, latex, non-lubricated (Trustex®, Kimono®)	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Condoms, latex, lubricated (Trustex®, Kimono®, Aimsco®, Fantasy®)	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Condoms, non-latex, lubricated (Durex® Avanti)	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Condoms, female (FC2® Female Condom)	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Spermicides, Intravaginal (Over-the-counter)								
Encare (nonoxynol-9) 100 mg suppository	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Gynol II (nonoxynol-9) 3% gel	0	0	$0.00	$0.00	0	0 (0%)	F	No change
VCF® (nonoxynol-9) 28% vaginal film	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Nonoxynol-9 (VCF®) 4% Gel/PF Applicator	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Today Contraceptive Sponge® (nonoxynol-9) 1000 mg	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Other Contraceptives, Intravaginal (Prescription-only)								
Phexxi™ (lactic acid, citric acid monohydrate, and postassium bitartrate) 1.8 %-1 %-0.4 % vaginal gel	0	0	$0.00	$0.00	0	0 (0%)	F	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

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Gaucher Disease

Executive Summary

CLASS OVERVIEW

Gaucher disease (GD) is the one of the most common lysosomal storage diseases and is caused by an enzyme deficiency of glucocerebrosidase, which results in the abnormal accumulation of glycolipids within cellular lysosomes. It occurs in approximately 1 in 40,000 to 60,000 births in the United States (1 in 75,000 births worldwide) and its most common form, type 1 GD (GD1), is most prevalent in those of Ashkenazi-Jewish descent. Types 2 and 3 GD are less common and occur equally among other ethnic groups. It is estimated that about 20,000 people in the United States have this disease. GD may present at any age with major clinical manifestations including splenomegaly, hepatomegaly, thrombocytopenia, anemia, bleeding, osteopenia, bone pain, pathologic fractures, bone crisis, growth retardation, enlarged liver and spleen, and brown pigmentation of the skin. Cerezyme® (imiglucerase), Vpriv® (velaglucerase alfa), and Elelyso® (taliglucerase alfa) are IV therapies used as enzyme-replacement therapy (ERT) while Zavesca® (miglustat) and Cerdelga® (eliglustat) are oral glucosylceramide synthase inhibitors, also known as substrate reduction therapy (SRT). Both ERT and SRT are used in non-neuronopathic GD1. Zavesca® (miglustat) should only be considered for treatment in patients with whom ERT is not an option. Like ERT, Cerdelga® (eliglustat) may sometimes be used first-line. However, guidelines currently recommend both SRT therapies as second-line to ERT in most patients.

UTILIZATION FINDINGS

There were no claims and no prior authorization requests.

RECOMMENDATIONS

- No changes

CLINICAL SUMMARY

Gaucher disease (GD) is the one of the most common lysosomal storage diseases and is caused by an enzyme deficiency of glucocerebrosidase (GBA), which results in the abnormal accumulation of glycolipids within cellular lysosomes. It occurs in approximately 1 in 40,000 to 60,000 births in the United States (1 in 75,000 births worldwide) and its most common form, type 1 GD (GD1), is most prevalent in those of Ashkenazi-Jewish descent. Types 2 and 3 GD (GD2, GD3) are less common and occur equally among other ethnic groups. It is estimated that about 20,000 people in the United States have this disease. GD may present at any age with major clinical manifestations including splenomegaly, hepatomegaly, thrombocytopenia, anemia, bleeding, osteopenia, bone pain, pathologic fractures, bone crisis, growth retardation, enlarged liver and spleen, and brown pigmentation of the skin.

GD is an autosomal recessive disorder caused by mutations in the GBA gene located on chromosome 1q21. There are over 200 distinct mutations, although only four account for most cases. Disease onset, severity, and clinical manifestations vary with genotype. The c.1226A>G mutation is encountered most commonly in non-Jewish-Europeans and Ashkenazi-Jews and accounts for 53% of mutant alleles. The c.1448T>C mutation is common in Sweden and Northern Europe and accounts for 18% of mutants. The c84dupG allele is represented in approximately 7% of mutant alleles. Most individuals with this disease develop GD1. GD1 does not involve the central nervous system (CNS) while types 2 and 3 have CNS involvement and type 3 being chronic involvement. Type 1 GD has a slow progression with a chance of reduced life expectancy while type 2 occurs rapidly and results in death by 2 years of age. Type 3 GD has variable progression with a shortened life expectancy but this may depend on the subtype. Diagnosis is confirmed through the discovery of reduced GBA activity in peripheral leukocytes and also confirmed by mutation analysis. Early identification is crucial in order to initiate treatment and prevent irreversible complications.

Enzyme replacement therapy (ERT) is indicated in non-neuronopathic GD1 and prescribed based on patient population and disease severity or progression. ERT with Cerezyme® (imiglucerase), Vpriv® (velaglucerase alfa), or Elelyso® (taliglucerase alfa) may be used in symptomatic children (having malnutrition, growth retardation, impaired psychomotor development, and/or fatigue) and symptomatic adult patients (e.g. platelet count < 60,000/microL, liver > 2.5 times normal size, spleen > 15 times normal size, or radiologic evidence of skeletal disease) having GD1 with clinically significant manifestations. ERT is also an off-label option in patients with chronic neuronopathic GD3 that have visceral manifestations and in patients at risk for GD3. Cerezyme® (imiglucerase) is approved in Canada for the treatment of GD3 but is not FDA-approved in the US for this use. ERT is not appropriate for patients with acute neuronopathic GD2. There is limited data from head-to-head studies but current studies suggest comparable efficacy among ERT treatments.

Substrate-Reduction Therapy (SRT) reduces glycolipid accumulation by decreasing synthesis of glucocerebroside, the substrate of the deficient enzyme in GD, and is usually considered alternative therapy to ERT. Both Cerdelga® (eliglustat) and Zavesca® (miglustat) inhibit glucosylceramide synthase. However, Cerdelga® has a broader indication as first-line therapy for the long-term treatment of adult patients with GD1 who are CYP2D6 extensive metabolizers, intermediate metabolizers, or poor metabolizers. Patients who are CYP2D6 ultra-rapid metabolizers may not achieve adequate concentrations of eliglustat to achieve a therapeutic effect. Zavesca® is restricted as monotherapy for adults with mild to moderate GD1 for whom ERT is not a therapeutic option (e.g. due to allergy, hypersensitivity, or poor venous access). It is also used off-label for Niemann-Pick Type C disease. SRT has been associated with mild to moderate diarrhea in 85-90% of patients and a 6-7% weight reduction in 60% of patients, which usually resolves within the first year of treatment. Long term adverse events include peripheral neuropathy, transient tremor, and cognitive impairment.

Venglustat is a novel glucosylceramide synthase inhibitor currently in phase 3 trials for GD that blocks the formation of glucosylceramide, similar to Cerdelga® (eliglustat). Both agents are manufactured by Sanofi; data for venglustat is expected to be released in the spring of 2024. In July 2023, AvroBio announced they withdrew their consideration of potential stem cell therapy AVR-RD-02 and Regenxbio's GBA1 gene therapy is in phase 2 trials with an estimated primary completion date of 2028.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Enzyme Replacement Therapy		
Elelyso® (taliglucerase alfa)	Enzyme replacement therapy for type 1 Gaucher Disease	Treatment-naïve: 60 units/kg administered every other week as a 60- to 120-minute intravenous infusion. Patients switching from imiglucerase: Initiate Elelyso® intravenous treatment (60- to 120-minute infusion) with the same units/kg imiglucerase dosage and subsequently administer Elelyso® every other week.
Vpriv® (velaglucerase alfa)	Long-term enzyme replacement therapy for type 1 Gaucher disease	60 units/kg every 2 weeks; adjust dose based upon disease activity, range: 15-60 units/kg
Cerezyme ® (imiglucerase)	Long-term enzyme replacement therapy for type 1 Gaucher disease that results in one or more of the following: anemia, thrombocytopenia, bone disease, hepatomegaly or splenomegaly	Initial range: 2.5 units/kg IV three times weekly, up to 60 units/kg every 2 weeks
Glucosylceramide Synthase Inhibitors		
Cerdelga® (eliglustat)	Long-term treatment of type 1 Gaucher disease in adults who are CYP2D6 extensive, intermediate, and poor metabolizers	• Extensive and Intermediate metabolizers: 84 mg twice daily • Poor metabolizers: 84 mg once daily
Miglustat (Zavesca®)	• Monotherapy for treatment of mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option • *Niemann-Pick Type C disease (off-label use)*	• 100 mg TID; may be reduced to 100 mg 1-2 times daily in patients with ADRs • *Niemann-Pick Type C disease (off-label use) Oral: 200 mg 3 times daily*

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Enzyme Replacement Therapy		
Elelyso® (taliglucerase alfa)	None	None
Vpriv® (velaglucerase alfa)		
Cerezyme ® (imiglucerase)		
Glucosylceramide Synthase Inhibitors		
Cerdelga® (eliglustat)	None	• Use in extensive metabolizers with moderate or severe hepatic impairment • Use in intermediate metabolizers or poor metabolizers with any degree of hepatic impairment • Concomitant use of a moderate or strong CYP2D6 inhibitor with a moderate or strong CYP3A inhibitor in extensive metabolizers or intermediate metabolizers • Concomitant use of a strong CYP3A inhibitor in poor metabolizers or intermediate metabolizers • Concomitant use of a moderate or strong CYP2D6 inhibitor in extensive metabolizers with mild hepatic impairment
Miglustat (Zavesca®)		None

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Enzyme Replacement Therapy	
Elelyso® (taliglucerase alfa) Vpriv® (velaglucerase alfa) Cerezyme ® (imiglucerase)	**Concerns related to adverse effects:** • The development of IgG anti-drug antibodies (ADA) has been reported but the clinical significance unknown • Serious hypersensitivity reactions, including anaphylaxis may occur • Dizziness and fatigue have been observed with therapy (Elelyso® only) **Disease-related concerns:** • Pulmonary hypertension/pneumonia has been observed during treatment but may be related to a complication of Gaucher disease (Cerezyme® only) **Dosage form specific issues:** • Some dosage forms may contain polysorbate 80 (Tweens) which may cause hypersensitivity in some patients (Cerezyme® only) **Other warnings/precautions:** • Experienced health care provider: Should be administered under the supervision of a health care provider experienced in treatment of Gaucher disease (Cerezyme® only) • Registry: A registry has been established and all patients with Gaucher disease, and physicians who treat Gaucher disease are encouraged to participate (Cerezyme® only)
Glucosylceramide Synthase Inhibitors	
Cerdelga® (eliglustat)	**Concerns related to adverse effects:** • May cause arrhythmias including increases in ECG intervals at substantially elevated eligustat plasma concentrations **Disease-related concerns:** • Avoid use in patients with preexisting cardiac disease (CHF, recent acute MI, bradycardia, heart block, ventricular arrhythmia), long QT syndrome, and in combination with Class IA and Class III antiarrhythmic medications (has not been studied) • Use is contraindicated in extensive metabolizers with moderate to severe hepatic impairment and intermediate metabolizers or poor metabolizers with any degree of hepatic impairment; concomitant use of moderate or strong CYP2D6 inhibitor in extensive metabolizers with mild hepatic impairment is also contraindicated • Avoid use in intermediate metabolizers with any degree of renal impairment and in extensive metabolizers with ESRD **Other warnings/precautions:** • A registry has been established and all patients with Gaucher disease, and healthcare providers who treat Gaucher disease are encouraged to participate
Miglustat (Zavesca®)	**Concerns related to adverse effects:** • Diarrhea has been observed in a majority of patients and many also reported weight loss within the first 12 months of treatment • Peripheral neuropathy has been reported • Mild decrease in platelet counts (without bleeding) has been observed in patients with type 1 Gaucher disease switched from enzyme replacement therapy • New-onset or exacerbations of existing tremor may occur typically within the first month of treatment and may resolve over time or respond to dose reduction **Disease-related concerns:** • Use with caution in patients with renal impairment

Medication	Warnings/Precautions
	Other warnings/precautions: • Should be administered under the supervision of a physician experienced in treatment of Gaucher disease • A registry has been established and all patients with Gaucher disease, and healthcare providers who treat Gaucher disease are encouraged to participate

PRACTICE GUIDELINES

Expert Review of Endocrinology & Metabolism Review Article

Gary SE, Ryan E, Steward AM, et al. Recent advances in the diagnosis and management of Gaucher disease. Expert Review of Endocrinology & Metabolism. 2018: 13(2):107-118.

Approved First-Line Therapies for Gaucher Disease

Enzyme Replacement Therapy (imiglucerase, velaglucerase alfa, taliglucerase alfa): When administered prior to irreversible skeletal manifestations, most patients do extremely well, with correction of disease parameters. Although ERT dramatically improves the systemic symptoms of GD, virtually eliminating splenectomy as a treatment, neurological manifestations are not impacted by available therapies. Despite this, ERT has improved the quality of life of those with GD in many ways. For example, after years of ERT, some patients with GD are often able to take 'drug holidays,' or temporary delays in enzyme administration of up to a few months, without redevelopment of symptoms. Early administration of ERT has also been shown to positively impact the growth of children. Furthermore, ERT has been shown to decrease bleeding during pregnancy, delivery, and postpartum and improves overall outcomes of mothers who have suffered previous miscarriages. Characteristics:

- Recombinant enzyme
- Administered intravenously
- Few adverse events
- No demonstration of superiority between the three available ERTs
- Very costly, life-long therapy
- Not effective for GD2

Substrate Reduction Therapy (eliglustat tartrate and miglustat): SRT is an alternate treatment strategy. While ERT aims to rectify the absence and/or inactivity of glucocerebrosidase (GCase), SRT decreases glucocerebroside (GlcCer) production, making residual GCase activity sufficient to cleave the remaining lysosomal GlcCer. SRT was predicted to be more appealing to patients because it is administered orally, unlike ERT. Additionally, it was predicted to cost less, act on tissues not affected by ERT, and avoid potential immune responses that may be associated with infused proteins. Although miglustat improved several hallmark features of GD, including hemoglobin concentrations, platelet counts, hepatosplenomegaly, and bone density, several adverse effects were reported. These included diarrhea, weight loss, tremor, and peripheral neuropathy. Characteristics:

- Administered orally
- Approved for use in adults but not children
- Dosage and use depends on rate of CYP2D6 metabolism
- More frequent adverse events than ERT
- Similar cost to ERT, life-long therapy
- Not effective for GD2

ACMG Standards and Guidelines

Wang RY, Bodamer OA, Watson MS, et al. Lysosomal storage diseases: Diagnostic confirmation and management of presymptomatic individuals. Genetics in Medicine. 2011; 13(5):457-484.

- GD1: The reference treatment is enzyme replacement therapy (ERT) with Cerezyme®. Approximately 15% of treated patients develop IgG antibodies against the recombinant enzyme and about half of these patients show mild to moderate allergic adverse events. Vpriv® was recently approved and Elelyso® (called Uplyso® at the time) was in development at the time that these guidelines were published. Vpriv® and Elelyso® as parity to Cerezyme® or as an alternative to Cerezyme® in patients who develop IgG antibodies or adverse events was

implied. An alternative to ERT is substrate removal therapy (SRT). Only Zavesca® was approved at the time that this guideline was published. SRT (Zavesca®) was shown to be effective concerning hepatosplenomegaly, anemia, and thrombocytopenia but improvements of bone disease were delayed and limited. SRT is similarly effective as a low-dose treatment with ERT but less effective than standard or high-dose enzyme replacement. Therefore, SRT is currently* only recommended as second-line therapy for adults with GD1, which either show severe side effects on ERT or refuse to receive ERT and have mild to moderate disease.

- GD2/GD3: Due to rapid clinical progression, there is no specific therapy available for patients presenting with GD2. For patients with GD3, HSCT is no longer recommended. Studies with ERT, SRT, and combined treatment were ambivalent.

The Journal of Pediatrics

Martins AM, Valadares ER, Porta G, et al. Recommendations on Diagnosis, Treatment, and Monitoring for Gaucher Disease. 2009; 155(4): S10-S18.

- ERT with imiglucerase is the current standard of care for the treatment of GD and has been proven to improve the clinical manifestations of GD and enhance quality of life in patients with GD. ERT with imiglucerase is recommended for all patients with type 1 and type 3 GD, regardless of age, who has symptoms with mild, moderate, or severe clinical manifestations.
    - Nonneuronopathic form (Type 1): The dose of imiglucerase depends on GD type, patient age, organ involvement, severity, extent, and progression of the disease. The ideal dose for a patient is sufficient to maintain full or partial reversal of signs and symptoms of the disease. Some studies suggest that a dose-response effect of imiglucerase exists for several clinical manifestations, which underscores previous recommendations that dosage must be individualized according to each patient's clinical scenario and progression. In children, therapeutic intervention should occur as soon as possible and at the necessary dose to attain growth potential and avoid serious and irreversible manifestations of GD.
    - Chronic Neuronopathic Form (Type 3): The initial recommended dose of imiglucerase for patients with type 3 GD is 120 U/kg/2 weeks. Adults with mild systemic disease and stable neurologic involvement may have maintenance doses adjusted gradually in 15% to 25% reductions every 6 months, depending on response, until 60 U/kg every 2 weeks is attained. All patients at risk for development of neurologic disease (such as carriers of L444P/L444P, D409H/D409H or L444P/D409H genotypes) must receive the minimum dose of 60 U/kg/2 weeks and continue to be carefully monitored every 6 months. Siblings of patients with the same genotype and neurologic involvement must be treated as if they exhibit neurologic disease.

Recent clinical studies (2015) suggest a broader indication for Cerdelga®. Please see Clinical Summary or Clinical Trials section for more information.

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Mistry PK, Balwani M, Charrow J, et al. Real-world effectiveness of eliglustat in treatment-naïve and switch patients enrolled in the International Collaborative Gaucher Group Gaucher Registry. American Journal of Hematology. 2020; 95(9): 1038–1046.	Real-world effectiveness study of 6,341 patients enrolled in the ICGG Gaucher Registry as of January 2019. Of the 466 patients treated with eliglustat, 231 met the inclusion criteria of known eliglustat treatment dates, confirmed Gaucher disease type 1 with a reported diagnosis date, known splenectomy status (including date of splenectomy if splenectomized), and baseline and 2-year data while on eliglustat only for at least one of the key clinical parameters (hemoglobin concentration, platelet count, liver volume, spleen volume, bone pain, or bone crisis).	• Endpoints: change in mean hemoglobin, mean platelet count, mean spleen volume, mean liver volume, and median spine Z-score
Results: In treatment-naïve patients, mean hemoglobin increased from 12.4 to 13.4 g/dL (P = 0.004, n = 18), mean platelet count increased from 113 to 156 × 109/L (P < .001, n = 17); mean spleen volume decreased from 7.4 to 3.5 multiples of normal (MN) (P = 0.02, n = 7); mean liver volume remained normal (n = 7), and median spine Z-score was unchanged (−1.3 to −1.2, n = 6). In non-splenectomized switch patients, mean hemoglobin remained stable/non-anemic (n = 167); mean platelet count remained stable/normal (n = 165); mean spleen volume decreased from 3.3 to 2.8 MN (P < .001, n = 64); mean liver volume remained normal (n = 63), and median lumbar spine Z-score improved from −0.7 to −0.4 (P = .014, n = 68). In splenectomized switch patients, mean hemoglobin remained stable/non-anemic (n = 31); mean platelet count increased from 297 to 324 × 109/L (non-significant, n = 29); mean liver volume remained normal (n = 13); median spine Z-score improved from −0.8 to −0.6 (non-significant, n = 11). Median chitotriosidase decreased in all groups (P < .01 for all). **Conclusion**: Improvements in the endpoints studied were consistent with eliglustat clinical trial results that demonstrate a long-term clinical benefit in treatment-naïve patients and stability in enzyme replacement therapy switch patients.		
Citation	**Design**	**Endpoints**
Cox TM, Drelichman G, et al. Eliglustat compared with imiglucerase in patients with Gaucher's disease type 1 stabilized on enzyme replacement therapy: a phase 3, randomized, open-label, non-inferiority trial. Lancet. 2015 Jun; 385(9985):2355-62.	A phase III, randomized, multinational, open-label, non-inferiority trial enrolled adults aged 18 and older and received ERT for 3 years or more for Gaucher disease. Patients were randomized 2:1 to receive either oral eliglustat or imiglucerase infusions for 12 months.	• Composite primary efficacy endpoint: percentage of patients who hematological variables and organ volumes remained stable for 10 months
Results: 84 of 99 patients (85%) who completed eliglustat treatment and 44 of 47 patients (94%) who completed imiglucerase treatment met the composite primary endpoint (between-group difference -8·8%; 95% CI -17.6 to 4.2). The lower bound of the 95% CI of -17.6% was within the prespecified threshold for non-inferiority. Dropouts occurred due to palpitations (one patient on eliglustat), myocardial infarction (one patient on eliglustat), and psychotic disorder (one patient on imiglucerase). 97 of 106 patients (92%) in the eliglustat group had treatment-emergent adverse events, as did 42 of 53 (79%) in the imiglucerase group (mostly mild or moderate in severity). There were no reported deaths. **Conclusion**: Oral eliglustat was found to be noninferior to imiglucerase at maintaining hematological and organ volume stability in adults with Gaucher disease type 1 already controlled by intravenous ERT. This study helped to justify the use of eliglustat as first-line or maintenance therapy as it may be a useful therapeutic option.		
Citation	**Design**	**Endpoints**

Mistry PK, Lukina E, Ben Turkia H, et al. Effect of oral eliglustat on splenomegaly in patients with Gaucher disease type 1: the ENGAGE randomized clinical trial. JAMA. 2015 Feb;313(7):695-706.	Phase 3, randomized, double-blind, placebo-controlled trial included eligible patients with splenomegaly plus thrombocytopenia and/or anemia. Of the 72 patients screened, 40 were enrolled. The goal was to determine whether eliglustat safely reverses clinical manifestations in untreated adults with GD1. Patients were stratified by spleen volume and randomized 1:1 to receive eliglustat (50 or 100 mg twice daily; n = 20) or placebo (n = 20) for 9 months.	• Primary efficacy endpoint: percentage change in spleen volume in multiples of normal from baseline to 9 months • Secondary efficacy end points: change in hemoglobin level and percentage changes in liver volume and platelet count
Results: Least-square mean spleen volume decreased by 27.77% (95% CI, -32.57% to -22.97%) in the eliglustat group (from 13.89 to 10.17 multiples of normal) vs. an increase of 2.26% (95% CI, -2.54% to 7.06%) in the placebo group (from 12.50 to 12.84 multiples of normal) for an absolute treatment difference of -30.03% (95% CI, -36.82% to -23.24%; P < .001). For the secondary endpoints, the least-square mean absolute differences between groups all favored eliglustat, with a 1.22 g/dL increase in hemoglobin level (95% CI, 0.57-1.88 g/dL; P < .001), 6.64% decrease in liver volume (95% CI, -11.37% to -1.91%; P = .007), and 41.06% increase in platelet count (95% CI, 23.95%-58.17%; P < .001). One patient in the eliglustat group withdrew (non-treatment related); 39 of the 40 patients transitioned to an open-label extension study. No serious adverse events occurred. **Conclusion**: Treatment with eliglustat resulted in significant improvements in spleen volume, hemoglobin level, liver volume, and platelet count over a 9 month study period. Authors claim that the clinical significance is unknown and long-term follow up to compare eliglustat with ERT is necessary. The clinical significance of these findings is uncertain. Longer-term follow up is necessary for comparison with the standard of care, enzyme replacement therapy.		
Citation	**Design**	**Endpoints**
Cox T, Lachmann R, et al. Novel oral treatment of Gaucher's disease with N-butyldeoxynojirimycin (OGT 918) to decrease substrate biosynthesis. Lancet. 2000 Apr 29;355(9214):1481-5.	1-year open-label study included 28 adults (7 with previous splenectomies) that were unable or unwilling to receive ERT. Patients were started on 100 mg oral OGT 918 three times daily.	• Primary endpoints: liver and spleen volume were measured by computed tomography or magnetic resonance imaging at baseline and at months 6 and 12, and biochemical and hematological variables monthly, including chitotriosidase activity (a sensitive marker of Gaucher disease activity).
Results: Baseline liver volumes were 1.1-2.7 times normal and spleen volumes 5.1-24.8 times normal. At 12 months, mean liver and spleen volumes were significantly lowered by 12% (95% CI 7.8-16.4) and 19% (14.3-23.7), respectively (p<0.001 for these endpoints). **Conclusion**: Decrease of substrate formation by OGT 918 improves key clinical features of nonneuronopathic Gaucher disease. Further research is needed.		
Citation	**Design**	**Endpoints**
Schiffmann R, Fitzgibbon EJ, Harris C, et al. Randomized, controlled trial of miglustat in Gaucher's disease type 3. Ann Neurol. 2008;64(5):514.	4-month, phase II, open-label clinical trial of miglustat in GD3 was conducted in two phases. During the initial 12 months, patients were randomized 2:1 to receive miglustat or "no miglustat treatment." The randomized phase was followed by an optional 12-month extension phase in which all patients received miglustat. All patients received ERT during the 24-month period.	• Primary efficacy end points: change from baseline to months 12 and 24 in vertical saccadic eye movement velocity as determined by the peak amplitude versus amplitude regression line slope. • Secondary end points: changes in neurological and neuropsychological assessments, pulmonary function tests, liver and spleen organ volumes,

		hematological and clinical laboratory assessments, and safety evaluations.
Results: Thirty patients were enrolled of whom 21 were randomized to miglustat and 9 to "no miglustat treatment." Twenty-eight patients entered the 12-month extension phase. No significant between-group differences in vertical saccadic eye movement velocity or in the other neurological or neuropsychological evaluations were observed. Organ volumes and hematological parameters remained stable in both treatment groups, but improvement in pulmonary function and decrease of chitotriosidase levels were observed with miglustat compared with patients receiving ERT alone. **Conclusion**: Miglustat does not appear to have significant benefits on the neurological manifestations of GD3. Miglustat may have positive effects on systemic disease (pulmonary function and chitotriosidase activity) in addition to ERT in patients with GD3. This study helped to justify the indication of miglustat only for mild to moderate GD1 in adults (no benefits for neurologic manifestations).		

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (01-01-2024 to 03-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Enzyme Replacement Therapy								
Elelyso® (taliglucerase alfa) 200 unit IV solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Vpriv® (velaglucerase alfa) 400 unit IV solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Cerezyme® (imiglucerase) 400 unit IV solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Substrate Replacement Therapy								
Cerdelga® (eliglustat) 84 mg oral capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Miglustat 100 mg oral capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

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

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Drug Name: Ridaura® (auranofin)

Manufacturer: Prometheus Laboratories Inc.

Approval Date: April 24, 1985

Marketing Date: May 24, 1985

Recommendation

- No changes

Prescribing Information

Indication

Ridaura® (auranofin) is indicated in the management of adults with active classical or definite rheumatoid arthritis (RA) [per American Rheumatism Association (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 (NSAIDs).

Mechanism of Action

The mechanism of action of auranofin is not understood. In patients with adult RA, auranofin may modify disease activity as manifested by synovitis and associated symptoms and reflected by laboratory parameters such as erythrocyte sedimentation rate (ESR). There is no substantial evidence, however, that gold-containing compounds induce remission of RA.

Dosage and Administration

Two capsules (6 mg) by mouth daily. If response remains inadequate after 6 months increase to 9 mg (3 mg three times daily). If response to 9 mg dose remains inadequate after 6 months, discontinue. Transferring from Injectable gold: First discontinue injectable agent, then start oral therapy with auranofin 6 mg daily.

Black Box Warning

Auranofin contains gold and, like other gold-containing drugs, can cause gold toxicity, signs of which include: fall in hemoglobin, leukopenia below 4,000 WBC/cu mm, granulocytes below 1,500/cu mm, decrease in platelets below 150,000/cu mm, proteinuria, hematuria, pruritus, rash, stomatitis or persistent diarrhea. Therefore, the results of recommended laboratory work should be reviewed before writing each auranofin prescription. Like other gold preparations, auranofin is only indicated for use in selected patients with active RA. Physicians planning to use auranofin should be experienced with chrysotherapy and should thoroughly familiarize themselves with the toxicity and benefits of auranofin.

In addition, the following precautions should be routinely employed:

- The possibility of adverse reactions should be explained to patients before starting therapy.
- Patients should be advised to report promptly any symptoms suggesting toxicity.

Adverse Reactions

Reactions occurring in > 1% of auranofin-treated patients:

- Gastrointestinal: loose stools or diarrhea (47%), abdominal pain (14%), nausea with or without vomiting (10%), constipation, anorexia, flatulence, dyspepsia, dysgeusia
- Dermatological: rash (24%), pruritus (17%), hair loss, urticaria
- Mucous Membrane: stomatitis (13%), conjunctivitis, glossitis
- Hematological: anemia, leukopenia, thrombocytopenia, eosinophilia
- Renal: proteinuria, hematuria
- Hepatic: elevated liver enzymes

Use in Specific Populations, Pregnancy

Use of auranofin by pregnant women is not recommended. Furthermore, women of childbearing potential should be warned of the potential risks of auranofin therapy during pregnancy. There are no adequate and well-controlled auranofin studies in pregnant women.

Drug Interactions

In a single patient-report, there is the suggestion that concurrent administration of auranofin and phenytoin may have increased phenytoin blood levels.

How Supplied

Oral capsules: 3 mg

Price

$2,684

(Per month for maximum dosing, based on WAC.)

Clinical Studies

Completed

Title	Auranofin is safe and superior to placebo in elderly-onset rheumatoid arthritis PMID: 9291856
Design	Two-year prospective double-blind placebo-controlled clinical trial
Population	N=65 Elderly-onset rheumatoid arthritis (EORA), defined as onset at age > 60 years
Arms	Auranofin 3 mg BID or placebo for 2 years Prednisolone starting at 7.5 or 20 mg daily was used as a rescue drug in patients with intolerable joint pain and stiffness and with C-reactive Protein (CRP) >= 20 (was tapered down according to guidelines)
Endpoint(s)	Primary – Efficacy of auranofin as compared to placebo measured by primary clinical variables: • Changes in joint pain • Number of swollen joints • Health Assessment Questionnaire score • Radiographic damage score of hands (Larsen-Dale index) Secondary – Evaluate safety of auranofin as compared to placebo measured by: • Total number of adverse events • Reasons for withdrawals and discontinuations
Inclusion Criteria	• RA, according to the American College of Rheumatology (ACR) 1987 criteria, or oligoarthritis (at least three swollen joints) associated with PMR-like symptoms
Exclusion Criteria	• Patients with temporal arthritis or polymyalgia rheumatica (PMR) without arthritis • Patients with major arthropathies other than EORA • Patients previously treated with gold-containing drugs • Patients on oral prednisolone for other reasons than EORA or doses > 20 mg daily within the 4 weeks preceding study • Chronic inflammatory bowel disease (IBD) • Liver or kidney disease
Results	Primary endpoint: • No statistically significant differences between the treatment groups could be demonstrated during the treatment period. • The auranofin group consumed significantly less prednisolone 2.64 (0-11.85) mg/day, compared to 5.0 (0-18.33) mg/day in the placebo group (P=0.006) Secondary endpoint: • The total number of adverse events tended to be higher in the auranofin group: 8.5 events per patient compared with 7.5 events per patient in the placebo group. • 10% of patients on auranofin and 41% of patients on placebo withdrew due to adverse events • Additionally, 16% on auranofin and 29% on placebo treatment withdrew due to lack of effect
Conclusion	Auranofin is safe, superior to placebo and has steroid-sparing capacity in the treatment of elderly-onset RA (EORA).

Interpretation	Auranofin demonstrates clinical efficacy in patients with EORA when compared to placebo. It is unclear why there were more adverse events in the placebo group but the adverse effects due to auranofin are generally mild and tolerated. The steroid-sparing effect could prove useful for those who cannot tolerate steroids for the treatment of EORA.

Title	Efficacy and safety of auranofin in patients with active early rheumatoid arthritis PMID: 7758062
Design	Single-arm, non-randomized, non-blinded trial
Population	N=48; 35 completed the trial but all were used in the determination of adverse events 7 males, 28 females; majority aged 50-59 (Min 27-Max 71) 1:2 ratio having < 1 year to 1-5 year duration and Class 1 to 2 3:4 ratio having Stage I to Stage II
Arms	Auranofin 3 mg twice daily after morning and evening meals for 12 months + NSAIDs +/- prednisolone 5 mg or 2.5 mg (8 patients used oral steroids)
Endpoint(s)	On the first day of the trial and after 3, 6, and 12 months of treatment, clinical symptoms, modified Lansbury index, CRP, ESR, rheumatoid factor, and the patients' assessments of severity of pain, judged using a visual analog scale (VAS), were evaluated.
Inclusion Criteria	Diagnosis of RA that satisfied the diagnostic standards set in 1987 by the ACR, was of less than 5 years' duration, and was of stage I or II and class 1 or 2 according to the Steinbrocker system.
Exclusion Criteria	• Patients under 18 years of age • Women of childbearing potential
Results	Statistically significant improvement in clinical symptoms, modified Lansbury index, C-reactive protein, erythrocyte sedimentation rate, rheumatoid factor, and the patients' assessments of severity of pain, judged using a VAS after 12 months of treatment. Mean duration of morning stiffness and mean grip strength was statistically significantly lower from 6 months to the duration of the study. ESR, mean number of painful joints, was statistically significantly improved after 3 months and for the duration of the study. The modified Lansbury index (includes duration of morning stiffness, grip strength, ESR, and articular index) was statistically significantly improved after 6 months and for the duration of the study. The RA test result was positive for all patients at the beginning of the study but became negative in 1, 2, and 4 patients after month 3, 6, and 12 respectively. The CRP test was positive for all patients in the beginning of the trial but showed improvement. Pain assessed using VAS was significantly reduced after 6 months of treatment, but statistical significance was lost at 12 months. Self-reported general impressions and the global improvement ratings were improved. No adverse events were observed during the treatment period.
Conclusion	Auranofin combined with NSAIDs and/or steroids shows significant improvement in both objective and subjective factors in the assessment of RA with no observable adverse events.
Interpretation	Although this study shows improvement with auranofin, it is important to observe the meaningful impact that NSAIDs and/or oral steroids (8 of 35 patients used steroids) have on an inflammatory condition like RA. Many of these improvements only occurred after 3 months of use and arguably the most important outcome, pain, lost statistical significance at 12 months. Other studies showed GI adverse events with auranofin, but this study did not. The small sample size (35 completed the study)

	implies low statistical power and poor study design (not randomized and single arm) reduces the value of this study. Larger, placebo-controlled trials are necessary to obtain an adequate conclusion.

Title	Comparison of auranofin, methotrexate, and the combination of both in the treatment of rheumatoid arthritis. A controlled clinical trial PMID: 1536666
Design	Prospective, controlled, double-blind, multicenter trial
Population	N=335 (211 completed trial) No baseline differences in age, sex, race, disease duration, or disease severity
Arms	• Auranofin 3 mg BID + placebo • Methotrexate (MTX) 2.5 mg q12 hours for 3 doses per week + placebo • Auranofin 3 mg BID + MTX 2.5 mg q12 hours for 3 doses per week Every patient was allowed to take aspirin and/or NSAID provided the dosage had been stable for 1 month and was kept constant for the duration of the trial. Prednisone therapy at a stable dose for 1 month prior to study entry was maintained if <=10 mg/day (or equivalent).
Endpoint(s)	• Response to treatment in all patients entering the trial • Response to treatment in patients completing the 48-week trial • Time to response • Patient withdrawals

Inclusion Criteria	• Patients ≥ 18 years old
	• Definite or classic RA of > 6 months duration with onset after age 16 with ≥ 6 swollen joints capable of responding to drug therapy and ≥ 2 of the following:
	  ○ 9 or more joints tender on pressure
	  ○ 45 minutes or more of AM stiffness
	  ○ ESR of ≥ 28 mm/hr
	• Unsuccessful treatment with conventional doses of ≥ 2 NSAIDs and/or salicylates
	• No antimalarial agents, intraarticular corticosteroids or parenteral corticosteroids for the 2 months prior to study start and no phenylbutazone for the 1 month prior to study start
	• Patients never received treatment with gold, penicillamine, immunosuppressives or cytotoxic medications (including methotrexate)
	• Patients and sexual partners either had no childbearing potential or were practicing successful contraception for ≥ 3 months before the study start

Exclusion Criteria	• ACR exclusion criteria for RA • Seronegative spondylarthropathy, mixed connective tissue disease • Psoriasis • RA functional class IV • Concomitant treatment with another experimental drug • History or presence of malignancy • Acute or chronic infection • Active peptic ulcer disease (PUD) or IBD • Bone marrow hypoplasia • Concomitant treatment with an anticoagulant • Insulin-dependent diabetes mellitus (IDDM)

	• Regular alcohol intake of > 14 oz of 100-proof liquor or equivalent/week • Elevated hepatic enzymes, serum creatinine > normal • Positive Hep-B surface antigen • Proteinuria, thrombocytopenia, leukopenia
Results	Patients taking auranofin monotherapy had a slower onset of response than did patients taking MTX alone or in combination. Withdrawals because of adverse drug reactions were slightly more common for patients taking combination therapy, but the differences were not statistically significant. Withdrawals because of lack of response were more common for single-drug therapy, with the difference between auranofin and the combination group reaching statistical significance. No unexpected adverse drug effects were identified, and all reactions resolved without sequelae. Except for fewer withdrawals because of lack of response, combination therapy did not demonstrate any advantage in efficacy over single-drug treatment within the time frame of the study.
Conclusion	There was no difference in efficacy between combination MTX and auranofin versus single drug therapy, but withdrawal from the study was the smallest in the combination group. Both MTX and auranofin had similar efficacy but patients taking MTX alone or in combination had an earlier onset of benefit than patients taking auranofin. Adverse drug events were more common in the combination group, with the toxicities seeming additive and not synergistic.
Interpretation	This is one of the few randomized, controlled trials with a sufficient patient population that tests the safety and efficacy of auranofin. Auranofin and MTX have similar efficacy according to this study. However, the onset of benefit for auranofin is delayed at 8-12 weeks compared to MTX which had a 6-week onset. The combination therapy only increases the risks of additive adverse events and therefore should be avoided. However, it is important to note that each drug has a unique set of risks (i.e., MTX more commonly increases liver enzymes and leukopenia while auranofin more likely increases the risk of GI distress, rash, and mucosal ulcers).

Title	Low-Dose Methotrexate Compared With Auranofin In Adult Rheumatoid Arthritis PMID: 2180405
Design	36-week double-blind, randomized, multicenter study
Population	N=281 Patients with adult-onset, definite, or classic RA of more than 6 months duration No statistically significant differences in demographic or clinical characteristics between groups
Arms	• MTX 7.5 mg once weekly + placebo for 36 weeks • Auranofin 3 mg BID + placebo for 36 weeks If inadequate response, dose was increased up to MTX 15 mg/week or auranofin 9 mg/day.
Endpoint(s)	Primary: • Physician global assessment of disease activity • Patient global assessment • Number of joints with tenderness and/or pain on pressure or passive motion • Number of joints with swelling Secondary: • Joint pain/tenderness index

	• Joint swelling index • ESR • Duration of morning stiffness • 50-foot unaided walk time • Grip strength
Inclusion Criteria	• Diagnosed with adult-onset, definite, or classic RA of more than 6 months • Inadequate response to at least 2 NSAIDs • Active disease, defined as the presence of at least 3 of the following: >=6 painful or tender joints, >=3 swollen joints, morning stiffness of >=45 minutes duration, and a Westergren ESR >=28 mm/hr.
Exclusion Criteria	• Patients who previously received therapy with either gold salts (oral or parenteral), D-penicillamine (DP), MTX, or cytotoxic drugs • Patients who had previously used antimalarial drugs or sulfasalazine which were discontinued due to factors other than toxicity or lack of efficacy • Active PUD or IDDM • Serum transaminase or bilirubin level greater than twice the upper limit of normal (ULN) • History of alcoholism or unwillingness to limit alcohol consumption to 2 drinks per week • Serum creatinine > ULN or a creatinine clearance <50 mL/minute • Thrombocytopenia or leukopenia • Serious coexisting illness • Functional class I or IV • History of malignancy • Recent major surgery • Pulmonary fibrosis if the FEV1 or carbon monoxide diffusing capacity <60% of predicted • Women of childbearing potential including sexual partners of male patients were required to be practicing an accepted method of birth control
Results	There was a statistically significant improvement from baseline for all efficacy measures at weeks 12, 24, and 36 for both treatment groups, but mean improvement favored MTX. The response with MTX occurred earlier and was consistently greater than that with auranofin. Intent-to-treat analysis showed significantly greater improvement with MTX for painful and swollen joint counts and physician and patient global assessments of disease activity. There was a higher frequency of adverse events in the auranofin group and more auranofin-treated patients were withdrawn from the study.
Conclusion	Both MTX and auranofin demonstrated effectiveness in improving the standard measures of RA activity but the response with MTX was “superior” and occurred earlier. Auranofin has less tolerated adverse events leading to patient withdrawal from the study
Interpretation	MTX has both a safety and efficacy benefit over auranofin for patients who had not received prior treatment with other second-line agents. Although the study did not test for superiority, MTX had consistently better outcomes and the clinical benefit occurred earlier than auranofin, justifying MTX’s place in RA guidelines as a first line agent.

Ongoing

None

Guidelines

Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2021;73(7):924-939.

The 2021 American College of Rheumatology Guidelines for the Treatment of Rheumatoid Arthritis do not include any recommendations for gold compounds due to their infrequent use and/or lack of new data.

Clinical Opinions

Gold has demonstrated efficacy in controlling disease activity and radiographic progression of RA compared to placebo. However, two meta-analyses showed reduced efficacy of auranofin compared to MTX and sulfasalazine. Additionally, auranofin is less effective than gold sodium thiomalate (GST), the parenteral form of gold, but it also has fewer adverse effects. Infliximab has also demonstrated superiority when compared to auranofin on the effect on radiological erosion scores. According to one systematic review, auranofin appears to be efficacious in the short-term (6-month) treatment of patients with RA and has a small but clinically and statistically significant benefit on disease activity.

The use of gold is further limited by its side effect profile. Common side effects include dermatitis/stomatitis, pruritis, enterocolitis and metallic taste. Serious adverse reactions including persistent and significant proteinuria, hematologic toxicity, pulmonary toxicity, hepatitis, enterocolitis, and neuropathy can occur. Due to the potential for toxicity, baseline and monthly monitoring of complete blood count (CBC) with differential, platelet count, and urinalysis should be taken.

Gold therapy may be appropriate for patients with early and mild disease requiring less effective therapies. It may also be considered for use in the following circumstances: concerns regarding immunosuppression, coexisting chronic infection, contraindications to or failure of other therapies, lack of availability of other medications, and pregnancy planning in select women in whom treatment options may be limited. In summary, it is difficult to justify the use of auranofin due to its inferior efficacy, absence in clinical guidelines, and high cost compared to other agents for RA.

Utilization 1/1/2024 to 3/31/2024

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Ridaura 3 mg capsule	0	0	$0.00	$0.00	0	0 (0%)	**NF**	No change

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

Alternatives

Drug Name^	Formulary Status	Dosage Form	Price*

Methotrexate	F	2.5 mg oral tablets	$142
Leflunomide (Arava®)	F	10 mg, 20 mg oral tablets	$492
Enbrel® (etanercept)	F-PA	50 mg/mL SQ auto-injector, cartridge, pre-filled syringe; 25 mg/0.5 mL SQ pre-filled syringe, kit; 25 mg SQ vial	$8,459
Humira® (adalimumab)	NF	10 mg/0.1 mL, 20 mg/0.2 mL, 40 mg/0.4 mL, 40 mg/0.8 mL SQ pre-filled syringe	$1,560 - $15,782¥

^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 28 days 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). Price is based on maximum dosing for rheumatoid arthritis.*

¥2023 biosimilar entrants for Humira® have a WAC price of nearly 10% of brand Humira®; this pricing range reflects current average WAC of the 11 biosimilar entrants up to current WAC of brand Humira ®. Additionally, price based on dosing when combined with methotrexate. Dosing (and price) can be doubled for patients not taking methotrexate.

