PHARMACY & THERAPEUTICS COMMITTEE

Tuesday, December 17th, 2024
5:00pm – 7:00pm

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

Location: Microsoft Teams
Meeting ID: 274 205 345 92
Password: kdZByF

YOU MAY SUBMIT COMMENTS ON ANY AGENDA ITEM OR ON ANY ITEM NOT ON THE AGENDA, IN WRITING VIA MAIL TO "ATTN: ALLIANCE PHARMACEUTICAL AND THERAPEUTICS COMMITTEE" 1240 SOUTH LOOP ROAD, ALAMEDA, CA 94502; OR THROUGH E-COMMENT AT bochoa@alamedaalliance.org . YOU MAY WATCH THE MEETING LIVE BY LOGGING IN VIA COMPUTER AT THE FOLLOWING LINK: Microsoft Teams Meeting OR MAY LISTEN TO THE MEETING BY CALLING