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Recommendation:

- No changes

Formulary, step therapy required *For drugs without specific criteria	
Therapeutic Classes (AHFS)	N/A
Medications	Formulary, step therapy required medications without specific 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	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	**Initial criteria for approval:**
	• Appropriate diagnosis/indication for requested medication or meets off-label criteria below AND
	• *Off-label criteria:*
	  ○ No other formulary medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia AND
	  ○ Medication is being requested for an accepted off-label use and is listed in the standard clinical decision support resources (as noted in Covered uses section above) OR requested use can be supported by at least two published peer reviewed clinical studies
	• The quantity requested does not to exceed FDA approved or off-label dose (Requests for quantities above indicated Quantity Limits will be reviewed on a case by case basis) AND
	• Documentation provided that patient has had sufficient prior trial/failure or contraindication/inability to use required step therapy drug(s) OR
	• Provider has demonstrated knowledge of step therapy requirements AND
	• Medical justification why required step therapy drug(s) would be ineffective or have the potential to cause harm or deterioration of the member's condition OR
	• Medical justification why the requested drug would be superior to the required step therapy drug(s).
	
	Criteria for re-authorization:
	• Patient is stable and continuing the medication

Criteria Statement	Medications for drugs without specific criteria, where step therapy is required, are reserved for members who have tried and failed, or have an inability to use the current step therapy medications, or no other formulary medication with a medically accepted use for the patient's specific diagnosis is to be used, as referenced in the medical compendia, is available and medication is being requested and is listed in the standard clinical decision support resources or requested use can be supported by at least two published peer reviewed clinical studies.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Non-formulary and prior authorization required oral liquid formulations	
Therapeutic Classes (AHFS)	N/A
Medications	Non-formulary and prior authorization-required oral liquid formulations, where solid oral dosage forms exist
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	**Non-formulary and prior authorization-required oral liquid formulations, where solid oral dosage forms exist are approved when the following criteria are met:** • Documentation of difficulty swallowing, inability to swallow, or unable to use oral tablet/capsule formulation.
Criteria Statement	Non-formulary and prior authorization-required oral liquid formulations, where solid oral dosage forms exist are reserved for members who have difficulty swallowing or are unable to swallow tablets or capsules.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Cholinesterase Inhibitors	
Therapeutic Classes (AHFS)	Parasympathomimetic (cholinergic agents)
Medications	Formulary, PA required galantamine (Razadyne) tablets and solution galantamine (Razadyne ER) capsules rivastigmine (Exelon) patches Non-formulary, PA required Donepezil (Aricept) 23mg tablet Adlarity (donepezil) 5 mg/day weekly patch
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 conditions are met, the request will be approved for up to 12 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.

PA Review Criteria	Criteria for approval
	• Galantamine tablet, galantamine ER capsule, or donepezil (Aricept) 23mg tablet are approved when the following criteria is met:
	  ○ Documentation of a trial/failure/contraindication to rivastigmine capsule or donepezil (Aricept) 5mg or 10mg tablet
	• Rivastigmine (Exelon) patches and Adlarity (donepezil) patches are approved when the following criteria is met:
	  ○ Documentation of a compliance issue or intolerance with oral therapy
	• Galantamine solution is approved when ONE of the following criteria is met:
	  ○ Documentation of a trial/failure/contraindication to rivastigmine capsule or donepezil (Aricept)
	  ○ Documentation of difficulty or inability to swallow

Criteria Statement	Galantamine tablet, galantamine ER capsule, or donepezil (Aricept) 23mg tablet are reserved for members who have used (or cannot/should not use) rivastigmine capsule or donepezil 5mg or 10mg tablet. Rivastigmine patches and Adlarity patches are reserved for members who have an intolerance to or compliance issue with oral therapy. Galantamine solution is reserved for members who have used (or cannot/should not use) rivastigmine capsule or donepezil OR have difficulty or inability to swallow.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

febuxostat (Uloric)	
Therapeutic Classes (AHFS)	Antigout agents
Medications	Formulary, PA required: febuxostat (Uloric)
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	**All of the following conditions must be met:** • Patient has a diagnosis of gout AND • Documented contraindication to or trial and failure of allopurinol 600 mg per day for at least 90 consecutive days in the last 365 days. AND • For patients with CKD, renal adjustment of allopurinol to the maximum tolerated dose is required for at least 90 consecutive days in the last 365 days.
Criteria Statement	Febuxostat (Uloric) is reserved for members who have gout and who have used (or cannot/should not use) allopurinol.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Lamotrigine ER	
Therapeutic Classes (AHFS)	Anticonvulsants, miscellaneous
Medications	Formulary, PA required Lamotrigine ER (Lamictal XR) 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	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	Lamotrigine ER is approved when the following criteria are met: • Documentation the patient having compliance issues using immediate release lamotrigine or is already stable on lamotrigine ER
Criteria Statement	Lamotrigine ER is reserved for members who are having compliance issues using immediate release lamotrigine or are already stable on lamotrigine ER.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Levalbuterol (Xopenex/Xopenex HFA)	
Therapeutic Classes (AHFS)	Beta-adrenergic agonists
Medications	Formulary, step therapy required Levalbuterol HFA 45 mcg inhaler (Xopenex HFA) Levalbuterol 0.31mg/3 ml, 0.63 mg/3 ml, 1.25 mg/3 ml, 1.25mg/0.5 ml solution for (Xopenex)
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	Levalbuterol HFA or solution for nebulization is approved when the following criteria are met: • Documentation of a trial and failure of albuterol HFA or albuterol solution for nebulization
Criteria Statement	Levalbuterol HFA or levalbuterol solution for nebulization is reserved for members who have used (or cannot/should not use) albuterol HFA or albuterol solution for nebulization.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Remove Gen7T and Synera as they have been discontinued.

Lidocaine Patch	
Therapeutic Classes (AHFS)	ANTIPRURITICS AND LOCAL ANESTHETICS
Medications	Formulary-PA Lidocaine (Lidoderm) 5% transdermal patch Non-Formulary ZTlido (lidocaine) 1.8% patch Lidocaine 4% patch Lidaflex (lidocaine) 4% patch ~~Gen7T (lidocaine) 3.5% patch~~ ~~Synera (lidocaine/tetracaine) 70mg/70mg patch~~ Any other 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	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months (for up to a maximum of #90 patches per 30 days) **Later Approvals** 12 months (for up to a maximum of #90 patches per 30 days) If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	**CRITERIA FOR AUTHORIZATION for lidocaine 5% patch** • Diagnosis of neuropathic pain AND • Documented trial and failure or intolerance to gabapentin at least 1800mg per day for 90 days in the last 365 days OR documented trial and failure or intolerance to pregabalin at least 300mg per day for 90 days in the last 365 days AND • Documented trial of a therapeutic dose and duration of one other formulary alternative (e.g., duloxetine, venlafaxine, amitriptyline) in the last 365 days OR • Member is using over 50 mg morphine equivalence/day for 3 months. **CRITERIA FOR AUTHORIZATION for non-formulary patches** • The member meets the criteria for lidocaine 5% patch, as outlined in the section above AND • Documented trial and failure or intolerance to lidocaine 5% patch
Criteria Statement	Lidocaine 5% patches are reserved for members with neuropathic pain who have used (or cannot/should not use) gabapentin 1800 mg (or more) OR pregabalin 300mg (or more) AND one other formulary alternative (e.g., duloxetine, venlafaxine, amitriptyline). Non-formulary patches are reserved for members with neuropathic pain who have used (or cannot/should not use) gabapentin 1800 mg (or more) OR pregabalin 300mg (or more) AND one other formulary alternative (e.g., duloxetine, venlafaxine, amitriptyline) AND who have used (or cannot/should not use) lidocaine 5% patches.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Potassium-removing agents	
Therapeutic Classes (AHFS)	Potassium-removing agents
Medications	Formulary, quantity limit Lokelma (sodium zirconium cyclosilicate) Formulary, step therapy required, quantity limit Veltassa (patiromer) powder packets
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	Step-therapy Criteria • For Veltassa, documented (consistent with pharmacy claims data), OR for new members to the health plan consistent with medical chart history) documentation of trial and failure, intolerance, or contraindication to Lokelma
Criteria Statement	Veltassa is reserved for members who have used (or cannot/should not use) Lokelma.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Minor wording change for clarity

Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	
Therapeutic Classes (AHFS)	Immunomodulatory agents
Medications	**<u>Non-Preferred</u>** **Ocrevus (ocrelizumab)** **Rituxan (rituximab)** **Ruxience (rituximab-pvvr) - biosimilar** **Truxima (rituximab-abbs) - biosimilar** **Riabni (rituximab-arrx) - biosimilar** **Rituxan Hycela (rituximab/hyaluronidase)** **Lemtrada (alemtuzumab)** **Tysabri (natalizumab)** **Briumvi (ublituximab-xiiy)** **Any other newly marketed healthcare professional administrable DMT for MS indicated for the listed diagnoses**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Tysabri or Briumvi: • Primary Progressive MS (PPMS) Lemtrada: • Primary Progressive MS (PPMS) • Clinically Isolated Syndrome (CIS)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Member must be age appropriate per prescribing information (PI) **NOTE: Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	**Initial Approval** 12 months **Later Approval** 12 months: If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For requests for Tysabri for the indication of Crohn's disease, please see the Specialty Biological Agents for Crohn's Disease policy **** When the biosimilar is indicated, the member must have documented dates of trial and failure, intolerance, inability to use, or contraindication to the biosimilar medication prior to the brand medication approval, OR the currently available biosimilar product does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested, in addition to meeting all applicable criteria below.** **<u>Initial Authorization</u>** <u>Clinically Isolated Syndrome (CIS), Relapsing Remitting MS (RRMS), Secondary Progressive MS (SPMS)</u> ○ Diagnosis of CIS, RRMS, or SPMS ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

	○ Documented trial of BOTH preferred agents or a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing these therapies. ○ Preferred agents: glatiramer and dimethyl fumarate (Tecfidera) OR ○ For members with "highly active" MS requesting Lemtrada (alemtuzumab), Tysabri (natalizumab) or rituximab, a trial with Gilenya (fingolimod) alone will be acceptable. ○ If the request is for Ocrevus (ocrelizumab), Briumvi (ublituximab-xiiy), or rituximab, documentation of the following: ○ Attestation that the member has been screened for and does not have active hepatitis B virus (HBV) ○ Attestation that the member has received all non-live immunizations for rituximab according to immunization guidelines or has a documented medical reason for not receiving recommended immunizations ○ If the request is for Rituxan Hycela (rituximab/hyaluronidase) or brand Rituxan, all of the above AND documented medical reason why the member cannot use a rituximab biosimilar product. ○ If the request is for Tysabri (natalizumab), documentation of the following ○ Member does not have a history of progressive multifocal leukoencephalopathy (PML) ○ Documentation consistent with pharmacy claims data indicating the member is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications Primary Progressive Multiple Sclerosis (PPMS) ○ Diagnosis of PPMS ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature ○ If the request is for Ocrevus (ocrelizumab) or rituximab, documentation of the following has been submitted ○ Attestation that the member has been screened for and does not have active HBV ○ Member has received all non-live immunizations for rituximab, according to immunization guidelines or has a documented medical reason for not receiving recommended immunizations ○ If the request is for Rituxan Hycela (rituximab/hyaluronidase) or brand Rituxan, all of the above AND documented medical reason why the member cannot use a rituximab biosimilar product. **Reauthorization** CIS ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature ○ Documentation was provided that the prescriber has reviewed the risks and benefits of continuing DMT versus stopping. PPMS, RRMS, or SPMS ○ Documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit)

	○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature ○ If the request is for Lemtrada (alemtuzumab), documentation of the following ○ At least 12 months has or will have elapsed since previous treatment ○ If the request is for Tysabri (natalizumab), documentation of the following has been submitted ○ Member does not have a history of PML ○ Documentation consistent with pharmacy claims data was submitted indicating the member is not currently using any antineoplastic, immunosuppressant, or immunomodulating medications **Continuation of Therapy~~/Grandfathering~~ Provision**: Members with history (within the past 90 days) of a non-formulary product (or the past 12 months for Lemtrada) ar**e** not required to try a preferred agent prior to receiving the non-preferred product.
Criteria Statement	Ocrevus (ocrelizumab), rituximab, Briumvi (ublituximab-xiiy), Lemtrada (alemtuzumab), and Tysabri (natalizumab) are reserved for members with multiple sclerosis who have tried and failed or have a reason not to use both of the following agents: glatiramer or dimethyl fumarate (Tecfidera). Rituxan/ Rituxan Hycela (rituximab) is reserved for members with multiple sclerosis who have tried and failed or have a reason not to use a rituximab biosimilar product AND both of the following agents: glatiramer or dimethyl fumarate (Tecfidera).
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Remove generic Antara as it has been discontinued

Fenofibrates	
Therapeutic Classes (AHFS)	Fibric acid derivatives
Medications	Formulary, with quantity limit (30/30) (pays at point-of-sale): fenofibrate nanocrystallized 48, 145 mg fenofibrate 54, 160 mg fenofibrate micronized 67, 134, 200 mg gemfibrozil 600mg Non-formulary (non-preferred, requires prior authorization): fenofibric acid [choline] (Trilipix) 45, 135 mg cap fenofibrate (Lipofen) 50, 150 mg cap fenofibrate (Fenoglide) 40, 120 mg tab fenofibrate micronized 43, 130 mg cap fenofibric acid (Fibricor) 35, 105 mg tab ~~fenofibrate micronized (Antara) 30, 90mg cap~~ 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	Non-preferred strengths and formulations of fenofibrate are approved when the following criteria are met: • Documentation of a trial and failure of at least 3 of the following: gemfibrozil 600mg, fenofibrate 54mg, 160mg, 48 mg, 145 mg, 67 mg, 134mg, or 200 mg tablets/capsules.
Criteria Statement	Non-formulary fenofibrates are reserved for members who have used (or cannot/should not use) 3 of the following drugs: gemfibrozil 600mg, fenofibrate 54mg, 160mg, 48 mg, 145 mg, 67 mg, 134mg, or 200 mg tablets/capsules
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Remove STC information, as this refers to FDB

Nutritional formulas, infant formulas ~~(STC C5F C5C)~~	
Therapeutic Classes (AHFS)	Caloric agents
Medications	Nutritional formulas, infant formulas ~~(STC C5F C5C)~~
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	N/A
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	N/A
PA Review Criteria	**CRITERIA FOR AUTHORIZATION** **These products/services are delegated to California Home Medical Equipment (CHME). Please call CHME by phone at 1-800-906-0626 or fax the prescription to CHME at 1-650-357-8551.**
Criteria Statement	N/A
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Lipotropics	
Therapeutic Classes (AHFS)	Antilipemic agents, miscellaneous
Medications	Formulary, quantity limit (120/30) omega-3-acid ethyl esters (Lovaza) Formulary, PA required icosapent ethyl (Vascepa) 0.5gm & 1gm 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/Re-Approval** If all conditions are met, the request will be approved for up to 12 months with a limit of 120 capsules per 30 days. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.

PA Review Criteria	**Initial Authorization**
	
	Cardiovascular risk reduction icosapent ethyl (Vascepa)
	• Member has a diagnosis of moderate hypertriglyceridemia (pre-treatment triglyceride ≥ 150 mg/dL) and ONE of the following is true:
	  ○ Member is ≥ 45 years of age and has established cardiovascular disease as evidenced by a history of at least ONE of the following:
	  ▪ Myocardial infarction or acute coronary syndrome
	  ▪ Stroke or transient ischemic attack
	  ▪ Coronary artery disease with stable angina
	  ▪ Coronary or other arterial revascularization
	  ▪ Peripheral vascular disease
	  ▪ Aortic aneurism
	  ○ Member is ≥ 50 years of age, has diabetes mellitus and at least TWO of the following:
	  ▪ Men ≥ 55 years or women ≥ 65 years
	  ▪ Cigarette smoker or stopped smoking within the past 3 months
	  ▪ Hypertension (pretreatment blood pressure ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic)
	  ▪ HDL-C ≤ 40 mg/dL for men or ≤ 50 mg/dL for women
	  ▪ High-sensitivity C-reactive protein > 3.0 mg/L
	  ▪ Renal dysfunction (CrCl > 30 mL/min and < 60 mL/min)
	  ▪ Retinopathy
	  ▪ Micro- or macro-albuminuria
	  ▪ Ankle-brachial index (ABI) < 0.9 without symptoms of intermittent claudication
	• Member is taking and will continue on maximum tolerated statin dose while receiving icosapent ethyl (Vascepa), or documentation has been provided that the member is not able to tolerate a statin.
	• Documentation was provided indicating provider has counseled member on smoking cessation (if applicable) and following a "heart healthy diet."

	• The request is for an FDA approved dose. **Triglyceride reduction** • Member has a diagnosis of severe hypertriglyceridemia (pre-treatment triglyceride level ≥ 500 mg/dL). • Member has tried and failed an OTC fish oil or omega-3-ecid ethyl ester (generic Lovaza) • Documentation was provided indicating provider has counseled member on smoking cessation (if applicable) and following a "heart healthy diet." • The request is for an FDA approved dose. **Reauthorization** • Documentation was provided that the member has obtained clinical benefit from medication (e.g. triglyceride lowering from baseline by documentation of labs or provider attestation) • For cardiovascular risk reduction, the member will continue on maximum tolerated statin dose, or documentation has been provided that the member is not able to tolerate a statin. • The request is for an FDA approved dose.
Criteria Statement	For the diagnosis of hypertriglyceridemia, icosapent ethyl (Vascepa) is reserved for members who have used (or cannot/should not use) plain omega-3 fatty acid/fish oil capsules or omega-3-acid ethyl esters (Lovaza) but still have high triglycerides of 500 mg/dL or greater. For the indication of cardiovascular risk reduction, icosapent ethyl (Vascepa) is reserved for members who have used (or cannot/should not use) a statin, have documentation of cardiovascular disease OR are age ≥50 with diabetes with risk factors, but still have high triglycerides of 150 mg/dL or greater.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Long acting opioids		
Therapeutic Classes (AHFS)	Analgesics, narcotics	
Medications	**Prior authorization required:** Morphine sulfate ER (MS Contin) 15, 30, 60, 100, 200 mg tablet -**Preferred** Oxycodone HCl ER 10, 15, 20, 30, 40, 60, 80 mg Methadone 5, 10 mg tablet Methadone 10 mg/ml 5 mg/ml. 10 mg/5 ml solution Fentanyl (Duragesic) 12, 25, 50, 75, 100 mcg/h transdermal patch **Non-Formulary** Morphine ER (Kadian, Avinza) capsule Fentanyl (Duragesic) 37.5, 62.5, 87.5, mcg/h transdermal patch Oxymorphone ER tablet Hydromorphone ER tablet Hydrocodone ER (Zohydro ER) capsule Hydrocodone (Hysingla) ER tablet Nucynta ER tablet Tramadol ER capsule (Conzip) Tramadol ER (Ryzolt ER) Xtampza ER capsule Buprenorphine patch (Butrans) Any other non-formulary long-acting opioid medication	
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	Methadone for use in treatment of opioid use disorder is not a covered indication	
Required Clinical Information	See "**PA Review Criteria**" below	
Age Restrictions	N/A	
Prescriber Restrictions	N/A	
Coverage Duration	**Approval for initial and renewal when not otherwise specified**	If all of the conditions are met, the request will be approved for up to a 12 month duration.
	Initial approval for LTC or SNF requests	Approval duration limit is up to a 30-day supply with 1 refill (up to a total duration of 60 days)
	Partial Approval for chronic users	Partial approval duration limit for members with chronic use is up to a 3 month supply If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.

PA Review Criteria	**All requests must be reviewed by a clinical pharmacist first and then forwarded to AAH for review**
	
	****Members who are on at least 90 MME with a continuous 6 months utilization, please use Partial Approval Authorization Criteria for Chronic Opioid Users.**
	
	If the member has a diagnosis of cancer, sickle cell disease, or is on hospice/palliative care please automatically authorize for up to 12 months (member must meet non-formulary criteria if request is for non-formulary medication)
	
	Criteria to start treatment for ALL drugs: administration location other than SNF/LTC*:
	***Please note for requests for members in SNF/LTC see separate criteria section below**
	• Documentation member has met all of the following:
	  ○ Clinic notes containing diagnosis and rationale for needing long-acting opioids for severe chronic pain requiring around-the-clock opioid treatment requiring more than 90 days of therapy.
	  ○ Previous use of an equianalgesic short-acting opioid and/or the total dose increase is not greater than 50% from the previous average daily dose
	  ○ Current and adherent to at least one non-opioid adjuvant (e.g., NSAIDs, tri-cyclic antidepressant, SNRI, gabapentin).
	  ○ Non-pharmacologic treatments (e.g., acupuncture, physical therapy, chiropractic adjustment, etc.) have been discussed with the member, if applicable
	  ○ The member is not opioid naïve (defined as no opioid claims in last 90 days)
	  ○ The member is not on another long-acting opioid OR documentation/attestation that member is switching from one long-acting opioid to another has been submitted.
	• For members with a high-risk condition stated in the CDC guidelines (ex. sleep apnea or other causes of sleep-disordered breathing, renal or hepatic insufficiency, older adults, pregnant women, depression or other mental health conditions, or alcohol or other substance use disorders) the prescriber attests to discussing the heightened risks of opioid use and has educated the member on naloxone use and has considered prescribing naloxone
	
	Criteria for the use of morphine sulfate ER tablets (MS Contin)
	• See “Criteria to start treatment for ALL drugs”
	
	Criteria for the use of fentanyl (Duragesic) 12, 25, 50, 75, 100 mcg/h transdermal patch, oxycodone ER (OxyContin) tablets, and methadone 5, 10, mg tablet, 10 mg/ml, 5mg/5 ml, 10 mg/5ml solution
	• See “Criteria to start treatment for ALL drugs”
	• Documentation of trial and failure, intolerance, contraindication to extended-release morphine sulfate [MS Contin])
	• For methadone, the prescriber attests naloxone has been prescribed for the member
	• For methadone liquid, documented reason (i.e. inability to swallow) or inability to use oral tablet formulation
	
	Criteria for non-formulary long-acting opioid medications
	• See “Criteria to start treatment for ALL drugs”

	• Documentation of trial and failure, intolerance, or contraindication to extended-release morphine sulfate [MS Contin]) AND at least one other formulary-prior authorization required medication • If the request is for non-formulary fentanyl 37.5, 62.5, or 87.5 mcg/h patches, the member must have documentation of trial and failure, contraindication, or inability to use fentanyl 12, 25, 50, 75, 100 mcg/h transdermal patches • If a non-formulary strength of fentanyl patch is requested, return with suggestion of separate patches (ex: 37.5mcg/hr, suggestion of 12mcg/hr + 25mcg/hr separate patches) **<u>Criteria for requests for an opioid regimen above 500 morphine milligram equivalents (MME) per day, approve if:</u>** o For members who are on 6 months of continuous utilization, refer to partial approval authorization criteria for chronic opioid users Approve if: o The criteria to start treatment for ALL drugs, above, and drug-specific criteria (i.e. criteria for the use of fentanyl patches) are met AND all of the additional following criteria are met: ▪ The member has been referred to a pain management specialist ▪ Documentation is provided that the prescribing provider has reviewed the CURES database for the member, and the member is not receiving opioids from any other prescriber outside the requesting provider's practice ▪ Documentation is provided that the prescriber reviewed the potential risks of ultra-high dose opioid use with the member ▪ Documentation is provided that the prescriber has evaluated the member's treatment history for evidence of benefit with opioid titration in terms of function as well as pain score goals ▪ Documentation is provided that the member has received a prescription for naloxone and education for use ▪ The provider attests that the member has no known opioid overdose episodes in the last year (i.e., hospitalizations or use of naloxone) ▪ Documentation is provided that urine drug screens are being utilized to assess for illicit drug use and/or compliance. **<u>Criteria for Skilled Nursing Facility (SNF) or Long-Term Care Facility (LTC) initial requests. Approval duration limit is up to a 30-day supply with 1 refill (up to a total duration of 60 days)</u>**: • Formulary and non-formulary opioids will be approved as a part of continued treatment from the hospital OR when started and administered in the SNF or LTC. • Formulary and non-formulary opioids should not be denied unless more than a 60 day supply is requested, or the request is deemed unsafe by reviewer • If the request is for a brand name opioid when a generic is available, it will be partialed for a generic unless they meet following: o The member must use the authorized generic (if available), if made by the maker of the brand-name product OR o The member must use the biosimilar product when available, prior to the approval of the brand OR o The member must use a generic formulation with the same inactive ingredients as the brand name product (if available) o AND, the member must try and have documented adverse reaction to three (3) different generic formulations. If there are fewer than 3

	formulations available, the member must try all available generic formulations before the brand name product will be approved. • If the request is for a brand name opioid when a generic is NOT available, the request will be partialed for up to a 30-day supply with 1 refill (up to a total duration of a 60-day supply). • Subsequent requests will be reviewed using the initial criteria. **Partial Approval Authorization Criteria for Chronic Opioid Users:** • Members with a total opioid utilization of at least 90 MME AND 6 months of continuous utilization are eligible for 3 months approval until a treatment plan is provided. o Clinic notes and claims history will be used to confirm the above. o Members who are new to the plan must have a list of specific dates when they were on opioids. • Criteria above (e.g. Criteria to start treatment for ALL drugs, Criteria for fentanyl patches, Criteria for non-formulary medications, etc.) do NOT need to be met for a partial approval for chronic opioid users. • Subsequent requests will be reviewed using the same partial approval criteria for chronic opioid users. If the prescriber provides a treatment plan, the request will be approved up to the duration of the treatment plan with a maximum of a 1 year approval. **Reauthorization criteria for administration locations other than SNF/LTC** • Documentation (clinic notes or chart notes) showing why longer treatment is needed: should include treatment plan, non-pharmacological treatment (e.g., acupuncture, physical therapy, chiropractic adjustment, etc.), titration or tapering plan (if applicable).
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Serotonin Receptor Agonists (Triptans)	
Therapeutic Classes (AHFS)	Selective serotonin agonists
Medications	**FORMULARY STATUS** Formulary, Pays at Point-of-Sale (First Line), within quantity limits (QL) • Sumatriptan (Imitrex) tablets: QL 18/30 • Rizatriptan (Maxalt & Maxalt- MLT) tablets and ODT: QL 12/30 • Naratriptan (Amerge) tablets: QL 9/30 **FORMULARY STATUS** step-therapy required (Second Line, after trial and failure of sumatriptan tablets), within QL 6/30 • Zolmitriptan (Zomig) tablet • Zolmitriptan (Zomig-ZMT) ODT • Sumatriptan (Imitrex) nasal spray **FORMULARY STATUS** Non-preferred, prior authorization required (Third Line) • Sumatriptan (Imitrex) injection **FORMULARY STATUS** Non-formulary, prior authorization required (Last Line) • Almotriptan (Axert) • Frovatriptan (Frova) • Eletriptan (Relpax) • Sumatriptan/naproxen (Treximet) • Zembrace SymTouch (sumatriptan) • Onzetra Xsail (sumatriptan) • Migranow (Sumatriptan/menthol/camphor) 50 mg tablet/gel kit • Tosymra (sumatriptan) 10mg nasal spray • Zolmitriptan (Zomig) nasal spray **Any other newly marketed serotonin receptor agonists (triptans) treatment 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), 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, not to exceed 12 tablets per 30 days, 2 injections kits (4 injections) per 30 days, and 6 nasal spray units (1 box) per 30 days **Later Approvals** 12 months, not to exceed 12 tablets per 30 days, 2 injections kits (4 injections) per 30 days, and 6 nasal spray units (1 box) per 30 days If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Criteria for authorization:** **First line agents:** • An automatic approval for first line agents sumatriptan tablet, rizatriptan tablets or ODT, or naratriptan tablets at the point-of-sale will occur if the quantities prescribed do not exceed quantity limits. **Second line agents:**

Serotonin Receptor Agonists (Triptans)	
	• Second line agents will pay automatically, at the point-of-sale if the quantities prescribed do not exceed quantity limits and the members has a history of paid claims for sumatriptan tablets **Third line agent:** • **For sumatriptan (Imitrex) injection, approve if:** o Documented trial and failure at therapeutic doses or intolerance, contraindication, or inability to use oral formulary alternatives sumatriptan tablets or naratriptan tablets AND rizatriptan ODT. o Diagnosis of migraine headaches OR o Diagnosis of cluster headaches **Last line agents:** • **For non-formulary triptans, approve if:** o Documented trial and failure at therapeutic doses or intolerance, contraindication, or inability to use 1) sumatriptan tablets/nasal spray and 2) rizatriptan tablets/ODT and 3) naratriptan tablets and then 4) zolmitriptan tablets/ODT. o Requests for sumatriptan/naproxen (Treximet) should be directed to using the two individual agents **Criteria for Quantities Greater Than Allowed Per 30 Days:** If the patient requires doses greater than the set limits after meeting approval the following conditions must be met: • Documentation provided that member is on prophylactic therapy. AND/OR • Documentation of medical necessity for increased quantity despite optimal prophylactic therapy.
Criteria Statement	Second line agents are reserved for members who have used (or cannot/should not use) sumatriptan tablets. Third line agent sumatriptan injection is reserved for members who have used (or cannot/should not use) sumatriptan tablets or naratriptan tablets AND rizatriptan ODT and have a diagnosis of migraine headaches or cluster headaches. Third line agents/non-formulary triptans are reserved for members who have used (or cannot/should not use) 1) sumatriptan tablets/nasal spray and 2) rizatriptan tablets/ODT and 3) naratriptan tablets and 4) zolmitriptan tablets/ODT.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Pregabalin (Lyrica and Lyrica CR)	
Therapeutic Classes (AHFS)	Anticonvulsants, miscellaneous
Medications	Formulary, quantity limit (90/30) Pregabalin (Lyrica) 25, 50, 75, 100, 150, 200, 225, 300 mg capsule Formulary, prior authorization required Pregabalin (Lyrica CR) 82.5, 165, 330 mg ER tablet Pregabalin (Lyrica) 20 mg/ml 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
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 pregabalin (LYRICA) liquid OR ER tablet REQUESTS** • Documentation of trial and failure of, intolerance, or inability to use pregabalin IR oral capsules (i.e. difficulty swallowing for the liquid formulation) **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. AND • The dose requested is supported by the Medical Compendia or current treatment guidelines
Criteria Statement	Pregabalin (Lyrica) oral solution and ER tablets are reserved for members who cannot use pregabalin IR oral capsules (for example, unable or difficulty swallowing).
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Rufinamide (Banzel)	
Therapeutic Classes (AHFS)	Anticonvulsants, Miscellaneous
Medications	Formulary, PA required • Rufinamide (Banzel) tablet • Rufinamide (Banzel) 40mg/ml 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), and the Drug Package Insert.
Exclusion Criteria	None
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	Member must be ≥ 1 year old. Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	None.
Coverage Duration	**Initial/ Later Approval**: If all criteria are met, approve for up to a 12 month duration for up to 16 tablets/day of 200 mg and 8 tablets/day for 400 mg or the liquid equivalent. 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 • Diagnosis of Lennox-Gastaut syndrome AND • Member ≥ 1 years old AND • Patient is currently receiving another anticonvulsant medication at a therapeutic dosage and seizures are not controlled
Criteria Statement	Rufinamide (Banzel) tablets or liquid are reserved for patients at least 1 year of age, with a diagnosis of Lennox-Gastaut syndrome, and are already taking another anti-seizure medication at a therapeutic dose.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Corrected minor grammar error to be consistent with package insert

vigabatrin (Sabril)	
Therapeutic Classes (AHFS)	Anticonvulsants, Miscellaneous
Medications	Formulary, PA required • Vigabatrin (Sabril) powder packet and vigabatrin (Sabril) 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), and the Drug Package Insert.
Exclusion Criteria	None
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 specialist in treatment of seizure disorders.
Coverage Duration	**Initial Approval** 3 months **Later Approval** 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	**Initial criteria:** Diagnosis of refractory ~~partial complex~~ complex partial seizures • Member is ≥ 2 years of age • Seizures remain uncontrolled with adequate trial of formulary oral antiepileptic medication • Documentation vigabatrin (Sabril) will be used in combination with other anticonvulsants Diagnosis of infantile spasms (powder for oral suspension) • Member is age 1 month to 2 years • Vigabatrin (Sabril) is being used as monotherapy **Reauthorization criteria:** • Documentation has been provided that demonstrates reduction or stabilization of seizure frequency • Dose and age are within FDA approved limits, per diagnosis
Criteria Statement	**Vigabatrin powder for oral suspension:** Vigabatrin (Sabril) powder for oral suspension is reserved for members who are aged 1 month to 2 years who have a diagnosis of infantile spasms and are not on any other anti-seizure medications at the same time. **Vigabatrin (Sabril) tablet:** Vigabatrin (Sabril) tablet and vigabatrin (Sabril) powder for oral suspension are reserved for members who have a diagnosis of refractory ~~partial complex~~ complex partial seizures, who are at least 2 years of age, and are still having seizures, despite taking another anti-seizure medication, and will take vigabatrin (Sabril) in combination with the other anti-seizure medication.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Remove Zolpimist as it has been discontinued

Sedative Hypnotics	
Therapeutic Classes (AHFS)	Anxiolytics, sedatives, and hypnotics, misc
Medications	ramelteon (Rozerem) Edluar (zolpidem SL) zolpidem (Intermezzo) sublingual tablet ~~Zolpimist (zolpidem oral solution)~~ Belsomra (suvorexant) doxepin (Silenor) tablet DayVigo (lemborexant) tablet Quviviq (daridorexant) tablet Any other 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** — If all criteria are met, approve for up to a 6 month duration; if all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review. **Reauthorization** — If all criteria are met, approve for up to a 12 month duration; 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
	Ramelteon (Rozerem)
	• Diagnosis of insomnia.
	• Documented trial and failure, contraindication, or intolerance to one of the following: zolpidem (Ambien) IR or ER, eszopiclone (Lunesta) or zaleplon (Sonata) for at least 2 weeks (14 days) of therapy.
	  ○ For requests for members aged 65 or older OR for members with a history of substance abuse, only a diagnosis of insomnia is required
	
	Doxepin (Silenor) tablet
	• Diagnosis of insomnia.
	• Documented trial and failure, contraindication, or intolerance to one of the following: zolpidem (Ambien) IR or ER, eszopiclone (Lunesta), or zaleplon (Sonata) AND ramelteon (Rozerem) AND doxepin concentrate for at least 2 weeks (14 days) of therapy
	  ○ For members aged 65 or older, only diagnosis of insomnia AND documented trial and failure, contraindication, or intolerance to doxepin concentrate AND ramelteon (Rozerem) for at least 2 weeks (14 days) of therapy is required
	
	Edluar, zolpidem (Intermezzo)~~, Zolpimist~~
	• Diagnosis of insomnia.

	• Documented trial and failure, contraindication, or intolerance to TWO of the following: zolpidem (Ambien) IR or ER, eszopiclone (Lunesta), or zaleplon (Sonata) for at least 2 weeks (14 days) of therapy • Documented trial and failure or intolerance to ramelteon (Rozerem) for at least 2 weeks (14 days) of therapy. **<u>DayVigo, Quviviq, or Belsomra</u>** • Diagnosis of insomnia. • Documented trial and failure, contraindication, or intolerance to TWO of the following: zolpidem (Ambien) IR or ER, eszopiclone (Lunesta), or zaleplon (Sonata) for at least 2 weeks (14 days) of therapy • Documented trial and failure or intolerance to ramelteon (Rozerem) for at least 2 weeks (14 days) of therapy. o For members aged 65 or older, only diagnosis of insomnia AND documented trial and failure, contraindication, or intolerance to doxepin concentrate AND ramelteon (Rozerem) for at least 2 weeks (14 days) of therapy is required • For Belsomra requests, the criteria above must be met AND documented trial and failure, contraindication, or intolerance to DayVigo is required • For Quviviq requests, the criteria above must be met AND documented trial and failure, contraindication, or intolerance to DayVigo AND Belsomra is required
Criteria Statement	Ramelteon is reserved for members with insomnia who are older than 65 years OR have history of substance abuse OR who have used (or cannot/should not use) one of the following: zolpidem IR or ER, eszopiclone, or zaleplon for at least 2 weeks. Edluar, zolpidem (Intermezzo), or Zolpimist are reserved for members who have insomnia and who have used (or cannot/should not use) ramelteon and at least two of the following, zolpidem IR or ER, eszopiclone, or zaleplon AND ramelteon (Rozerem) for at least 2 weeks. DayVigo, Quviviq, or Belsomra are reserved for members who have insomnia and who have used (or cannot/should not use) two of the following: zolpidem IR or ER, eszopiclone, or zaleplon AND ramelteon for at least 2 weeks. If a member is 65 or older, DayVigo is reserved for members who have a diagnosis of insomnia and who have used (or cannot/should not use) doxepin concentrate and ramelteon for at least 2 weeks. If a member is 65 or older, Belsomra is reserved for members who have a diagnosis of insomnia and who have used (or cannot/should not use) doxepin concentrate and ramelteon and DayVigo. If a member is 65 or older, Quviviq is reserved for members who have a diagnosis of insomnia and who have used (or cannot/should not use) doxepin concentrate and ramelteon and DayVigo and Belsomra. Doxepin (Silenor) is reserved for members who have insomnia who have used (or cannot/should not use) one of the following: zolpidem IR or ER, eszopiclone, or zaleplon AND ramelteon AND doxepin concentrate. If a member is 65 or older, doxepin (Silenor) is reserved for members who have a diagnosis of insomnia and used (or cannot/should not use) doxepin concentrate.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Epidiolex (cannabidiol)	
Therapeutic Classes (AHFS)	Anticonvulsant – Cannabinoid type
Medications	Formulary, PA required Epidiolex (cannabidiol)
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 specialist in treatment of seizure disorders.
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: • Clinical diagnosis of Lennox-Gastaut syndrome, Dravet syndrome or Tuberous Sclerosis complex • Documented trial and failure or intolerance to at least two antiepileptic drugs within the member's lifetime • • Patient is currently taking a stable dose of at least one other antiepileptic medication • Member's weight • Dose is within FDA approved limits Reauthorization: • Documentation has been provided that demonstrates reduction or stabilization of seizure frequency • Member's weight • Dose is within FDA approved limits
Criteria Statement	Epidiolex is reserved for members who have Lennox-Gastaut syndrome, Dravet syndrome or Tuberous Sclerosis complex who have used (or cannot/should not use) at least two antiepileptic drugs within the member's lifetime and are taking a stable dose of at least one other antiepileptic medication.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Tiagabine (Gabitril)	
Therapeutic Classes (AHFS)	Anticonvulsants, Miscellaneous
Medications	Formulary, PA required • Tiagabine (Gabitril)
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	None
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 specialist in treatment of seizure disorders.
Coverage Duration	**Initial Approval** 6 months **Later Approvals** 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 • Diagnosis of partial seizures AND • Seizures remain uncontrolled with adequate trial of one formulary oral antiepileptic medication AND • Documentation tiagabine will be used in combination with other anticonvulsants
Criteria Statement	**Tiagabine (Gabitril)** tablet is reserved for members who have a diagnosis of partial seizures and are still having seizures, despite taking another anti-seizure medication, and will take tiagabine (Gabitril) in combination with the other anti-seizure medication.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Topiramate (Topamax) sprinkles	
Therapeutic Classes (AHFS)	ANTICONVULSANTS, MISCELLANEOUS
Medications	Formulary, Prior Authorization Required Topiramate (Topamax) sprinkles Non-Formulary Topiramate (Qudexy) XR sprinkle 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), 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
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	CRITERIA FOR AUTHORIZATION • Diagnosis of epilepsy or migraine prophylaxis AND • Documentation of inability to swallow generic topiramate tablets AND • For topiramate (Qudexy) XR sprinkle capsule, trial and failure or contraindication to use both topiramate tablets AND topiramate (Topamax) sprinkles
Criteria Statement	Topiramate (Topamax) sprinkles are reserved for members who have epilepsy or require migraine prophylaxis and cannot swallow topiramate tablets. Qudexy (topiramate) XR sprinkle capsules are reserved for members who have epilepsy or require migraine prophylaxis and cannot swallow topiramate tablets and who have used (or cannot/should use) topiramate (Topamax) sprinkles.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Change to treatment summary in recommended regimens for patients who have failed Mavyret treatment and require Vosevi

Hepatitis C Medications: All requests must be reviewed by a clinical pharmacist first and then forwarded to AAH for review

MAVYRET (glecaprevir/ pibrentasvir) - PREFERRED AGENT
SOFOSBUVIR /VELPATASVIR (GENERIC EPCLUSA)-PREFERRED AGENT
LEDIPASVIR /SOFOSBUVIR (GENERIC HARVONI)-PREFERRED AGENT

ZEPATIER (elbasvir/ grazoprevir)
VOSEVI (sofosbuvir/ velpatasvir/ voxilaprevir)
EPCLUSA (sofosbuvir/velpatasvir)
HARVONI (ledipasvir/ sofosbuvir)
SOVALDI (sofosbuvir)
PEG-INTRON (peginterferon alfa-2b) PEGASYS (peginterferon alfa-2a)
RIBAVIRIN
VIEKIRA PAK (ombitasvir, paritaprevir, ritonavir and dasabuvir)
ANY OTHER NEWLY MARKETED AGENT for treatment of Hepatitis C

NOTE: Where applicable and appropriate: MAVYRET (glecaprevir/pibrentasvir), SOFOSBUVIR/VELPATASVIR (GENERIC EPCLUSA), or LEDIPASVIR/SOFOSBUVIR (GENERIC HARVONI) are the PREFERRED AGENTS for Hepatitis C requests unless a documented medical reason has been provided (intolerance, hypersensitivity, contraindication, etc.) why the member is not able to use Mavyret, sofosbuvir/velpatasvir (generic Epclusa), or ledipasvir/sofosbuvir (generic Harvoni).

All initial requests MUST meet the following requirements:

1. Life expectancy ≥ 12 months.
2. Lab testing required before starting treatment (copy of results required) if required for treatment selection per AASLD guidelines
    - Genotype must be provided if:
        - Genotype testing required for all who are not going to receive Mavyret or generic Epclusa
        - Genotype testing required for generic Epclusa in treatment naive patients with compensated cirrhosis
        - Genotype testing required for patients who do not qualify for simplified treatment (treatment-experienced, have or had decompensated cirrhosis (Child-Pugh B and C), have ESRD, are HIV positive, have current HBV infection (positive for HbsAg), are pregnant, have known or suspected hepatocellular carcinoma, or have had a liver transplant)
2. Provider has addressed all potential drug interactions with Hepatitis C regimen (including discontinuation of the interacting drug, dose reduction, or counseling of the patient of the risks associated with the use of both medications), AND
3. **Dose and Duration of Therapy: (SEE TREATMENT SUMMARY THAT FOLLOWS)**: Approvals of requests will be consistent with package labeling or current guidelines, at FDA approved dosing. These regimens are subject to change as newly marketed agents become available. Pediatric patients will be limited to one tablet/packet per day. Medications must be dose consolidated to 1 tablet/packet daily, as appropriate.
   ALL regimens are for 28 day supply per fill.

Hepatitis C Treatment Summary
*****For all charts, sofosbuvir/velpatasvir (generic Epclusa) and ledipasvir/sofosbuvir (generic Harvoni) refer to their generic formulations*****

Treatment Naïve			
Genotype	**Treatment Option**	**Duration**	
		No Cirrhosis	**Compensated Cirrhosis (Child-Pugh A)**
All	**Mavyret**	**8 weeks**	**8 weeks**
All^	**sofosbuvir/velpatasvir (generic Epclusa)**	**12 weeks**	**12 weeks**

^Genotype testing required; for genotype 3 with compensated cirrhosis, only use sofosbuvir-velpatasvir (generic Epclusa) if no Y93H resistance

Treatment Experienced, with and without compensated cirrhosis		
Genotype	**Prior Treatment**	**Preferred Regimen**
All	**Sofosbuvir-based and Zepatier treatment failures, including:** Sovaldi + ribavirin ± interferon Harvoni Epclusa Zepatier	12 weeks Vosevi (± ribavirin)^
	Mavyret treatment failures Mavyret only	16 weeks Mavyret + Sovaldi + ribavirin 12 weeks Vosevi (± ribavirin)[a]
	Multiple DAA treatment failures, including: Vosevi Sovaldi + Mavyret	16 weeks Mavyret + Sovaldi + ribavirin* 24 weeks Vosevi + ribavirin

^Add ribavirin for 12 weeks in patients with genotype 3 and cirrhosis, if no contraindications

[a] Add ribavirin if the patient has compensated cirrhosis

*Extension of treatment to 24 weeks should be considered in extremely difficult cases (eg, genotype 3 with cirrhosis) or failure following Sovaldi + Mavyret.

Unique patient populations Refer to current AASLD guidelines @ http://www.hcvguidelines.org/ For all unique and key populations: NOTE: If Mavyret, sofosbuvir/velpatasvir (generic Epclusa), or ledipasvir/sofosbuvir (generic Harvoni) are recommended treatment options, they are preferred unless medical reason provided that member is unable to use Mavyret, sofosbuvir/velpatasvir (generic Epclusa), or ledipasvir/sofosbuvir (generic Harvoni).
HIV/HCV Coinfection
Decompensated Cirrhosis (Child-Pugh B or C)
Recurrent HCV Infection Post-Transplant
HCV-Uninfected Transplant Recipients Receiving Organs From HCV-Viremic Donors
Renal Impairment
Kidney Transplant
Pregnancy
Pediatrics *Medications should be dose consolidated to no more than one tablet/packet daily if possible.

Last Review/Revision Date: ~~6/2023~~6/2024

Recommendation:

- No changes

Short acting opioid containing products		
Therapeutic Classes (AHFS)	OPIATE AGONISTS	
Medications	Short-acting opioid containing products	
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	N/A	
Coverage Duration	**Approval for initial and renewal when not otherwise specified** **Initial approval for LTC or SNF requests** **Partial Approval for chronic users** **Later Approvals**	If the criteria are met, the request will be approved for up to six months duration; if the criteria are not met, the request will be referred to a clinical reviewer for medical necessity review Approval duration limit is up to a 30-day supply with 1 refill (up to a total duration of 60 days) Partial approval duration limit for members with chronic use is up to a 3 month supply If the criteria are met, the request will be approved for up to six month duration; if the criteria are not met, the request will be referred to a clinical reviewer for medical necessity review ****If a member does not meet the criteria but is actively tapering off of opioids and the prescriber has explained medical necessity, the request should be approved for 6 months****
PA Review Criteria	****All requests for narcotics must be reviewed by a clinical pharmacist**** ****Members who are on at least 90 MME with a continuous 6 months utilization, please use Partial Approval Authorization Criteria for Chronic Opioid Users.** **If the member has a diagnosis of cancer, sickle cell disease, or is on hospice/palliative care please automatically authorize for up to 12 months (member must meet non-formulary criteria if request is for non-formulary medication with the exception of ALL formulations of short acting oxycodone products which will be approved for 12 months)** Day supply limits apply to opioid naive patients. <u>Initial Authorization</u>: **treatment for administration location other than SNF/LTC*: *Please note for requests for members in SNF/LTC see separate criteria section below** • Documentation member has met all of the following: ○ Documented diagnosis of pain. ○ The member has tried and failed two non-opioid containing pain medications (e.g. acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], tri-cyclic antidepressant, SNRI, gabapentin).	

	○ Non-pharmacologic treatments (e.g., acupuncture, physical therapy, chiropractic adjustment, etc.) have been discussed with the member, if applicable ○ The prescriber has justified the medical necessity for dosing above the current quantity limit (for medications with quantity limits) or day supply limit (i.e. active tapering) ○ The member is not taking concurrent benzodiazepines. If the member is taking benzodiazepines, the prescriber has provided documentation as to why, and attests to discussing with the member the risks of using opioids and benzodiazepines concurrently, and has outlined a plan for tapering if appropriate. ○ The member is not taking concurrent muscle relaxants that are classified as controlled substances. If the member is taking muscle relaxants classified as controlled substances, the prescriber has provided documentation as to why, and attests to discussing with the member the risks of using opioids and muscle relaxants concurrently, and has outlined a plan for tapering if appropriate. ○ If the request is for a non-formulary short acting opioid, the member must meet the above criteria AND one of the following conditions: ▪ Documented trial and failure or intolerance with up to three formulary medications used to treat the documented diagnosis. For medications where there is only one preferred agent, only that agent must have been ineffective or not tolerated. ▪ No other formulary medication has a medically accepted use for the member's specific diagnosis as referenced in the medical compendia. ▪ All other formulary medications are contraindicated based on the member's diagnosis, other medical conditions, or other medication therapy. • If the request is for an opioid regimen above 500 morphine milligram equivalents (MME) per day, see below: ○ For members who are on 6 months of continuous utilization, refer to partial approval authorization criteria for chronic opioid users • Approve if: ○ The criteria for initial authorization, above, are met AND all of the additional following criteria are met: ▪ The member has been referred to a pain management specialist ▪ Documentation is provided that the prescribing provider has reviewed CURES database for the member, and the member is not receiving opioids from any other prescriber outside the requesting provider's practice ▪ Documentation is provided that the prescriber reviewed the potential risks of ultra-high dose opioid use with the member ▪ Documentation is provided that the prescriber has evaluated the member's treatment history for evidence of benefit with opioid titration in terms of function as well as pain score goals ▪ Documentation is provided that the member has received a prescription for naloxone and education for use ▪ The provider attests that the member has no known opioid overdose episodes in the last year (i.e., hospitalizations or use of naloxone) ▪ Documentation is provided that urine drug screens are being utilized to assess for illicit drug use and/or compliance.

Criteria for Skilled Nursing Facility (SNF) or Long-Term Care Facility (LTC) initial requests. Approval duration limit is up to a 30-day supply with 1 refill (up to a total duration of 60 days):

- Formulary and non-formulary opioids can be approved as a part of continued treatment from the hospital OR when started and administered in the SNF or LTC.
- Formulary and non-formulary opioids should not be denied unless more than 60 days supply is requested, or the request is deemed unsafe by reviewer
- If the request is for a brand name opioid when a generic is available, it will be partialed for generic unless they meet the following:
    - The member must use the authorized generic (if available), if made by the maker of the brand-name product OR
    - The member must use the biosimilar product when available, prior to the approval of the brand OR
    - The member must use generic formulation with the same inactive ingredients as the brand name product (if available)
    - AND, the member must try and have documented adverse reaction to three (3) different generic formulations. If there are fewer than 3 formulations available, the member must try all available generic formulations before the brand name product will be approved.
- If the request is for a brand name opioid when a generic is NOT available, the request will be partialed up to a 30-day supply with 1 refill (up to a total duration of 60 days supply)
- Subsequent requests will be reviewed using initial criteria

Partial Approval Authorization Criteria for Chronic Opioid Users

- Members with a total opioid utilization of at least 90 MME AND 6 months of continuous utilization are eligible for 3 months approval until a treatment plan is provided.
    - Clinic notes and claims history will be used to confirm the above
    - Members who are new to the plan must have a list of specific dates when they were on opioids
- Criteria above (e.g. initial authorization) do NOT need to be met for partial approval for chronic opioid users.
- Subsequent requests will be reviewed using partial approval criteria for chronic opioid users. If the provider provides a treatment plan, the request will be approved up to duration of treatment plan with a maximum of 1 year of approval.

Reauthorization Criteria for administration locations other than SNF/LTC

- The prescriber has explained the medical necessity for continued dosing above the current quantity limit (for medications with quantity limits) and if the dose is not being titrated, has provided medical justification explaining why the dose cannot be decreased
- The provider has submitted documentation of the member's response to the requested medication (ex. Improvement in severity level of pain, improvement in ADL's, etc.)
- The member is not taking concurrent benzodiazepines. If the member is taking benzodiazepines, the prescriber has provided documentation as to why, and attests to discussing with the member the risks of using opioids and benzodiazepines concurrently, and has outlined a plan for tapering if appropriate.
- Non-pharmacologic treatments (e.g., acupuncture, physical therapy, chiropractic adjustment, etc.) have been discussed with the member and/or

	the member has tried and failed appropriate non-pharmacological alternatives for pain • The member is not taking concurrent muscle relaxants that are classified as controlled substances. If the member is taking muscle relaxants classified as controlled substances, the prescriber has provided documentation as to why, and attests to discussing with the member the risks of using opioids and muscle relaxants concurrently and has outlined a plan for tapering if appropriate. • For members over 500 daily MME, the reauthorization criteria above, are met AND all of the additional following criteria are met: o The member has been referred to a pain management specialist o Documentation is provided that the prescribing provider has reviewed CURES database for the member, and the member is not receiving opioids from any other prescriber outside the requesting provider's practice o Documentation is provided that the prescriber reviewed the potential risks of ultra-high dose opioid use with the member o Documentation is provided that the prescriber has evaluated the member's treatment history for evidence of benefit with opioid titration in terms of function as well as pain score goals o Documentation is provided that the member has received a prescription for naloxone and education for use o The provider attests that the member has no known opioid overdose episodes in the last year (i.e., hospitalizations or use of naloxone) o Documentation is provided that urine drug screens are being utilized to assess for illicit drug use and/or compliance.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Hemlibra (emicizumab-kxwh)	
Therapeutic Classes (AHFS)	Hemostatics
Medications	Hemlibra (emicizumab-kxwh)
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	N/A
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be a hematologist
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	**All requests must be reviewed by a clinical pharmacist first and then forwarded to AAH for review**
	
	Initial Authorization:
	Documentation submitted indicates the following:
	• Documentation of patient weight
	• Dose requested is within FDA approved limits
	• Severe hemophilia A AND one of the following
	  ○ Member has tried Factor VIII products and is not well-managed due to limited venous access (attestation must be submitted from prescriber)
	  ○ Request is for routine prophylaxis in patients with a diagnosis of severe hemophilia A **WITH** Factor VIII inhibitors and history of spontaneous or traumatic bleeding episode
	  ○ Request is for routine prophylaxis in patients with a diagnosis of severe hemophilia A ***WITHOUT*** Factor VIII inhibitors and patient requires management with Factor VIII products at a total weekly dose of >100 U/kg (attestation must be submitted by prescriber)
	
	Re-Authorization:
	• Documentation submitted indicates a clinical benefit was observed (e.g. reduction in bleeding episodes, improved quality of life)
	• Documentation of patient weight
	• Dose requested is within FDA approved limits

Criteria Statement	Hemlibra is reserved for patients who have a diagnosis of severe hemophilia A with one of the following: not a candidate for Factor VIII products due to limited venous access, routine prophylaxis in patients with Factor VIII inhibitors and spontaneous/traumatic bleeding episodes, or without Factor VIII inhibitors and requires management with Factor VIII products at a total weekly dose of >100 U/kg .
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Aptiom (eslicarbazepine)	
Therapeutic Classes (AHFS)	Anticonvulsants, miscellaneous
Medications	Formulary, PA required Aptiom (eslicarbazepine) 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	Member must be 4 years of age or older Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a neurologist or specialist in treatment of seizure disorders.
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 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	Initial criteria for authorization: • Dose is within FDA approved limits • Diagnosis of partial onset seizures for monotherapy or adjunctive therapy • Documented trial and failure or intolerance to at least two formulary medications that are used to treat partial onset seizures as monotherapy or adjunctive therapy (e.g., carbamazepine, levetiracetam, phenytoin) Reauthorization criteria • Dose is within FDA approved limits • Documentation has been provided that demonstrates reduction or stabilization of seizure frequency
	Aptiom is reserved for members with partial onset seizures as monotherapy or adjunctive therapy who have used (or cannot/should not use) two other formulary medications (e.g., carbamazepine, levetiracetam, phenytoin) used to treat this diagnosis.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Alprazolam (Xanax)	
Therapeutic Classes (AHFS)	BENZODIAZEPINES (ANXIOLYTIC,SEDATIVE/HYPNOTIC)
Medications	Non-formulary Alprazolam oral tablets (0.25mg, 0.5mg, 1mg and 2mg) Alprazolam oral ER tablets (0.5mg, 1mg, 2mg and 3mg) Alprazolam oral disintegrating tablets (0.25mg, 0.5mg, 1mg and 2mg)
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	Psychiatry
Coverage Duration	**Initial Approval** 3 months **Later Approvals** 3 months If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	**CRITERIA FOR AUTHORIZATION** • Request is for alprazolam oral tablets: o Diagnosis of anxiety or panic disorders o Clinic notes to show trial and failure of at least 3 formulary benzodiazepines for at least 2 weeks (14 days) of therapy each (for example – clonazepam, diazepam and lorazepam) • Request is for alprazolam oral disintegrating (ODT) tablets: o Diagnosis of anxiety or panic disorder o Clinic notes to show trial and failure of at least 3 formulary benzodiazepines for at least 2 weeks (14 days) of therapy each AND o Inability to swallow or another medical reason why alprazolam oral tablets cannot be used • Request is for alprazolam oral ER tablets: o Diagnosis of panic disorder o Clinic notes to show trial and failure of at least 3 formulary benzodiazepines for at least 2 weeks (14 days) of therapy each AND o Trial and failure of alprazolam oral tablets **RE-AUTHORIZATION** Documentation of clinical benefit and/or titration schedule for discontinuation (if applicable). Treatment plan should also be given for those on long term treatment (more than 3 months of therapy).
	Alprazolam oral tablets are reserved for members who have used (or cannot/should not use) 3 formulary benzodiazepines for at least 2 weeks (14 days) of therapy each. Alprazolam oral disintegrating (ODT) tablets are reserved for members who have used (or cannot/should not use) 3 formulary benzodiazepines for at least 2 weeks (14 days) of therapy each AND who cannot/should not use alprazolam oral tablets or cannot swallow. Alprazolam ER tablets are reserved for members who have used (or cannot/should not use) 3 formulary benzodiazepines for at least 2 weeks (14 days) of therapy each AND who cannot/should not use alprazolam oral tablets.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Rectiv (nitroglycerin) ointment	
Therapeutic Classes (AHFS)	Skin and Mucous Membrane Agents, Misc.
Medications	Non-Formulary Rectiv (nitroglycerin) rectal ointment 0.4%
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 a phosphodiesterase type 5 (PDE5) inhibitors (e.g. sildenafil, vardenafil, tadalafil).
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for a one-time coverage duration of up to 3 weeks. If conditions are not met, the request will be sent to a clinical reviewer for medical necessity review.

PA Review Criteria	The following criteria must be met for initial requests:
	• Dose is appropriate per label or supported by compendia/standard of care guidelines
	• Diagnosis of moderate to severe pain associated with chronic anal fissures for at least 6 weeks
	• Prescriber attestation that the patient has a documented history (within past 60 days) of trial of at least two conservative treatments for the underlying cause of the anal fissure:
	  ○ High-fiber diet or fiber supplements
	  ○ Sitz baths
	  ○ Topical analgesia/ medicated creams (e.g. hydrocortisone rectal suppository or topical cream, zinc oxide)
	  ○ Laxative or stool softeners (e.g. psyllium, docusate)
	
	The following criteria must be met for re-authorization requests:
	• Dose continues to be appropriate per label or supported by compendia/standard of care guidelines
	• Documentation submitted indicates a clinical benefit was observed and rationale for continuation of treatment

Criteria Statement	Rectiv is reserved for members with moderate to severe pain associated with chronic anal fissures for at least 6 weeks. The member should have used (or cannot/should not use) other conservative treatments for the underlying cause of the anal fissure.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Diuretics	
Therapeutic Classes (AHFS)	Loop Diuretics, Thiazide-like Diuretics
Medications	Formulary, step therapy required Bumetanide tablet Metolazone tablet (quantity limit 30/30)
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	Bumetanide step therapy criteria: • Documentation of a trial and failure or intolerance to torsemide 100 mg or furosemide 80 mg required. Metolazone step therapy criteria: • Documentation of a trial and failure or intolerance to hydrochlorothiazide AND furosemide required.
	Bumetanide is reserved for members who have used (or cannot/should not use) torsemide 100 mg or furosemide 80 mg. Metolozone is reserved for members who have used (or cannot/should not use) hydrochlorothiazide AND furosemide.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Sleep Disorder Therapy	
Therapeutic Classes (AHFS)	Wakefulness-Promoting Agents, Central Nervous System Agents, Misc.
Medications	Formulary, PA required Armodafinil (Nuvigil) 50, 150, 200, 250 mg tablet Modafinil (Provigil) 100, 200 mg tablet Non-Formulary, PA required Sunosi (solriamfetol) 75, 150 mg tablet Wakix (pitolisant) 4.45, 17.8 mg tablet Sodium oxybate (Xyrem) solution Xywav (oxybate salts) 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	See "**PA Review Criteria**" below
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Per prescribing information
Prescriber Restrictions	Sleep specialist, neurologist, psychiatrist, or other specialist in the treatment of the member's diagnosis (does not apply for diagnosis of shift-work disorder)
Coverage Duration	**Initial Approval** If the criteria are met, requests for modafinil or armodafinil will be approved for up to a 12 month duration. Requests for Sunosi or Wakix will be approved for up to 6 months. Requests for sodium oxybate (Xyrem) or Xywav will be approved for up to a 3 month duration. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review. **Later Approvals** If all conditions are met, the request will be approved for up to 12 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	**For all requests:** • Appropriate diagnosis/indication for requested medication • Medication is being prescribed at an FDA approved dose **Modafinil/armodafinil initial authorization:** • For a diagnosis of obstructive sleep apnea (OSA) documentation that the member has been compliant with or is unable to use positive airway pressure [continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), or automatic positive airway pressure (APAP)]. • If request is for armodafinil, member must meet above criteria AND documentation of trial and failure, contraindication or intolerance to modafinil. **Sunosi initial authorization**: • Documented trial and failure of, or inability to use, modafinil or armodafinil • For members with OSA: ○ Documentation that the member has been compliant with or is unable to use positive airway pressure (CPAP, BPAP, or APAP) **Wakix initial authorization**: • For a diagnosis of narcolepsy without cataplexy: documented trial and failure of (or medical reason for not using), BOTH of the following:

	○ Modafinil or armodafinil ○ Sunosi (solriamfetol) • For a diagnosis of narcolepsy with cataplexy: documented trial and failure of, or medical reason for not using, the following: ○ Dextroamphetamine **<u>Sodium oxybate (Xyrem) or Xywav initial authorization:</u>** • Medication is not being taken concurrently with sedative hypnotics • If member has a history of substance abuse, documentation has been provided that prescriber has referred the member for substance abuse disorder treatment. • For a diagnosis of narcolepsy without cataplexy: ○ Documented trial and failure of, or a medical reason for not using, ALL of the following: ▪ Modafinil or armodafinil ▪ Sunosi (solriamfetol) ▪ Wakix (pitolisant) • For a diagnosis of narcolepsy with cataplexy: ○ Documented trial and failure of each of, or a medical reason for not using BOTH of the following: ▪ Dextroamphetamine ▪ Wakix (pitolisant) • For a diagnosis of idiopathic hypersomnia (Xywav only): ○ Patient has a documented trial and failure of, or a medical reason for not using, the following: ▪ Modafinil or armodafinil **<u>Criteria for reauthorization:</u>** • Documentation has been submitted indicating member has experienced a clinical benefit from treatment (e.g. improvement on Epworth Sleepiness Score) • For members with cataplexy: Documentation has been provided that there has been a reduction in frequency of cataplexy attacks.
Criteria Statement	Modafinil is reserved for members who have a diagnosis of obstructive sleep apnea, who use or have used (or cannot/should not use) positive airway pressure [continuous positive airway pressure (CPAP), bilevel positive airway pressure (BPAP), or automatic positive airway pressure (APAP)]. Armodafinil is reserved for members who have used (or cannot/should not use) modafinil For members with obstructive sleep apnea (OSA), Sunosi is reserved for those who have used (or cannot/should not use) positive airway pressure (CPAP, BPAP, or APAP) and modafinil/armodafinil. For members without OSA, Sunosi is reserved for those who have used (or cannot/should not use) modafinil/armodafinil. Wakix is reserved for members who have a diagnosis of narcolepsy without cataplexy and have used (or cannot/should not use) modafinil/ armodafinil and Sunosi. Wakix is reserved for members who have a diagnosis of narcolepsy with cataplexy and have used (or cannot/should not use) dextroamphetamine. For members without cataplexy, sodium oxybate (Xyrem) or Xywav are reserved for those who have used (or cannot/should not use) modafinil/armodafinil, Sunosi, and Wakix. For members with narcolepsy with cataplexy, sodium oxybate (Xyrem) or Xywav are reserved for those who have used (or cannot/should not use) dexamphetamine and Wakix.

	For members with idiopathic hypersomnia, Xywav is reserved for those who have used (or cannot/should not use) modafinil/armodafinil.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Palforzia	
Therapeutic Classes (AHFS)	ALLERGENIC EXTRACTS (THERAPEUTIC)
Medications	Non-Formulary Palforzia (peanut [Arachis hypogaea] allergen powder-dnfp)
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	• Initiation: Patient is age 4-17 years. • Up dosing and maintenance: Patient is age ≥ 4 years
Prescriber Restrictions	Prescriber is a specialist in the area of allergy/immunology
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 conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization**: Palforzia is approved when all of the following criteria are met: • Patient has a confirmed diagnosis of peanut allergy • For patients starting initial dose escalation (new to therapy) ○ Patient has not had severe or life-threatening anaphylaxis within the previous 60 days • Patient will follow a peanut-avoidant diet • Patient has been prescribed and has acquired (as demonstrated by pharmacy claims or documentation) injectable epinephrine • No history of eosinophilic esophagitis or other eosinophilic gastrointestinal disease • Patient does not have uncontrolled asthma **Criteria for Re-Authorization:** Palforzia is approved for re-authorization when all of the following criteria are met • Patient will follow a peanut-avoidant diet • Patient is able to tolerate at least the 3 mg dose daily • Patient is able to comply with the daily dosing requirements • Patient does not have recurrent asthma exacerbations or persistent loss of asthma control • Patient has been prescribed and has acquired (as demonstrated by pharmacy claims or documentation) injectable epinephrine
Criteria Statement	Palforzia is reserved for members with an allergy to peanuts, who will follow a peanut-avoidant diet, who have not experienced anaphylaxis in the previous 60 days, don't have uncontrolled asthma, and have been prescribed injectable epinephrine.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Streamlining language and abbreviations

Gonadotropin Releasing Hormone Antagonists	
Therapeutic Classes (AHFS)	ANTIGONADTROPINS
Medications	Formulary, PA required Oriahnn (elagolix, estradiol, and norethindrone acetate) capsule Orilissa (elagolix) Non-Formulary Myfembree (relugolix, estradiol, and norethindrone acetate)
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	• Pregnancy • History of osteoporosis • History of hepatic impairment (Myfembree, Oriahnn), or severe hepatic impairment (Orilissa)
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	18 years or older
Prescriber Restrictions	Prescriber is an obstetrician/gynecologist
Coverage Duration	**Initial/Re-Approval** If the criteria are met, the request will be approved for (a maximum treatment duration of): • Initial Authorization: 6 months • Subsequent Authorizations: 6 months • Eligible maximum treatment duration: 24 months If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	**Initial Authorization for all requests:** • Medication is prescribed at an FDA approved dose • If patient is of childbearing potential, prescriber attests the patient is not currently pregnant • Prescriber attests the patient does not have a history of osteoporosis • Prescriber attests they have reviewed the patient's liver function **For a diagnosis of endometriosis associated with moderate to severe pain:** • Request is for Orilissa or Myfembree only • Documented trial and failure or medical reason for not using an analgesic pain reliever (e.g., NSAIDs, COX-2 inhibitors) taken in combination with combined estrogen progestin oral contraceptive pills (OCPs): o If one of the following drugs has been tried previously, a trial of OCPs is not required: progestins, gonadotropin releasing hormone (GnRH) agonists, danazol, or aromatase inhibitors (e.g., anastrozole, letrozole) **For a diagnosis of diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids):** • Request is for Oriahnn or Myfembree only • Documented trial and failure or medical reason for not using estrogen-progestin contraceptive therapy • If one of the following drugs has been tried previously, a trial of estrogen-progestin contraceptive therapy is not required: o ~~gonadotropin-releasing hormone (~~GnRH~~)~~ agonists, o progestin-releasing intrauterine device

	○ tranexamic acid • If the request is for Myfembree, there is a documented trial and failure of Oriahnn, or medical reason why Oriahnn cannot be used **Reauthorization:** • Documentation or provider attestation of positive clinical response (i.e., reduction in pain, reduced menstrual bleeding) • Maximum lifetime treatment duration based on previous dosing and/or hepatic functioning has not been exceeded • Medication is prescribed at an FDA approved dose
Criteria Statement	Orilissa and Myfembree are reserved for members who have a diagnosis of endometriosis associated with moderate to severe pain who have used (or cannot/should not use) an analgesic pain reliever (e.g., NSAIDs, COX-2 inhibitors) taken in combination with combined estrogen progestin oral contraceptive pills (OCPs), however if one of the following drugs has been tried previously, a trial of OCPs is not required: progestins, ~~gonadotropin-releasing hormone (~~GnRH~~)~~ agonists, danazol, or aromatase inhibitors (e.g., anastrozole, letrozole). Oriahnn and Myfembree are reserved for members who have a diagnosis of heavy menstrual bleeding associated with uterine fibroids who have used (or cannot/should not use) estrogen-progestin contraceptive therapy OR one of the following: ~~gonadotropin-releasing hormone (~~GnRH~~)~~ agonists, progestin-releasing intrauterine devices, or tranexamic acid. Myfembree is reserved for members who have used (or cannot/should not use) Oriahnn.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Update diagnostic requirement wording for simplicity

Lupkynis	
Therapeutic Classes (AHFS)	Immunosuppressive Agents
Medications	Formulary, PA required Lupkynis (voclosporin)
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 rheumatologist, nephrologist or other specialist in the treatment of autoimmune disorders
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 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	**Initial Authorization** • Member must have a diagnosis of ~~systemic lupus erythematosus (SLE) with a diagnosis of~~ lupus nephritis (LN) Class III, IV, or V • Documentation that the member has a baseline eGFR > 45 mL/min/1.73m^2 • Documentation of the member's urine protein/creatinine ratio (UPCR) is provided • Member is concurrently being treated with background immunosuppressive therapy, or has a medical reason for not using background immunosuppressive therapy • Member is NOT concurrently being treated with cyclophosphamide • Medication is prescribed at an FDA approved dose **Reauthorization** • Documentation of improvement in renal function (i.e. reduction in UPCR or no confirmed decrease from baseline eGFR ≥ 20%) • Medication is prescribed at an FDA approved dose
	Lupkynis is reserved for members with a ~~diagnosis of systemic lupus erythematosus (SLE) with a~~ diagnosis of lupus nephritis (LN) Class III, IV, or V and a baseline eGFR > 45 mL/min/1.73m^2, who have used (or cannot/should not use) background immunosuppressive therapy (and will continue using it), and is NOT currently using cyclophosphamide.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Radicava ORS (edaravone)	
Therapeutic Classes (AHFS)	Anticonvulsants, miscellaneous
Medications	Radicava ORS (edaravone)
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
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	**Initial:** • Member must have a diagnosis of ALS • Member must have a documented baseline evaluation of functionality using the revised ALS functional rating scale (ALSFRS-R) score ≥ 2 • Member's disease duration is 2 years or less • Member has a baseline forced vital capacity (FVC) of ≥ 80% • Member has been on riluzole (Rilutek), is beginning therapy as an adjunct to treatment with Radicava, or provider has provided a medical reason why patient is unable to use riluzole • Dose is within FDA approved limits **Reauthorization:** • Member is not ventilator-dependent • Provider documents clinical stabilization in symptoms (e.g. stabilization of ALSFRS-R score) • Dose is within FDA approved limits
Criteria Statement	Radicava ORS are reserved for members with a diagnosis of ALS, with a disease duration of 2 years or less, with a documented baseline evaluation of functionality using the revised ALS functional rating scale (ALSFRS-R) score ≥ 2 and a baseline forced vital capacity (FVC) of ≥ 80%, who is taking riluzole (Rilutek) or has used (or cannot/ should not use) riluzole (Rilutek).
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Daybue (trofinetide)	
Therapeutic Classes (AHFS)	CENTRAL NERVOUS SYSTEM AGENTS, MISC.
Medications	Daybue (trofinetide)
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	According to package insert
Prescriber Restrictions	Prescribed by a neurologist
Coverage Duration	**Initial Approval** 3 months **Later Approvals** 6 months If criteria are not met, request will be sent to a clinical reviewer for medical necessity review.

PA Review Criteria	**Initial Authorization:**
	• Medication is prescribed at an FDA approved dose
	• Diagnosis of classic or typical Rett syndrome (RTT)
	• Documentation or attestation of mutation of the MECP2 gene
	• Documentation of patient weight
	• Documentation or provider attestation of all the following:
	  ○ RTT Clinical Severity Scale rating of 10–36
	  ○ Clinical Global Impression–Severity (CGI-S) score of ≥4
	  ○ Baseline Rett Syndrome Behavior Questionnaire (RSBQ) score
	
	Re-Authorization:
	• Documentation or provider attestation of positive clinical response (i.e., decrease from baseline in RSBQ score, decrease in Clinical Global Impression–Improvement (CGI-I, etc.)
	• Medication is prescribed at an FDA approved dose

Criteria Statement	Daybue is reserved for members with a diagnosis of classic or typical Rett syndrome (RTT), with a mutation of the MECP2 gene, with documentation or provider attestation of all the following: RTT Clinical Severity Scale rating of 10–36, Clinical Global Impression–Severity (CGI-S) score of ≥4, and Baseline Rett Syndrome Behavior Questionnaire (RSBQ) score, with a documented patient weight.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Filspari	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS
Medications	Filspari (sparsentan)
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	• Pregnancy • Coadministration with renin-angiotensin-aldosterone system (RAAS) inhibitors, endothelin receptor antagonists, or aliskiren
Required Clinical Information	See "other criteria"
Age Restrictions	According to package insert
Prescriber Restrictions	Prescriber must be a nephrologist
Coverage Duration	**Initial Approval** 9 months **Later Approvals** 12 months If criteria are not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	**Initial Authorization:** • Medication is prescribed at an FDA approved dose • Diagnosis of primary immunoglobulin A nephropathy (IgAN) verified by biopsy • Total urine protein ≥1.0 g/day • eGFR ≥30 mL/min/1.73 m2 • Trial and failure with a maximized stable dose of ACE inhibitor or ARB **Re-Authorization:** • Documentation of positive clinical response as evidenced by a decrease in urine protein-to-creatinine ratio (UPCR) • Medication is prescribed at an FDA approved dose
Criteria Statement	Filspari is reserved for members with a diagnosis of primary immunoglobulin A nephropathy (IgAN) verified by biopsy, with a total urine protein ≥1.0 g/day and eGFR ≥30 mL/min/1.73 m2, who have used (or cannot/should not use) a maximized stable dose of angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) medication.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Joenja	
Therapeutic Classes (AHFS)	IMMUNOMODULATORY AGENTS
Medications	Joenja (leniolisib)
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	Per prescribing information.
Prescriber Restrictions	Prescriber must be an immunologist, hematologist, medical geneticist, or other prescriber who specializes in the treatment of genetic or immunologic disorders.
Coverage Duration	**Initial Approval** 6 months **Later Approvals** 12 months If criteria are not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	**Initial Authorization:** • Documentation of APDS/PASLI-associated PIK3CD/PIK3R1 mutation, confirmed by genetic testing. • Documentation of nodal and/or extranodal lymphoproliferation, history of repeated oto-sino-pulmonary infections and/or organ dysfunction (e.g., lung, liver) • Prescriber attests that the member is not currently taking immunosuppressive medication • Prescriber attests that female patients have been advised of the potential risk to a fetus, will use effective contraception and have had a negative pregnancy test prior to initiation of treatment • Medication is being prescribed at an FDA approved dose **Reauthorization:** • Documentation has been submitted indicating member has experienced a clinical benefit from treatment (e.g., decreased lymph node size, increase in percentage of naïve B cells) • Prescriber attests that female patients will use effective contraception and have had a negative pregnancy test • Medication is being prescribed at an FDA approved dose
Criteria Statement	Joenja is reserved for members with a diagnosis activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS/PASLI-associated PIK3CD/PIK3R1 mutation) confirmed by genetic testing, with documentation of nodal and/or extranodal lymphoproliferation, history of repeated oto-sino-pulmonary infections and/or organ dysfunction (e.g., lung, liver), who is not currently taking immunosuppressive medication, and female patients have been advised of the potential risk to a fetus, will use effective contraception and have had a negative pregnancy test prior to initiation of treatment.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Skyclarys (omaveloxolone)	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS
Medications	Skyclarys (omaveloxolone)
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	Per prescribing information
Prescriber Restrictions	Prescriber must be a neurologist or specialist with expertise in treating patients with Friedreich's Ataxia.
Coverage Duration	**Initial Approval** 6 months **Later Approvals** 12 months If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	**Initial Authorization:** • Diagnosis of Friedreich's Ataxia, confirmed via genetic testing (must submit documentation) • Modified Friedreich's Ataxia Rating Scale (mFARS) score ≥20 and ≤80 • Medication is prescribed at an FDA approved dose **Re-Authorization:** • Documentation or provider attestation of positive clinical response to Skyclarys therapy (i.e. improvement in symptoms, slowing of disease progression, etc.) • Medication is prescribed at an FDA approved dose
Criteria Statement	Skyclarys is reserved for members with a diagnosis of Friedreich's Ataxia, confirmed via genetic testing, and a modified Friedreich's Ataxia Rating Scale (mFARS) score ≥20 and ≤80.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Update coverage duration language for clarity

Leqembi	
Medications	Leqembi (lecanemab-irmb)
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	Patients with moderate to severe Alzheimer's Disease (AD) Patients with neurodegenerative disease caused by a condition other than AD
Required Clinical Information	See "other criteria"
Age Restrictions	age 50-90 years
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	For initial authorization: the request will be approved ~~in accordance with the FDA-indicated titration schedule~~ for ~~up to~~ 6 months For reauthorization: if all of the conditions are met, the request will be approved for 6 months.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization**
	• Diagnosis of mild cognitive impairment (MCI) caused by AD or mild AD consistent with Stage 3 or Stage 4 Alzheimer's disease as evidenced by at least one of the following:
	  ○ Clinical Dementia Rating Global (CDR-G) score of 0.5-1.0 and a Memory Box score of 0.5 or greater
	  ○ Mini-Mental State Examination (MMSE) score ≥ 22 and ≤ 30
	  ○ Wechsler Memory Scale IV-Logical Memory (subscale) II (WMS-IV LMII) score at least 1 standard deviation below age-adjusted mean
	• The request is for an FDA approved dose
	• Documentation of BOTH of the following:
	  ○ Recent, within past year, positive results for the presence of beta-amyloid plaques on a positron emission tomography (PET) scan or cerebrospinal fluid testing
	  ○ Recent, within past year, baseline Magnetic Resonance Imaging (MRI) scan
	• Physician has assessed baseline disease severity utilizing an objective measure/tool (i.e., Alzheimer's Disease Assessment Scale-Cognitive Subscale [ADAS-Cog-14], Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory-Mild Cognitive Impairment version [ADCS-ADL-MCI], Clinical Dementia Rating Sum of Boxes [CDR-SB], etc.)
	• No recent (past 1 year) history of stroke, seizures or transient ischemic attack (TIA), or findings on neuroimaging that indicate an increased risk for intracerebral hemorrhage.
	
	Reauthorization
	• The request is for an FDA approved dose

	• Patient continues to have a diagnosis of mild cognitive impairment (MCI) caused by AD or mild AD consistent with Stage 3 or Stage 4 Alzheimer's disease as evidenced by at least one of the following:
	  ○ CDR-G score of 0.5-1.0 and a Memory Box score of 0.5 or greater
	  ○ MMSE score of 22-30
	  ○ Wechsler Memory Scale IV-Logical Memory (subscale) II (WMS-IV LMII) score at least 1 standard deviation below age-adjusted mean
	• Provider attestation of safety monitoring and management of amyloid related imaging abnormalities (ARIA) and intracerebral hemorrhage, as recommended per the manufacturer's prescribing information.
	• Documentation that member has experienced clinical benefit from the medication (such as: stabilization or decreased rate of decline in symptoms from baseline on CDR-SB, ADAS-Cog14, or ADCS MCI-ADL scales)
	• No recent (past 1 year) history of stroke, seizures or TIA
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.

Last Review Date	~~9/2023~~6/2024

Recommendation:

- No changes

B-Cell Maturation Antigen (BCMA) Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy	
Medications	Abecma (idecabtagene vicleucel), Carvykti (ciltacabtagene autoleucel)
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	Member must be 18 years or older Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber must be an oncologist, hematologist or other appropriate specialist
Coverage Duration	If all the criteria are met, the initial request will be approved for a one –time infusion per lifetime.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization**
	• Member has a diagnosis of relapsed or refractory multiple myeloma (RRMM)
	• Member must have received at least 4 prior lines of therapy, which must include ALL of the following:
	  ○ An immunomodulatory agent (e.g. lenalidomide, pomalidomide, thalidomide)
	  ○ A proteasome inhibitor (e.g. bortezomib, carfilzomib, ixazomib)
	  ○ An anti-CD38 monoclonal antibody (e.g. daratumumab, isatuximab)
	• Member does not have an active infection
	• Member will be screened for cytomegalovirus (CMV), hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines
	• Member will not receive live virus vaccines for at least 6 weeks prior to the start of lymphodepleting chemotherapy and until immune recovery following treatment
	• Member has not previously received a BCMA CAR-T therapy
	
	Re-authorization:
	• Treatment exceeding 1 dose per lifetime will not be authorized.
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.

Last Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Naglazyme	
Medications	Naglazyme (galsulfase)
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 the criteria are met, the initial request will be approved for up to a 6 month duration; reauthorization requests will be approved for up to 12 months.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization**
	• Diagnosis of Mucopolysaccharidosis VI as confirmed by one of the following:
	  ○ Enzyme assay demonstrating a deficiency in N-acetygalactosamine 4-sulfatase (arylsulfatase B) enzyme activity
	  ○ DNA testing
	• Patient's weight
	• Dosing is consistent with FDA-approved labeling or is supported by compendia or standard of care guidelines
	
	Reauthorization
	• Documentation of clinical response was submitted with request (i.e., stabilization or improvement in 12-minute walk test [12-MWT], 3-minute stair climb test, urinary glycosaminoglycan (GAG) levels)
	• Patient's weight
	• Dosing is consistent with FDA-approved labeling or is supported by compendia or standard of care guidelines
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.

Last Review Date	~~6/2023~~6/2024

Recommendation:

- No changes

Radicava (edaravone)	
Medications	Radicava (edaravone)
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 neurologist
Coverage Duration	If the criteria are met, requests will be approved for up to 6 month duration;
Maximum Billable Units	Variable
Other Criteria	**Initial:** • Member must have a diagnosis of ALS • Member must have a documented baseline evaluation of functionality using the revised ALS functional rating scale (ALSFRS-R) score ≥ 2 • Member's disease duration is 2 years or less • Member has a baseline forced vital capacity (FVC) of ≥ 80% • Member has been on riluzole (Rilutek), is beginning therapy as an adjunct to treatment with Radicava, or provider has provided a medical reason why patient is unable to use riluzole • Dose is within FDA approved limits **Reauthorization:** • Member is not ventilator-dependent • Provider documents clinical stabilization in symptoms (e.g. stabilization of ALSFRS-R score) • Dose is within FDA approved limits If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.
Last Review Date	~~6/2023~~6/2024

Alameda Alliance for Health (IHSS)

Q2 2024 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
Xolair Subcutaneous Solution Auto-injector 75 MG/0.5ML	NF to F-PA
Xolair Subcutaneous Solution Auto-injector 150 MG/ML	NF to F-PA
Xolair Subcutaneous Solution Prefilled Syringe 300 MG/2ML	NF to F-PA
Xolair Subcutaneous Solution Auto-injector 300 MG/2ML	NF to F-PA
Opill Oral Tablet 0.075 MG	NF to F
Glucagon-like peptide 1 (GLP-1) agonists and Dipeptidyl peptidase-4 (DPP-4) inhibitor	Claims for a GLP-1 will no longer reject when a member has recent history of use of a DPP-4 (and vice versa) and will instead send an educational message to the pharmacy

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	Medi-Cal
Effective Date	04/01/2021
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date ~~Approval / Revision Date~~	TBD~~3/28/2023~~
Compliance Committee Approval Date	TBD

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. ~~Requests are to be tracked as a new excel for each update/request (old excels must be kept for historical record keeping) in the following drive folder: W:\DEPT_Project Management\Active Projects\20_0XX - RX Carve-out\Transition Documents\Rx Carve Out Magellan DU request. The Excel is to be titled in the format: "DU for Magellan – [DELEGATE PARTNER NAME] – Date of Request".~~

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

III. Maintenance ~~and tracking a list~~ of Designated Users List and U~~u~~tilization of Medi-Cal Rx Okta~~secure Alliance Pharmacy~~ Portal

~~A. The Alliance will receive the reports monthly via a secure file transfer protocol or other secure method. These Alliance specific User_Access_Audit_Report_MCP020 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 reports will be provided by the 5th business day of each month for the prior month. 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.~~

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.

~~B.~~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 ~~Magellan~~ Prime Therapeutics via forwarding an updated DHCS-6520-Medi-Cal MCP Designated User System Access Request Form requesting

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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**

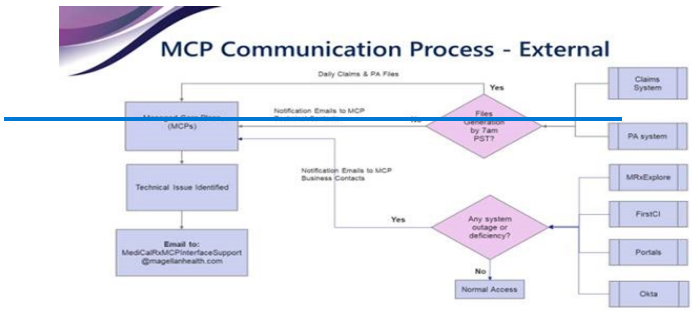
A. MCP Pharmacy Portal Access:
1. Users may access the Medi-Cal Rx secure MCP Pharmacy Portal at: https://medi-calrx.dhcs.ca.gov/home/
2. Users may also choose to access the Okta SSO Prime Therapeutics Tool directly at: https://ciam.primetherapeutics.com/ ~~https://magellanhealthsso.okta.com~~

B. Use and Navigation of the MCP Pharmacy Portal:
1. Access to the Health Plan Portal is available only to approved users. If access has been granted, an individual can enter the secured area of the Health Plan Portal.
2. Clicking on the Health Plan Portal button on the Medi-Cal Rx Web Portal Home page will prompt a HIPAA notification which users must click AGREE to continue.
3. Users with credentials will be able to log into the secured area of the Health Plan Portal using the Okta℠ SSO tool via ~~Magellan Health~~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. ~~or SABA LMS.~~

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 ~~Magellan~~ 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@~~magellanhealth.com~~PrimeTherapeutics.com and Carbon Copy internal stakeholders so that they are informed when Medi-Cal Rx secure MCP Pharmacy Portal is down.

Field Code Changed



~~B. Maintenance and Tracking List of Business MCP Notification Contacts~~

~~1. Once monthly, or as needed, AAH designated pharmacy technician will update the list containing Business MCP Notification Contacts who would like to receive notification around system outage or deficiency issues, related to applications like MRxExplore, FirstCI, Portals, and Okta. This list is to include names, emails and phone numbers of each individual Business MCP contact. This list is stored in: W:\DEPT_Project Management\Active Projects\20_0XX - RX Carve-out\Transition Documents and is an excel document titled "Business MCP Notification Contacts".~~

~~A. When internal stakeholders request to be added to the DU list, the pharmacy technician should ask if they would like to be added to the Business MCP Notification Contacts list. If so, then technician will add to the respective file and drive.~~

~~2. This list will be submitted via email to the Magellan Iteration Manager Associate monthly, or as needed (every time list is updated).~~

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DEFINITIONS / ACRONYMS

a. PBM: Pharmacy Benefit Manager (Currently, ~~Magellan~~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 (~~Magellan~~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

REVISION HISTORY

4/13/2021, 6/15/2021, 6/21/2022, 3/28/2023, 3/19/2024, 4/8/24

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	Medi-Cal, Group Care (IHSS)
Effective Date	7/17/2023
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	3/19/2024
Compliance Committee Approval Date	TBD

POLICY STATEMENT

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

PROCEDURE

I. Prior Authorization Process Guidelines

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

B. The Alliance utilizes evidence-based prior authorization criteria approved by the P&T Committee. Prior authorization criteria are developed and reviewed annually and are based established by organizations such as Medi-Cal guidelines (if for Medi-Cal line of business),

Milliman Care Guidelines, Food and Drug Administration (FDA), National Comprehensive Cancer Network (NCCN), UpToDate, and National Institutes of Health (NIH). The Alliance covers pharmaceuticals in accordance with 42 CFR section 438.900 et seq, to ensure parity in medical/surgical, mental health, and substance abuse benefits and treatment.

II. Prior Authorization Procedures

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

B. Required information provided on all requests should include:

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

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

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

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

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

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

B. Pre-Service/Post-Service Review for Pharmacy Technician (PT)
    A. Upon receipt of the authorization request, the PT will review the request for:
        (1) Member eligibility
        (2) Completeness of the request
            (a) Presence of medical codes,
            (b) Presence of medical records
    B. Once the authorization request review is complete, the PT enters the authorization

request into the clinical information system and routes it to the appropriate UM PT processing queue.

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

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

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

(b) The PT Reviewer workflow includes:

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

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

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

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

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

(a) The hierarchal criteria process:

(i) Regulatory and contractual requirements

(ii) Evidence based guidelines

(iii) Alliance specific guidelines

(iv) National medical association consensus

(v) Medical necessity/medical judgement

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

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

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

i. Name and title of person spoken to

ii. Phone number called (if different from one already noted in the PA system)
iii. What specific information was requested

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

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

~~V. Continuity of Care for Covered Services for Members Receiving Pharmaceutical Treatment~~

~~A. Anthem~~

~~1. Member may request up to 6 months for continuity of care service to continue an active course of treatment.~~

~~2. Active Course of Treatment is defined as a course of treatment in which a member is actively engaged with a provider prior to January 1, 2024, and following the prescribed or ordered course of treatment as outlined by the provider for a particular medical condition as in DHCS 2024 Medi-Cal Managed Care Plan Transition Policy Guide.~~

~~B. Medi-Cal Beneficiaries who newly enroll in Medi-Cal managed care from Medi-Cal fee-for service, on or after January 1, 2024 (i.e., Adult Expansion)~~

~~1. Member may request up to 90 days for continuity of care service following AAH enrollment and until reassessment as in APL 23-022.~~

~~C. LTC Members~~

~~1. ICF-DD~~

~~A. Member may request up to 90 days for continuity of care service following AAH enrollment and until reassessment as in APL 23-023.~~

~~2. Subacute~~

~~A. Member may request up to 6 months for continuity of care service following AAH enrollment and or duration of TAR (which ever duration is shorter) as in APL 23-027.~~

~~3. LTC-SNF~~

~~A. Member may request up to 90 days for continuity of care service following AAH enrollment and until reassessment as in APL 23-004.~~

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V. Continuation of Therapy

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

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

4. Date medication was started and date last given/filled

VI. Annual Review of PAD Prior Authorization and UM Criteria

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

VII. Monitoring of the PA process

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

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

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

DEFINITIONS / ACRONYMS

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

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Utilization Management
Claims
Benefit Configuration
Member Services
Provider Relations
Communications and Outreach

RELATED POLICIES AND PROCEDURES

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

REVISION HISTORY

6/20/2023, 12/19/2023, 3/19/2024

REFERENCES

- NCQA UM 12, Element A**,** B, D
- Alliance Provider Manual
- Health & Safety Code, Sections 1363.5, 1367.01, 1367.21, 1367.215, 1373.96
- Senate Bill 855 – Mental Health as a Medical Necessity
- DHCS All Plan Letter 22-012 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx
- DHCS All Plan Letter 22-032 Continuity of Care for Medi-Cal Beneficiaries Who Newly Enroll in Medi-Cal Managed Care from Medi-Cal FFS, and for Medi-Cal Members who Transition into a New Medi-Cal Managed Care Health Plan on or after January 1, 2023
- DHCS APL 23-004 Skilled Nursing Facilities -- Long Term Care Benefit Standardization And Transition Of Members To Managed Care
- DHCS APL 23-027, Subacute Care Facilities -- Long Term Care Benefit Standardization and Transition of Members to Managed Care
- DHCS APL 23-023 – Intermediate Care Facilities for Individuals with Developments Disabilities – Long Term Care Benefit Standardization and Transition of Members to Managed Care
- DHCS Contract #23-30212, Exhibit A – Scope of Work
- 2024 Medi-Cal Managed Care Plan Transition Policy Guide

MONITORING

This policy will be reviewed annually to ensure effectiveness.

APPENDIX

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

Type of Request	NCQA	DHCS	DMHC	**Alliance**
Prospective, Urgent	72 hours	72 hours	72 hours	**72 hours**
Prospective, Non-Urgent	Medi-Cal: 14 calendar days Group Care: 15 calendar days	5 business days	5 business days	**5 business days**
Post-service	30 calendar days	30 calendar days	30 calendar days	**30 calendar days**

Alameda Alliance for Health
1240 South Loop Road
Alameda, CA 94502
Phone Number: **1.510.747.4567**
Toll-Free: **1.877.932.2738**
People with hearing and speaking impairments (CRS/TTY): **711/1.800.735.2929**

www.alamedaalliance.org

90-Day Supply on Maintenance Medications

Medications are available for Alliance Group Care Members through choice in-network retail pharmacies or Walgreens Mail Service pharmacy. Prescriptions are filled with generic versions, when available and medically necessary. Certain medications are subject to prior authorization (PA) review by Alameda Alliance for Health (Alliance).

This list may not include all 90-day maintenance medications as product updates are being made periodically. Questions about drugs not included on this list should be directed to the Alliance Pharmacy Services Department at **1.510.747.4541**. Products in red are new additions to the list.

Asthma & COPD

Arnuity Ellipta
Atrovent HFA
Combivent
Flovent Diskus
Flovent HFA
Fluticasone/Salmeterol blister w/device
Fluticasone/Salmeterol Respiclick
Montelukast
Qvar Redihaler
Spiriva HandiHaler
Spiriva Respimat
Stiolto Respimat
Theophylline
Tudorza Pressair

Blood Pressure & Heart Health

Acetazolamide
Aliskiren
Aliskiren/Amlodipine
Amiloride
Amiodarone
Amlodipine/Benazepril
Aspirin/Dipyridamole
Atenolol
Atenolol/Chlorthalidone
Azilsartan
Benazepril
Benazepril/HCTZ
Bisoprolol Bisoprolol/HCTZ
Bumetanide

Blood Pressure & Heart Health (cont.)

Candesartan
Captopril
Carvedilol
Chlorthalidone
Cilostazol
Clonidine
Clopidogrel
Digoxin
Diltiazem
Dipyridamole
Dronedarone
Enalapril
Enalapril/HCTZ
Eprosartan

Blood Pressure & Heart Health (cont.)

Eprosartan/HCTZ
Felodipine
Flecainide
Fosinopril
Furosemide
Guanfacine
Hydralazine
Hydrochlorothiazide
Indapamide
Irbesartan
Irbesartan/HCTZ
Isoproterenol
Isosorbide Dinitrate
Isosorbide Mononitrate
Labetalol
Lisinopril
Lisinopril/HCTZ
Methyldopa
Methyldopa/HCTZ
Metolazone
Metoprolol Succinate
Metoprolol Tartrate
Mexiletine
Midodrine
Minodixidil
Nadolol
Niacin
Nicardipine
Nifedipine
Nitroglycerin
Olmesartan

Blood Pressure & Heart Health (cont.)

Pentoxifyline
Pindolol
Prazosin
Propafenone
Propranolol
Propranolol/HCTZ
Quinidine gluconate
Quinidine sulfate
Ramipril
Reserpine
Sotalol
Spironolactone
Spironolactone/HCTZ
Telmisartan
Telmisartan/HCTZ
Terazosin
Triamterene/HCTZ
Valsartan/HCTZ
Verapamil
Warfarin

Diabetes

Chlorpropamide
Glimepiride
Glipizide
Glyburide
Glyburide, micronized
Glyburide/Metformin
Metformin
Nateglinide
Pioglitazole/Metformin

Diabetes (cont.)

Pioglitazone
Rosiglitazone
Rosiglitazone/Metformin
Tolazamide
Tolbutamide

Gastrointestinal Health

Balsalazide
Sulfasalazide
Ursodiol

Gout

Allopurinol
Probenecid

High Cholesterol

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

Liver Disease
Adefovir
Baraclude solution
Entecavir
Lamividine
Tenofovir 300mg tablets
Vemlidy
Viread

Men's Health
Alfuzosin
Doxazosin
Finasteride
Tamsulosin
Terazosin

Mental Health
Bupropion
Duloxetine
Escitalopram
Fluoxetine
Mirtazapine
Paroxetine
Sertraline
Trazodone

Miscellaneous
Cabergoline
Fludrocortisone
Hydroxychloroquine
Hydroxyurea
Leflunomide
Methazolamide

Miscellaneous
Methotrexate
Methylsulfate
Neostigmine

Myasthenia Gravis
Edrophonium Chloride
Physostigmine Salicylate
Pyridostigmine Bromide

Osteoporosis & Paget's Disease
Alendronate
Calcitonin (Salmon)
Raloxifene

Parkinson's & Alzheimer's
Bromocriptine
Carbidopa/Levodopa
Donepezil
Entacapone
Pramipexole
Ropinirole

Seizures & Epilepsy
Carbamazepine
Clobazam
Clonazepam
Divalproex sodium
Ethosuximide
Ezogabine
Gabapentin
Levetiracetam
Levetiracetam NaCl

Seizures & Epilepsy
Phenobarbital
Phenytoin
Primidone
Rufinamide
Tiagabine
Topiramate
Valproic Acid
Zonisamide

Thyroid Conditions
Armour Thyroid
Levothyroxine
Liothyronine
Methimazole
Propylthiouracil

Transplant
Azathioprine
Mycophenolate Mofetil
Mycophenolate Sodium
Tacrolimus

Urinary Incontinence & Retention
Bethanechol
Desmopressin
Oxybutinin

Vitamins & Nutritional Health
B Complex with Vitamin C
Calcitriol
Calcium Acetate 667 mg
Calcium Carbonate

Vitamins & Nutritional Health

Calcium Carbonate/Vitamin D2
Calcium Carbonate/Vitamin D3
Calcium Citrate/Vitamin D2
Calcium Citrate/Vitamin D3
Calcium Glubionate
Calcium Gluconate
Calcium Lactate
Calcium Phosphate/Vitamin D3
Cholecalciferol (Vitamin D3)
Cyanocobalamin (Vitamin B-12)
Ferrous Sulfate
Folic Acid
Folic Acid with Multivitamins
Magnesium Oxide
Multivitamins
Potassium Bicarbonate
Potassium Chloride
Pyridoxine
Thiamine

Women's Health

Estradiol
Estrogens, Conjugated
Estrogens, Conjugated/Medroxyprogesterone Acetate
Estrogens, Esterified
Estrogens, Esterified/Methyltestosterone
Norethindrone Acetate/Ethinyl Estradiol

ALAMEDA Alliance FOR HEALTH

Up to 365-Day Supply on Contraceptives

Generic products are listed under **LABEL NAME** by their ingredient components.

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
ALYACEN 1/35	NORETHINDRONE & ETHINYL ESTRADIOL	1 MG-35MCG	TABLET
ALYACEN 7/7/7	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/0.75MG/1MG- 35MCG	TABLET
AMETHIA	LEVONORGESTREL & ETHINYL ESTRADIOL & ETHINYL STRADIOL	0.15MG-30MCG/10MCG 3 MONTH DOSE PACK	TABLET
AMETHIA LO	LEVONORGESTREL/ETHINYL ESTRADIOL & ETHINYL ESTRADIOL	0.10MG-20MCG/10MCG 3 MONTH DOSE PACK	TABLET
AMETHYST	ETHINYL ESTRADIOL & LEVONORGESTREL	90MCG-20MCG	TABLET
APRI	ETHINYL ESTRADIOL & DESOGESTREL	0.15MG-0.03MG	TABLET
BALZIVA	ETHINYL ESTRADIOL & NORETHINDRONE	0.4MG-35MCG	TABLET
BEYAZ	DROSPIRENONE/ ETHINYL ESTRADIOL/ LEVOMEFOLATE CALCIUM	3MG-0.02MG-0.45MG	TABLET
BRIELLYN	ETHINYL ESTRADIOL & NORETHINDRONE	0.4MG-35MCG	TABLET
CAMRESE	LEVONORGESTREL/ETHINYL ESTRADIOL & ETHINYL ESTRADIOL	0.15MG-30MCG 3 MONTH DOSE PACK	TABLET
CAMRESE LO	ETHINYL ESTRADIOL & LEVONORGESTREL	0.10MG-20MCG 3 MONTH DOSE PACK	TABLET
CONCEPTROL	NONOXYNOL 9	4%	VAGINAL GEL
CONDOMS	CONDOMS, LATEX, LUBRICATED	N/A	TOPICAL
DROSPIRENONE-ETHINYL ESTRADIOL	DROSPIRENONE-ETHINYL ESTRADIOL	3MG-0.03MG	TABLET
ELLA	ULIPRISTAL	30MG	TABLET
ENSKYCE	DESOGESTREL & ETHINYL ESTRADIOL	0.15MG-0.03MG	TABLET
GENERESS FE	NORETHINDRONE & ETHINYL ESTRADIOL & FERROUS FUMARATE	0.8MG-25MCG/75MG	TABLET
GIANVI	DROSPIRENONE & ETHINYL ESTRADIOL	3MG-20MCG	TABLET

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
GILDESS 1.5/30	NORETHINDRONE & ETHINYL ESTRADIOL	1.5MG-30MCG	TABLET
GILDESS 1/20	NORETHINDRONE & ETHINYL ESTRADIOL	1MG-20MCG	TABLET
GILDESS FE 1/20	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1MG-20MCG/75MG	TABLET
GILDESS FE 1.5/30	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1.5MG-30MCG/ 75MG	TABLET
GYNOL II	NONOXYNOL 9	3%	VAGINAL GEL
INTROVALE	LEVONORGESTREL & ETHINYL ESTRADIOL	0.15MG-30MCG	TABLET
JOLESSA	LEVONORGESTREL & ETHINYL ESTRADIOL	0.15MG-30MCG	TABLET
JUNEL 1.5/30	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL	1.5-0.03MG	TABLET
JUNEL 1/20	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL	1MG-20MCG	TABLET
JUNEL FE 1.5/30	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1.5-0.03MG	TABLET
JUNEL FE 1/20	NORETHINDRONE ACETATE & ETHINYL ESTRADIOL & FERROUS FUMARATE	1MG-20MCG	TABLET
KARIVA	DESOGESTREL-ETHINYL ESTRADIOL	0.15MG/0.02MG-0.01MG	TABLET
LEVONORGESTREL-ETHINYL ESTRADIOL	LEVONORGESTREL-ETHINYL ESTRADIOL	0.1MG-20MCG (84)/10MCG (7) 3 MONTH PACK	TABLET
LEVONORGESTREL-ETHINYL ESTRADIOL	LEVONORGESTREL-ETHINYL ESTRADIOL	0.1MG-20MCG	TABLET
LEVONORGESTREL-ETHINYL ESTRADIOL	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-30MCG 3 MONTH PACK	TABLET
LEVONORGESTREL	LEVONORGESTREL	0.75 MG	TABLET
LEVONORGESTREL	LEVONORGESTREL	1.5 MG	TABLET
LO LOESTRIN FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-10MCG/75MG	TABLET
LOMEDIA 24 FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-20MCG/75MG	TABLET
LORYNA	DROSPIRENONE & ETHINYL ESTRADIOL	3MG-20MCG	TABLET
LOW-OGESTREL	NORGESTREL & ETHINYL ESTRADIOL	0.3MG-30MCG	TABLET
LUTERA	LEVONORGESTREL & ETHINYL ESTRADIOL	0.1MG-20MCG	TABLET
MARLISSA	LEVONORGESTREL & ETHINYL ESTRADIOL	0.15MG-30MCG	TABLET

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
MICROGESTIN 1.5/30	NORETHINDRONE & ETHINYL ESTRADIOL	1.5MG-30MCG	TABLET
MICROGESTIN 1/20	NORETHINDRONE & ETHINYL ESTRADIOL	1MG-20MCG	TABLET
MICROGESTIN FE 1.5/30	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1.5MG-30MCG/ 75MG	TABLET
MICROGESTIN FE 1/20	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-20MCG/75MG	TABLET
MINASTRIN 24 FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG-20MCG/75MG	TABLET
NATAZIA	DIENOGEST & ESTRADIOL VALERATE	3MG/2MG-2MG/ 2MG-3MG-1MG	TABLET
NECON 0.5/35	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG-35MCG	TABLET
NECON 1/35	NORETHINDRONE & ETHINYL ESTRADIOL	1MG-35MCG	TABLET
NECON 1/50	NORETHINDRONE-MESTRANOL	1MG-50MCG	TABLET
NECON 10/11	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG-35MCG/ 1MG-35MCG	TABLET
NECON 7/7/7	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/0.75MG/1MG-35MCG	TABLET
NEXPLANON	ETONOGESTREL	68MG	SUBDERMAL
NORETHINDRONE	NORETHINDRONE	0.35MG	TABLET
NORGESTIMATE-ETHINYL ESTRADIOL	NORGESTIMATE-ETHINYL ESTRADIOL	0.25MG-35MCG	TABLET
NORGESTIMATE-ETHINYL ESTRADIOL	NORGESTIMATE-ETHINYL ESTRADIOL	0.18MG/0.215MG/ 0.25MG-25MCG	TABLET
NORGESTIMATE-ETHINYL ESTRADIOL	NORGESTIMATE-ETHINYL ESTRADIOL	0.18MG/0.215MG/ 0.25MG-35MCG	TABLET
NORINYL 1+50	NORETHINDRONE-MESTRANOL	1MG-50MCG	TABLET
NORTREL 1/35	NORETHINDRONE & ETHINYL ESTRADIOL	1 MG-35MCG	TABLET
NORTREL 7/7/7	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/0.75MG/ 1MG-35MCG	TABLET
NUVARING	ETONOGESTREL/ETHINYL ESTRADIOL	0.12MG-0.015MG	VAGINAL RING
OGESTREL	NORGESTREL & ETHINYL ESTRADIOL	0.5MG-50MCG	TABLET
PORTIA	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-0.03MG	TABLET
QUARTETTE	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-20MCG/ 0.15MG-25MCG 3 MONTH DOSE PACK	TABLET
QUASENSE	LEVONORGESTREL-ETHINYL ESTRADIOL	0.15MG-30MCG 3 MONTH DOSE PACK	TABLET
RECLIPSEN	DESOGESTREL-ETHINYL ESTRADIOL	0.15MG-0.03MG	TABLET

LABEL NAME	GENERIC NAME	STRENGTH	DOSAGE FORM
SAFYRAL	DROSPIRENONE-ETHINYL ESTRADIOL-LEVOMEFOLATE	3MG-0.03MG-0.451MG	TABLET
TILIA FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG/20MCG-30MCG-35MCG (75MG)	TABLET
TODAY CONTRACEPTIVE SPONGE	NONOXYNOL 9	1000MG	VAGINAL SPONGE
TRI-LEGEST FE	NORETHINDRONE & ETHINYL ESTRADIOL (FERROUS FUMARATE)	1MG/20MCG-30MCG-35MCG (75MG)	TABLET
TRI-NORINYL	NORETHINDRONE & ETHINYL ESTRADIOL	0.5MG/1MG/0.5MG-35MCG	TABLET
TRI-LO-SPRINTEC	NORGESTIMATE-ETHINYL ESTRADIOL	0.18MG/0.215MG/ 0.25MG-25MCG	TABLET
TRIVORA	LEVONORGESTREL/ETHINYL ESTRADIOL	0.05MG-0.075MG-0.125MG/ 0.03MG-0.04MG-0.03MG	TABLET
VAGINAL CONTRACEPTIVE FILM	NONOXYNOL 9	28%	VAGINAL FILM
VAGINAL CONTRACEPTIVE FOAM	NONOXYNOL 9	12.5%	VAGINAL FOAM
VELIVET TRIPHASIC REGIMEN	DESOGESTREL/ETHINYL ESTRADIOL	0.1MG-0.125MG-0.15MG/25MCG	TABLET
VESTURA	DROSPIRENONE-ETHINYL ESTRADIOL	3MG-20MCG	TABLET
XULANE	NORELGESTROMIN-ETHINYL ESTRADIOL	4.86MG-0.53MG	TRANSDERMAL PATCH
ZENCHENT FE	NORGESTIMATE-ETHINYL ESTRADIOL (FERROUS FUMARATE)	0.4MG-35MCG/75MG	TABLET
ZOVIA 1/35E	ETHYNODIOL DIACETATE-ETHINYL ESTRADIOL	1MG-35MCG	TABLET
ZOVIA 1/50E	ETHYNODIOL DIACETATE-ETHINYL ESTRADIOL	1 MG-50MCG	TABLET

If you need help reading this document or would like a different format, please call the Alliance Member Services Department at **1.510.747.4567**.

Si necesita ayuda para leer este documento, o le gustaría tenerlo en un formato diferente, llame al Departamento de Servicios al Miembro de Alliance al **1.510.747.4567**.

如果您需要幫助閱讀此文檔或需要不同的格式，請致電Aliiance計畫成員服務處，電話：**1.510.747.4567**。

Nếu quý vị cần giúp đỡ đọc tài liệu này hoặc muốn một định dạng khác, vui lòng gọi cho Ban Dịch vụ Hội viên Alliance theo số **1.510.747.4567**.

Kung kailangan mo ng tulong sa pagbasa ng dokumentong ito o kung gusto mo ng ibang format, mangyaring tumawag sa Alliance Member Services Department sa **1.510.747.4567**.

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

PHARMACY & THERAPEUTICS COMMITTEE

Record of Committee Meeting Minutes

Tuesday, March 19, 2024 | 5:00pm – 7:00pm

Status	Voting Committee Members	Organization	Initials	Officer / Notes
P	Donna Carey, MD	Interim Chief Medical Officer-Alliance	DC	Chairman
P	Helen Lee, PharmD	Senior Director of Pharmacy Services – Alliance	HL	Co-Chair
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	
A	Steve O'Brien, MD	CMO - Alliance	SO	Chairman

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	Role / Department
P	Natalee Felten	PerformRx	Formulary Management & Drug Utilization Review
	Pat DeHoratius	PerformRx	Manager Formulary/DUR
	Barrie Cheung	PerformRx	Regional Pharmacy Director
P	Rahel Negash, PharmD	Alameda Alliance	Pharmacy Supervisor
P	Ramon Tran Tang, PharmD	Alameda Alliance	Clinical Pharmacist
A	Jefferey Bencini, Pharm D	Alameda Alliance	Clinical Pharmacist
P	Timothy Tong, Pharm D	Alameda Alliance	Clinical Pharmacist
A	Beverly Juan, MD	Alameda Alliance	Medical Director
A	Sanjay Bhatt, MD	Alameda Alliance	Medical Director
A	Darryl Crowder	Alameda Alliance	Provider Relations
P	Bibek Sandhu, PharmD, MBA	PillarRX	Consulting Pharmacist

Other Guests	

Follow-up Items:

Clerk of the Committee: Antonio Hoy

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
I) Call to Order	D. Carey	• Conflict of Interest Check/Disclosure • Agenda Overview	Called to order at 5:10PM	
II) Informational Updates	D. Carey H. Lee	Informational Updates • Anthem - As many of you know we have a transition from dual county to a single plan in terms of Anthem and Alliance. - We absorbed about 86,000 members from Anthem. - We had close to 100,000 new members that joined Alliance in 2024. It has been a huge transition, and our volume production line has increased. The transition was very smooth. - We did a continuity of care which meant that even if members were seen at a private facility or private physician that was not in our network prior to January our contracting team did a really great job of trying to make sure we contracted with all of the providers that Anthem contracted with so there would be the continuity of care and continuity of treatment. That is inclusive for DME equipment, pharmacy services, and medical and clinical care. PB: how many patients went to Kaiser? DC: In order for someone to move from Anthem to Kaiser they need to have a family member who is in Kaiser or had previous insurance with Kaiser. The majority of people came to the Alliance. HL: Minimum number went to Kaiser. We gained over 120,000 plus patients. • ICF-DD, Adult Expansion • CAL-AIM initiatives • DHCS Routine Survey - The routine DHCS Survey is coming in June and the date is to be determined. I believe it is from June 17th through June 28th. Mainly it will be about access and then UM. So pharmacy might be a part of that UM and G&A, Fraud Waste Abuse, and emergency services sessions. We will find out as we go. • CGM - Continuous Glucose Monitor will get redirected to the state effective July 1st of 2024. Initially we were trying to move it earlier but because of Anthem and ICF -DD Adult Expansion we decided to give them an extra six months as it is required for Anthem patients to satisfy COC policy per APL. This is the reason why we are pushing out to July 1st, 2024. • Medi-Cal Rx - As of March 15th, 2024, the state processed over 39.479 million pos pharmacy paid claims. - And spent over 3.9 billion dollars. - There were a little less than 180,000 prior authorizations. They also received about 145,000 phone calls.		

- MDAC
  - These are some of the drugs that we recommend to the contract drug list as known as their supplemental formulary list. We reviewed a total of eight medications. We recommend adding to formulary with prior authorization except the generic insulin aspart and the combination product to be added to formulary without PA requirement.
  - Most indications were for Rheumatoid Arthritis, DMD, congestive heart failure, Type I and II diabetes and ALS and chronic weight management.

MCDAC Drug	Indication	CDL Status	**Recommendation** Based on - Safety, Efficacy, Essential Need, Misuse Potential, etc.
Amjevita (adalimumab-atto) 20mg/0.4ml prefilled syringe, 40mg/0.8ml prefilled syringe and 40mg/0.8ml prefilled sureclick autoinjector	Rheumatoid Arthritis (RA), Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease (CD), Ulcerative Colitis (UC) and Plaque Psoriasis	F-PA	Keep F-PA
Emflaza (deflazacort) 6mg, 18mg, 30mg, 36mg and 22.75mg/ml suspension	Duchenne muscular dystrophy (DMD) in patients ≥ 2 years old	F-PA	Keep F-PA
Furoscix (furosemide) 80mg/10ml prefilled cartridge co-packaged w/one on-body infusor	Congestion due to fluid overload in adult patients with NYHA class II and class III chronic heart failure	F-PA	Keep F-PA
Inpefa (sotagliflozin) 200mg and 400mg tablets	Heart failure; Cardiovascular risk reduction	F-PA	Keep F-PA
Insulin aspart vial 100u/ml 10ml vial, 100 u/ml penfill 3ml, 100u/ml flexpen 3ml	Type 1 and Type 2 Diabetes	F	Keep F
Insulin aspart protamine-Insulin aspart mix 70/30 suspension 10ml vial and 3ml flexpen	Type 1 and Type 2 Diabetes	F	Keep F
Radicava (edaravone) ORS and Radicava ORS starter kit	Amyptotrophic lateral sclerosis (ALS)	F-PA	Keep F-PA
Zepbound (tirzepatide) 2.5mg/0.5ml, 5mg/0.5ml, 7.5mg/0.5ml, 10mg/0.5ml, 12.5mg/0.5ml, and 15mg/0.5ml pen	Chronic weight management	F-PA	Keep F-PA

III) Pharmacy Utilization Reports (Quarter 4, 2024) — H.Lee

(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 1,474 claims for 1,011 members and cost $1,119,278, which is a decrease of $7,941 in spend from the previous quarter.
- Biktarvy remains at number one, claims have gone up by 5, and there is one additional member since the previous quarter.
- Vemlidy is up to number 2 with 44 claims for 19 members. This medication is managed via the Hepatitis B MRG, which was loosened during Q4 2022 P&T to require trial and failure of, or reason not to use, entecavir (previously generic Viread and entecavir).
- Ozempic is at numbers 3, 4 and 28, with 141 total claims for 72 members. There was an increase of 8 claims and of 4 members from the previous quarter.
- Tagrisso is at number 5 with 3 claims for one member. Utilization has not changed since the previous quarter. This medication is managed via the Oncology MRG.

- Top 50 Drugs by Cost (Medi-Cal)
  - The top 50 drugs accounted for 31,667 claims for 27,121 members and cost $41,548,265.19, which is an increase of $1,442,357.83 in spend from the previous quarter.
  - Ozempic has fallen from the number 2 to number 3, with 1,474 claims for 1,182 members. This is a decrease of 10 claims from last quarter.
  - Humira is down to number 4 from the number 3 spot with 109 claims for 87 members. This is a decrease of 8 claims since last quarter.
  - Stelara has moved up to the number 2 spot from number 5, with 56 claims for 40 members. This is an increase of 14 claims from last quarter.
  - Jardiance 25mg has fallen from number 4 to number 5 with 1,397 claims for 1,310 members. This is an increase of 47 claims from last quarter.
  - Biktarvy remains at the number 1 spot with 676 claims for 543 members. An increase of 29 claims from the last quarter. Top 50 PA Reviewed Drugs by Volume (IHSS)

- Top 50 PA Reviewed Drugs by Volume (IHSS)
  - Top 50 PA requests = 134. There were 191 total PA requests for quarter 4.
    - 64 requests (48%) were approved. This approval rate is lower, by 1%, than what was observed last quarter.
    - 70 requests (52%) were denied or partially approved.
  - Jardiance 10mg is at numbers 1 & 2 with 20 total requests and 10 approvals (50%).
    - The formulary alternative is Steglatro, with trial and failure of metformin.
  - Vemlidy 25 mg is down to number 3 and had a total of 9 requests, from which there were 6 approvals (67%).
    - Vemlidy requires a diagnosis of Hepatitis B, and trial and failure of, intolerance to, or inability to use entecavir tablets.
  - Entecavir is at number 4 with 8 requests and 3 approvals (38%). This is 3 more requests than the previous quarter.
    - Entecavir requires a diagnosis of Hepatitis B and an appropriate dose
  - Lidocaine 5% patch is at number 5 and had 7 requests with 3 approvals (43%).

- This medication requires a diagnosis of neuropathic pain and a trial and failure of gabapentin or pregabalin and one other formulary alternative used for neuropathic pain or morphine MME < 50 for 3 months.

- Linzess, Ozempic 0.25-0.5mg/dose, and Restasis all have 4 requests.
  - Linzess requires a diagnosis of irritable bowel syndrome with constipation (IBS-C) with trial and failure of soluble fiber OR a diagnosis of chronic idiopathic constipation with trial and failure of soluble fiber and 2 other formulary laxatives.
  - Ozempic requires a trial and failure of metformin.
  - Restasis multidose requires trial and failure of cyclosporine (Restasis) 0.05% dropperette (generic) and two different artificial tear products, one of which must be high viscosity artificial tears.

- Top 50 PA Reviewed Drugs by Volume (Medi-Cal)
  - The top 50 drugs accounted for 179,112 claims for 160,306 members and cost $3,981,958.05.
  - Albuterol remains at the number 1 spot with 13,546 claims for 11,403 members. An increase of 2,268 claims from last quarter.
  - Ibuprofen moved up to number 2 from number 3 with 7,845 claims for 7,104 members. This is an increase of 108 claims from last quarter.
  - Fluticasone remains at number 4 with 7,384 claims for 6,819 members. There was an increase of 116 claims from last quarter.
  - Aspirin has fallen from number 2 to number 3 with 7,839 claims for 7,265 members. This is a decrease of 56 claims from last quarter.
  - Diclofenac gel has risen from the number 7 spot to number 5 with 5,441 claims for 4,785 members. This is an increase of 505 claims from last quarter.

IV) E-Voting Material/Consent Agenda

B. Ochoa

Monographs/Class Reviews	Changes
Inhaled Corticosteroids/Long-Acting Beta-Agonists (ICS/LABA) class review	• No changes
First generation antihistamines class review	• No changes
Opioid containing antitussives class review	• No changes
Zepbound monograph	• No changes
Methergine monograph	• No changes
Medication Request Guidelines	**Changes**
Inhaled Corticosteroids/Long-Acting Beta-Agonists (ICS/LABA) Combinations MRG (part of ICS/LABA class review)	• Change Advair HF to reflect generic availability • Add new NF medication Airsupra
Oxbryta (voxelotor)	• Minor formatting updates
Angiotensin II Receptor Blockers and Renin Inhibitors	• Remove eprosartan and Tekturna from policy. Off market.
Histamine H2 Receptor Antagonists	• Cimetidine 300 mg/5 ml oral solution is discontinued. Remove from policy.
Ophthalmic Antihistamines	• No changes
Verquvo	• No changes
Siklos (hydroxyurea)	• No changes
Tadalafil (Cialis) for BPH	• No changes
Altoprev (lovastatin ER) and Fluvastatin, Fluvastatin ER	• No changes
Arikayce (amikacin)	• No changes
Long-Acting Muscarinic /Long-Acting Beta Agonist/ Corticosteroid inhaled Triple Combination Products Long-Acting Muscarinic /Long-Acting	• No changes
Savella (milnacipran) tablet	• No changes
Fexofenadine-pseudoephedrine	• No changes

Approved via e-voting:
Yes: 6
No: 0
Abstained: 0

		Injectable Anticoagulants	• No changes			
		Atovaquone (Mepron)	• No changes			
		Thrombocytopenia Agents	• No changes			
		Travoprost (Travatan Z) ophthalmic drops	• No changes			
		Pyridostigmine (Mestinon)	• No changes			
		Antifibrotic Respiratory Tract Agents	• No changes			
		Cystic Fibrosis Agents	• No changes			
		Elmiron (pentosane polysulfate sodium)	• No changes			
		Linezolid	• No changes			
		Symlin (pramlintide)	• No changes			
		Corticosteroid Preparations to Treat Hemorrhoids	• No changes			
		Physician Administered Drug (PAD) Guidelines	**Changes**			
		Emergency Use Authorization (EUA) Drugs/Products for COVID-19	• Add in formulation check for appropriateness			
		Tzield	• No changes			
		Ophthalmic indications for bevacizumab	• No changes			
		Interim Formulary Updates				
		• See p. 137 in packet				
		Summary of PAD Updates				
		• See p. 140 in packet				
		Pharmacy Policy & Procedure Updates				
		• RX-001 – RX-014	• Format updates and Annual Review			
		ED Oversight Updates				
		• None				
		90 Day Maintenance List Updates				
		• None				
		P&T Meeting Minutes				
		• P&T Meeting Minutes Q4 December 19, 2023				

Interim Formulary Changes

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

Medication	Formulary Change
Humira Pediatric Crohns Start Subcutaneous Prefilled Syringe Kit 80 MG/0.8ML	F-PA to NF
Humira Pediatric Crohns Start Subcutaneous Prefilled Syringe Kit 80 MG/0.8ML & 40MG/0.4ML	F-PA to NF
Humira Pen Subcutaneous Pen-injector Kit 40 MG/0.4ML	F-PA to NF
Humira Pen Subcutaneous Pen-injector Kit 40 MG/0.8ML	F-PA to NF
Humira Pen Subcutaneous Pen-injector Kit 80 MG/0.8ML	F-PA to NF
Humira Pen-CD/UC/HS Starter Subcutaneous Pen-injector Kit 40 MG/0.8ML	F-PA to NF
Humira Pen-CD/UC/HS Starter Subcutaneous Pen-injector Kit 80 MG/0.8ML	F-PA to NF
Humira Pen-Pediatric UC Start Subcutaneous Pen-injector Kit 80 MG/0.8ML	F-PA to NF
Humira Pen-Ps/UV/Adol HS Start Subcutaneous Pen-injector Kit 40 MG/0.8ML	F-PA to NF
Humira Pen-Psor/Uveit Starter Subcutaneous Pen-injector Kit 80 MG/0.8ML & 40MG/0.4ML	F-PA to NF
Humira Subcutaneous Prefilled Syringe Kit 10 MG/0.1ML	F-PA to NF
Humira Subcutaneous Prefilled Syringe Kit 20 MG/0.2ML	F-PA to NF

		Humira Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	F-PA to NF		
		Humira Subcutaneous Prefilled Syringe Kit 40 MG/0.8ML	F-PA to NF		
		Rinvoq Oral Tablet Extended Release 24 Hour 15 MG	F-PA to NF		
		Rinvoq Oral Tablet Extended Release 24 Hour 30 MG	F-PA to NF		
		Rinvoq Oral Tablet Extended Release 24 Hour 45 MG	F-PA to NF		
		Cosentyx (300 MG Dose) Subcutaneous Solution Prefilled Syringe 150 MG/ML	F-PA to NF		
		Cosentyx Sensoready (300 MG) Subcutaneous Solution Auto-injector 150 MG/ML	F-PA to NF		
		Cosentyx Sensoready Pen Subcutaneous Solution Auto-injector 150 MG/ML	F-PA to NF		
		Cosentyx Subcutaneous Solution Auto-injector 300 MG/2ML	F-PA to NF		
		Cosentyx Subcutaneous Solution Prefilled Syringe 150 MG/ML	F-PA to NF		
		Cosentyx Subcutaneous Solution Prefilled Syringe 75 MG/0.5ML	F-PA to NF		
		Skyrizi (150 MG Dose) Subcutaneous Prefilled Syringe Kit 75 MG/0.83ML	F-PA to NF		
		Skyrizi Pen Subcutaneous Solution Auto-injector 150 MG/ML	F-PA to NF		
		Skyrizi Subcutaneous Solution Prefilled Syringe 150 MG/ML	F-PA to NF		
		Stelara Subcutaneous Solution 45 MG/0.5ML	F-PA to NF		
		Stelara Subcutaneous Solution Prefilled Syringe 45 MG/0.5ML	F-PA to NF		
		Stelara Subcutaneous Solution Prefilled Syringe 90 MG/ML	F-PA to NF		
		Taltz Subcutaneous Solution Auto-injector 80 MG/ML	F-PA to NF		
		Taltz Subcutaneous Solution Prefilled Syringe 80 MG/ML	F-PA to NF		

		Cimzia Starter Kit Subcutaneous Prefilled Syringe Kit 6 X 200 MG/ML	F-PA to NF		
		Cimzia Subcutaneous Kit 2 X 200 MG	F-PA to NF		
		Cimzia Subcutaneous Prefilled Syringe Kit 2 X 200 MG/ML	F-PA to NF		
		Skyrizi Intravenous Solution 600 MG/10ML	F-PA to NF		
		Skyrizi Subcutaneous Solution Cartridge 180 MG/1.2ML	F-PA to NF		
		Skyrizi Subcutaneous Solution Cartridge 360 MG/2.4ML	F-PA to NF		
		Zeposia 7-Day Starter Pack Oral Capsule Therapy Pack 4 x 0.23MG & 3 x 0.46MG	F-PA to NF		
		Zeposia Oral Capsule 0.92 MG	F-PA to NF		
		Zeposia Starter Kit Oral Capsule Therapy Pack 0.23MG & 0.46MG & 0.92MG	F-PA to NF		
		Zeposia Starter Kit Oral Capsule Therapy Pack 0.23MG &0.46MG 0.92MG(21)	F-PA to NF		
		inFLIXimab Intravenous Solution Reconstituted 100 MG	NF to F-PA		
		Inflectra Intravenous Solution Reconstituted 100 MG	NF to F-PA		
		Avsola Intravenous Solution Reconstituted 100 MG	NF to F-PA		
		Renflexis Intravenous Solution Reconstituted 100 MG	NF to F-PA		
		Siliq Subcutaneous Solution Prefilled Syringe 210 MG/1.5ML	NF to F-PA		
		Olumiant Oral Tablet 1 MG	NF to F-PA		
		Olumiant Oral Tablet 2 MG	NF to F-PA		
		Olumiant Oral Tablet 4 MG	NF to F-PA		
		Entyvio Intravenous Solution Reconstituted 300 MG	NF to F-PA		
		Entyvio Subcutaneous Solution Pen-injector 108 MG/0.68ML	NF to F-PA		
		All claims	Increase in dollar limit per claim pay at point-of-sale allowance from $1000 to $1500		

Zenpep Oral Capsule Delayed Release Particles 60000-189600 UNIT	NF to F-AL (min 21 years)
Penbraya Intramuscular Suspension	NF to F-QL-AL (0.5ml per dose) (2 fills per lifetime) (max age 25 years)
Ibrance capsules and tablets	NF to F-PA
Verzenio tablets	NF to F-PA

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.

Physician Administered Drug (PAD) Prior authorization (PA) list Updates

HCPCS Code	HCPSC Description	Action
J9258	PACLITAXEL PROTEIN-BOUND PARTICLES (TEVA)	Add PA Requirement
J9072	CYCLOPHOSPHAMIDE	Add PA Requirement
J9286	GLOFITAMAB-GXBM (COLUMVI)	Add PA Requirement
J9321	EPCORITAMAB-BYSP (EPKINLY)	Add PA Requirement
J9324	PEMETREXED (PEMRYDI RTU)	Add PA Requirement
J0217	VELMANASE ALFA-TYCV (LAMZEDE)	Add PA Requirement
J1304	TOFERSEN (QALSODY)	Add PA Requirement

J1413	DELANDISTROGENE MOXEPARVOVEC (ELEVIDYS)	Add PA Requirement		
J1412	VALOCTOCOGENE ROXAPARVOVEC-RVOX (ROCTAVIAN)	Add PA Requirement		
J2508	PEGUNIGALSIDASE ALFA-IWXJ (ELFABRIO)	Add PA Requirement		
J9333	ROZANOLIXIZUMAB-NOLI INJECTION (RYSTIGGO)	Add PA Requirement		
J9334	EFGARTIGIMOD ALFA-FCAB AND HYALURONIDASE-QVFC (VYVGART)	Add PA Requirement		
J0224	OXLUMO (LUMASIRAN)	Add PA Requirement		
J0219	AVALGLUCOSIDASE ALFA-NGPT	Add PA Requirement		
J3490	UNCLASSIFIED DRUGS	Remove PA		
J0135	HUMIRA (ADALIMUMAB) 20MG	Remove PA		
J1325	INJECTION EPOPROSTENOL 0.5 MG	Remove PA		
J2941	INJECTION, SOMATROPIN, 1 MG	Remove PA		
J7191	FACTOR VIII AHF PORCINE PER IU	Remove PA		
J7504	LYMPHCYT GLOB EQUINE PARNTRAL 250MG	Remove PA		
J7511	LYMPHCYT GLOB RABBIT PARNTRAL 25MG	Remove PA		
J7599	IMMUNOSUPPRESSIVE DRUG NOC	Remove PA		
J7685	TOBRAMYCIN INHAL CP THRU DME 300 MG	Remove PA		
J9160	ONTAK (DENILEUKIN DIFTITOX) 300 MCG	Remove PA		
J9999	NOT OTHWISE CLASS ANTINEOPLSTC DRUG	Remove PA		

V) New Business	N. Felten	**<u>New PADs</u>** **NF**-Let's start on part 246. We have a new policy with Pompe Disease Agents **<u>Pompe disease agents</u>** - And this policy covers Lumizyme, Nexviazyme, and and two newest agents Pombilit and Opfolda used for Pompe disease which is a rare genetic condition that causes muscle weakness over time. Pombiliti is IV and Opfolda is an oral capsule given together every week. - They cost about $50,000 a month. For the policy, we are asking for a specialist to prescribe, and the policy is broken up into two sections for infantile onset where only Lumizyme is indicated and then late onset where all the medications are indicated. - For infantile onset, we are looking for diagnosis confirmation by either assay or genetic testing, appropriate dose, and no duplication of therapy. And then late onset, looking for onset via the same methods, measurable signs and symptoms, results of a baseline walk test, forced vital capacity, and again no duplication of therapy. - Separately for Pombiliti and Opfolda, patients' trial and failure of another enzyme therapy, trial and failure of Lumizyme or Nexvfiazyme per package labeling. **<u>Zulresso</u>** - On page 248, we have a new policy for Zulresso, this is an IV infusion used to treat postpartum depression in patients 15 years and up. It did come out several years ago but today we have an accomplished new pharmacy policy for Zerzue. So postpartum depression is the most common post-natal psychiatric complication. This is a onetime 60-hour continuous infusion. It is about $34,000 per infusion and the policy asks for prescriber that is either a psychiatrist or OBGYN. A diagnosis of moderate to severe postpartum depression with a validated screening tool result, onset of an episode within 6 months of delivery, and also enrollment in the REMS program and patient weight.	Move to approve: 1st:DB 2nd:IL	

- Any questions on these two, so far?

Adzynma

- Moving onto 249, we have a new Adzynma policy. This is a new IV infusion for prophylactic for on demand enzyme replacement therapy in adults and peds with cTTP. This is a rare disorder that affects approximately less than 1000 people in the US. It's administered daily for 3 days and sometimes beyond until 2 days after the acute event has resolved.
- The pricing is about $18,000 per month but varies based on weight and length of therapy. For the policy, we are asking for a specialist prescriber with confirmed diagnosis, by both of these methods listed. Attestation that patient has not been diagnosed with any other TTP disorder and if it's being used for prophylaxis, at least one previous event and also patient weight.

New MRGs

Now we will move on to the new MRG's on the pharmacy side starting on page 250. The first is Presbyopia agents. This policy covers both Vuity and Qlosi which are brand names of pilocarpine solution.

Presbyopia Agents

- These are interesting because they are indicated for presbyopia-or the inability of the eyes to focus on nearby objects. They are both indicated in very specific age ranges based on the trials and you'll see that there are age restrictions.
- The price is about $115 per 5ML. Qlosi is not yet listed but we have heard it will be comparable based on what we've seen. For the policy, we are looking for the diagnosis, correct age, trial and failure of glasses or contact lenses.

Zurzuvae

- On page 251, we have a policy for Zurzuvae and this is a new medication with an oral formulation.
- So, the last was IV for the treatment of PPD in adults. It is taken once daily for 14 days. The price is about $16,000 for a fourteen-day course and the policy is very similar to the one we just went over for Zulresso. As you can see here, except for the REMS requirement as this drug is not part of any REMS program.
- I'll stop here for any questions.

Dificid

		- OK on page 252, we have a new policy for Dificid which is not a not a new drug, however we have seen new PA requests for it. - Though we are creating a drug specific policy, it is indicated for the initial C-Diff infection. - The policy asks for a specialist, correct dose, and reason why patient cannot use oral vancomycin. - The approval is for a ten duration and the cost for a 10-day course is about $5000. **Fabhalta** - And then finally on page 253, we have a new policy for Fabhalta. This is the first oral concomitant inhibitor on the market. It is indicated for the treatment of adults with PNH. It's given twice daily. - It has a box warning for serious infection caused by incapsulated bacteria which you can see in the second bullet point. - The price is about $45,000 per month and the policy is very similar to our IV concomitant inhibitor polices that you may be familiar with. - We are asking for a specialist, an appropriate dose, documentation of diagnosis, and hemoglobin less than 10. **Questions:** Before we move onto our class reviews on page 254, are there any questions? DC-Natalie we are going ahead and do our vote now. HL-we will wait until the end. DC- Oh you want to wait until the end, OK. Sorry, never mind. (laughs). I am just making sure. NF-Ok I will keep going until you stop me. DC-yes, thank you.		
VI) Class Reviews, Monographs, and Recommendations	N. Felten	**Casgevy monograph** **Recommendation:** - OK, first monograph is Casgevy. This is the new cellular gene therapy consisting of stem cells edited by CRISPR technology. It's indicated for patients 12 and up with either sickle cell disease or recurrent Vaso occlusive crisis for transfusion dependent beta thalassemia. Patients are required to undergo HSC mobilization followed by apheresis to obtain CD34 positive cells for Casgevy manufacturing, then full myeloablative conditioning. The price of this drug alone 2.2		

		million dollars per one time treatment. It is estimated that there is approximately 1300-1500 individuals in the country with transfusion dependent beta thalassemia and we do have a policy revised starting on page 266. We are adding Casgevy to our previous policy for Zynteglo. Just to note, Casgevy is indicated for patients 12 and up and Zenteglo doesn't have an age restrictions. - The exclusion criteria will now include repeat use of the same agent or subsequent other agents. The requirement for transfusion will remain the same and (if you scroll down a little bit and we are amending the statement for no family match stem cell doners to simply no prior stem cell transplant or gene treatment in particular so if few patients match and has to do very young and there are concerns with graph verses host or graph reduction with stem cell transplant and this drug would not have those complications. Just as interest, the manufacturer of Casgevy is working on a warranty program from what we read and what that means if the member fails the treatment the manufacturer may reimburse part of the original cost of the drug on some kind of prorated schedule so we will share more about that if we hear any concrete details. **Comments:**		
		Lyfgenia monograph **a. New PAD: Gene Therapy for Sickle Cell Disease** - Moving on to the Lyfgenia monograph which is on page 268. So, this is another new gene therapy released for sickle cell only so it doesn't have the dual indication and this is little bit different instead of CRISPR technology, it works on the CD34 positive cells that have been transduced with a lentiviral vector. Otherwise, the process is pretty similar to Casgevy. The price for this one is 3.1 million dollars for the drug and unlike Lyfgenia which does have a black box warning, for hematologic malignancies, Casgevy does have a black box warning. **Recommendation:** - There is a new policy for this on page 274. For this policy we are looking for a specialist prescriber, correct diagnosis, at least 2 severe Vaso-occlusive events as defined by these bullet points, Documentation that the member has been taking Hydroxyurea at the max tolerated dose or reason not to take and has been compliant for 6 months. Also, pregnancy has been ruled out prior to the initiation of treatment and also has no prior stem cell transplant or gene therapy treatment. Of note, I did look up administration centers a couple weeks ago for these and Casgevy. The closet one is Duarte, California. The second closet is San Antonio, For Lyfgenia, there is going to be an administration center in Palo Alto but both companies are working on implementing more treatment centers and you'll see that when you look at their web site. It's easy to see where they are located just in case a concern of which therapy to use.		

		Any questions on those? **Comments:**		
		Direct oral anticoagulants class review - Moving onto page 276, we have the direct oral anticoagulants for review and there were 100 claims for 39 members. The total cost is $54,000. The average cost per claim was $549. The most highly utilized medication was Eliquis. **Recommendation:** - The recommendation for this class review is to change brand Pradaxa 75mg and 150mg capsules from formulary back to non-formulary. The reason for this was for a time, they were about the same price. However, the available generic are once again more cost effective. **Comments:**		
		SGLT2s class review - On page 304, is the SGLT2 inhibitors class review. There were 168 claims for 80 members. And there was a total cost of about $70, 000 with the average cost per claim was $432. The most highly utilized claim was Steglatro. **Recommendation:** - We would like to change Farxiga XR from formulary PA to formulary step therapy with a trial or failure of Metformin. These drugs have a multitude of indications. - They are just not for diabetes anymore. - They are for heart failure. They are for kidney disease. And based on the diagnosis they would need to try and fail more than Metformin. We are also recommending having the same step therapy requirement that Steglatro to have consistency within the class and also change Steglujan from formulary step therapy to formulary PA. We don't have any utilization of that medication. **Comments:** Any Questions? PB-can you just restate, I am little lost. What page is this again? 339? NF-yes PB- can you just restate, OK. NF-The step therapy drugs? PB-yea NF-Previously SGLT2, our preferred agents, we had trial and failure of metformin and for metformin containing products. That was historically from when this class was only indicated for diabetes. However, as they gained indications and particularly Farxiga that the gained indications for things like Heart failure or kidney disease so no longer makes sense to only require only trial and failure of Metformin but also require trial and failure of these other drugs listed here if there are using for those other indications. PB-got it, so your recommendations at the top and trial and fail Steglatro and Farxiga to be able to get other SGL2 inhibitors, right? NF-yes PB- So the difference is because Jardiance has a specific indication.		

		NF- The indications for Farxiga and Jardiance are pretty similar to each other but previously we only preferred the Steglatro, so we are now preferring two additional agents. We are expanding the availability here to include Farxiga and Xigduo PB-OK, thanks NF-OK any other questions on this class review? And just to restate this, previously we had a combined policy for SGL2, but it was a little cumbersome to have their individualized indications, so we are putting the SGL2 inhibitors into their own policies and this is it		
VII) Medication Request Guidelines	R. Negash	The committee has reviewed and discussed the following updates and additions to the Medication Review Guidelines (MRG) Guideline (Changes): **Emflaza** - We're changing the name because we're including another product, Agamree. Instead of calling this the Emflaza policy, we'll call it the corticosteroids for Duchene Muscular Dystrophy. - As a result of adding that additional product we'll have more updates to the PA review criteria. - We're also adding a line under prescriber restrictions that says that any provider who specializes to treat DMD can also request for these products. With the PA criteria section the change here is to allow for a general diagnosis of DMD, an example can be some these genetic testing, we're just looking for copies of the results that show that the diagnosis is appropriate instead of requiring any specific parameters. That's just based on the addition of a new drug here. - We're also removing some of these bullet points that are only specific to Emflaza. For instance, that first bullet point that says patient need an onset of weakness before 5 years of age, we're removing it because it's specific to Emflaza. - The other bullet points there that relates to requirement for calcium and vitamin D, also based on eye exam and BMD screening, we're removing it since these are more monitoring parameters rather than a means to deny a request. - Also, another update is with prednisone, instead of making it a weight based requirement, it will be a general trial and failure of prednisone over a 12 month period. The reauthorization section is getting simplified, we're just looking for clinical benefit and appropriate FDA dose when we get request to continue therapy. **Comments:** DC: What's the age for this? RN: These are for adults. NF: Do you mean Agamree? The indication for the age range? DC: Yes, because of the change in the weight based dosing. NF: It's indicated for anyone that's over or equal to 2 years of age, so can be for adults or children. Guideline (Changes): **Corlanor (ivabradine)** - Under the Initial Authorization section, we're just adding the wording in there for our adult patients.		

- Also, looking for stable symptomatic chronic heart failure. We're also updating the NYHA class from 2 to 4.
- We're adding language to be specific for Peds patients, for those over 6 months here we're looking for a member that has a stable heart failure with the appropriate class due to dilated cardiomyopathy, then also ejection fraction less than 45%, and then also looking for a sinus rhythm with elevated heart rates.
- We generally don't see a lot of these requests from Peds, but we just sometimes put it in there for them.
- Those are the changes for this policy, the reauthorization criteria remains unchanged here.

Comments:

Guideline (Changes): **Ezetimibe (Zetia)**

- The change here is that we're adding an additional diagnosis of homozygous sitosterolemia. That's just to include all the appropriate FDA changes.
- There's no other changes on this policy.

Comments:

Guideline (Changes): **Estrogen Patches and Injectables – RETIRE**

- Here we're proposing to retire just because we've removed the age limits on this product and our previous P&T, so we won't really get the requests since it's a formulary quantity limit.

Comments:

Guideline (Changes): **Pulmonary Arterial Hypertension (PAH) Criteria**

- Here we're updating the policy to include that these products are vasodilators.
- We're also adding Liqrev oral suspension.
- As we can see for Ambrisentan and Bosentan we're allowing a medical reason why they can't use these products when we get requests for Opsumit. We can also see the Liqrev oral suspension.
- There are no more changes on this.

Comments:

Guideline (Changes): **Brilinta (ticagrelor) tablet**

- Pg. 352 we're just making 2 changes here, under PA Review Criteria that first bullet point that's struck is duplicative, the 30-day quantity limit is already noted in the coverage section above.
- We're also adding the requirement of combination with Aspirin on one bullet point.
- Below that at the top of the next page, you can see where the consolidation with the other bullet point is being struck.

- There are no other changes on this Brillinta policy.

Comments:

Guideline (Changes): **GLP-1 Agonists, SGLT2 inhibitors, DPP-4 Inhibitors and Combinations**

- On Pg. 354 this is what we discussed earlier, we had a GLP-1, SGLT-2, and DPP-4.
- Natalee went through SGLT-2 inhibitor updates, and I'll go through the GLP-1 and DPP-4.
- We're proposing to retire this combination policy since we're splitting them up.
- Under the Review Criteria section we can see the old policy and how it was structured. We see criteria for Heart failure, chronic kidney disease, and Diabetes.
- The GLP-1 policy is on pg. 357. So, this one is a new policy we see the same structure as the SGLT-2 where we have our step therapy preferred products. There's 4 Trulicity, Ozempic, Rybelsus, and Mounjaro.
- The medications that require a pa are Byetta and Victoza.
- Under the PA review criteria section, you see that requests will require metformin. So, when we get a prescription for Trulicity per se it will pay if the patient has tried Metformin recently. It will not pay if they didn't, so to answer those questions about weight management.
- They won't get the medication if they have not tried Metformin. If they are taking these products just for weight management, it will not go through without a pa.
- If the request is for a pa required product, they need to try a step therapy product first.
- For the DPP-4 Inhibitors again you'll see the same line up with the same therapy products and then the pa required products.
- Under Pa review criteria we do find that same treatment failure of Metformin requirement and then treatment failure for step therapy products if there's a pa required medication that comes in. Very similar logic to the previous policy.

Comments:
PB: What is the relative cost of the SGLT-2 inhibitor vs. the GLP-1 Agonist?
NF: In general, the SGLT-2 inhibitors are going to be a lot cheaper, right now our 2 most cost effective of the SGLT-2 are either going to be Steglatro or Farxiga. They are running around $340/ month. The other ones are more expensive, such as Jardiance, hence, we're not preferring it. When we're talking about the GLP-1 they are in the range anywhere of $1100-$1200/ month.
PB: Why would we not want to have them try the SGLT-2 first? Or as a second to Metformin?
NF: I'd have to look back at the algorithm to make sure I'm saying the right thing. I can follow up via email for that.
HL: Dr. Bayard in this case has something to do with the rebate arrangement.

Guideline (Changes): **Parkinson's Disease Agents**

- We're proposing to change the initial approval creation. Instead of 1 month for all it will on be for Tasmar as it does have more risk potential and 12 months for all others.
- There's no other changes on this policy.

Comments:

Guideline (Changes): **PCSK-9 Monoclonal Antibodies (mAbs)**

- Pg. 361 under PA Review Criteria you see the first change to show and add language to specifically indicate that we're looking for baseline levels when we get requests and we're looking at LDL.
- Below that we're seeing that same baseline language, just to be clear.
- Also, for requests that come in for secondary ASCVD, we do want to see that they have both the appropriate conditions. A history of multiple major ASCVD events with multiple factors involved.
- The second item that we want to see with those requests are LDL remaining above 55 or non HDL above 85 when they are on an LDL lowering therapy.
- The other change that we see here is for patients that are not at very high risk. So, we see those LDL's and non HDL levels at 70 and 100 despite the use of LDL lowering therapy.
- This policy doesn't have any additional updates.

Comments:

Guideline (Changes): **Xolair (omalizumab) for Asthma and Urticaria**

- Pg. 364 with this policy we're just rewording the exclusion criteria so basically this is saying that they should just be on Xolair and not another pulmonary biologic therapy at the same time.
- Under coverage duration we're increasing from 4 months initially to 6. Since there's no clear clinical reason why they can't be on 6, and it just makes for a smoother request review when we receive these cases.
- No other changes to this policy at this time.

Comments:

Guideline (Changes): **Agents for Atopic Dermatitis**

- Pg. 366 the changes here are to the prescriber restrictions section. This is expansion here, so if we get requests, it can either be prescribed by or in consultation with the appropriate specialists.
- Then we're also including Immunologist here.
- Pg. 367 we're also adding language here just to emphasize that we can get provider attestation for the appropriate diagnosis. That's just for a more thorough review.
- There's no other changes on this policy.

Comments:

Guideline (Changes): **Pulmonary Biologics for Asthma and Eosinophilic Conditions**

		- Pg. 369 we see similar changes here, we're just adding language in the prescriber restriction section to state that we can get these requests directly from the prescriber or if a provider is in consultation with any of the indicated specialists. - There's no other changes for this MRG. **Comments:** Guideline (Changes): **Biologic Agents for Nasal Polyposis** - Pg. 373 This is for the prescriber restrictions section again it's the same as the update we saw in the previous policy in the sense that we'll take direct request from prescribers or other specialists or providers who have consultation with the appropriate prescriber. - There's no other changes that we see here. **Comments:** No changes recommended at this time. No further discussion.		
VIII) Physician Administered Drug (PAD) Policies	N.Felten	Guideline (Changes): **Oxlumo (lumasiran)** - This was previously Oxlumo, we added the newest agent Rivfloza that just came out. We're changing the name to be inclusive. - These are very expensive medications, Oxlumo is about $700K a year, and Rivfloza is about $750K a year. That varies because the doses are weight based. - Here we're going to separate the metabolic testing requirements based more specifically on what end points each drug is approved for. - Rivfloza is only approved for urinary oxalate reduction, and Oxlumo is approved for both urinary and plasma oxalate. - We would like to add a kidney function requirement for Rivfloza as it's part of the drug indication and adding in an exclusion for using both drugs concurrently. - Rivfloza is approved for 9 and older, no defined age for Oxflumo but since our patients are 12 and up there's no distinction there. Guideline (Changes): **Rituximab** - Pg. 377 for Oncology we're just adding detail to the initial authorization, and adding in reauthorization criteria, so we have a more complete policy. - Pg. 378 for rheumatoid arthritis, the recommendation is to add in a disease state specific bullet point list. This is because previously we had a policy that was all inclusive of all the specialty biologic demards, however, we don't have that anymore, so we need to add that detail back into this policy and you will be familiar with them as they are the same as our previous policy. - Pg. 379 for GPA, EGPA, and MPA we're going to add in a requirement that rituximab is being used concurrently with IV glucocorticoids. **Comments:**		

		PB: On the rituximab it's used for other autoimmune diseases as well, right? NF: Yes. Lots of them. PB: So, you're just calling out specific ones for this guideline? I think Lupus and Myasthenia are also some of them. What's the plan for those other autoimmune diseases it's being used for? NF: In terms of indications, we have some that are on label, and we have some that are off label. Generally, we include the labeled ones and then we refer to the off-label policies for rituximab and other drug indications. PB: So, you're saying those other ones are off label, the ones I mentioned? NF: Which ones specifically? PB: Lupus and Myasthenia Gravis. NF: Lupus is off label and myasthenia gravis is also off label. Guideline (Changes): **Immunoglobulin Therapy (IVIG)** - Pg. 383 you can see the section for chronic inflammatory demyelinating polyneuropathy. - We're adding that the use of corticosteroids is not required for the pure motor variety and the guidelines it's recommended that IVIG treatment is the first choice for pure motor IPD. Guideline (Changes): **Reblozyl (luspatercept-aamt)** - Pg. 385 here we're updating the myelodysplastic syndrome section to account for the new indication to treat anemia without previous ESA agent use in adult patients with very low to intermediate risk myelodysplastic syndrome who may require red blood cell transfusion. - So, the new indication for those patents regardless of their erythropoietin levels allows them to have myelodysplastic syndrome with or without ring sideroblasts to qualify for treatment. We're taking all the parts out about that.		
IX) Informational Updates on New Developments in Pharmacy	N. Felten	<u>New Product Review</u> • New Products were discussed.		

BRAND NAME	GENERIC NAME/DOSAGE FORM	RECOMMENDATION
Immphentiv	phenylephrine 0.5 mg/5 ml, 1 mg/10 ml intravenous vial	Non-formulary
Meropenem	meropenem 2 g intravenous vial	Non-formulary
Adalimumab-aacf	adalimumab-aacf 40 mg/0.8 ml subcutaneous auto-injector	Non-formulary
Augtyro	repotrectinib 40 mg oral capsules	Non-formulary
Zemaira	alpha1-proteinase inhibitor (human) 4000 mg, 5000 mg intravenous vials	Non-formulary
Xalkori	crizotinib 20 mg, 50 mg, 150 mg oral pellet capsules	Non-formulary
Cabtreo	clindamycin phosphate/ adapalene/benzoyl peroxide 1.2%-0.15%-3.1% topical gel	Non-formulary
Truqap	capivasertib 160 mg, 200 mg oral tablets	Non-formulary
Amjevita	adalimumab-atto 20 mg/0.2 ml, 40 mg/0.4 ml subcutaneous syringe; 40 mg/0.4 mL, 80 mg/0.8 ml subcutaneous auto-injector	Non-formulary

			Adzynma	ADAMTS13, recombinant-krhn 500 unit, 1500 unit intravenous vials	Non-formulary (see new PAD)			
			Loqtorzi	toripalimab-tpzi 240 mg/6 ml intravenous vial	Non-formulary			
			Yuflyma	adalimumab-aaty 80 mg/0.8 mL subcutaneous auto-injector	Non-formulary			
			Jylamvo	methotrexate 2 mg/ml oral solution	Non-formulary			
			Ogsiveo	nirogacestat 50 mg oral tablets	Non-formulary			
			Bijuva	estradiol/progesterone 0.5 mg-100 mg oral capsule	Non-formulary			
			Coxanto	oxaprozin 300 mg oral capsules	Non-formulary			
			Fabhalta	iptacopan 200 mg oral capsules	Non-formulary (see new MRG)			
			Rezipres	ephedrine hydrochloride 47 mg/10 ml intravenous vial	Non-formulary			
			Casgevy	exagamglogene autotemcel intravenous suspension	Non-formulary (see new PAD)			
			Lyfgenia	lovotibeglogene autotemcel intravenous suspension	Non-formulary (see new PAD)			

			Vevye	cyclosporine 0.1% ophthalmic solution	Non-formulary			
			iDose TR	travoprost 75 mg intracameral implant	Non-formulary			
			Zituvio	sitagliptin 25 mg, 50 mg, 100 mg oral tablets	Non-formulary (see updated MRG)			
			Zoryve	roflumilast 0.3% topical foam	Non-formulary			
			Breyna	budesonide/formoterol 80 mcg-4.5 mcg, 160 mcg-4.5 mcg inhaler	Non-formulary			
			Penbraya	meningococcal groups A, B, C, W, and Y intramuscular vaccine	F-QL-AL (0.5ml per dose) (2 fills per lifetime) (max age 25 years) (already added via CRF)			
			Wainua	eplontersen 45 mg/0.8 ml subcutaneous auto-injector	Non-formulary			
			Ixchiq	chikungunya intramuscular vaccine, live	Non-formulary			
			Zenpep	pancrelipase 60,000 units (lipase)-189,600 units (protease)-252,600 units (amylase) delayed-release oral capsules	F-AL (min 21 years) (already added via CRF)			
			Iwilfin	eflornithine 192 mg oral tablets	Non-formulary			

			Bosulif	bosutinib 50 mg, 100 mg oral capsules	Non-formulary			
			Zilbrysq	zilucoplan 16.6 mg/0.416 ml, 23 mg/0.574 ml, 32.4 mg/0.81 ml subcutaneous syringe	Non-formulary			
			Agamree	vamorolone 40 mg/ml oral suspension	Non-formulary (see updated MRG)			
			Tramadol	tramadol 25 mg oral tablet	Non-formulary			
			Hemlibra	emicizumab-kxwh 300 mg/2 ml subcutaneous vial	Non-formulary			
			Combogesic	ibuprofen/acetaminophen 300 mg-1000 mg/100 ml intravenous vial	Non-formulary			
			Rivfloza	nedosiran 128 mg/0.8 ml, 160 mg/ml subcutaneous syringe; nedosiran 80 mg/0.5 ml subcutaneous vial	Non-formulary (see updated PAD)			
			Udenyca	pegfilgrastim-cbqv 6 mg/0.6 ml subcutaneous syringe with on-body injector	Non-formulary			
			DefenCath	taurolidine/heparin 40.5 mg-3000 units/3 ml instillation vial	Non-formulary			
X) Old Business		None						

XI) Public Comment	N. Felten	• No comment		
Adjournment	D. Carey	• P&T Committee Member Forms **Meeting adjourned at 6:23PM**	None	

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New Physician Administered Drug (PAD) Guidelines Alameda Q2 2024 P&T

New

Amtagvi	
Medications	Amtagvi (lifileucel)
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	• Uncontrolled brain metastases • Melanoma of uveal or ocular origin • Systemic steroid therapy for any reason
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	According to package insert
Prescriber Restrictions	Prescriber must be an oncologist
Coverage Duration	If all of the criteria are met, the initial request will be approved for a one-time treatment
Other Criteria	**Initial Authorization:** • Diagnosis of unresectable or metastatic melanoma (Stage IIIc or Stage IV) • Member must have progressed through at least one prior systemic therapy including a PD-1/PD-L1 blocking antibody and, if BRAF V600 mutation–positive, a BRAF inhibitor or BRAF inhibitor in combination with a MEK inhibitor • Member must have at least one resectable lesion (or aggregate of lesions resected) of a minimum 1.5 cm in diameter post-resection • Eastern Cooperative Oncology Group (ECOG) score of 0 or 1 • Medication is prescribed at an FDA approved dose **The safety and effectiveness of repeat administration of Amtagvi has 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 P&T Review Date	6/2024

New

Lenmeldy	
Medications	Lenmeldy (atidarsagene 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	N/A
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age According to package insert
Prescriber Restrictions	Prescribed by a neurologist or geneticist
Coverage Duration	If all of the criteria are met, the initial request will be approved for a one-time treatment

Other Criteria	**Initial Authorization:**
	• Member has diagnosis of one of the following metachromatic leukodystrophies (MLD):
	  ○ Pre-symptomatic late infantile (PSLI) MLD
	  ○ Pre-symptomatic early juvenile (PSEJ) MLD
	  ○ Early symptomatic early juvenile (ESEJ) MLD
	• Documentation patient has both of the following:
	  ○ Arylsulfatase A (ARSA) activity below the normal range (normal range 31-198 nmol/mg/h)
	  ○ Identification of two disease-causing ARSA alleles
	• Medication is prescribed at an FDA approved dose
	
	The safety and effectiveness of repeat administration of Lenmeldy has 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 P&T Review Date	6/2024

New Medication Request Guidelines (MRGs) Alameda Q2 2024 P&T

New

Filsuvez	
Therapeutic Classes (AHFS)	Skin and Mucous Membrane Agents, Misc
Medications	Filsuvez (birch triterpenes)
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	• Other forms of epidermolysis bullosa, such as epidermolysis bullosa simplex, kindler epidermolysis bullosa • Concurrent use of Filsuvez and Vyjuvek
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age Per prescribing information
Prescriber Restrictions	Prescriber must be a dermatologist, geneticist, or specialist experienced in the treatment of epidermolysis bullosa
Coverage Duration	**Initial Approval** 3 months **Later Approvals** 6 months If conditions are not met, the request will be sent to a clinical reviewer
PA Review Criteria	**Initial Authorization:** • Patient has a diagnosis of dystrophic or junctional epidermolysis bullosa, with genetic mutation(s) confirmed via genetic testing • Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected • Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated • Medication is prescribed at an FDA approved dose, and maximum dispensable amount is not exceeded o Documentation of size of treatment area(s) and frequency of dressing changes is required. One tube of Filsuvez covers up to 250 cm^2 surface area. Requests exceeding use more than once daily will not be approved. **Re-Authorization:** • Documentation or provider attestation of positive clinical response (i.e. improvement in wound appearance, wound closure, healing, etc.) • Documentation indicating need for continued treatment is needed (either to partially healed wounds or to other wound sites) • Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected • Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated • Medication is prescribed at an FDA approved dose, and maximum dispensable amount is not exceeded. o Documentation of size of treatment area(s) and frequency of dressing changes is required. One tube of Filsuvez covers up to 250 cm^2

	surface area. Requests exceeding use more than once daily will not be approved.
Criteria Statement	Filsuvez is reserved for members who have a diagnosis of dystrophic or junctional epidermolysis bullosa with wound(s) that do not appear infected, clean with adequate granulation tissue, excellent vascularization and no evidence of squamous cell carcinoma.
Last P&T Review Date	06/2024

New

Complement Inhibitors for the Treatment of Myasthenia Gravis	
Therapeutic Classes (AHFS)	Complement Inhibitors
Medications	Zilbrysq (zilucoplan) 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	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age ≥ 18 years
Prescriber Restrictions	Prescribed by a neurologist or rheumatologist
Coverage Duration	Initial request: 6 months Continuation of therapy: 12 months If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review

PA Review Criteria	**Initial Authorization:**
	• Diagnosis of generalized myasthenia gravis (gMG)
	  ○ Patient has a positive serological test for Anti-AChR antibodies
	• Patient has a Myasthenia Gravis Foundation of America (MGFA) clinical classification of class II, III or IV
	• Patient has tried and failed, or has contraindication, to one of the following:
	  ○ Two (2) or more conventional therapies (i.e. acetylcholinesterase inhibitors, corticosteroids, non-steroidal immunosuppressive therapies)
	  ○ Failed at least 1 conventional therapy and required chronic plasmapheresis or plasma exchange or intravenous immunoglobulin
	• Medication is prescribed at an FDA approved dose
	• No concurrent use of Vyvgart, Vyvgart Hytrulo, Rystiggo, Soliris, or Ultomiris
	• Documentation patient complies with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal infections in patients receiving a complement inhibitor
	
	Re-Authorization:
	• Provider has submitted documentation of clinical response to therapy (e.g., reduction in disease severity, improvement in quality-of-life scores, MG-ADL scores, etc).
	• Medication is prescribed at an FDA approved dose.

Criteria Statement	Zilbrysq is reserved for members who have a diagnosis of generalized myasthenia gravis clinical classification of class II, III or IV and have tried and failed 2 or more conventional therapies or at least 1 conventional therapy and required chronic plasmapheresis or plasma exchange or intravenous immunoglobulin, and who have complied with the ACIP current vaccination recommendations against meningococcal infections in patients receiving a complement inhibitor.
Last P&T Review Date	6/2024

New

Eohilia	
Therapeutic Classes (AHFS)	Glucocorticoids
Medications	Eohilia (budesonide)
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	Prescribed by gastroenterologist, allergist, immunologist, or other provider who specializes in the treatment of eosinophilic esophagitis (EoE)
Coverage Duration	If the criteria are met, the request will be approved for 3 months Reauthorization requests will not be approved as Eohilia has not been shown to be safe and effective for the treatment of EoE for longer than 12 weeks If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review
PA Review Criteria	• Diagnosis of EoE as confirmed by esophageal biopsy indicating ≥15 eosinophils per high-power field (eos/hpf) • Member must have experienced dysphagia for at least 4 days over a 2-week period • Documented trial and failure, intolerance, or contraindication to one proton pump inhibitor (PPI) at a maximally tolerated dose for a minimum of 8 weeks • Documented trial and failure, intolerance, or contraindication to an inhaled corticosteroid that can be swallowed (i.e., fluticasone, ciclesonide, mometasone, etc.) • Request is for an FDA-approved dose
Criteria Statement	Eohilia is reserved for members who have a diagnosis of eosinophilic esophagitis (EoE), who have experienced dysphagia and have tried and failed or were unable to use PPI at a maximally tolerated dose for at least 8 weeks and inhaled corticosteroid that can be swallowed.
Last P&T Review Date	6/2024

New

Wegovy	
Therapeutic Classes (AHFS)	Incretin Mimetics
Medications	Wegovy (semaglutide) injection ****Please Note: If the request is for Wegovy 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 Wegovy for a diagnosis of weight reduction and maintenance for overweight or obesity • Concurrent use of any glucagon-like-peptide-1 receptor agonist • Personal history of Type 1 or Type 2 diabetes • Personal or family history of medullary thyroid carcinoma • Multiple Endocrine Neoplasia syndrome type 2
Required Clinical Information	See “PA Review Criteria”
Age Restrictions	Member must be ≥ 45 years of age
Prescriber Restrictions	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	**<u>Initial Authorization:</u>**
	• 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:
	  o Prior myocardial infarction
	  o Prior stroke
	  o 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)
	• Documentation is provided patient's Hb A1c ≤ 6.5%
	
	<u>Re-Authorization:</u>
	• 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

Criteria Statement	Wegovy is reserved for members who are overweight or obese, have an established cardiovascular disease, receive standard of care treatment for CVD, have Hb A1c ≤ 6.5% and do not have diabetes.
Last P&T Review Date	6/2024

Drug Name: Rezdiffra (resmetirom)

Manufacturer: Madrigal Pharmaceuticals

Approval Date: 3/14/2024

Marketing Date: 3/19/2024

Prescribing Information

Indication

In conjunction with diet and exercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis).

This indication is approved under accelerated approval based on improvement of NASH and fibrosis. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Limitations of Use

Use of Rezdiffra™ should be avoided in patients with decompensated cirrhosis.

Mechanism of Action

Resmetirom is a partial agonist of the thyroid hormone receptor-beta (THR-β). Resmetirom produced 83.8% of the maximum response compared to triiodothyronine (T3), with a half maximal effective concentration of 0.21 µM in an in vitro functional assay for THR-β activation. The same functional assay for thyroid hormone receptor-alpha (THR-α) agonism showed 48.6% efficacy for resmetirom relative to T3, with a half maximal effective concentration of 3.74 µM. THR-β is the major form of THR in the liver, and stimulation of THR-β in the liver reduces intrahepatic triglycerides, whereas actions of thyroid hormone outside the liver, including in heart and bone, are largely mediated through THR-α.

Dosage and Administration

The recommended dosage of Rezdiffra™ is based on actual body weight. For patients weighing:

- <100 kg, the recommended dosage is 80 mg orally once daily
- ≥100 kg, the recommended dosage is 100 mg orally once daily

Black Box Warning

None

Adverse Reactions

Most common (reported in at least 5% of patients and higher compared to placebo): Diarrhea, nausea, pruritus, vomiting, constipation, abdominal pain, and dizziness

Serious: Hepatotoxicity and gallbladder-related adverse reactions

Use in Specific Populations, Pregnancy

There are no available data on Rezdiffra™ use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus related to underlying NASH with liver fibrosis, such as increased risks of gestational diabetes, hypertensive complications, preterm birth, and postpartum hemorrhage.

In animal reproduction studies, adverse effects on embryo-fetal development occurred in pregnant rabbits treated with resmetirom at 3.5 times the maximum recommended dose during organogenesis. These effects were associated with maternal toxicity, whereas no embryo-fetal effects were observed at lower dose levels with better tolerance in pregnant rabbits. No embryo-fetal developmental effects occurred in pregnant rats treated with resmetirom or the metabolite MGL-3623. A pre- and postnatal development study in rats with maternal dosing of resmetirom during organogenesis through lactation showed a decrease in birthweight and increased incidence of stillbirths and mortality (postnatal days 1-4) at 37 times the maximum recommended dose.

Drug Interactions

Strong or Moderate CYP2C8 Inhibitors: Resmetirom is a CYP2C8 substrate. Concomitant use with a strong or moderate CYP2C8 inhibitor can increase resmetirom C_{max} and area under the curve (AUC), which may increase the risk of Rezdiffra™ adverse reactions. Concomitant use of Rezdiffra™ with strong CYP2C8 inhibitors (e.g., gemfibrozil) is not recommended. The dosage of Rezdiffra™ should be reduced if used concomitantly with a moderate CYP2C8 inhibitor (e.g., clopidogrel).

Organic Anion-Transporting Polypeptides (OATP) 1B1 and OATP1B3 Inhibitors: Resmetirom is an OATP1B1 and OATP1B3 substrate. Concomitant use with OATP1B1 and OATP1B3 inhibitors may increase resmetirom C_{max} and AUC, which may increase the risk of Rezdiffra™ adverse reactions. Concomitant use of Rezdiffra™ with OATP1B1 or OATP1B3 inhibitors (e.g., cyclosporine) is not recommended.

Statins (Atorvastatin, Pravastatin, Rosuvastatin, or Simvastatin): Rezdiffra™ increased plasma concentrations of some statins (atorvastatin, pravastatin, rosuvastatin and simvastatin), which may increase the risk of adverse reactions related to these drugs. Rosuvastatin and simvastatin dosage should be limited to 20 mg daily and pravastatin and atorvastatin dosage should be limited to 40 mg daily.

CYP2C8 Substrates: Resmetirom is a weak CYP2C8 inhibitor. Resmetirom increases exposure of CYP2C8 substrates, which may increase the risk of adverse reactions related to these substrates. Patients should be monitored more frequently for substrate-related adverse reactions if Rezdiffra™ is co-administered with CYP2C8 substrates where minimal concentration changes may lead to serious adverse reactions.

How Supplied

Oral tablets: 60 mg, 80 mg, 100 mg

Price

$3,950

(Per month, based on WAC.)

Clinical Studies

Ongoing

Title	A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis (MAESTRO-NASH) NCT: 03900429 PMID: 38324483
Design	Phase 3, 54-month, randomized, double-blind, placebo-controlled trial to determine if 80 or 100 mg resmetirom as compared with placebo resolves NASH and/or reduces fibrosis on liver biopsy and prevents progression to cirrhosis and/or advanced liver disease
Population	N=966 Demographic and baseline characteristics were balanced between treatment and placebo groups. Overall, the median age of patients at baseline was 58 years, 56% were female, 21% were Hispanic, 89% were White, 3% were Asian, and 2% were Black or African American. Median body mass index (BMI) was 35 kg/m^2 and median body weight was 99 kg.
Arms	Patients were randomized 1:1:1 to receive either placebo (N=321), resmetirom 80 mg once daily (N=322), or resmetirom 100 mg once daily (N=323), in addition to lifestyle counseling on nutrition and exercise
Endpoint(s)	Primary: • NASH resolution (including a reduction in the nonalcoholic fatty liver disease [NAFLD] activity score by ≥2 points; scores range from 0 to 8, with higher scores indicating more severe disease) with no worsening of fibrosis at week 52 • Improvement (reduction) in fibrosis by at least one stage with no worsening of the NAFLD activity score at week 52 Secondary: • Reduction of low-density lipoprotein cholesterol (LDL-C) levels at week 24
Inclusion Criteria	• Adults ≥ 18 years of age • Biopsy-confirmed NASH and a fibrosis stage of F1B, F2, or F3 (stages range from F0 [no fibrosis] to F4 [cirrhosis]) • NAFLD Activity Score (NAS) of at least 4
Exclusion Criteria	• History of significant alcohol consumption for a period of more than 3 consecutive months within 1 year prior to screening • Regular use of drugs historically associated with NAFLD • Thyroid diseases including active hyperthyroidism and untreated clinical hypothyroidism (defined by thyroid stimulating hormone [TSH] >7 IU/L with symptoms of hypothyroidism or >10 IU/L without symptoms) • History of bariatric surgery or intestinal bypass surgery within the 5 years prior to randomization

	• Recent significant weight gain or loss • Hemoglobin A1c (HbA1c) ≥ 9.0% • Glucagon-like peptide 1 (GLP-1) agonist, high dose Vitamin E (> 400 IU/day), or pioglitazone therapy unless stable dose for 24 weeks prior to biopsy • Presence of cirrhosis on liver biopsy defined as stage 4 fibrosis • Diagnosis of hepatocellular carcinoma (HCC) • Model for End-Stage Liver Disease (MELD) score ≥12 • Hepatic decompensation • Chronic liver diseases other than NASH • Active autoimmune disease • Serum alanine aminotransferase (ALT) >250 U/L
Results	Primary: • NASH resolution with no worsening of fibrosis was achieved in 25.9% of the patients in the 80 mg resmetirom group and 29.9% of those in the 100 mg resmetirom group, as compared with 9.7% of those in the placebo group (P<0.001 for both comparisons with placebo) • Fibrosis improvement by at least one stage with no worsening of the NAFLD activity score was achieved in 24.2% of the patients in the 80 mg resmetirom group and 25.9% of those in the 100 mg resmetirom group, as compared with 14.2% of those in the placebo group (P<0.001 for both comparisons with placebo) Secondary: • The change in low-density lipoprotein cholesterol levels from baseline to week 24 was −13.6% in the 80 mg resmetirom group and −16.3% in the 100 mg resmetirom group, as compared with 0.1% in the placebo group (P<0.001 for both comparisons with placebo) • Diarrhea and nausea were more frequent with resmetirom than with placebo; the incidence of serious adverse events was similar across trial groups: 10.9% in the 80 mg resmetirom group, 12.7% in the 100 mg resmetirom group, and 11.5% in the placebo group
Conclusion	Both the 80 mg dose and the 100 mg dose of resmetirom were superior to placebo with respect to NASH resolution and improvement in liver fibrosis by at least one stage.
Interpretation	Results from the MAESTRO-NASH trial demonstrate that resmetirom helped patients with NASH resolution and liver fibrosis improvement. Additional data will be necessary to confirm the clinical benefit of resmetirom. This study is still ongoing and will measure clinical benefit on the composite endpoint of progression to cirrhosis, hepatic decompensation events, liver transplant, and mortality.
Completion Date	January 2028

Title	A Phase 3 Study to Evaluate Safety and Biomarkers of Resmetirom in Patients With Non-alcoholic Fatty Liver Disease (NAFLD), MAESTRO-NAFLD-Open-Label-Extension (MAESTRO-NAFLD-OLE)

	NCT: 04951219
Design	Phase 3, 52-week, multi-center, open-label, active treatment extension study to evaluate safety and tolerability of once daily, oral administration of resmetirom
Completion Date	April 2026

Title	A Phase 3 Study to Evaluate the Effect of Resmetirom on Clinical Outcomes in Patients With Well-compensated NASH Cirrhosis (MAESTRO-NASH-OUTCOMES) NCT: 05500222
Design	Phase 3, multi-national, multicenter, double-blind, randomized, placebo-controlled study in participants with well-compensated (Child-Pugh A) NASH cirrhosis.
Completion Date	January 2027

Guidelines

Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77(5):1797-1835.

Clinical guidelines have not been updated since the approval of Rezdiffra™. Current treatment recommendations as follows:

- Patients with NAFLD who are overweight or obese should be prescribed a diet that leads to a caloric deficit. When possible, diets with limited carbohydrates and saturated fat and enriched with high fiber and unsaturated fats (e.g., Mediterranean diet) should be encouraged due to their additional cardiovascular benefits.
- Patients with NAFLD should be strongly encouraged to increase their activity level to the extent possible. Individualized prescriptive exercise recommendations may increase sustainability and have benefits independent of weight loss.
- Bariatric surgery should be considered as a therapeutic option in patients who meet criteria for metabolic weight loss surgery, as it effectively resolves NAFLD or NASH in the majority of patients without cirrhosis and reduces mortality from cardiovascular disease (CVD) and malignancy.
- There are currently no FDA-approved medications for the treatment of NAFLD, but drugs approved to treat associated comorbidities with potential benefit in NAFLD may be considered in the appropriate clinical setting.
- Semaglutide can be considered for its approved indications (type 2 diabetes mellitus [T2DM]/obesity) in patients with NASH, as it confers a cardiovascular benefit and improves NASH.
- Pioglitazone improves NASH and can be considered for patients with NASH in the context of patients with T2DM.
- Vitamin E can be considered in select individuals as it improves NASH in some patients without diabetes.
- Available data on semaglutide, pioglitazone, and vitamin E do not demonstrate an antifibrotic benefit, and none has been carefully studied in patients with cirrhosis.

- Metformin, ursodeoxycholic acid, dipeptidyl peptidase-4, statins, and silymarin are well studied in NASH and should not be used as a treatment for NASH as they do not offer a meaningful histological benefit.

Clinical Opinions

NAFLD is the most common chronic liver condition in Western populations and is most often associated with comorbid obesity and type 2 diabetes. NASH is the most severe form of NAFLD and is characterized by an abnormal accumulation of fat in the liver. NASH affects an estimated 1.5% to 6.5% of U.S. adults. People with NASH are more likely to develop serious liver complications such as cirrhosis or liver cancer than individuals with NAFLD who do not have NASH. Due to its potential to cause serious liver complications, NASH is expected to become the leading cause of liver transplantation between 2020 and 2025. Prior to the approval of Rezdiffra™, there were no FDA-approved treatments for NAFLD or NASH. Common treatment strategies included management of obesity, type 2 diabetes, and cardiovascular risk factors, particularly because CVD is the leading cause of death in NASH patients. Off-label therapies such as vitamin E and pioglitazone are used in some patients with NASH, but there is limited data to support their use. Semaglutide is also used off-label, particularly in patients with concomitant type 2 diabetes and obesity, due to its weight loss and CVD reduction effects.

Rezdiffra™ (resmetirom) is a once-daily, oral, THR-β selective agonist. It is the first NASH treatment to be approved by the FDA, after dozens of other molecules have failed to show benefit in this patient population. Rezdiffra™ was approved under the FDA's accelerated approval pathway based on improvement of NASH and fibrosis in clinical trials. In the phase 3 MAESTRO-NASH trial, Rezdiffra™ met both its primary endpoints of NASH resolution with a ≥2 point reduction in the NAFLD activity score with no worsening of fibrosis and an improvement in fibrosis by at least one stage with no worsening of the NAFLD activity score after 52 weeks. The MAESTRO-NASH trial is still ongoing and will be used as the confirmatory trial to verify clinical benefit and potentially support full approval of Rezdiffra™. Although Rezdiffra™ is the first FDA-approved treatment for NASH, there are many therapies in the pipeline that will be expected over the next few years. Most notably, there are 4 GLP-1 receptor agonists in Phase 2 and 3 trials for NASH: semaglutide, tirzepatide, survodutide, and efinopegdutide. Agents in Phase 2 trials (i.e., tirzepatide, survodutide, and efinopegdutide) could be approved for NASH in 2027, while semaglutide could be approved for NASH as early as 2025.

Alternatives

None

Medication Request Guideline

New:

Rezdiffra	
Therapeutic Classes (AHFS)	Hepatotropics
Medications	Rezdiffra (resmetirom)
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	• Patients with decompensated cirrhosis
	• Patient with thyroid disease including:
	  ○ active hyperthyroidism
	  ○ untreated hypothyroidism (TSH >7 IU/L with symptoms of HT or >10 IU/L without symptoms

Required Clinical Information	See "PA Review Criteria"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age According to package insert
Prescriber Restrictions	Prescriber must be a hepatologist, gastroenterologist, or a specialist in the treatment of liver disease
Coverage Duration	**Initial Approval** Up to a 12 month duration **Later Approvals** Up to a 12 month duration 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 noncirrhotic nonalcoholic steatohepatitis (NASH) 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 • The drug is being prescribed at an FDA approved dose according to the member's weight **Re-Authorization:** • The member has clinically benefited from the medication (e.g. the resolution of steatohepatitis and no worsening of liver fibrosis, or at least one stage improvement in liver fibrosis and no worsening of steatohepatitis) • The member continues to have a fibrosis stage of ≤ 3 • The drug is being prescribed at an FDA approved dose according to the member's weight
Criteria Statement	Rezdiffra is reserved for members who have a diagnosis of noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis stage F2 to F3, who were provided lifestyle counseling on nutrition and exercise, and avoid excess alcohol intake.
Last P&T Review Date	6/2024

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PERFORMRx℠

Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists
Executive Summary

CLASS OVERVIEW

Migraine is a disabling disease with high individual and societal costs. Migraine is ranked as the third most prevalent disease in the world, as well as the third highest cause of disability in persons younger than age 50. Migraines affect 12% of the U.S. population, women more than men, and has a higher prevalence in middle age. The pathophysiology of migraine is multifactorial, influenced by both genetics and the environment. According to the International Classification of Headache Disorders, third edition (ICHD-3) criteria, migraines are classified as episodic or chronic, based on frequency of occurrence. Episodic migraines are defined as occurring fewer than 15 days per month. Chronic migraines are defined as occurring 15 or more days per month, having migraine features for eight days, and lasting for more than three months. In the U.S., episodic migraines are estimated to comprise 90% of cases, and chronic migraines 10% of cases. Migraines are treated acutely with abortive medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and triptans, and prophylactically with antiepileptics, antidepressants, and antihypertensives.

CGRP antagonists are a fairly new class of agents. The mechanism of action has not been fully elucidated; however, stimulation of the trigeminal ganglion and subsequent release of CGRP are thought to be migraine triggers by mediating pain transmission from intracranial vessels to the central nervous system and the vasodilatory component of neurogenic inflammation. There are currently four injectable CGRP antagonists: Aimovig® (erenumab-aooe), Ajovy® (fremanezumab-vfrm), Emgality® (galcanezumab-gnlm), and Vyepti® (eptinezumab-jjmr). All injectable CGRP antagonists are indicated for the preventative treatment of migraines and are administered subcutaneously (SQ), with the exception of Vyepti®, which is administered intravenously (IV). There are also three oral CGRP antagonists, Ubrelvy® (ubrogepant), Nurtec® ODT (rimegepant), and Qulipta® (atogepant). Ubrelvy® is indicated for acute migraine treatment, while Qulipta® is indicated for migraine prevention. Nurtec® ODT, meanwhile, is currently the only CGRP antagonist indicated for both acute and prophylactic treatment of migraine. Additionally, in 2023, Zavzpret™ (zavegepant) was approved as the first intranasal CGRP antagonist and is indicated for acute migraine treatment.

UTILIZATION FINDINGS

There were 7 claims for 4 members, for a total cost of $5,576 and an average cost per claim of $797. The most highly utilized medication was Emgality 120 mg/mL subcutaneous injection, with 5 claims, followed by Zavzpret 10mg nasal spray with 2 claims. There were 4 prior authorizations with 2 approvals (50%).

RECOMMENDATIONS

- Change from F-PA to NF to maintain favorable pricing on currently preferred products Emgality and Ubrelvy and obtain favorable pricing on Ajovy
    - Aimovig (erenumab-aooe) 70 mg/mL, 140 mg/ml subcutaneous auto-injectors
    - Nurtec ODT (rimegepant) 75 mg oral disintegrating tablets
    - Reyvow (lasmiditan) 50 mg and 100 mg oral tablets
- Change from NF to F-PA due to availability of preferred pricing
    - Add Zavzpret (zavegepant) 10 mg nasal spray to the formulary with a PA requirement

CLINICAL SUMMARY

The pathophysiology of migraine is multifactorial, influenced by both genetics and the environment. It was previously thought that the migraine headache was caused by the dilation of blood vessels, while the aura (sensory disturbances such as flashes of light or blind spots) was a result of vasoconstriction. It is now suggested that migraines are the result of a long sequence of changes in the body, including activation of the trigeminovascular system, and stimulation of the trigeminal ganglion resulting in release of various vasoactive neuropeptides, such as substance P, CGRP, and neurokinin A. According to the ICHD-3 criteria, migraines are classified as episodic or chronic, based on frequency of occurrence. Episodic migraines are defined as occurring <15 days per month; chronic migraines are defined as occurring on ≥ 15 days per month, having migraine features for eight days, and lasting for >3 months. In the U.S., episodic migraines are estimated to comprise 90% of cases, and chronic migraines 10% of cases.

Prophylactic treatment of migraines generally consists of the use of antiepileptics, antidepressants, and antihypertensives. Propranolol, timolol, divalproex sodium, valproic acid, and topiramate carry FDA labeled indications to prevent migraine, with no reference to migraine type (e.g., episodic or chronic). Amitriptyline carries an off-label indication for migraine prophylaxis, while Botox® (onabotulinum toxinA) is FDA approved to treat chronic migraine. American Academy of Neurology (AAN) guidelines related to the prevention of episodic migraine published in 2012 recommend as follows:

- Level A (established efficacy): divalproex sodium, sodium valproate, topiramate, propranolol, timolol, and frovatriptan (for menstrually related migraine [MRM] prevention).
- Level B (probable efficacy): amitriptyline, venlafaxine, atenolol, nadolol, naratriptan (MRM), and zolmitriptan (MRM).

The symptomatic, or acute treatment of migraine, consists of abortive medications, including NSAIDs, acetaminophen, and triptans. NSAIDs with reported efficacy in randomized trials for acute migraine include aspirin, ibuprofen, naproxen, and diclofenac. Acetaminophen is an effective abortive agent in some patients and can be used in combination with NSAIDs. Triptans are considered to be "specific" treatments for acute migraines and are highly efficacious at treating migraines. The choice of triptan is generally individualized, and patients who do not respond well to one triptan may respond to another. Ergots, including dihydroergotamine, have also been found to have some efficacy at treating acute migraine. American Headache Society (AHS) guidelines related to acute migraine treatment published in 2015 recommend as follows:

- Level A (established efficacy): almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan), and dihydroergotamine
- Level B (probable efficacy): acetaminophen, aspirin, diclofenac, ibuprofen, naproxen, butorphanol, sumatriptan/naproxen, acetaminophen/aspirin/caffeine, prochlorperazine, droperidol, chlorpromazine, metoclopramide, and octreotide

CGRP antagonists are a fairly new class of migraine agents. The mechanism of action has not been fully elucidated; however, stimulation of the trigeminal ganglion and subsequent release of CGRP are thought to be migraine triggers by mediating pain transmission from intracranial vessels to the central nervous system and the vasodilatory component of neurogenic inflammation. Aimovig® (erenumab-aooe), Ajovy® (fremanezumab-vfrm), and Emgality® (galcanezumab-gnlm) are all subcutaneous injectable monoclonal antibodies and indicated for the preventative treatment of migraines. Galcanezumab is currently the only CGRP antagonist that also has an indication for preventative treatment of cluster headache during cluster episodes in adults. Vyepti® (eptinezumab-jjmr) is also indicated for migraine prevention, however, it is the only CGRP antagonist that is administered IV and is done so once every 3 months.

In early 2020, Ubrelvy® (ubrogepant) and Nurtec™ ODT (rimegepant), were both approved for the acute treatment of migraine. Unlike the large monoclonal antibody CGRP antagonists, both ubrogepant and rimegepant are small molecule CGRP antagonists that pass through the blood brain barrier and can stop an acute migraine in progress. In May 2021, rimegepant received a second indication for the preventive treatment of episodic migraine in adults, making it the first CGRP antagonist indicated for both acute and prophylactic treatment of migraine. Rimegepant for migraine prevention is taken every other day, with the dose being the same strength as the one used for acute migraine treatment. In August

2021, Qulipta® (atogepant) became the third oral CGRP antagonist to hit the market. Dosed once daily, it is only indicated for the preventative treatment of migraine in adults, and cannot be used for acute migraine treatment. It should be noted that like the injectable CGRP antagonists, atogepant is indicated for both episodic and chronic migraine prevention, whereas rimegepant is only indicated for episodic migraine prevention. Zavzpret™ (zavegepant), approved in 2023, is the newest CGRP antagonist on the market. It is indicated for acute migraine treatment and is the only drug in this class that is administered intranasally. Looking forward in the pipeline, no novel CGRP antagonists are in development as the class is fairly saturated. However, an oral formulation of zavegepant is currently in phase 3 trials for migraine prevention.

With regards to management of CGRP antagonists, the AHS provided updated recommendations in 2021 for integrating new migraine treatments into clinical practice. For migraine prevention, the AHS recommends initiating CGRP antagonists in patients with migraine who have an inadequate response or an inability to tolerate (due to side effects) at least 2 of the following medications: topiramate, divalproex sodium/valproate sodium, beta-blocker (metoprolol, propranolol, timolol, atenolol, nadolol), tricyclic antidepressant (amitriptyline, nortriptyline), and serotonin-norepinephrine reuptake inhibitor (venlafaxine, duloxetine). For acute migraine treatment, the AHS recommends initiating CGRP antagonists in patients who have either an inadequate response to two or more oral triptans, or a contraindication to or inability to tolerate triptans.

Questions have been raised about the possibility of concurrent use of prophylactic CGRP antagonists and acute migraine CGRP antagonists. To date, there is very limited data with regards to concurrent use. Current evidence is primarily limited to case reports, which have demonstrated no safety issues and positive migraine results. Additionally, the current labeling for CGRP antagonists do not outright prohibit concurrent use. Therefore, it is a very realistic possibility that patients can be put on both prophylactic CGRP antagonists and acute migraine CGRP antagonists, which may pose an enormous financial burden for payers. Payers may want to consider restricting concomitant use due to the high costs and because some may consider it a form of duplicate therapy. It should be noted though, that among patients taking prophylactic CGRP antagonists, utilization of acute migraine treatments should ideally decline over time. There is also the theory that the acute migraine CGRP antagonists may be effective for migraine prevention and that use of the prophylactic CGRP antagonists may be impacted in the future.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Injectable CGRP Antagonists		
Aimovig® (erenumab-aooe)	Preventive treatment of migraine in adults	70 SQ once a month; some patients may benefit from 140 mg SQ monthly
Ajovy® (fremanezumab-vfrm)		225 mg SQ monthly or 675 mg SQ every 3 months
Vyepti® (eptinezumab-jjmr)		100 mg IV every 3 months; some patients may benefit from a dosage of 300 mg
Emgality® (galcanezumab-gnlm)		240 mg SQ once as a loading dose, followed by 120 mg SQ monthly
	Preventative treatment of cluster headache during cluster episodes in adults	300 mg SQ at the onset of the cluster period and then once monthly until the end of the cluster period
Oral CGRP Antagonists		
Ubrelvy® (ubrogepant)	Acute treatment of migraine with or without aura in adults	50 to 100 mg orally as a single dose; may repeat once based on response and tolerability after ≥2 hours; max dose of 200 mg per 24 hours
Nurtec® ODT (rimegepant)		75 mg orally as a single dose; max dose of 75 mg per 24 hours
	Preventive treatment of episodic migraine in adults	75 mg orally every other day
Qulipta® (atogepant)	Preventive treatment of episodic or chronic migraine in adults	Episodic migraine: 10 mg, 30 mg, or 60 mg orally once daily
		Chronic migraine: 60 mg orally once daily
Intranasal CGRP Antagonists		
Zavzpret™ (zavegepant)	Acute treatment of migraine with or without aura in adults	One spray (10 mg) in 1 nostril as a single dose; max dose of one spray (10 mg) per 24 hours

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Injectable CGRP Antagonists		
Aimovig® (erenumab-aooe)	None	None
Ajovy® (fremanezumab-vfrm)		
Emgality® (galcanezumab-gnlm)		
Vyepti® (eptinezumab-jjmr)		
Oral CGRP Antagonists		
Ubrelvy® (ubrogepant)	None	Concomitant use of strong CYP3A4 inhibitors
Nurtec® ODT (rimegepant)		None
Qulipta® (atogepant)		
Intranasal CGRP Antagonists		
Zavzpret™ (zavegepant)	None	None

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Injectable CGRP Antagonists	
Aimovig® (erenumab-aooe)	Concerns related to adverse effects: - Constipation, including cases with serious complications resulting in hospitalization and surgery, has been reported. Concurrent use of medications that decrease GI motility may increase the risk for more severe constipation and the potential for constipation-related complications. - Hypersensitivity reactions, including rash, angioedema, and anaphylaxis, have been reported. Most reactions are mild to moderate and occur within hours after administration, but some may be delayed for >1 week. - Hypertension: New-onset and worsening of preexisting hypertension, including cases requiring pharmacological treatment or hospitalization, have been reported. Onset most frequently reported after the initial dose and within 7 days of administration but may occur at any time. Disease related concerns: - Cardiovascular disease: May cause hypertension; use with caution in patients with hypertension or risk factors for hypertension.
Ajovy® (fremanezumab-vfrm)	Concerns related to adverse effects: - Hypersensitivity reactions, including rash, pruritus, drug hypersensitivity, and urticaria, have been reported. Most reactions were mild to moderate and were reported from within hours to 1 month after administration. Disease-related concerns: - Cardiovascular disease: Patients with a history of significant cardiovascular disease, vascular ischemia, or thrombotic events, such as cerebrovascular accident, transient ischemic attacks, deep vein thrombosis, or pulmonary embolism were excluded from clinical trials. Use with caution in these patients. Dosage form specific issues: - Polysorbate 80: May contain polysorbate 80 (also known as Tweens). Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals. Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates after receiving parenteral products containing polysorbate 80. Other warnings/precautions: - Immunogenicity: Anti-fremanezumab antibodies and neutralizing antibodies may develop.
Emgality® (galcanezumab-gnlm)	Concerns related to adverse effects: - Hypersensitivity reactions, including anaphylaxis, angioedema, dyspnea, rash, and urticaria have been reported. Reactions may occur days after administration and may be prolonged. Disease-related concerns: - Cardiovascular disease: Patients with electrocardiogram (ECG) abnormalities compatible with an acute cardiovascular event and patients with a recent history of stroke, myocardial infarction, unstable angina, percutaneous coronary intervention, coronary artery bypass grafting, deep vein thrombosis, or pulmonary embolism were excluded from clinical trials. Use with caution in these patients.

Medication	Warnings/Precautions
	- Peripheral vascular disease: Patients with history of stroke, intracranial or carotid aneurysm, intracranial hemorrhage, vasospastic angina or Raynaud disease, or clinical evidence of peripheral vascular disease were excluded from cluster headache clinical trials. Use with caution in these patients. Dosage form specific issues: - Polysorbate 80: May contain polysorbate 80. Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals. Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates after receiving parenteral products containing polysorbate 80. Other warnings/precautions: - Appropriate use: Patients on any other migraine or cluster headache preventive treatment and patients with medication overuse headache were excluded from clinical trials. Use with caution in these patients. - Immunogenicity: Anti-galcanezumab antibodies and neutralizing antibodies may develop.
Vyepti® (eptinezumab-jjmr)	Dosage form specific issues: - Polysorbate 80: May contain polysorbate 80. Hypersensitivity reactions, usually a delayed reaction, have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals. Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates after receiving parenteral products containing polysorbate 80.
Oral CGRP Antagonists	
Ubrelvy® (ubrogepant)	Concerns related to adverse reactions: - Signs of hypersensitivity reactions, including anaphylaxis, dyspnea, facial or throat edema, pruritus, rash, and urticaria, have occurred minutes, hours, or days after administration; majority of reactions were not serious and occurred within hours after administration. Disease-related concerns: - Dose reduction required in severe hepatic impairment. - Use is not recommended in patients with end-stage renal impairment; dose reduction required in severe renal impairment. Other warnings/precautions: - Appropriate use: Only indicated for treatment of acute migraine; not indicated for prevention of migraine.
Nurtec® ODT (rimegepant)	Concerns related to adverse effects: - Hypersensitivity reactions, including dyspnea, rash, and delayed serious reactions, have been reported. Disease-related concerns: - Use is not recommended in patients with severe hepatic impairment. - Use is not recommended in patients with end-stage renal disease. Other warnings and precautions: - Appropriate use: The safety of using more than 18 doses in a 30-day period has not been established.
Qulipta® (atogepant)	Concerns related to adverse effects:

Medication	Warnings/Precautions
	- Anaphylaxis, dyspnea, facial edema, pruritus, rash, and/or urticaria may occur. Hypersensitivity reactions may occur days after administration. Disease-related concerns: - Use is not recommended in patients with severe hepatic impairment. - Dose reduction or avoidance of use required in severe and end-stage renal impairment.
Intranasal CGRP Antagonists	
Zavzpret™ (zavegepant)	Concerns related to adverse effects: - Hypersensitivity reactions, including facial swelling and urticaria, may occur. Disease-related concerns: - Use is not recommended in patients with severe hepatic impairment. - Use is not recommended in patients with severe renal impairment (CrCl <30 mL/min). Other warnings/precautions: - Appropriate use: The safety of treating more than 8 migraines in a 30-day period has not been established.

7

PRACTICE GUIDELINES

US Department of Veterans Affairs (VA)/Department of Defense (DoD) Clinical Practice Guideline for Management of Headache (2023).

Pharmacotherapy

- Migraine – Preventative
  - We recommend candesartan or telmisartan for the prevention of episodic migraine (Strong for; Reviewed, New-replaced).
  - We recommend erenumab, fremanezumab, or galcanezumab for the prevention of episodic or chronic migraine (Strong for; Reviewed, New-replaced).
  - We suggest intravenous eptinezumab for the prevention of episodic or chronic migraine (Weak for; Reviewed, New-added).
  - We suggest lisinopril for the prevention of episodic migraine (Weak for; Reviewed, Not changed).
  - We suggest oral magnesium for the prevention of migraine (Weak for; Not reviewed, Not changed).
  - We suggest topiramate for the prevention of episodic and chronic migraine (Weak for; Reviewed, New-replaced).
  - We suggest propranolol for the prevention of migraine (Weak for; Reviewed, Not changed).
  - We suggest valproate for the prevention of episodic migraine (Weak for; Reviewed, New-replaced).
  - We suggest memantine for the prevention of episodic migraine (Weak for; Reviewed, New-added).
  - We suggest atogepant for the prevention of episodic migraine (Weak for; Reviewed, New-added).
  - We suggest onabotulinumtoxinA injection for the prevention of chronic migraine (Weak for; Reviewed, Not changed).
  - We suggest against abobotulinumtoxinA or onabotulinumtoxinA injection for the prevention of episodic migraine (Weak against; Reviewed, Not changed).
  - There is insufficient evidence to recommend for or against rimegepant for the prevention of episodic migraine (Neither for nor against; Reviewed, New-added).
  - We suggest against the use of gabapentin for the prevention of episodic migraine (Weak against; Reviewed, New-replaced).
  - There is insufficient evidence to recommend for or against levetiracetam for the prevention of episodic migraine (Neither for nor against; Reviewed, New-added).
- Migraine – Abortive
  - We recommend eletriptan, frovatriptan, rizatriptan, sumatriptan (oral or subcutaneous), the combination of sumatriptan and naproxen, or zolmitriptan (oral or intranasal) for the acute treatment of migraine (Strong for; Reviewed, New-replaced).
  - We recommend aspirin/acetaminophen/caffeine for the acute treatment of migraine (Strong for; Reviewed, New-added).
  - We suggest acetaminophen, aspirin, ibuprofen, or naproxen for the acute treatment of migraine (Weak for; Reviewed, Amended).
  - We suggest rimegepant or ubrogepant for the acute treatment of migraine (Weak for; Reviewed, New-added).
  - We suggest against intravenous ketamine for the acute treatment of migraine (Weak against; Reviewed, Amended).
  - There is insufficient evidence to recommend for or against lasmiditan for the acute treatment of migraine (Neither for nor against; Reviewed, New-added).
- Cluster Headache – Preventive
  - We suggest galcanezumab for the prevention of episodic cluster headache (Weak for; Reviewed, Not changed).
  - We suggest against galcanezumab for the prevention of chronic cluster headache (Weak against; Reviewed, New-added).

- There is insufficient evidence to recommend for or against verapamil for the prevention of episodic or chronic cluster headache (Neither for nor against; Reviewed, New-added).

- Cluster Headache – Abortive
  - We suggest subcutaneous sumatriptan (6 mg) or intranasal zolmitriptan (10 mg) for the acute treatment of cluster headache (Weak for; Reviewed, New-replaced).
  - We suggest the use of normobaric oxygen therapy for the acute treatment of cluster headache (Weak for; Not reviewed, Amended).

Non-pharmacologic Therapy

- We suggest non-invasive vagus nerve stimulation for the acute treatment of episodic cluster headache (Weak for; Reviewed, Not Changed).
- We suggest physical therapy for the management of tension-type, migraine, or cervicogenic headache (Weak for; Reviewed, New-replaced).
- We suggest aerobic exercise or progressive strength training for the prevention of tension-type and migraine headache (Weak for; Not reviewed, Amended).
- There is insufficient evidence to recommend for or against the following behavioral interventions for the treatment and/or prevention of headache (Neither for nor against; Reviewed, New-replaced):
  - Biofeedback and smartphone application-based heartrate variability monitoring
  - Cognitive behavioral therapy
  - Mindfulness-based therapies
  - Progressive muscle relaxation
- There is insufficient evidence to recommend for or against acupuncture, dry needling, or yoga for the treatment and/or prevention of headache (Neither for nor against; Reviewed, New-replaced).
- There is insufficient evidence to recommend for or against dietary trigger avoidance for the prevention of headache (Neither for nor against; Not Reviewed).
- There is insufficient evidence to recommend for or against any form of neuromodulation for the treatment and/or prevention of migraine (Neither for nor against; Reviewed, New-replaced):
  - Non-invasive vagus nerve stimulation
  - Supraorbital, or external trigeminal, nerve stimulation
  - Remote electrical neurostimulation
  - External combined occipital and trigeminal neurostimulation system
  - Repetitive transcranial magnetic stimulation
  - Transcranial direct current stimulation

Comparative Effectiveness and Combination Therapies

- There is insufficient evidence to recommend for or against any specific medication over another for the acute treatment of migraine (Neither for nor against; Reviewed, New-added).
- There is insufficient evidence to recommend for or against any specific medication over another for the prevention of migraine headache, tension headache, or cluster headache (Neither for nor against; Reviewed, New-added).
- There is insufficient evidence to recommend for or against any specific combination of therapies for the prevention of headache (Neither for nor against; Reviewed, New-replaced).

VA/DoD Recommendation Definitions

Strength of Recommendation	General Corresponding Text	Definition
Strong for/Strong against	We recommend…/We recommend against…	The Work Group is highly confident that desirable outcomes outweigh undesirable outcomes and vice-versa
Weak for/Weak against	We suggest…/We suggest against…	The Work Group is less confident of the balance between desirable and undesirable outcomes

Evidence Reviewed	Recommendation Category	Definition

Strength of Recommendation	General Corresponding Text	Definition
Reviewed	New-added	New recommendation
	New-replaced	Recommendation from previous clinical practice guideline was carried forward and revised
	Not changed	Recommendation from previous clinical practice guideline was carried forward but unchanged
	Amended	Recommendation from previous clinical practice guideline was carried forward with a nominal change
	Deleted	Recommendation from previous clinical practice guideline was deleted
Not Reviewed	Not changed	Recommendation from previous clinical practice guideline was carried forward but unchanged
	Amended	Recommendation from previous clinical practice guideline was carried forward with a nominal change
	Deleted	Recommendation from previous clinical practice guideline was deleted

Ailani J, Burch RC, Robbins MS; Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. Headache. 2021 Jul;61(7):1021-1039. doi: 10.1111/head.14153. Epub 2021 Jun 23.

Acute Treatment

- All patients with a confirmed diagnosis of migraine should be offered a trial of acute pharmacological and/or nonpharmacologic treatment
- Acute treatments considered effective or probably effective based on reviews of available evidence are presented in Table 1

Table 1 – Acute treatments with evidence of efficacy in migraine

Established Efficacy	Probably Effective
Triptans	Ergotamine
Ergotamine derivatives	Other forms of dihydroergotamine
Gepants	NSAIDs: flurbiprofen, ketoprofen, IV and intramuscular (IM) ketorolac
Lasmiditan	IV magnesium (in migraine with aura)
NSAIDs: aspirin, celecoxib oral solution, diclofenac, ibuprofen, naproxen	Isometheptene-containing compounds
Combination analgesic: acetaminophen + aspirin + caffeine	Antiemetics: chlorpromazine, droperidol, metoclopramide, prochlorperazine, promethazine

Criteria for Initiating Acute Treatment with Gepants, Ditans, or Neuromodulatory Devices

Use is appropriate when ALL of the following are met:

A. Prescribed/recommended by a licensed clinician
B. Patient is at least 18 years of age
C. Diagnosis of ICHD-3 migraine with aura, migraine without aura, or chronic migraine
D. Either of the following:
    a. Contraindications to or inability to tolerate triptans
    b. Inadequate response to two or more oral triptans, as determined by EITHER of the following

10

i. Validated acute treatment patient-reported outcome questionnaire (Migraine Treatment Optimization Questionnaire [mTOQ], Migraine Assessment of Current Therapy [Migraine-ACT], Patient Perception of Migraine Questionnaire-Revised [PPMQ-R], Functional Impairment Scale [FIS], Patient Global Impression of Change [PGIC])
ii. Clinical attestation

Preventative Treatment

- Patients with migraine should be considered for preventive treatment in any of the following situations:
  - Attacks significantly interfere with patients' daily routines despite acute treatment
  - Frequent attacks (Table 2)
  - Contraindication to, failure, or overuse of acute treatments, with overuse defined as:
    - 10 or more days per month for ergot derivatives, triptans, opioids, combination analgesics, and a combination of drugs from different classes that are not individually overused
    - 15 or more days per month for nonopioid analgesics, acetaminophen, and NSAIDs
  - Adverse events with acute treatments
  - Patient preference

Table 2 – Criteria for identifying patients for preventive treatment

Prevention should be…	Headache days/month	Degree of disability required[a]
Offered	6 or more	None
	4 or more	Some
	3 or more	Severe
Considered	4 or 5	None
	3	Some
	2	Severe

[a]As can be measured by the Migraine Disability Assessment Scale, Migraine Physical Function Impact Diary, or Headache Impact Test.

Table 3 – Medications with evidence of efficacy in migraine prevention

Established Efficacy		Probably Effective	
Oral	**Parenteral**	**Oral**	**Parenteral**
Candesartan	Eptinezumab	Amitriptyline	OnabotulinumtoxinA + CGRP monoclonal antibody
Divalproex sodium	Erenbumab	Atenolol	
Frovatriptan (short-term prevention of MRM)	Fremanezumab	Lisinopril	
Metoprolol	Galcanezumab	Memantine	
Propranolol	OnabotulinumtoxinA	Nadolol	
Timolol		Venlafaxine	
Topiramate			
Valproate sodium			

Criteria for Initiating Treatment with Monoclonal Antibodies to CGRP or its Receptor

Use is appropriate when A, B, and either C, D, or E are met

A. Prescribed by a licensed clinician
B. Patient is at least 18 years of age
C. Diagnosis of ICHD-3 migraine with or without aura (4–7 monthly headache days) and both of the following:
   a. Inability to tolerate (due to side effects) or inadequate response to an 8-week trial at a dose established to be potentially effective of at least 2 of the following:
      1. Topiramate
      2. Divalproex sodium/valproate sodium
      3. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
      4. Tricyclic antidepressant: amitriptyline, nortriptyline
      5. Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine

6. Other Level A or B treatments (established efficacy or probably effective) according to AAN scheme for classification of evidence

b. At least moderate disability (Migraine Disability Assessment [MIDAS] ≥11, Headache Impact Test [HIT-6] >50)

D. Diagnosis of ICHD-3 migraine with or without aura (8–14 monthly headache days) and inability to tolerate (due to side effects) or inadequate response to an 8-week trial of at least 2 of the following:
   a. Topiramate
   b. Divalproex sodium/valproate sodium
   c. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
   d. Tricyclic antidepressant: amitriptyline, nortriptyline
   e. Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
   f. Other Level A or B treatments (established efficacy or probably effective) according to AAN scheme for classification of evidence

E. Diagnosis of ICHD-3 chronic migraine and EITHER a or b:
   a. Inability to tolerate (due to side effects) or inadequate response to an 8-week trial of at least 2 of the following:
      1. Topiramate
      2. Divalproex sodium/valproate sodium
      3. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
      4. Tricyclic antidepressant: amitriptyline, nortriptyline
      5. Serotonin-norepinephrine reuptake inhibitor: venlafaxine, duloxetine
      6. Other Level A or B treatments (established efficacy or probably effective) according to AAN scheme for classification of evidence
   b. Inability to tolerate or inadequate response to a minimum of 2 quarterly injections (6 months) of onabotulinumtoxinA

<u>Criteria for Continuation of Monoclonal Antibodies to CGRP or its Receptor or Neuromodulation Therapy</u>

Reauthorization after initial use is appropriate when EITHER of the following criteria are met:

A. Reduction in mean monthly headache days of at least moderate severity of ≥50% relative to the pretreatment baseline (diary documentation or medical professional attestation)
B. A clinically meaningful improvement in ANY of the following validated migraine-specific patient-reported outcome measures:
   a. MIDAS
      i. Reduction of ≥5 points when baseline score is 11–20
      ii. Reduction of ≥30% when baseline scores >20
   b. Migraine Physical Function Impact Diary (MPFID)
      i. Reduction of ≥5 points
   c. HIT-6
      i. Reduction of ≥5 points

Mayans L, Walling A. Acute Migraine Headache: Treatment strategies. AAFP. 2019; 97(4):243-251.

- Nonsteroidal anti-inflammatory drugs are a first-line treatment for mild to moderate migraine. The choice of medication should be based on availability and adverse effect profile (Evidence Rating A).
- Triptans are a first-line treatment for moderate to severe migraine. Several triptans are available with different pharmacokinetics and routes of administration (Evidence Rating A).
- The choice of triptan should be individualized based on the patient's migraine characteristics and on the route of administration, pharmacokinetics, and cost (Evidence Rating C).
- Dopamine antagonist antiemetics are second-line treatments for migraine (Evidence Rating B).

12

- Parenteral dihydroergotamine (DHE 45), magnesium sulfate, valproate, and opioids should be reserved for refractory migraine because of adverse effects, weaker evidence of effectiveness, and/or abuse potential (Evidence Rating B).

American Academy of Family Physicians (AAFP) Evidence Rating Definitions

Evidence Rating	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

Marmura MJ, Silberstein SD, Schwedt J. Evidence Assessment of Migraine Pharmacotherapies. AHS. 2015; 55(1):3-20.

- The triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) and dihydroergotamine (nasal spray, inhaler) are effective at treating migraine (Level A).
- Ergotamine and other forms of dihydroergotamine are probably effective (Level B).
- Acetaminophen, NSAIDs (aspirin, diclofenac, ibuprofen, and naproxen), opioids (butorphanol nasal spray), sumatriptan/naproxen, and the combination of acetaminophen/aspirin/caffeine are probably effective (Level B).
- The antiemetics, prochlorperazine, droperidol, chlorpromazine, and metoclopramide are probably effective (Level B).
- Octreotide is probably not effective (Level B).
- There is inadequate evidence for butalbital, phenazone, tramadol, methadone, intranasal lidocaine, and corticosteroids (Level C).

Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-Based Guideline Update: Pharmacologic Treatment for Episodic Migraine Prevention in Adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology 78 (2012): 1337 – 45.

Level A. The following medications are established as effective and should be offered for migraine prevention:

- Antiepileptic drugs (AEDs): divalproex sodium, sodium valproate, topiramate
- β-Blockers: metoprolol, propranolol, timolol
- Triptans: frovatriptan (for short-term MRM prevention)

Level B. The following medications are probably effective and should be considered for migraine prevention:

- Antidepressants: amitriptyline, venlafaxine
- β-Blockers: atenolol, nadolol
- Triptans: naratriptan, zolmitriptan (for short-term MRM)

Level C. The following medications are possibly effective and may be considered for migraine prevention:

- ACE inhibitors: lisinopril
- Angiotensin receptor blockers: candesartan
- α-Agonists: clonidine, guanfacine
- AEDs: carbamazepine
- β-Blockers: nebivolol, pindolol

Level U. Evidence is conflicting or inadequate to support or refute the use of the following medications for migraine prevention:

- AEDs: gabapentin
- Antidepressants

    - Selective serotonin reuptake inhibitor/selective serotonin-norepinephrine reuptake inhibitors: fluoxetine, fluvoxamine
    - Tricyclics: protriptyline
- Antithrombotics: acenocoumarol, warfarin, picotamide
- β -Blockers: bisoprolol
- Calcium-channel blockers: nicardipine, nifedipine, nimodipine, verapamil
- Acetazolamide

Level A negative. The following medication is established as ineffective and should not be offered for migraine prevention:

- Lamotrigine

Level B negative. The following medication is probably ineffective and should not be considered for migraine prevention:

- Clomipramine

Level C negative. The following medications are possibly ineffective and may not be considered for migraine prevention:

- Acebutolol
- Clonazepam
- Nabumetone
- Oxcarbazepine
- Telmisartan

Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache. 2016;56(7):1093-106.

Acute Therapy of Cluster Headache:

Level A. The following medications are established as effective and should be offered for acute treatment of cluster headache:

- Sumatriptan (subcutaneous injection)
- Zolmitriptan (nasal spray)
- Oxygen

Level B. The following medications are probably effective and should be considered for acute treatment of cluster headache:

- Sumatriptan (nasal spray)
- Zolmitriptan (oral)
- Sphenopalatine ganglion stimulation

Level C. The following medications are possibly effective and may be considered for acute treatment of cluster headache:

- Cocaine/lidocaine (nasal spray)
- Octreotide (subcutaneous)

Level U. Evidence is conflicting or inadequate to support or refute the use of the following medications for acute treatment of cluster headache:

- Dihydroergotamine (nasal spray)
- Somatostatin
- Prednisone

Prophylactic Therapy of Cluster Headache:

Level A. The following medications are established as effective and should be offered for prophylactic treatment of cluster headache:

- Suboccipital steroid injection

Level B. The following medications are probably effective and should be considered for prophylactic treatment of cluster headache:

- Civaminde (nasal spray)

Level C. The following medications are possibly effective and may be considered for prophylactic treatment of cluster headache:

- Lithium
- Verapamil
- Warfarin
- Melatonin

Level U. Evidence is conflicting or inadequate to support or refute the use of the following medications for prophylactic treatment of cluster headache:

- Frovatriptan
- Capsaicin(intranasal)Prednisone
- Nitrate tolerance
- Prednisone

Level B negative. The following medication is probably ineffective and should not be considered for prophylactic treatment of cluster headache:

- Sodium valproate
- Sumatriptan
- Deep brain stimulation

Level C negative. The following medications are possibly ineffective and may not be considered for prophylactic treatment of cluster headache:

- Cimetidine/chlorpheniramine
- Misoprostol
- Oxygen (hyperbaric)
- Candesartan

AAN and AHS Recommendation Definitions

Classification of Recommendations	Definition
Level A	Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)*
Level B	Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)
Level C	Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)
Level U	Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome > 5 and the lower limit of the confidence interval is > 2).

Evidence Rating	Definition
Class I	A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required: a. concealed allocation b. primary outcome(s) clearly defined c. exclusion/inclusion criteria clearly defined d. adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias. e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required* 1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority.

Evidence Rating	Definition
	2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective). 3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment. 4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.
Class II	A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b–e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.
Class III	All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement. **
Class IV	Studies not meeting Class I, II or III criteria including consensus or expert opinion.

* Note that numbers 1–3 in Class Ie. are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

16

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Goadsby PJ, Reuter U, Hallström Y, et al. A Controlled Trial of Erenumab for Episodic Migraine. N Engl J Med. 2017 Nov 30;377(22):2123-2132.	Randomized (1:1:1), double blind, placebo-controlled, phase 3 study in adults with episodic migraine. 955 subjects were randomized to receive erenumab 70 mg monthly, 140 mg monthly or placebo.	• Primary: change in mean monthly migraine days from baseline over the last three months of the double-blind treatment phase of the study (months 4, 5 and 6) • Secondary: 50% or greater reduction in mean migraine days per month, change in the number of days of use of acute migraine-specific medication, and change in scores on the physical-impairment and everyday-activities domains of the Migraine Physical Function Impact Diary (scale 0-100 with higher scores representing greater migraine burden)
Results: By months 4 through 6, the number of mean monthly migraine days was reduced by 3.2 in the 70 mg erenumab group and by 3.7 in the 140 mg erenumab group, compared with 1.8 days in the placebo group (p<0.001 for both comparisons). A 50% or greater reduction in the mean number of migraine days per month was achieved for 43.3% of patients in the 70 mg erenumab group and 50.0% of patients in the 140 mg erenumab group, as compared with 26.6% in the placebo group (p<0.001 for both comparisons). The number of days of use of acute migraine-specific medication was reduced by 1.1 days in the 70 mg erenumab group and by 1.6 days in the 140 mg erenumab group, as compared with 0.2 days in the placebo group (p<0.001 for both comparisons). Physical-impairment scores improved by 4.2 and 4.8 points in the 70 mg and 140 mg erenumab groups, respectively, as compared with 2.4 points in the placebo group (p<0.001 for both comparisons), and everyday-activities scores improved by 5.5 and 5.9 points in the 70 mg and 140 mg erenumab groups, respectively, as compared with 3.3 points in the placebo group (p<0.001 for both comparisons). The rates of adverse events were similar between erenumab and placebo. **Conclusion**: Erenumab administered subcutaneously at a monthly dose of 70 mg or 140 mg significantly reduced migraine frequency, the effects of migraines on daily activities, and the use of acute migraine-specific medication over a period of 6 months. The long-term safety and durability of the effect of erenumab require further study.		
Citation	**Design**	**Endpoints**

Dodick DW, Ashina M, Brandes JL, et al. ARISE: A Phase 3 randomized trial of erenumab for episodic migraine. Cephalalgia. 2018 May;38(6):1026-1037.	Randomized (1:1), double-blind, placebo-controlled, phase 3 study in adults with episodic migraine. 577 subjects were randomized to receive erenumab 70 mg monthly or placebo.	• Primary: change from baseline at month 3 in mean monthly migraine days • Secondary (at month 3): ≥50% reduction in monthly migraine days, change in acute migraine-specific medication treatment days, and ≥5-point reduction in Physical Impairment and Impact on Everyday Activities domain scores measured by the Migraine Physical Function Impact Diary
Results: Patients receiving erenumab experienced -2.9 days change in monthly migraine days, compared with -1.8 days for placebo, least-squares mean (95% CI) treatment difference of -1.0 (-1.6, -0.5) ($p < 0.001$). A ≥ 50% reduction in monthly migraine days was achieved by 39.7% (erenumab) and 29.5% (placebo) of patients (OR: 1.59 (95% CI: 1.12, 2.27) ($p = 0.010$). Migraine-specific medication treatment days were reduced by -1.2 (erenumab) and -0.6 (placebo) days, a treatment difference of -0.6 (-1.0, -0.2) ($p = 0.002$). The ≥ 5-point reduction rates in Migraine Physical Function Impact Diary - Physical Impairment were 33.0% and 27.1% [OR: 1.33 (0.92, 1.90) ($p = 0.13$)] and in Migraine Physical Function Impact Diary - Everyday Activities were 40.4% and 35.8% [OR: 1.22 (0.87, 1.71) ($p = 0.26$)]. Safety and adverse event profiles of erenumab were similar to placebo. Most frequent adverse events were upper respiratory tract infection, injection site pain, and nasopharyngitis. **Conclusion**: As a preventive treatment of episodic migraine, erenumab at a dosage of 70 mg monthly significantly reduced migraine frequency and acute migraine-specific medication use.		
Citation	**Design**	**Endpoints**
Reuter U, Goadsby PJ, Lanteri-minet M, et al. Efficacy and tolerability of erenumab in patients with episodic migraine in whom two-to-four previous preventive treatments were unsuccessful: a randomised, double-blind, placebo-controlled, phase 3b study. Lancet. 2018;392(10161):2280-2287.	Randomized, double-blind, placebo-controlled phase 3 study in adults with episodic migraine. 246 subjects were randomized to receive erenumab 140 mg monthly or placebo.	• Primary: percentage of patients with a 50% response in the reduction of monthly migraine days at month 3
Results: At week 12, 30% of patients in the erenumab group had a 50% or greater reduction from baseline in the mean number of monthly migraine days, compared with 14% in the placebo group (odds ratio, 2.7 [95% CI, 1.4-5.2]; p=0.002). The tolerability and safety profiles of erenumab and placebo were similar. The most frequent treatment-emergent adverse event was injection site pain, which occurred in seven (6%) participants in both groups. **Conclusion**: Compared with placebo, erenumab was efficacious in patients with episodic migraine who previously did not respond to or tolerate between two and four previous migraine preventive treatments. Erenumab might be an option for patients with difficult-to-treat migraine who have high unmet needs and few treatment options.		
Citation	**Design**	**Endpoints**
Dodick DW, Silberstein SD, Bigal ME, et al. Effect of Fremanezumab Compared With Placebo for Prevention of Episodic Migraine: A Randomized Clinical Trial. JAMA. 2018 May 15;319(19):1999-2008.	Randomized (1:1:1), double-blind, placebo-controlled phase 3 study in adults with episodic migraine. 875 subjects were randomized to receive fremanezumab 225 mg monthly, fremanezumab 675 mg once (quarterly), or placebo.	• Primary: mean change from baseline in the monthly average number of migraine days (12 weeks); percentage of participants with adverse events (12 weeks).

Results: From baseline to 12 weeks, mean migraine days per month decreased from 8.9 days to 4.9 days in the fremanezumab monthly dosing group, from 9.2 days to 5.3 days in the fremanezumab single-higher-dose group, and from 9.1 days to 6.5 days in the placebo group. This resulted in a difference with monthly dosing vs placebo of –1.5 days (95% CI, –2.01 to –0.93 days; p < 0.001) and with single higher dosing vs placebo of –1.3 days (95% CI, –1.79 to –0.72 days; p < 0.001). The most common adverse events that led to discontinuation were injection site erythema (n = 3), injection site induration (n = 2), diarrhea (n = 2), anxiety (n = 2), and depression (n = 2). **Conclusion**: Among patients with episodic migraine in whom multiple medication classes had not previously failed, subcutaneous fremanezumab, compared with placebo, resulted in a statistically significant 1.3- to 1.5-day reduction in the mean number of monthly migraine days over a 12-week period. Further research is needed to assess effectiveness against other preventive medications and in patients in whom multiple preventive drug classes have failed and to determine long-term safety and efficacy.		
Citation	**Design**	**Endpoints**
Silberstein SD, Dodick DW, Bigal ME, et al. Fremanezumab for the Preventive Treatment of Chronic Migraine. N Engl J Med. 2017 Nov 30;377(22):2113-2122.	Randomized (1:1:1), double-blind, placebo-controlled phase 3 study in adults with chronic migraine. 1130 subjects were randomized to receive fremanezumab 225 mg monthly, fremanezumab 675 mg once (quarterly), or placebo.	• Primary: mean change from baseline in the monthly average number of headache days of at least moderate severity (12 weeks); adverse events
Results: The least-squares mean (±SE) reduction in the average number of headache days per month was 4.3±0.3 with fremanezumab quarterly, 4.6±0.3 with fremanezumab monthly, and 2.5±0.3 with placebo (p<0.001 for both comparisons with placebo). The percentage of patients with a reduction of at least 50% in the average number of headache days per month was 38% in the fremanezumab-quarterly group, 41% in the fremanezumab-monthly group, and 18% in the placebo group (p<0.001 for both comparisons with placebo). The most common adverse events reported in clinical trials include injection site induration, erythema, and pruritus. Abnormalities of hepatic function occurred in 5 patients in each fremanezumab group (1%) and 3 patients in the placebo group (<1%). Mild transient elevations in liver enzyme levels occurred, and the levels reverted to normal without discontinuation of the trial regimen. **Conclusion**: Fremanezumab as a preventive treatment for chronic migraine resulted in a lower frequency of headache than placebo in this 12-week trial. Injection-site reactions to the drug were common. The long-term durability and safety of fremanezumab require further study.		
Citation	**Design**	**Endpoints**
Detke HC, Goadsby PJ, Wang S, Friedman DI, Selzler KJ, Aurora SK. Galcanezumab in chronic migraine: The randomized, double-blind, placebo-controlled REGAIN study. Neurology. 2018;91(24):e2211-e2221.	Randomized (2:1:1), double-blind, placebo-controlled phase 3 study in adults with chronic migraine. 1113 subjects were randomized to receive placebo, galcanezumab 120 mg, or galcanezumab 240 mg.	• Primary: Mean change from baseline to month 3 in the number of monthly migraine headache days
Results: Both galcanezumab dose groups demonstrated greater overall mean reduction in the number of monthly migraine headache days compared to placebo (placebo -2.7, galcanezumab 120 mg -4.8, galcanezumab 240 mg -4.6) (p < 0.001 for each dose compared to placebo). There were no clinically meaningful differences between galcanezumab doses and placebo on any safety or tolerability outcome except for a higher incidence of treatment-emergent injection-site reaction (p < 0.01), injection-site erythema (p < 0.001), injection-site pruritus (p < 0.01), and sinusitis (p < 0.05) in the galcanezumab 240-mg group relative to placebo. **Conclusion**: This interventional study provides Class I evidence that galcanezumab is superior to placebo in the reduction of the number of monthly migraine headache days.		
Citation	**Design**	**Endpoints**
Stauffer VL, Dodick DW, Zhang Q, Carter JN, Ailani J, Conley RR. Evaluation of Galcanezumab for the Prevention of Episodic Migraine: The EVOLVE-1 Randomized Clinical Trial. JAMA Neurol. 2018 Sep 1;75(9):1080-1088.	Randomized, double-blind, placebo-controlled phase 3 study in adults with episodic migraine. 862 subjects were randomized to receive galcanezumab (240 mg starting dose followed by 120 mg or 240 mg monthly) or placebo	• Primary: Mean change from baseline to month six in the number of monthly migraine headache days

Results: Average reduction of 4.7 migraine days per month for 120 mg and 4.6 days for 240 mg compared with 2.8 days for PBO (p<0.001 for both). **Conclusion**: Galcanezumab 120-mg and 240-mg monthly provided clinical benefits and improved functioning with a low rate of adverse events.		
Citation	**Design**	**Endpoints**
Goadsby PJ, Dodick DW, Leone M, et al. Trial of Galcanezumab in Prevention of Episodic Cluster Headache. N Engl J Med. 2019;381(2):132-141.	Randomized, double-blind, placebo-controlled phase 3 study in adults with episodic cluster headache. A total of 106 patients were randomized to receive galcanezumab (300 mg) or placebo.	• Primary: Mean change from baseline in the weekly frequency of cluster headache attacks across 3 weeks after receipt of the first dose • Secondary: Percentage of patients who had a reduction from baseline of at least 50% in the weekly frequency of cluster headache attacks at week 3
Results: The mean reduction in the weekly frequency of cluster headache attacks across weeks 1-3 was 8.7 attacks in the galcanezumab group, as compared with 5.2 in the placebo group (difference, 3.5 attacks per week; 95% CI, 0.2 to 6.7; P = 0.04). The percentage of patients who had a reduction of at least 50% in headache frequency at week 3 was 71% in the galcanezumab group and 53% in the placebo group. There were no substantial between-group differences in the incidence of adverse events, except that 8% of the patients in the galcanezumab group had injection-site pain. **Conclusion**: Galcanezumab administered subcutaneously at a dose of 300 mg once monthly reduced the weekly frequency of attacks of episodic cluster headache across weeks 1-3 after the initial injection, as compared with placebo.		
Citation	**Design**	**Endpoints**
Dodick DW, Goadsby PJ, Lucas C, et al. Phase 3 randomized, placebo-controlled study of galcanezumab in patients with chronic cluster headache: Results from 3-month double-blind treatment. Cephalalgia. 2020;:333102420905321.	Randomized, double-blind, placebo-controlled phase 3 study in adults with chronic cluster headache. A total of 237 patients were randomized to receive galcanezumab (300 mg) or placebo.	• Primary: Mean change from baseline in the weekly frequency of cluster headache • Secondary: Percentage of patients who had a reduction from baseline of at least 50% in the weekly frequency of cluster headache
Results: The primary endpoint was not met; mean change in weekly attack frequency was -4.6 for placebo vs. -5.4 for galcanezumab (p = 0.334). Key secondary endpoints also were not met. Injection site-related treatment-emergent adverse events were more common in the galcanezumab group than the placebo group, with significantly more injection site erythema. **Conclusion**: Treatment with galcanezumab 300 mg did not achieve its primary and key secondary endpoints. This study underscores the potential distinct biology of chronic cluster headaches as well as the significant unmet need for safe, effective, and well-tolerated preventive treatment. The safety profile of galcanezumab in chronic cluster headache consistent with that observed in trials of episodic cluster headache and migraine.		
Citation	**Design**	**Endpoints**
Ashina M, Saper J, Cady R, et al. Eptinezumab in episodic migraine: A randomized, double-blind, placebo-controlled study (PROMISE-1). Cephalalgia. 2020;:333102420905132.	Randomized, double-blind, placebo-controlled, parallel-group, phase 3 study in adults with episodic migraine. A total of 888 subjects were randomized to receive eptinezumab 30 mg, eptinezumab 100 mg, eptinezumab 300 mg, or placebo.	• Primary: Mean change from baseline in monthly migraine days over 3 months

Results: Eptinezumab 100 mg and 300 mg met the primary endpoint, significantly reducing mean monthly migraine days across months 1-3 compared with placebo (100 mg, -3.9, p = 0.0182; 300 mg, -4.3, p = 0.0001; placebo, -3.2). Eptinezumab 30 mg was not found to be statistically significant when compared with placebo. Treatment-emergent adverse events were reported by 58.4% (30 mg), 63.2% (100 mg), 57.6% (300 mg), and 59.5% (placebo) of patients; adverse events reported by ≥2% of eptinezumab-treated patients at an incidence greater than placebo included: upper respiratory tract infection (30 mg, 11.4%; 100 mg, 9.9%; 300 mg, 10.3%; placebo, 7.2%), and fatigue (30 mg, 2.3%; 100 mg, 3.6%; 300 mg, 3.6%; placebo, <1%). **Conclusion**: Eptinezumab (100 mg or 300 mg) significantly reduced migraine frequency, was well tolerated, and had an acceptable safety profile when used for the preventive treatment of migraine in adults with episodic migraine.		
Citation	**Design**	**Endpoints**
Dodick DW, Lipton RB, Ailani J, et al. Ubrogepant for the Treatment of Migraine. N Engl J Med. 2019;381(23):2230-2241.	Randomized, double-blind, placebo-controlled phase 3 study in adults at least a one-year history of migraine and two to eight migraine attacks of moderate or severe intensity per month. A total of 1072 subjects were randomized to receive ubrogepant 50 mg, ubrogepant 100 mg, or placebo.	• Primary: Freedom from pain at 2 hours after the initial dose and absence of the most bothersome migraine-associated symptom (MBS) at 2 hours
Results: The percentage of participants who had freedom from pain at 2 hours was 11.8% in the placebo group, 19.2% in the 50-mg ubrogepant group (P = 0.002), and 21.2% in the 100-mg ubrogepant group (P<0.001). The percentage of participants who had freedom from MBS at 2 hours was 27.8% in the placebo group, 38.6% in the 50-mg ubrogepant group (P = 0.002), and 37.7% in the 100-mg ubrogepant group (P = 0.002). The most common adverse events were nausea, somnolence, and dry mouth; these events were more frequent in the 100-mg ubrogepant group. Serious adverse events reported within 30 days in the ubrogepant groups included appendicitis, spontaneous abortion, pericardial effusion, and seizure; none of the events occurred within 48 hours after the dose. **Conclusion**: A higher percentage of participants who received ubrogepant than of those who received placebo had freedom from pain and absence of the most bothersome symptom at 2 hours after the dose. The most commonly reported adverse events were nausea, somnolence, and dry mouth. Further trials are needed to determine the durability and safety of ubrogepant for acute migraine treatment and to compare it with other drugs for migraine.		
Citation	**Design**	**Endpoints**
Lipton RB, Dodick DW, Ailani J, et al. Effect of Ubrogepant vs Placebo on Pain and the Most Bothersome Associated Symptom in the Acute Treatment of Migraine: The ACHIEVE II Randomized Clinical Trial. JAMA. 2019;322(19):1887-1898.	Randomized, double-blind, placebo-controlled phase 3 study in adults with at least a one-year history of migraine and two to eight migraine attacks of moderate or severe intensity per month. A total of 1686 subjects were randomized to receive ubrogepant 25 mg, ubrogepant 50 mg, or placebo.	• Primary: Freedom from pain at 2 hours after the initial dose and absence of MBS at 2 hours
Results: Pain freedom at 2 hours was reported by 21.8% of participants in the ubrogepant 50-mg group, 20.7% in the ubrogepant 25-mg group, and 14.3% in the placebo group (absolute difference for 50 mg vs. placebo, 7.5%; 95% CI, 2.6% to 12.5%; P = .01; 25 mg vs. placebo, 6.4%; 95% CI, 1.5% to 11.5%; P = .03). Absence of MBS at 2 hours was reported 38.9% of participants in the ubrogepant 50-mg group, 34.1% in the ubrogepant 25-mg group, and 27.4% in the placebo group (absolute difference for 50 mg vs. placebo, 11.5%; 95% CI, 5.4% to 17.5%; P = .01; 25 mg vs. placebo, 6.7%; 95% CI, 0.6% to 12.7%; P = .07). The most common adverse events within 48 hours of any dose were nausea (50 mg, 2.0%; 25 mg, 2.5%; and placebo, 2.0%) and dizziness (50 mg, 1.4%; 25 mg, 2.1%; placebo, 1.6%). **Conclusion**: Among adults with migraine, acute treatment with ubrogepant compared with placebo led to significantly greater rates of pain freedom at 2 hours with 50-mg and 25-mg doses, and absence of the most bothersome migraine-associated symptom at 2 hours only with the 50-mg dose. Further research is needed to assess the effectiveness of ubrogepant against other acute treatments for migraine and to evaluate the long-term safety of ubrogepant among unselected patient population.		
Citation	**Design**	**Endpoints**

21

Croop R, Goadsby PJ, Stock DA, et al. Efficacy, safety, and tolerability of rimegepant orally disintegrating tablet for the acute treatment of migraine: a randomised, phase 3, double-blind, placebo-controlled trial. Lancet. 2019;394(10200):737-745.	Randomized, double-blind, placebo-controlled phase 3 study in adults with at least a one-year history of migraine and two to eight migraine attacks of moderate or severe intensity per month. A total of 1811 subjects were randomized to receive rimegepant (75 mg orally disintegrating tablet) or placebo.	• Primary: Freedom from pain and freedom from MBS 2 hours after the initial dose
Results: Rimegepant orally disintegrating tablet was superior to placebo for freedom from pain (21% vs. 11%, p<0.0001; risk difference 10%; 95% CI, 6 to 14) and freedom from MBS (35% vs. 27%, p=0.0009; risk difference 8%; 95% CI, 3 to 13). The most common adverse events were nausea (rimegepant [2%]; placebo [<1%]) and urinary tract infection (rimegepant [1%]; placebo [1%]). Treated participants reported no serious adverse events. **Conclusion**: In the acute treatment of migraine, a single 75 mg dose of rimegepant in an orally disintegrating tablet formulation was more effective than placebo. Tolerability was similar to placebo, with no safety concerns.		
Citation	**Design**	**Endpoints**
Lipton RB, Croop R, Stock EG, et al. Rimegepant, an Oral Calcitonin Gene-Related Peptide Receptor Antagonist, for Migraine. N Engl J Med. 2019;381(2):142-149.	Randomized, double-blind, placebo-controlled phase 3 study in adults with at least a one-year history of migraine and two to eight migraine attacks of moderate or severe intensity per month. A total of 1186 subjects were randomized to receive rimegepant (75 mg) or placebo.	• Primary: Freedom from pain and freedom from MBS 2 hours after the initial dose
Results: The percentage of patients who were pain-free 2 hours after receiving the dose was 19.6% in the rimegepant group and 12.0% in the placebo group (absolute difference, 7.6%; 95% CI, 3.3 to 11.9; P<0.001). The percentage of patients who were free from MBS 2 hours after the dose was 37.6% in the rimegepant group and 25.2% in the placebo group (absolute difference, 12.4%; 95% CI, 6.9 to 17.9; P<0.001). The most common adverse events were nausea and urinary tract infection. **Conclusion**: Treatment of a migraine attack with the oral CGRP antagonist rimegepant resulted in a higher percentage of patients who were free of pain and free from their most bothersome symptom than placebo.		
Citation	**Design**	**Endpoints**
Croop R, Lipton RB, Kudrow D, et al. Oral rimegepant for preventive treatment of migraine: a phase 2/3, randomised, double-blind, placebo-controlled trial. Lancet. 2021;397(10268):51-60.	Randomized, double-blind, multicenter, placebo-controlled phase 2/3 study in adults with at least a one-year history of migraine. A total of 747 subjects were randomized to receive rimegepant (75 mg) or placebo.	• Primary: Mean change from baseline in monthly migraine days in the last 4 weeks (weeks 9-12)
Results: Rimegepant was superior to placebo on the primary endpoint of change in the mean number of migraine days per month during weeks 9-12. The change from the observation period in mean number of migraine days per month during weeks 9-12 was -4.3 days with rimegepant and -3.5 days with placebo (least squares mean difference, -0.8 days; 95% CI, -1.46 to -0.20; P=0.0099). Thirty-six percent of patients who received rimegepant reported an adverse event, compared with 36% who received placebo. Seven (2%) participants who received rimegepant and four (1%) who received placebo discontinued the study due to an adverse event; no patients died. **Conclusion**: Taken every other day, rimegepant was effective for preventive treatment of migraine. Tolerability was similar to that of placebo, and no unexpected or serious safety issues were noted.		
Citation	**Design**	**Endpoints**

22

Ailani J, Lipton RB, Goadsby PJ, et al. Atogepant for the preventive treatment of migraine. N Engl J Med. 2021;385(8):695-706.	Randomized, double-blind, placebo-controlled phase 3 study in adults with at least a one-year history of migraine and 4 to 14 migraine days per month. A total of 873 subjects were randomized in a 1:1:1:1 ratio to receive atogepant (10 mg, 30 mg, or 60 mg) or placebo.	• Primary: Mean change from baseline in monthly migraine days over 12 weeks • Secondary: Headache days per month, reduction from baseline of at least 50% in the 3-month average of migraine days per month, quality of life, and scores on the Activity Impairment in Migraine–Diary (AIM-D)
Results: The changes from baseline across 12 weeks were −3.7 days with atogepant 10 mg, −3.9 days with atogepant 30 mg, −4.2 days with atogepant 60 mg, and −2.5 days with placebo. The mean differences from placebo in the change from baseline were −1.2 days with atogepant 10 mg (95% CI, −1.8 to −0.6), −1.4 days with atogepant 30 mg (95% CI, −1.9 to −0.8), and −1.7 days with atogepant 60 mg (95% CI, −2.3 to −1.2) (P<0.001 for all comparisons with placebo). Results for the secondary end points favored atogepant over placebo with the exceptions of the AIM-D Performance of Daily Activities score and the AIM-D Physical Impairment score for atogepant 10 mg. The most common adverse events were constipation (6.9% to 7.7% across atogepant doses) and nausea (4.4% to 6.1% across atogepant doses). Serious adverse events included one case each of asthma and optic neuritis in the atogepant 10 mg group. **Conclusion**: Oral atogepant once daily was effective in reducing the number of migraine days and headache days over a period of 12 weeks. Longer and larger trials are needed to determine the effect and safety of atogepant for migraine prevention.		
Citation	**Design**	**Endpoints**
Goadsby PJ, Dodick DW, Ailani J, et al. Safety, tolerability, and efficacy of orally administered atogepant for the prevention of episodic migraine in adults: a double-blind, randomised phase 2b/3 trial. Lancet Neurol. 2020;19(9):727-737.	Randomized, double-blind, placebo-controlled phase 2b/3 study in adults with at least a one-year history of migraine and 4 to 14 migraine days per month. A total of 795 subjects were randomized in a 2:1:2:2:1:1 ratio to receive placebo or atogepant 10 mg once daily, 30 mg once daily, 60 mg once daily, 30 mg twice daily, or 60 mg twice daily.	• Primary: Mean change from baseline in monthly migraine days over 12 weeks
Results: Across the 12-week treatment period, all five atogepant groups showed significant least-squares mean change from baseline in mean monthly migraine days vs. placebo: atogepant 10 mg once daily -4.0 (P=0.024), 30 mg once daily -3.8 (P=0.039), 60 mg once daily -3.6 (P=0.039), 30 mg twice daily -4.2 (P=0.0034), and 60 mg twice daily -4.1 (P=0.0031); placebo -2.9. The most common treatment-emergent adverse events across all groups were nausea (range 5% for 10 mg once daily to 12% for 60 mg once daily vs. 5% for placebo) and fatigue (1% for 10 mg once daily to 10% for 60 mg twice daily vs. 3% for placebo). Treatment-related adverse event frequency ranged from 18% for 10 mg once daily to 26% for 60 mg twice daily vs. 16% for placebo. Treatment-emergent adverse events leading to discontinuation were reported in 5% of atogepant participants and 3% of those randomized to placebo. All serious treatment-emergent adverse events were unrelated to treatment. **Conclusion**: All doses of oral atogepant were associated with a significant decrease in monthly migraine days over 12 weeks compared with placebo. Atogepant was safe and well tolerated over 12 weeks, supporting its use for the preventive treatment of migraine.		
Citation	**Design**	**Endpoints**
Croop R, Madonia J, Stock DA, et al. Zavegepant nasal spray for the acute treatment of migraine: A Phase 2/3 double-blind, randomized, placebo-controlled, dose-ranging trial. Headache. 2022;62(9):1153-1163.	Randomized, double-blind, placebo-controlled phase 2b/3 study in adults with at least a one-year history of migraine and two to eight migraine attacks of moderate or severe intensity per month. A total of 1673 subjects were randomized in a 1:1:1:1 ratio to receive zavegepant nasal spray 5, 10, 20 mg, or placebo.	• Primary: Freedom from pain and freedom from MBS 2 hours postdose

Results: Zavegepant 10 and 20 mg were more effective than placebo on the coprimary endpoints of pain freedom at 2 h postdose (placebo, 15.5%; 10 mg, 22.5% [P=0.0113]; 20 mg, 23.1% [P= 0.0055]) and freedom from MBS at 2 hours postdose (placebo, 33.7%; 10 mg, 41.9% [P= 0.0155]; 20 mg: 42.5% [P= 0.0094]). Findings for the 5 mg dose were not significant. The most common treatment-emergent adverse events with zavegepant 10 and 20 mg and placebo were dysgeusia (13.5% to 16.1% vs. 3.5%), nausea (2.7% to 4.1% vs. 0.5%), and nasal discomfort (1.3% to 5.2% vs. 0.2%). Most adverse events were mild or moderate and resolved without treatment. There was no signal of hepatotoxicity.
Conclusion: Zavegepant nasal spray, in single doses of 10 or 20 mg, was effective for the acute treatment of migraine, with a favorable safety profile. Additional research is needed to confirm its potential as a nonoral medication for the acute treatment of migraine.

Citation	Design	Endpoints
Lipton RB, Croop R, Stock DA, et al. Safety, tolerability, and efficacy of zavegepant 10 mg nasal spray for the acute treatment of migraine in the USA: a phase 3, double-blind, randomised, placebo-controlled multicentre trial. Lancet Neurol. 2023;22(3):209-217.	Randomized, double-blind, placebo-controlled, multicenter phase 3 study in adults with at least a one-year history of migraine and two to eight migraine attacks of moderate or severe intensity per month. A total of 1405 subjects were randomized in a 1:1 ratio to receive zavegepant 10 mg nasal spray or placebo.	• Primary: Freedom from pain and freedom from MBS 2 hours postdose

Results: Two hours after the treatment dose, more participants in the zavegepant group than in the placebo group had pain freedom (24% vs. 15%; risk difference, 8.8%; 95% CI, 4.5 to 13.1; P<0.0001) and freedom from MBS (40% vs. 31%; risk difference 8.7%; 95% CI, 3.4 to 13.9; P=0.0012). The most common adverse events in either treatment group (≥2%) were dysgeusia (21% in the zavegepant group vs. 5% in the placebo group), nasal discomfort (4% vs. 1%), and nausea (3% vs. 1%). No signal of hepatotoxicity due to zavegepant was identified.
Conclusion: Zavegepant 10 mg nasal spray was efficacious in the acute treatment of migraine, with favorable tolerability and safety profiles. Additional trials are needed to establish the long-term safety and consistency of effect across attacks.

Citation	Design	Endpoints
Sun W, Cheng H, Xia B, et al. Comparative efficacy and safety of five anti-calcitonin gene-related peptide agents for migraine prevention: a network meta-analysis. Clin J Pain. 2023;39(10):560-569.	Network meta-analysis conducted by searching PUBMED, EMBASE and the Cochrane Library, up to May 2022. Studies included involved patients diagnosed with episodic or chronic migraine and treated with erenumab, fremanezumab, eptinezumab, galcanezumab, atogepant, or placebo. A total of 24 studies were included.	• Primary: Mean change from baseline in monthly migraine days • Secondary: ≥50% reduction in monthly migraine days and adverse events

Results: Regarding efficacy, all interventions were superior to placebo with a statistically significant difference. The most effective intervention was monthly fremanezumab 225 mg in change from baseline of migraine days (standard mean difference, −0.49; 95% CI, −0.62 to −0.37) and ≥50% reduction rate (risk ratio, 2.98; 95% CI, 2.16 to 4.10), while the optimal choice for reducing acute medication days was monthly erenumab 140 mg (standard mean difference, −0.68; 95% CI, −0.79 to −0.58). In terms of adverse events, all therapies and placebo did not achieve statistical significance except for monthly galcanezumab 240 mg and quarterly fremanezumab 675 mg. There was no significant difference in discontinuation due to adverse events between interventions and placebo.
Conclusion: All anti-CGRP agents were more effective than placebo in migraine prevention. Overall, monthly fremanezumab 225 mg, monthly erenumab 140 mg, and daily atogepant 60 mg were effective interventions with fewer side effects.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (01-01-2024 to 03-31-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Injectable CGRP Receptor Antagonists								
Aimovig® (erenumab-aooe) 70 mg/mL, 140 mg/ml subcutaneous auto-injectors	0	0	$0.00	$0.00	0	0 (0%)	F-PA	F-PA -> NF
Ajovy® (fremanezumab-vfrm) 225 mg/1.5 mL subcutaneous auto-injector	0	0	$0.00	$0.00	1	0 (0%)	F-PA	No change
Ajovy® (fremanezumab-vfrm) 225 mg/1.5 mL subcutaneous prefilled syringe	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Emgality® (galcanezumab-gnlm) 120 mg/mL subcutaneous pen injector	5	3	$3,437.19	$687.44	1	1 (100%)	F-PA	No change
Emgality® (galcanezumab-gnlm) 100 mg/ml, 120 mg/mL subcutaneous prefilled syringes	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Vyepti® (eptinezumab-jjmr) 100 mg/ml intravenous solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Oral CGRP Receptor Antagonists								
Ubrelvy® (ubrogepant) 50 mg, 100 mg oral tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Nurtec® ODT (rimegepant) 75 mg oral disintegrating tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	F-PA -> NF
Qulipta™ (atogepant) 10 mg, 30 mg, 60 mg oral tablets	0	0	$0.00	$0.00	1	0 (0%)	NF	No change
Intranasal CGRP Receptor Antagonists								
Zavzpret™ (zavegepant) 10 mg nasal spray	2	1	$2,138.40	$1,069.20	1	1 (100%)	NF	NF -> F
TOTAL	7	4	$5,575.59	$796.51	4	2 (50%)		

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

Medication Request Guidelines

Recommendation:

- Adding Ajovy as a preferred product and updating criteria accordingly
- Moving Aimovig from formulary PA required to Non-formulary PA required

Calcitonin Gene-Related Peptide (CGRP) Antagonists for Headache Prevention	
Therapeutic Classes (AHFS)	CALCITONIN GENE-RELATED PEPTIDE ANTAGONISTS
Medications	Formulary, PA required Emgality (galcanezumab-gnlm) - PREFERRED Ajovy (fremanezumab-vfrm) - PREFERRED ~~Aimovig (erenumab-aooe)~~ Non-Formulary, PA required Aimovig (erenumab-aooe) Vyepti (eptinezumab-jjmr) Nurtec ODT (rimegepant)- if the request is for acute treatment of migraine please refer to the Acute Migraine Treatments criteria Qulipta (atogepant) 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** 6 months **Later Approvals** 6 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Criteria for Initial Authorization:** **Cluster Headache:** • Diagnosis of episodic cluster headache • Requested dose is within FDA approved dosing guidelines **Migraine Headache Prophylaxis:** • Diagnosis of episodic migraine or chronic migraine • Requested dose is within FDA approved dosing guidelines • Provider should note on the prior authorization request the number of headache days per month • Trial and failure (or a medical justification for not using e.g. hypersensitivity, baseline bradycardia or hypotension, adverse events experienced from previous trial, etc.) with at least one of the following:: 1. Beta-adrenergic blockers 2. Topiramate or divalproex ER or DR 3. A tricyclic antidepressant (TCA) (e.g. amitriptyline or nortriptyline) OR a serotonin norepinephrine reuptake inhibitor (SNRI) (e.g. venlafaxine or duloxetine) 4. Frovatriptan, zolmitriptan or naratriptan (for menstrual migraine prophylaxis) • If the medication request is for a Calcitonin Gene-Related Peptide Antagonist other than Emgality of Ajovy, the patient has a documented medical reason

Calcitonin Gene-Related Peptide (CGRP) Antagonists for Headache Prevention	
	(intolerance, hypersensitivity, contraindication, treatment failure etc) for not using Emgality or Ajovy to treat their medical condition. **Criteria for Re-Authorization:** **Episodic Cluster Headache:** • Documented reduction in the frequency of headaches (clinical benefit). **Migraine:** • Greater than or equal to a 50% reduction in the number of headache days per month relative to pre-treatment baseline (clinical benefit) • The provider should note on the prior authorization request the number of headache days per month
Criteria Statement	Emgality and Ajovy are~~is~~ reserved for members requiring migraine prophylaxis and who have used (or cannot/should not use) one medication to prevent migraines including beta-adrenergic blockers, topiramate or divalproex ER or DR, a tricyclic antidepressant, or a serotonin norepinephrine reuptake inhibitor, or frovatriptan zolmitriptan, or naratriptan. Non-preferred CGRPs are reserved for members requiring migraine prophylaxis and who have used (or cannot/should not use) one medication to prevent migraines including beta-adrenergic blockers, topiramate or divalproex ER or DR, a tricyclic antidepressant, or a serotonin norepinephrine reuptake inhibitor, or frovatriptan, zolmitriptan, or naratriptan AND who cannot/ should not take Emgality or Ajovy. Emgality is reserved for members with a diagnosis of episodic cluster headaches.
Last P&T Review Date	06/2024

27

Recommendation:

- Expanding prescriber restriction to allow for prescribing by or in consultation with a neurologist or additional specialist
- Update QL for Ubrelvy to align with labeled indication and package size
- Add Zavzpret to the Formulary, PA required section as preferred
- Add a quantity limit of 8 units per month to Zavzpret
- Remove Reyvow and Nurtec ODT from the formulary, and place them in newly created Non-formulary PA required section

Acute Migraine Treatments	
Therapeutic Classes (AHFS)	CALCITONIN GENE-RELATED PEPTIDE ANTAG., SELECTIVE SEROTONIN AGONISTS
Medications	Formulary, PA required Ubrelvy (ubrogepant) PREFERRED ~~Nurtec ODT (rimegepant) - if the request is for migraine prevention please refer to the Calcitonin Gene-Related Peptide (CGRP) Antagonists for Headache Prevention criteria~~ ~~Reyvow (lasmiditan)~~ Zavzpret (zavegepant) PREFERRED Non-formulary, PA required Nurtec ODT (rimegepant) - if the request is for migraine prevention please refer to the Calcitonin Gene-Related Peptide (CGRP) Antagonists for Headache Prevention Reyvow (lasmiditan) 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	~~Prescriber must be a neurologist~~ Prescribed by or in consultation with a neurologist, migraine specialist, pain specialist, or other specialist in the treatment of headaches
Coverage Duration	**Initial Approval** 3 months **Later Approvals** 6 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization:** Medications will be approved when all of the following criteria are met: • Diagnosis of migraine headache • Requested dose is within FDA approved dosing guidelines • Documented trial and failure of (or medical justification for not using) two triptan products • Attestation the patient was counseled regarding not driving or operating machinery until at least 8 hours after taking each dose (Reyvow only) • If the request is for a non-preferred agent, the member must have a documented trial of Ubrelvy or have a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing Ubrelvy or Zavzpret **Criteria for Re-Authorization:** • Documentation of improvement in migraine pain and symptom (s) (e.g., photophobia, nausea, phonophobia)

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28

Acute Migraine Treatments	
	Nurtec ODT QL of 8 units per month. **Reyvow QL of 8 units per month.** **Ubrelvy QL of ~~10~~ 16 units per month** **Zavzpret QL of 8 units per month** **Criteria for exceeding the quantity limit (note all of the above criteria must also be met)** • Documented trial and failure (or a medical justification for not using e.g. hypersensitivity, baseline bradycardia or hypotension, adverse events experienced from previous trial, etc.) with at least one drug from two categories below for at least 4 weeks EACH, at minimum effective doses: o Beta-adrenergic blockers o Topiramate or divalproex ER or DR o Amitriptyline or venlafaxine o Frovatriptan, zolmitriptan or naratriptan (for menstrual migraine prophylaxis)
Criteria Statement	Ubrelvy and Zavzpret are~~is~~ reserved for members with a diagnosis of migraine headaches who have used (or cannot/should not use) two triptan medications, and are within the quantity limits. Reyvow and Nurtec are reserved for members with a diagnosis of migraine headaches who have used (or cannot/should not use) two triptan medications AND Ubrelvy or Zavzpret and are within the quantity limits. Quantities exceeding the quantity limits are reserved for members who have used (or cannot/should not use) a member from two prophylactic migraine medication classes.
Last P&T Review Date	~~6/2023~~6/2024

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Recommendation:

- Change entecavir 0.5 and 1 mg tablets from F-PA to formulary status, as there are no medications that must be tried and failed prior to its use. There also would be limited to no off label use of this medication. No prior authorizations for this medication were denied during Q4 2023 or Q1 2024.
- Move entecavir 0.5 and 1 mg tablets from the Formular PA required section to the Formulary section to represent the new formulary status of the medication
- Remove entecavir from the PA Review Criteria where appropriate.

Hepatitis B Drugs		
Therapeutic Classes (AHFS)	Various	
Medications	Formulary Tenofovir disoproxil fumarate (Viread) 300 mg tablet Entecavir (Baraclude) 0.5, 1 mg tablets Formulary - PA required ~~Entecavir (Baraclude) 0.5, 1 mg tablets PREFERRED~~ Baraclude (entecavir) 0.05 mg/ml solution Adefovir (Hepsera) 10 mg tablet Lamivudine (Epivir HBV) 100 mg tablet Lamivudine (Epivir HBV) 25 mg/5 ml solution Viread 150mg, 200mg, 250mg tablet Vemlidy (tenofovir alafenamide fumarate) 25 mg tablet Non-formulary Viread (Tenofovir disoproxil fumarate) 40mg/gm oral powder **Any other 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**	For pregnant patients taking prophylaxis therapy for reduction of perinatal transmission of HBV: 6 months All other INITIAL requests: 12 months: Requests can be approved for up to a 90 day supply
	Later Approvals	For RENEWAL requests for patients undergoing chemotherapy: HBV prophylactic treatment is only approved for up to an additional 12 months upon completion of chemotherapy. RENEWAL requests will not be considered for perinatal prophylaxis after 3 months postpartum All other RENEWAL requests:12 months Requests can be approved for up to a 90 day supply

	Partial approvals - For situations where lab values required for later approvals/ renewals are missing either in full or in part should be granted for 3 months. *If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**INITIAL CRITERIA for adult population:** • Diagnosis of Hepatitis B; AND • Medication is being prescribed at an appropriate FDA approved dose (for age and weight); AND • ~~Request is for entecavir (Baraclude) tablet~~ ~~OR~~ • Requests for Vemlidy require trial and failure of, intolerance to, or inability to use entecavir (Baraclude) tablet AND • **For Immune-Active chronic hepatitis B (CHB)**: Elevation of ALT ≥2 ULN (above 50 U/L for females or 66 U/L for males) OR evidence of significant histological disease (significant inflammation and/or fibrosis); AND A) Elevated HBV DNA ≥ 2000 IU/mL (HBeAg negative); OR B) Elevated HBV DNA > 20,000 IU/mL (HBeAg positive). • **For Decompensated Cirrhosis:** Presence of decompensated cirrhosis and detectable serum HBV DNA. • **For Compensated Cirrhosis:** Presence of elevated HBV DNA ≥ 2000 IU/mL • **Prophylaxis for Transplant Recipients with Hepatitis B:** A) Patient is HBsAg-positive and undergoing liver transplantation, regardless of HBeAg status or HBV-DNA level pre-transplant; OR B) Patient is HBsAg-negative and received a HBsAg-negative but anti-HBc–positive graft; OR C) Patient has received a HBsAg-positive (non-liver) organ transplant. • **Pregnant Women (for perinatal transmission prophylaxis only; patient does not meet other eligibility categories):** A) Patient is HBsAg-positive pregnant women with an HBV DNA level >200,000 IU/mL; AND B) Patient is in the third trimester of pregnancy • **Undergoing Chemotherapy or Will Be Initiating Cytotoxic Chemotherapy**: A) Patient is HBsAg-positive, anti-HBc–positive regardless of baseline serum HBV DNA levels; OR B) Patient is HBsAg-negative, anti-HBc–positive; AND 1) Receiving anti-CD20 antibody therapy (e.g., rituximab); OR 2) Undergoing stem cell transplantation. • **Acute Symptomatic Hepatitis B** Patient has acute hepatitis B with acute liver failure OR has a protracted, severe course, as indicated by total bilirubin >3 mg/dL (or direct bilirubin

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	>1.5 mg/dL), international normalized ratio >1.5, encephalopathy, or ascites. ***For adults, if request is for adefovir (Hepsera) or lamivudine (Epivir HBV), documentation of treatment failure or contraindication to entecavir (Baraclude) tablet AND tenofovir disoproxil fumarate (Viread) 300 mg tablet must be provided.** ***If request is for oral solution/oral powder, medical justification for use (i.e. difficulty swallowing) must be provided.** **INITIAL CRITERIA for Treatment of CHB in children (ages 2 to <18 years):** • Diagnosis of Hepatitis B; AND • Medication is being prescribed at an appropriate FDA approved dose (for age and weight); AND • ~~Request is for entecavir (Baraclude) tablet~~ • Patient is HBeAg-positive with both: A) elevated ALT; AND B) measurable HBV-DNA levels ***For children, if request is for adefovir (Hepsera) or lamivudine (Epivir HBV), documentation of treatment failure or contraindication to entecavir (Baraclude) tablet or disoproxil fumarate (Viread) 300 mg tablet must be provided.** **For requests for Viread 150mg, 200mg, or 250mg tablet, documentation of weight required as rationale supporting why tenofovir disoproxil fumarate (Viread) 300 mg tablet cannot be used.** ***If request is for oral solution/oral powder, medical justification for use (i.e. difficulty swallowing) must be provided.** **RENEWAL CRITERIA** • Documented response to treatment shown by reduced HBV DNA levels. • If all other criteria are met but the necessary lab values have not been provided, a partial approval for 3 months may be granted. The partial approval should indicate what information is needed for ongoing approval.
Criteria Statement	N/A
Last P&T Review Date	6/2024~~12/2023~~

Alameda MRGs for review Q2 2024 P&T

Recommendation:

- Add new medication Wainua to policy along with formatting changes for clarity
- Remove the genetic test result requirement for thansthyretin variant for Vyndagel and Vyndamax since these drugs treat both the wild type and hereditary forms of cardiomyopathy, and to simplify it for the reviewing pharmacist to prevent inappropriate denials and delays in care

Transthyretin-mediated Amyloidosis Agents	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS
Medications	**Preferred:** Polyneuropathy – Amvuttra (vutrisiran), Wainua (eplontersen) Cardiomyopathy – Vyndaqel (tafamidis meglumine), Vyndamax (tafamidis) **Non-preferred**: Polyneuropathy – Tegsedi (inoterson) Or any other 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	Prescriber must be neurologist, cardiologist, or specialist in the treatment of amyloidosis
Coverage Duration	If all the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 6 months.

PA Review Criteria	**Initial Authorization:**
	• Regimen does not exceed FDA-approved dose/frequency
	• Patient has not undergone a liver or heart transplant
	• Patient is not taking any of these agents concurrently: Tegsedi, Amvuttra, Vyndaqel, ~~or~~ Vyndamax, or Wainua
	
	If the request is for Amvuttra, Wainua, or Tegsedi: ~~, patient has diagnosis of polyneuropathy of hereditary transthyretin-mediated amyloidosis as evidenced by~~:
	• Patient has diagnosis of polyneuropathy of hereditary transthyretin-mediated amyloidosis as evidenced by ~~D~~documented transthyretin variant by genotyping
	• One of the following:
	  ○ Patient has baseline polyneuropathy disability (PND) score ≤ IIIb
	  ○ Patient has a baseline Familial Amyloid Polyneuropathy (FAP) Stage 1 or 2
	  ○ Patient has baseline neuropathy impairment (NIS) score ≥ 5 and ≤ 130
	• Patient has clinical signs/symptoms of neuropathy
	• For Tegsedi, patient has contraindication to/or previous trial and failure of use of Amvuttra or Wainua
	
	If the request is for Vyndaqel or Vyndamax: ~~, patient has diagnosis of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis as evidenced by all of the following:~~

	• Patient has a confirmed diagnosis of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis • ~~Documented transthyretin variant by genotyping or wild-type amyloidosis~~ • Documented amyloid deposit by biopsy or positive technetium 99m pyrophosphate (Tc 99m PYP) cardiac imaging • Patient has New York Heart Association (NYHA) functional class I, II, or III heart failure symptoms. **Re-authorization**: • Patient's regimen does not exceed FDA-approved dose/frequency for the agent • Patient has not undergone a liver or heart transplant • Patient is not taking any of these agents concurrently: Tegsedi, Amvuttra, Wainua, Vyndaqel or Vyndamax) • Documented positive clinical response to therapy from baseline (stabilization/slowing of disease progression, improved neurological impairment, motor functions, improved NIS score, stabilization/reduced rate of decline in 6 minute walk test, etc.) • If the request is for Vyndaqel/Vyndamax ○ Patient has continued NYHA functional class I, II, or III heart failure symptoms
Criteria Statement	Amvuttra, Wainua, and Tegsedi are reserved for members with a diagnosis of polyneuropathy of hereditary transthyretin-mediated amyloidosis who have not undergone a liver transplant, with clinical signs or symptoms of neuropathy. Tegsedi is reserved for members who have used (or cannot/should not use) Amvuttra or Wainua. Vyndaqel and Vyndamax are reserved for members with a diagnosis of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis who have documented amyloid deposit by biopsy or positive technetium 99m pyrophosphate (Tc 99m PYP) cardiac imaging and New York Heart Association (NYHA) functional class I, II, or III heart failure symptoms, who have not undergone a heart transplant.
Last P&T Review Date	~~9/2023~~6/2024

Recommendation:

- Update naming conventions to reflect generic availability of brand Vyvanse, lisdexamphetamine

Medications for Attention Deficit Hyperactivity Disorder (ADHD) and Narcolepsy	
Therapeutic Classes (AHFS)	Respiratory and CNS stimulants
Medications	**Formulary, with age limits and selected quantity limits** Atomoxetine (Strattera) 10 mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg Capsule Dexmethylphenidate (Focalin) 2.5mg, 5mg, 10mg tablet Dextroamphetamine (Dexedrine) 5mg, 10 mg Tablet Dextroamphetamine-amphetamine (Adderall) 5 mg, 7.5mg 10mg, 12.5mg, 15mg, 20mg, 30mg Tablet Dextroamphetamine-amphetamine ER (Adderall XR) 5mg, 10 mg, 15mg, 20mg, 25mg, 30mg 24Hr Capsule, Extended Release Guanfacine (Intuniv) ER 1mg, 2mg, 3mg, 4mg Tablet, Extended Release 24 Hr Methylphenidate (Ritalin) 5mg, 10mg, 20mg tablet Methylphenidate CD 10 mg, 20mg, 30mg, 40mg, 50mg, 60mg Biphasic 30-70 Capsule, Extended Release Methylphenidate ER 18mg, 27mg, 36mg, 54mg Tablet, Extended Release Methylphenidate LA 10 mg, 20mg, 30mg, 40mg, 60mg Capsule, Extended Release Biphasic 50-50 **Formulary PA** ~~Vyvanse (lisdexamfetamine)10 mg, 20mg, 30mg, 40mg, 50mg, 60mg, 70mg Capsule~~ Lisdexamfetamine (Vyvanse) 10mg, 20mg, 30mg, 40mg, 50mg, 60mg, 70mg Capsule ~~Vyvanse (lisdexamfetamine)10 mg, 20mg, 30mg, 40mg, 50mg, 60mg Chewable Tablet~~ Lisdexamfetamine (Vyvanse) 10 mg, 20mg, 30mg, 40mg, 50mg, 60mg Chewable Tablet Daytrana (methylphenidate transdermal) 10 mg/9Hr, 15mg/9Hr, 20mg/9Hr, 30mg/9Hr, 30mg/9Hr Daily Patch Qelbree (viloxazine) ER 100mg, 150mg, 200mg capsule *Any new dosage form, strength, or newly marketed medication indicated for ADHD
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	**Initial authorization**: • Appropriate diagnosis/indication and dose used for the requested medication for use in narcolepsy OR • Appropriate diagnosis/indication for requested medication- For use in adults, clinic notes are needed with Attention Deficit Hyperactivity Disorder (ADHD) diagnosis. If the request is from psychiatry, clinic notes are not required. AND • Appropriate dose of medication based on age and indication AND • If request is for a non-formulary or formulary, prior authorization-required medication, documented trial and failure or intolerance with three preferred formulary medications (if available) used to treat the documented diagnosis. For medications where there is only one preferred formulary agent, only that agent must have been ineffective or not tolerated OR • No other formulary medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia. OR • All other formulary medications are contraindicated based on the patient's diagnosis, other medical conditions, or other medication therapy **Re-authorization:** • The patient is using the medication at an appropriate dose for an approved indication and is stable and obtaining clinical benefit
Criteria Statement	CNS stimulants are reserved for members who have a diagnosis of attention deficit hyperactivity disorder (ADHD) or narcolepsy are using the medication at an appropriate dose based on their age, other medical conditions, and other concurrent medications, and if the request is for a non-formulary or formulary, prior authorization-required medication, formulary agents must be tried and failed first.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Add LAMA to criteria as another monotherapy treatment option since roflumilast can be used as an add-on treatment to either LABA or LAMA per guidelines

Roflumilast (Daliresp)	
Therapeutic Classes (AHFS)	Phosphodiesterase type 4 inhibitors
Medications	Formulary, PA required: Roflumilast (Daliresp)
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	18 years of age
Prescriber Restrictions	Prescribed by or in consultation with a pulmonologist
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 conditions must be met:** • Diagnosis of severe COPD associated with chronic bronchitis as indicated by FEV ≤ 50% predicted with nonreversible obstructive lung disease. • Patient has history of COPD exacerbations within the previous 1 year. • Documented trial and failure or intolerance with a preferred inhaled long-acting beta2-agonist/ long-acting muscarinic antagonist (LABA/LAMA) combination, or long-acting beta2-agonist/ long-acting muscarinic antagonist/ inhaled corticosteroid (LABA/LAMA/ICS) combination for a minimum of 4 weeks of therapy in the previous 60 days • Documentation roflumilast (Daliresp) is being used as add-on treatment in conjunction with at least one: long-acting beta2-agonist (LABA) or long-acting muscarinic antagonist (LAMA)
Criteria Statement	Roflumilast (Daliresp) is reserved for members who have severe chronic obstructive pulmonary disease (COPD) and chronic bronchitis who have history of exacerbations within the last year and who have used (or cannot/should not use) a preferred inhaled long-acting beta2-agonist/ long-acting muscarinic antagonist (LABA/LAMA) combination, or long-acting beta2-agonist/ long-acting muscarinic antagonist/ inhaled corticosteroid (LABA/LAMA/ICS) combination for a minimum of 4 weeks of therapy in the previous 60 days and who are using roflumilast (Daliresp) in addition to a long-acting beta2-agonist (LABA) inhaler or long-acting muscarinic antagonist (LAMA).
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Add new approved medications: Abilify Asimtufii, Uzedy, and Rykindo
- Update naming conventions to reflect generic availability of brand Risperdal Consta

Injectable Atypical Antipsychotic Medications	
Therapeutic Classes (AHFS)	Antipsychotic agents
Medications	Formulary, Prior Authorization Required Risperidone microspheres ER (Risperdal Consta) ~~(risperidone)~~ Invega Sustenna (paliperidone palmitate) Zyprexa Relprevv (olanzapine) Abilify Maintena (aripiprazole) Non-Formulary Invega Trinza (paliperidone palmitate) Invega Hafyera (paliperidone palmitate) Aristada (aripiprazole lauroxil) Aristada Initio (aripiprazole lauroxil) Perseris ER (risperidone) Abilify Asimtufii (aripiprazole) Uzedy (risperidone) Rykindo (risperidone) Any other 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** 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. **Reauthorization** If all conditions are met, the request will be approved for up to 12 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	CRITERIA FOR INITIAL AUTHORIZATION • Member has claims history or physician attestation that member has tolerated treatment with the oral agent of the drug that is being requested • The member has a long-term history (>3 months) of uncertain compliance or noncompliance with oral anti-psychotic medications **OR** the member has a documented medical reason (i.e. documented treatment failure to maximum doses and/or has intolerable side effects or drug interactions) for not using oral formulary atypical antipsychotic medication **OR** the prescriber attests that the member has stated preference for injectable atypical antipsychotic therapy • Request is for FDA approved indication at an approved dose. • If request if for Aristada Initio, only a single dose will be approved if documentation has been provided that the member is initiating Aristada • If request is for Invega Trinza, documentation has been provided that the member has been stable on Invega Sustenna for 4 months, and at the same dose for the last 2 months

	• If the request is for Invega Hafyera, documentation has been provided that the member has been stable on Invega Sustenna for 4 months and at the same dose for the last 2 months OR has been stable on Invega Trinza for the last 3 months CRITERIA FOR REAUTHORIZATION • Member has been compliant with filling their medication (documentation via claims fill history or provider attestation) OR documentation was provided indicating why member missed dosing • Request is for FDA approved indication at an approved dose. • Documentation submitted indicating member is stable and tolerating medication.
Criteria Statement	Injectable antipsychotics are reserved for members who have used (or cannot/should not use) formulary oral atypical antipsychotic medications.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Extend initial approval to 6 months for long-term prophylaxis to assess clinical benefit per guidelines
- Add 2 other mutations recognized for HAE with normal C1INH for completeness
- List out which medications are for acute treatment and prophylaxis to ensure requests are for appropriate drugs per indication

<table>
<tr><th colspan="2">Hereditary Angioedema (HAE)</th></tr>
<tr><td>Therapeutic Classes (AHFS)</td><td>COMPLEMENT INHIBITORS</td></tr>
<tr><td>Medications</td><td><u>Preferred:</u>
Orladeyo (berotralstat) oral capsule
Takhzyro (lanadelumab-flyo) SC injection
icatibant (Firazyr) SC injection
Haegarda (C1 esterase inhibitor, human) SC syringe
Cinryze (C1 esterase inhibitor, human) IV vial
Berinert (C1 esterase inhibitor, human) IV vial
Ruconest (C1 esterase inhibitor, recombinant) IV vial

<u>Non-Preferred:</u>
Kalbitor (ecallantide) SC syringe</td></tr>
<tr><td>Covered Uses</td><td>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.</td></tr>
<tr><td>Exclusion Criteria</td><td>N/A</td></tr>
<tr><td>Required Clinical Information</td><td>See “PA Review Criteria” below</td></tr>
<tr><td>Age Restrictions</td><td>Check AAH active CCS cases for members < 21 years of age</td></tr>
<tr><td>Prescriber Restrictions</td><td>Prescriber must be an immunologist, allergist, rheumatologist, or hematologist</td></tr>
<tr><td>Coverage Duration</td><td>Initial Approval
If criteria are met, the request will be approved as follows:
• Acute treatment: initial fill + 5 refills
• Pre-procedural prophylaxis: 1 treatment
• Long-term prophylaxis: Initial approval: <s>3</s> 6 months

Reauthorization
Long-term prophylaxis: Reauthorization:12 months

If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.</td></tr>
<tr><td>PA Review Criteria</td><td>All requests must meet the following criteria:
• Documentation submitted indicates the medication is being prescribed at FDA approved dose.
• The patient is not taking ACE inhibitors or estrogen containing oral contraceptives or hormone replacement therapy
• Documented diagnosis of one of the following:
▪ HAE with deficient or dysfunctional C1INH (e.g. type I, type II or acquired C1INH deficiency):
<table>
<tr><th>Deficiency Type</th><th>C4</th><th>C1INH antigenic level</th><th>C1INH functional level</th></tr>
<tr><td>Type I (deficiency of C1INH)</td><td>Low</td><td>Low</td><td>Low</td></tr>
<tr><td>Type II (dysfunction of C1INH)</td><td>Low</td><td>Normal or elevated</td><td>Low</td></tr>
</table></td></tr>
</table>

Acquired C1INH deficiency	Low	Low or normal	Low

- HAE with normal C1INH:
  - If known origin, documentation of results of confirmatory genetic test (e.g. mutations in gene for factor XII, angiopoietin-1, plasminogen, kininogen-1, myoferlin, heparan sulfate-glucosamine 3-O-sulfotransferase 6)
  - If unknown origin (U-HAE), documentation of a prolonged trial of high-dose non-sedating antihistamines

For acute treatment (Ruconest, Berinert, Kalbitor, icatibant):
- The patient is receiving only one agent for the treatment of acute attacks
- If the request is for a non-preferred agent, the member has documented trial and failure of or intolerance to a preferred agent or medical reason why the member cannot use a preferred agent.

For prophylaxis (Haegarda, Takhzyro, Cinryze, Orladeyo):
- Pre-procedural
  - Documentation that patient will be undergoing a medical, surgical, or dental procedure associated with mechanical impact to the upper aerodigestive tract and anticipated date of the procedure
- Long-term
  - Documentation of at least one HAE attack per month
  - The patient is receiving one prophylactic HAE medication only
  - If the request is for Cinryze, the patient has a documented trial and failure of, or intolerance to, Haegarda
  - If the request is for Takhzyro and the patient has been well controlled (e.g. attack free) for 6 months or more while receiving Takhzyro the patient will be receiving 300 mg every four weeks, or a medical reason has been provided why continued therapy with 300 mg every two weeks is necessary

Renewal Criteria:
For acute treatment:
- Documentation was submitted that the patient has clinically benefited from medication
- The medication is being prescribed at FDA approved dose.
- The patient is receiving no other medications for acute treatment

For prophylaxis:
- Documentation was submitted that the patient has clinically benefited from prophylactic therapy as demonstrated by a reduced number of attacks
- The medication is being prescribed at an FDA approved dose
- The patient is receiving no other medications for prophylaxis
- If the request is for Takhzyro and the patient has been well controlled (e.g. attack free) for 6 months or more while receiving Takhzyro the patient will be receiving 300 mg every four weeks, or a medical reason has been provided why continued therapy with 300 mg every two weeks is necessary

Treatments for hereditary angioedema are reserved for members with a diagnosis of hereditary angioedema (HAE) who are not using ACE inhibitors or estrogen containing oral contraceptives or hormone replacement therapy.
If a non-preferred agent is requested for acute treatment, the patient is receiving only one medication for the treatment of acute attacks, and has used (or cannot/should not use) a preferred agent.

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	If a non-preferred agent is requested for long-term prophylaxis, the patient is receiving only one medication for prophylaxis treatment, the member has a history of at least one attack and has used (or cannot/should not use) a preferred agent.
Last P&T Review Date	~~6/2023~~6/2024

Recommendation:

- Update to correct therapeutic class of antilipemic agents
- Update the policy based on expanded indication for cardiovascular risk reduction in patients who are unable to take statin therapy
- Separate and reorganize criteria based on two indications: hyperlipidemia and cardiovascular risk reduction
- Update with additional diagnosis for primary hyperlipidemia in the Hyperlipidemia section based on expanded indication
- For cardiovascular risk reduction indication, add criteria for members without established CVD but who are considered high risk for CVD with requirements based on CLEAR trial inclusion criteria
- Remove the requirement for ezetimibe trial for cardiovascular risk reduction indication since the trial showed improved cardiovascular outcomes with Nexletol/Nexlizet use as either monotherapy or add-on to statins
- Remove the requirement for continued use of statin therapy because Nexletol/Nexlizet can be used as monotherapy as a result of expanded indication
- Update reauthorization criteria by excluding requirements for continued use of statin and/or ezetimibe

Adenosine Triphosphate-Citrate Lyase (ACL) inhibitors	
Therapeutic Classes (AHFS)	~~Anticonvulsants, Miscellaneous~~ Antilipemic Agents, Miscellaneous
Medications	Formulary, PA required Nexletol (bempedoic acid) Nexlizet (bempedoic acid/ezetimibe) 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), and the Drug Package Insert.
Exclusion Criteria	None
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	18 years or older
Prescriber Restrictions	Prescriber must be a cardiologist or specialist in the treatment of lipid disorders
Coverage Duration	**Initial Approval** 3 months **Later Approval** 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	**Initial Authorization:** **All Requests:** • Member must have documentation of baseline low density lipoprotein cholesterol (LDL-C) • Member has tried and failed a high-intensity statin (i.e. atorvastatin 40-80 mg, rosuvastatin 20-40 mg) at maximum tolerated dose for 3 months via claim history or chart notes OR documentation has been provided that the member is not able to tolerate a statin • Documentation was provided indicating provider has counseled member on smoking cessation and following a "heart healthy diet" • Dose is appropriate per label or supported by compendia/standard of care guidelines

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For Hyperlipidemia:

- One of the following:
  - Member has a diagnosis of heterozygous familial hypercholesterolemia (FH)
  - Member has a diagnosis of primary hyperlipidemia
- ~~Member has a diagnosis of heterozygous familial hypercholesterolemia (FH)~~
  ~~OR~~
- Member has tried and failed ezetimibe at a maximum tolerated dose or documentation has been provided that the member is not able to tolerate ezetimibe

For Cardiovascular Risk Reduction:

- Member has established cardiovascular disease (documented history of coronary artery disease, symptomatic peripheral arterial disease, and or cerebrovascular atherosclerotic disease)
- Member does not have established cardiovascular disease but is considered high risk (one of the following):
  - Diabetes mellitus (type 1 or type 2) in females over 65 years of age or males over 60 years of age
  - A Reynolds Risk score > 30% or a SCORE Risk score > 7.5% over 10 years
  - A coronary artery calcium score >400 Agatston units at any time in the past.
- ~~Member has a diagnosis of hyperlipidemia and atherosclerotic cardiovascular disease (ASCVD) as evidenced by a history of least one of the following:~~
  - ~~Myocardial infarction or acute coronary syndrome,~~
  - ~~Stroke or transient ischemic attack,~~
  - ~~Coronary artery disease with stable angina,~~
  - ~~Coronary or other arterial revascularization,~~
  - ~~Peripheral vascular disease, or~~
  - ~~Aortic aneurysm~~
  - ~~Clinically significant CHD diagnosed by invasive or non-invasive testing (such as coronary angiography, stress test using treadmill, stress echocardiography, or nuclear imaging)~~
    ~~AND~~
- ~~Member must have a fasting LDL-C ≥ 70 mg/dL~~
- ~~Member has tried and failed a high-intensity statin (i.e. atorvastatin 40-80 mg, rosuvastatin 20-40 mg) at maximum tolerated dose for 3 months via claim history or chart notes OR documentation has been provided that the member is not able to tolerate a statin.~~
- ~~Member has tried and failed ezetimibe at a maximum tolerated dose or documentation has been provided that the member is not able to tolerate ezetimibe~~.
- ~~Member will continue on maximum tolerated statin dose while receiving Nexletol/Nexlizet or documentation has been provided that the member is not able to tolerate a statin.~~
- ~~Documentation was provided indicating provider has counseled member on smoking cessation and following a "heart healthy diet".~~
- ~~Dose is appropriate per label or supported by compendia/standard of care guidelines~~

Reauthorization:

- Documentation was provided that the member has obtained clinical benefit from medication (e.g. LDL-C lowering from baseline)
- Dose continues to be appropriate per label or supported by compendia/standard of care guidelines
- ~~Member will continue on:~~

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	○ maximum tolerated statin dose while receiving Nexlizet or documentation has been provided that the member is not able to tolerate a statin, OR ○ maximum tolerated statin and ezetimibe dose while receiving Nexletol OR ○ documentation has been provided that the member is not able to tolerate a statin and/or ezetimibe.
Criteria Statement	Nexletol and Nexlizet are reserved for members who have a diagnosis of heterozygous familial hypercholesterolemia (FH) OR a diagnosis of primary hyperlipidemia and atherosclerotic cardiovascular disease (ASCVD) who have used (or cannot/should not use) a high-intensity statin and ezetimibe, and who have received counseling on smoking cessation and are following a "heart healthy diet". In addition, drugs are reserved for members who have high risk or established atherosclerotic cardiovascular disease (ASCVD) and have used (or cannot/should not use) a high-intensity statin and received counseling on smoking cessation and following a "heart healthy diet".
Last P&T Review Date	9/20236/2024

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Recommendation

- Update the name of the policy and add criteria for the new indication for IgE-mediated food allergy
- Update exclusion criteria with concomitant use of Palforzia (arachis hypogaea allergen powder) and emergency treatment of allergic reactions with Xolair—limitation of Xolair use per PI
- Simplify language in prescriber restriction section

Xolair (omalizumab) for Asthma, ~~and~~ Urticaria, and IgE-Mediated Food Allergy	
Therapeutic Classes (AHFS)	RESPIRATORY TRACT AGENTS, MISCELLANEOUS
Medications	Xolair (omalizumab)
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	• Use of Xolair concomitantly with another pulmonary biologic (e.g, Cinqair, Fasenra, Dupixent, Tezspire, or Nucala) • Use of Xolair concomitantly with Palforzia • Use of Xolair for emergency treatment of allergic reactions, including anaphylaxis
Required Clinical Information	See "PA Review Criteria"
Age Restrictions	N/A
Prescriber Restrictions	~~**Asthma:**~~ ~~Pulmonologist or Allergist or one was consulted~~ ~~**Chronic Idiopathic Urticaria:**~~ ~~Allergist, Immunologist, Dermatologist, or one was consulted~~ Prescribed by an allergist/immunologist, pulmonologist, or dermatologist, or in consultation with one of these specialists
Coverage Duration	**Initial Approval** Up to a 6 month duration **Later Approvals** Up to a 6 month duration If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	****For nasal polyposis, please refer to the "Biologic Agents for Nasal Polyposis" policy**** **INITIAL AUTHORIZATION FOR ASTHMA:** • The patient has at least a 6 month history of moderate-to-severe asthma. • The drug is indicated for the patient's age and is prescribed at an approved dose according to the patient's weight and IgE level • Patient is taking maximally tolerated ICS/LABA combination in addition to a LAMA (e.g. tiotropium) for at least 3 months or there is a documented medical reason why the patient is unable to take these medications • Patient's asthma is uncontrolled as defined by having one of the following: o Frequent severe exacerbations requiring two or more bursts of systemic glucocorticoids (more than three days each) in the previous year o History of serious exacerbation: at least one hospitalization, intensive care unit stay, or mechanical ventilation in the previous year o Airflow limitation defined as a forced expiratory volume in 1 second (FEV1) less than 80% of predicted o Poor symptom control including at least THREE of the following:

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	▪ Asthma Control Questionnaire (ACQ) consistently > 1.5 or Asthma Control Test (ACT) < 20 ▪ Daytime asthma symptoms more than twice per week ▪ Use of an inhaled short acting B-2 agonist to relieve asthma symptoms more than twice per week (not including use prior to exercise) ▪ Limited physical activity due to asthma symptoms ▪ Nighttime awakening due to asthma symptoms • The patient has a positive documented immediate response on RAST test and/or skin prick test to at least 1 common allergen (e.g. dermatophagoides farinae, dermatophagoides pteronyssinus, dog, cat, or cockroach) and there is documented evidence that the positive skin tested allergen(s) is an asthma trigger (copy of results required). • Pre-treatment serum IgE levels must be greater than or equal to 30IU/mL **INITIAL AUTHROIZATION FOR CHRONIC IDIOPATHIC URTICARIA:** • The drug is indicated for the patient's age and is prescribed at an approved dose • The patient has a documented history of urticaria for at least 6 weeks • The patient requires oral steroids to control symptoms. • The patient remains symptomatic despite a minimum two week trial (or has medical reason for not utilizing) of two formulary second generation H1 antihistamines at the maximum tolerated dose INITIAL AUTHORIZATION FOR IgE-MEDIATED FOOD ALLERGY: • Diagnosis of IgE-mediated food allergy with documented allergy to one or more of the following foods: ○ Peanut, milk, egg, wheat, cashew, hazelnut, or walnut • Attestation Xolair will be used in conjunction with food allergen avoidance • The drug is being prescribed at an FDA approved dose according to the member's weight and IgE level **REAUTHORIZATION: AFTER 4 MONTHS OF THERAPY FOR ASTHMA OR CHRONIC IDIOPATHIC URTICARIA:** • Documentation submitted indicates that the member has benefited clinically from the medication (e.g. patient has marked improvement in pulmonary function tests such as FEV1 or peak expiratory flow rate, decrease in asthma exacerbations, decrease in skin manifestations or severe itching, and/or a decrease in inhaled or oral corticosteroid use since receiving Xolair therapy). • The prescribed dose is within approved FDA dosing guidelines.
Criteria Statement	N/A
Last P&T Review Date	~~3~~6/2024

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Recommendations:

- Include a reference to the Wegovy criteria for requests for Wegovy to reduce the risk a major adverse cardiovascular events

Anti-Obesity Medications	
Therapeutic Classes (AHFS)	GI drugs, miscellaneous; anorexigenic agents
Medications	Alli (orlistat) Xenical (orlistat) Phentermine (phentermine hcl) (Adipex-P) Phentermine (phentermine hcl) (Lomaira) Qsymia (phentermine/topiramate) Contrave (naltrexone/bupropion) Saxenda (liraglutide) Wegovy (semaglutide) Zepbound (tirzepatide) Any other newly marketed agent ****Please Note: If the request is for Wegovy to reduce the risk of major adverse cardiovascular events please refer to the Wegovy criteria*****
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to 6 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	**INITIAL CRITERIA FOR APPROVAL** Phentermine HCL (Adipex-P) • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc) or history of heart attack, despite diet and exercise. • For phentermine (Lomaira): trial and failure or medical reason for not using generic phentermine (Adipex-P) Alli: • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack despite diet and exercise. Qsymia • **For adults:** Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack, despite diet and exercise. **OR** ○ **For pediatrics**: BMI in the ≥95th percentile standardized for age and sex

	▪ https://www.cdc.gov/healthyweight/bmi/calculator.html • Documented trial and failure, contraindication, or intolerance to use phentermine HCL (Adipex-P) and topiramate as separate ingredients <u>Contrave</u> • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack, despite diet and exercise. • Documented trial and failure, contraindication, or intolerance to use Qsymia <u>Saxenda, Wegovy, and Zepbound</u> • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one weight-related comorbidity (such as diabetes, controlled hypertension, hyperlipidemia etc.) or history of heart attack, despite diet and exercise • Documented trial and failure, contraindication, or intolerance to use Qsymia AND Contrave <u>Xenical:</u> • Diagnosis of obesity (including documentation of BMI ≥ 30) OR BMI ≥27 and at least one cardiovascular comorbidity (such as diabetes, controlled hypertension, history of heart attack, etc.) despite diet and exercise. • Documented trial and failure, contraindication, or intolerance to Alli dosed at 120 mg (2 capsules) three times daily. **<u>REAUTHORIZATION CRITERIA FOR APPROVAL</u>** • Documented weight loss of 5% of body weight or more, compared with baseline • If a weight-related comorbidity was previously noted, an objective improvement compared with baseline is documented (e.g. reduction in blood pressure, cholesterol, hemoglobin A1c, etc.)
Criteria Statement	Phentermine is reserved for members who are obese with body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes or hypertension. Generic Lomaira is reserved for members who have used (or cannot/should not use) generic Adipex-P. Alli is reserved for members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack. Qsymia is reserved for adult members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack or pediatric members who are obese with a BMI in the ≥95th percentile standardized for age and sex and who have used (or cannot/should not use) phentermine and topiramate as separate ingredients. Contrave is reserved for members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack and who have used (or cannot/should not use) Qsymia. Saxenda,Wegovy, and Zepbound are reserved for members who are obese with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack and who have used (or cannot/should not use) Qsymia and Contrave.

	Xenical is reserved for obese members with a body mass index of ≥ 30 or ≥ 27 with a comorbidity such as diabetes, hypertension, or heart attack and who have used (or cannot/should not use) Alli.
Last P&T Review Date	~~12/2023~~6/2024

Alameda PADs for review Q2 2024 P&T

Recommendation:

- Retire. Biogen has announced they will discontinue the development and commercialization of Aduhelm and will terminate the ENVISION clinical study.

Aduhelm (aducanumab)	
Medications	Aduhelm (aducanumab)
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	Patients with moderate to severe Alzheimer's Disease (AD) Patients with neurodegenerative disease caused by other than AD
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be a neurologist
Maximum Billable Units	variable
Coverage Duration	**Initial Authorization** The request will be approved in accordance with the FDA-indicated titration schedule for up to 6 months **Reauthorization** If all of the conditions are met, the request will be approved for 6 months.

Other Criteria	**Initial Authorization**
	• Diagnosis of mild cognitive impairment (MCI) caused by AD or mild AD as evidenced by at least one of the following:
	  ○ Clinical Dementia Rating Global (CDR-G) score of 0.5 (very mild dementia)
	  ○ Repeatable Battery for Assessment of Neuropsychological Status (RBANS) delayed memory index (DMI) score ≤ 85 (low average)
	  ○ Mini-Mental State Examination (MMSE) score ≥ 24 (questionably significant impairment)
	• The request is for an FDA approved dose
	• Documentation of BOTH of the following:
	  ○ Recent, within past year, positive results for the presence of beta-amyloid plaques on a positron emission tomography (PET) scan or cerebrospinal fluid testing
	  ○ Recent, within past year, baseline Magnetic Resonance Imaging (MRI) scan
	• Not currently using blood thinners (except aspirin)
	• No recent (past 1 year) history of stroke or transient ischemic attack (TIA)
	Reauthorization
	• The request is for an FDA approved dose
	• Provider attestation of safety monitoring and management of amyloid related imaging abnormalities (ARIA) and intracerebral hemorrhage, as recommended per the manufacturer's prescribing information.
	• Patient continues to have a diagnosis of mild cognitive impairment (MCI) caused by AD or mild AD consistent with Stage 3 or Stage 4 Alzheimer's disease as evidenced by at least one of the following:
	  ○ CDR-G score of 0.5 (very mild dementia)
	  ○ RBANS DMI score ≤ 85 (low average)
	  ○ MMSE score of 24-30

	• Not currently using blood thinners (except aspirin) • No recent (past 1 year) history of stroke or TIA • Recent, within past year, positive results for the presence of beta-amyloid plaques on a positron emission tomography (PET) scan 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	9/2023

Recommendation:

- Add two new indications for Breyanzi (relapsed or refractory CLL and SLL)
- Reformat "other criteria" section by breaking it down by the specific type of leukemia and NHL and rearrange in an alphabetical order

Anti-CD19 CAR-T Immunotherapies	
Medications	Kymriah (tisagenlecleucel) Yescarta (axicabtagene ciloleucel) Tecartus (brexucabtagene autoleucel) Breyanzi (lisocabtagene maraleucel)
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	Patients with primary central nervous system lymphoma
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber must be an oncologist, hematologist or other appropriate specialist
Coverage Duration	If all the criteria are met, the initial request will be approved for a one –time infusion per lifetime.
Maximum Billable Units	Variable

Other Criteria	**Initial authorization:**
	• Patient must not have received prior anti-CD19 CAR-T therapy.
	• Patient will be screened for HBV, HCV, and HIV in accordance with clinical guidelines.
	• Patient does not have an active infection or inflammatory disorder.
	• Patient has a life expectancy greater than 12 weeks.
	• Patient will not receive live virus vaccines for at least 6 weeks prior to the start of lymphodepleting chemotherapy and until immune recovery following treatment.
	• Use is supported by a labeled indication or NCCN guidelines
	
	Leukemia
	
	For B-cell precursor Acute Lymphoblastic Leukemia (ALL):
	• If the request is for Kymriah
	  ○ Patient is 25 years of age or younger
	  ○ ALL that is refractory or in second or later relapse as defined by:
	  ▪ Second or greater bone marrow (BM) relapse or
	  ▪ Any BM relapse after allogeneic stem cell transplant (alloSCT) and greater than or equal to 6 months from SCT at the time of tisagenlecleucel infusion or
	  ▪ Primary refractory, defined as not achieving complete remission (CR) after 2 cycles of a standard chemotherapy regimen, or chemorefractory, defined as not achieving CR after 1 cycle of standard chemotherapy for relapsed leukemia or
	  ▪ Philadelphia chromosome–positive ALL intolerant of or with 2 failed lines of tyrosine kinase inhibitor (TKI) therapy or if TKI therapy is contraindicated or
	  ▪ Ineligible for alloSCT due to comorbid disease, contraindications to alloSCT conditioning regimen, lack of a suitable donor, prior SCT, or declined alloSCT after documented discussion about the role of SCT with a physician
	• If the request is for Tecartus
	  ○ Patient is 18 years of age or older

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- ALL that is relapsed or refractory
  - Primary refractory disease
  - First relapse if first remission ≤ 12 months
  - Relapsed or refractory disease after 2 or more lines of systemic therapy
  - Relapsed or refractory disease after alloSCT, provided patient is at least 100 days from SCT at the time of brexucabtagene infusion

For Chronic Lymphocytic Leukemia (CLL):

- If the request is for Breyanzi
  - Patient is 18 years of age of older
  - Patient has relapsed/refractory disease defined as failure of two or more lines of therapy, including a Bruton tyrosine kinase (BTK) inhibitor AND a B-cell lymphoma 2 (BCL-2) inhibitor

Non-Hodgkin's Lymphoma (NHL)

For Follicular Lymphoma (FL):

- If the request is for Kymriah or Yescarta:
  - Patient is 18 years of age or older
  - Patient has relapsed/refractory disease defined as failure of two or more lines of systemic therapy

For Large B-cell Lymphoma (LBCL), Diffuse Large B-cell Lymphoma (DLBCL) not otherwise specified, primary mediastinal high grade B-cell lymphoma, follicular lymphoma grade 3B, and DLBCL arising from follicular lymphoma:

- If the request is for Breyanzi, Kymriah, or Yescarta
  - Patient is 18 years of age or older
  - For Breyanzi ONE of the following:
    - Patient is refractory to first-line chemoimmunotherapy or relapsed within 12 months of first-line chemoimmunotherapy
    - Patient is refractory to first-line chemoimmunotherapy or relapsed after first-line chemoimmunotherapy and is not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age
    - Patient has failed two or more lines of systemic therapy
  - For Kymriah: Patient has relapsed/refractory disease defined as failure of two or more lines of systemic therapy
  - For Yescarta ONE of the following:
    - Patient is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy or
    - Patient has failed two or more lines of systemic therapy

For Mantle Cell Lymphoma (MCL):

- If the request is for Tecartus:
  - Patient is 18 years of age or older
  - Patient has relapsed/refractory disease defined as failure of BOTH of the following lines of therapy:
    - Chemoimmunotherapy such as an anti-CD20 monoclonal antibody (e.g. Rituxan) + any chemotherapeutic agent

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	▪ Bruton Tyrosine Kinase (BTK) Inhibitor (e.g. Calquence, Imbruvica, Brukinsa) **For Small Lymphocytic Lymphoma (SLL):** • If the request is for Breyanzi o Patient is 18 years of age or older ~~—~~Patient has received at least 2 prior lines of therapy including, a Bruton tyrosine kinase (BTK) inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor ~~**For other forms of NHL:**~~ ~~• If the request is for Breyanzi (lisocabtagene maraleucel), Kymriah (tisagenlecleucel), Yescarta (axicabtagene ciloleucel)~~ ~~o Use is supported by a labeled indication or NCCN guidelines~~ ~~o Patient is 18 years of age or older~~ ~~o For Breyanzi: ONE of the following:~~ ~~▪ Patient is refractory to first-line chemoimmunotherapy or relapsed within 12 months of first-line chemoimmunotherapy~~ ~~▪ Patient is refractory to first-line chemoimmunotherapy or relapsed after first-line chemoimmunotherapy and is not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age~~ ~~o For Kymriah: Patient has relapsed/refractory disease defined as failure of two or more lines of systemic therapy~~ ~~o For Yescarta: Patient is refractory to first-line chemoimmunotherapy or relapsed within 12 months of first-line chemoimmunotherapy OR has failed two or more lines of systemic therapy~~ **Re-authorization:** • Treatment exceeding 1 dose per lifetime will not be authorized. 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	~~6/2023~~6/2024

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Recommendation:

- Add an exclusion requirement that Spinraza and Evrysdi should not be used concomitantly, as they share a similar MOA.
- Remove the exclusion for Spinraza following Zolgensma. There is an ongoing phase 4, open label trial for Spinraza where the interim results show promise for both efficacy and safety in treating patients with Spinraza after Zolgensma.

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 ~~For Spinraza: Patient has previously received treatment with Zolgensma~~
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, or Upper Limb Module (ULM) 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, ULM score, 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	~~6/2023~~6/2024

Recommendation:

- Update policy based on expanded indication of Spevigo for GPP maintenance treatment in adult and pediatric patients, in addition to the existing indication for acute GPP flares
- Add coverage duration for maintenance treatment
- Separate initial authorization into two sections for each indication
- Add reauthorization section

Generalized Pustular Psoriasis (GPP) Agents	
Medications	Spevigo (spesolimab-abzo)
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"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a dermatologist or geneticist
Coverage Duration	Acute Flares (IV vial): If all of the criteria are met, the request will be approved for up to 2 doses. Maintenance Treatment (SQ syringe): If all criteria are met, the initial request will be approved for 12 months. Reauthorization requests will be approved for 12 months.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization**
	• Diagnosis of generalized pustular psoriasis (GPP)
	• If request is for an acute GPP flare (IV vial), Mmember ~~is~~ must be experiencing an acute flare of GPP of moderate to severe intensity as defined by ~~the patient~~ having all of the following:
	  ○ Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) total score of 3 or greater
	  ○ Presence of fresh pustules (new appearance or worsening of pustules)
	  ○ GPPPGA pustulation sub score of 2 or greater
	  ○ At least 5% of body surface area covered with erythema and the presence of pustules
	• ~~If member has previously received Spevigo treatment for a prior GPP flare, member must have achieved a clinical response, defined as achieving a GPPPGA score of 0 or 1, to previous treatment but is now experiencing a new flare~~
	• If request is for maintenance treatment of GPP (SQ syringe), member must have all of the following:
	  ○ History of at least two GPP flares in the past year of moderate to severe intensity
	  ○ GPPPGA score of 0 or 1
	  ○ Documented trial and failure, intolerance, or contraindication to ~~TWO~~ of the following: oral retinoids, methotrexate, and cyclosporine
	• Medication is prescribed at an FDA approved dose
	Reauthorization
	• If request is for an acute GPP flare (IV vial), member must have achieved a clinical response, defined as achieving a GPPPGA score of 0 or 1, to previous treatment and is now experiencing a new flare
	• If request is for maintenance treatment of GPP (SQ syringe), member must

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	have documentation of positive clinical response to therapy (i.e., reduction in GPP flares) • Medication is prescribed at 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	~~9/2023~~6/2024

Recommendation:

- Update exclusion criteria based on the approval of a new drug Filsuvez for this indication
- Define maximum authorization amount for Vyjuvek

Vyjuvek	
Medications	Vyjuvek (beremagene geperpavec-svdt)
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	• Other forms of epidermolysis bullosa, such as epidermolysis bullosa simplex, junctional epidermolysis bullosa, kindler epidermolysis bullosa • Concurrent use of Vyjuvek and Filsuvez
Required Clinical Information	See "other criteria"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a dermatologist, geneticist, or specialist experienced in the treatment of dystrophic epidermolysis bullosa.
Coverage Duration	If the criteria are met, the initial request will be approved for up to a 3 month duration; reauthorization requests will be approved for up to 6 months.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	• Patient has a diagnosis of dystrophic epidermolysis bullosa, with confirmed mutation(s) in the COL7A1 gene via genetic testing.
	• Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected
	• Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated
	• Medication is prescribed at an FDA approved dose, and maximum weekly dispensable amount is not exceeded
	  ○ Requests exceeding more than one vial per week will not be approved
	Re-Authorization:
	• Documentation or provider attestation of positive clinical response (i.e. improvement in wound appearance, wound closure, healing, etc.)
	• Documentation indicating need for continued treatment is needed (either to partially healed wounds or to other wound sites)
	• Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected
	• Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated
	• Medication is prescribed at an FDA approved dose, and maximum weekly dispensing amount is not exceeded
	  ○ Requests exceeding more than one vial per week 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	~~9/2023~~6/2024

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PERFORMRX NATIONAL NEW PRODUCTS REVIEW

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
2/20/2024	Alvaiz	eltrombopag 9 mg, 18 mg, 36 mg, 54 mg oral tablets	Teva	• Treatment of thrombocytopenia in adult and pediatric patients 6 years and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy; Alvaiz should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding • Treatment of thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy; Alvaiz should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy • Treatment of adult patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy	$6,884−$37,375 (dosing varies significantly depending on platelet count)	Promacta, Nplate, Doptelet, Tavalisse	Non-formulary

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
2/20/2024	Xolair	omalizumab 75 mg/0.5 mL, 150 mg/mL, 300 mg/2 mL subcutaneous auto-injector; 300 mg/2 ml subcutaneous syringe	Genentech	• Moderate to severe persistent asthma in adults and pediatric patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids • Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment • IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may occur with accidental exposure to one or more foods; to be used in conjunction with food allergen avoidance • Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment	$693−$11,080 (dosing & frequency varies significantly depending on serum IgE levels and body weight)	Dupixent, Nucala	F; PA (See updated MRG) (already added via CRF)
2/20/2024	Eohilia	budesonide 2 mg/10 ml oral suspension	Takeda Pharmaceuticals	• For 12 weeks of treatment in adult and pediatric patients 11 years of age and older with eosinophilic esophagitis (EoE)	$1,875	Omeprazole, Pantoprazole, Esomeprazole, Dupixent	Non-formulary (see new MRG)

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
2/27/2024	Amtagvi	lifileucel intravenous suspension	Iovance Biotherapeutics	• Treatment of adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor This indication is approved under accelerated approval based on objective response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).	$515,000 per one-time treatment	Keytruda, Opdivo, Braftovi + Mektovi, Cotellic + Zelboraf, Tafinlar + Mekinist	Non-formulary (see new PAD)
2/27/2024	Filsuvez	birch triterpenes 10% topical gel	Chiesi USA	• Treatment of wounds associated with dystrophic and junctional epidermolysis bullosa in adult and pediatric patients 6 months of age and older	$12,600−$54,000 (price varies significantly depending on how often patient utilizes product)	Vyjuvek	Non-formulary (see new MRG)
3/7/2024	FreeStyle Libre	FreeStyle Libre 3 Reader Device	Abbott Diabetes	• A real time continuous glucose monitoring (CGM) device with alarms capability indicated for the management of diabetes in persons age 4 and older.	$70	FreeStyle Libre 14 Day Reader Device, FreeStyle Libre 2 Reader Device, FreeStyle Libre Reader Device, Dexcom G6 Receiver Device, Dexcom G7 Receiver Device	Non-formulary
3/7/2024	Zymfentra	infliximab-dyyb 120 mg/ml subcutaneous syringe; 120 mg/ml subcutaneous auto-injector	Celltrion	Tumor necrosis factor (TNF) blocker indicated in adults for maintenance treatment of: • Moderately to severely active ulcerative colitis following treatment with an infliximab product administered intravenously • Moderately to severely active Crohn's disease following treatment with an infliximab product administered intravenously	$6,181	Infliximab, Inflectra, Remicade, Renflexis, Avsola	Non-formulary

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
3/12/2024	Opill	norgestrel 0.075 mg oral tablet	Perrigo	• To prevent pregnancy	$17−$25	Norethindrone	F (already added via CRF)
3/12/2024	Hemlibra	emicizumab-kxwh 12 mg/0.4 ml subcutaneous vial	Genentech	• For routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors	$47,018 for a 70 kg adult	Altuviiio, Eloctate, Advate, Esperoct, Jivi, Novoeight	Non-formulary
3/12/2024	Pemrydi RTU	pemetrexed 100 mg/10 ml, 500 mg/50 ml intravenous vials	Amneal Pharmaceuticals	• In combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations • In combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous NSCLC • As a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy • As a single agent for the treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy	$7,191 per 21-day cycle for an adult with a BSA of 1.7 m^2	Pemetrexed	Non-formulary
3/12/2024	RiVive	naloxone 3 mg nasal spray	Harm Reduction Therapeutics, Inc.	• To “revive” someone during an overdose from many prescription pain medications or street drugs such as heroin	$36 per package	Naloxone nasal spray	Non-formulary
3/12/2024	Yuflyma	adalimumab-aaty 20 mg/0.2 ml subcutaneous syringe	Celltrion	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn’s Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, Uveitis	$3,288 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yusimry, Hadlima, Abrilada	Non-formulary

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
3/26/2024	Alyglo	immune globulin (human)-stwk 5 g/50 ml, 10 g/100 ml, 20 g/200 ml intravenous vials	GC Biopharma	• Treatment of primary humoral immunodeficiency (PI) in adults	$1,490 per 50 ml vial (price varies significantly depending on patient's weight and dose)	Gamunex-C, Octagam, Flebogamma, Asceniv, Privigen, Bivigam, Panzyga	Non-formulary
3/26/2024	Rezdiffra	resmetirom 60 mg, 80 mg, 100 mg oral tablets	Madrigal Pharmaceuticals	• To be used in conjunction with diet and exercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) This indication is approved under accelerated approval based on improvement of NASH and fibrosis. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.	$3,950	None	Non-formulary (see new MRG)
4/2/2024	Simlandi	adalimumab-ryvk 40 mg/0.4 ml subcutaneous auto-injector	Teva Pharmaceuticals	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, Uveitis	$519 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yusimry, Yuflyma, Hadlima, Abrilada	Non-formulary
4/2/2024	Lenmeldy	atidarsagene autotemcel 1.8 to 11.8 x 10^6 CD34+ cells/ml intravenous suspension	Orchard Therapeutics	• Treatment of children with pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ) or early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD)	$4.25 million per one-time treatment	None	Non-formulary (see new PAD)
4/9/2024	Winrevair	sotatercept-csrk 45 mg, 60 mg subcutaneous vials	Merck Sharp & Dohme	• Treatment of adults with pulmonary arterial hypertension (PAH, WHO Group 1) to increase exercise capacity, improve WHO functional class (FC) and reduce the risk of clinical worsening events	$14,000 every 3 weeks for a 70 kg adult	Tadalafil, Sildenafil, Ambrisentan, Opsumit, Bosentan, Epoprostenol, Orenitram, Tyvaso, Ventavis, Uptravi	Non-formulary
4/9/2024	Spevigo	spesolimab-sbzo 150 mg/ml subcutaneous syringe	Boehringer Ingelheim Pharmaceuticals	• Treatment of generalized pustular psoriasis (GPP) in adults and pediatric patients 12 years of age and older and weighing at least 40 kg	$17,385 for maintenance dose	Methotrexate, Acitretin, Cyclosporine, Infliximab, Cosentyx, Taltz, Stelara, Tremfya	Non-formulary (see updated PAD)

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
4/9/2024	Voydeya	danicopan 50 mg, 100 mg oral tablets	Alexion Pharmaceuticals	• To be used as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH)	$5,508 (max dose)	Empaveli, Fabhalta	Non-formulary
4/9/2024	Baclofen	baclofen 15 mg oral tablets	TruPharma	• For the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity	$293 (max dose)	Tizanidine, Gabapentin, Dantrolene, Clonazepam, Diazepam	Non-formulary
4/9/2024	Opsynvi	macitentan/tadalafil 10 mg-20 mg, 10 mg-40 mg oral tablets	Actelion Pharmaceuticals	• For chronic treatment of pulmonary arterial hypertension (PAH, WHO Group I) in adult patients of WHO functional class (FC) II-III	$12,635	Opsumit + Tadalafil	Non-formulary
4/23/2024	Cyclophosphamide	cyclophosphamide 500 mg/5 ml, 1000 mg/10 ml, 2000 mg/20 ml intravenous vials	Sandoz	Treatment of adult patients with: • Malignant lymphomas (Stages III and IV of the Ann Arbor staging system), Hodgkin's lymphoma, lymphocytic lymphoma (nodular or diffuse), mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma • Multiple myeloma • Leukemias: chronic lymphocytic leukemia, chronic granulocytic leukemia (it is usually ineffective in acute blastic crisis), acute myelogenous and monocytic leukemia, acute lymphoblastic (stem-cell) leukemia (cyclophosphamide given during remission is effective in prolonging its duration) • Mycosis fungoides (advanced disease) • Neuroblastoma (disseminated disease) • Adenocarcinoma of the ovary • Retinoblastoma • Carcinoma of the breast	$421 per 5 ml vial (price varies depending on patient's weight and dosing frequency)	Bendamustine, Melphalan, Ifosfamide, Busulfan, Cisplatin, Oxaliplatin	Non-formulary

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
4/23/2024	Tyenne	tocilizumab-aazg 80 mg/4 ml, 200 mg/10 ml, 400 mg/20 ml intravenous vials	Fresenius Kabi	Rheumatoid Arthritis, Giant Cell Arteritis, Polyarticular Juvenile Idiopathic Arthritis, Systemic Juvenile Idiopathic Arthritis	$1,958 per 20 ml vial (dosing and price varies depending on indication and patient's weight)	Actemra, Adalimumab, Infliximab, Kineret, Orencia, Simponi, Cimzia, Rinvoq	Non-formulary
4/23/2024	Ogsiveo	nirogacestat 100 mg, 150 mg tablets	SpringWorks Therapeutics, Inc.	• For adult patients with progressing desmoid tumors who require systemic treatment	$29,000	None	Non-formulary
4/23/2024	Adalimumab-aaty	adalimumab-aaty 20 mg/0.2 ml, 40 mg/0.4 ml subcutaneous syringe; 40 mg/0.4 ml, 80 mg/0.8 ml subcutaneous auto-injector	Celltrion	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, Uveitis	$519 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yusimry, Hadlima, Abrilada, Simlandi	Non-formulary
4/30/2024	Xcopri	cenobamate 25 mg oral tablets	SK Life Science	• Treatment of partial-onset seizures in adult patients	$1,180 for maintenance dose	Pregabalin, Lacosamide Fycompa, Aptiom, Topiramate ER	Non-formulary
4/30/2024	Adalimumab-ryvk	adalimumab-ryvk 40 mg/0.4 ml subcutaneous auto-injector	Quallent Pharmaceuticals	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, Uveitis	$1,875 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yusimry, Hadlima, Abrilada, Yuflyma	Non-formulary
4/30/2024	Extencilline	penicillin G benzathine 1,200,000 units, 2,400,000 units intramuscular vials	Provepharm, Inc.	• Treatment of: o Erysipelas o Syphilis: early syphilis (primary and secondary) o Latent syphilis (except for neurosyphilis and presence of pathological CSF findings) o Yaws o Pinta • Prophylaxis of: o Rheumatic fever (chorea, rheumatic carditis) o Poststreptococcal glomerulonephritis o Erysipelas	$380 per 2,400,000 unit vial (dosing and price varies depending on indication and patient's weight)	Bicillin L-A, Penicillin G Potassium	Non-formulary

DATE ADDED	BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
5/7/2024	Libervant	diazepam 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg buccal films	Aquestive Therapeutics, Inc.	• Acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy between 2 to 5 years of age	$345 per dose	Diazepam rectal gel, Nayzilam, Valtoco	Non-formulary
5/7/2024	Anktiva	nogapendekin alfa inbakic-pmln 400 mcg/0.4 ml intravesical vial	Altor BioScience, LLC	• To be used with Bacillus Calmette-Guérin (BCG) for the treatment of adult patients with BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.	$35,800 (average monthly price) for maintenance dose	Keytruda, Adstiladrin	Non-formulary
5/7/2024	Ojemda	tovorafenib 100 mg oral tablets; 25 mg/mL oral suspension	Day One Biopharmaceuticals	• Treatment of patients 6 months of age and older with relapsed or refractory pediatric lowgrade glioma (LGG) harboring a BRAF fusion or rearrangement, or BRAF V600 mutation This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).	$33,916	Mekinist + Tafinlar	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.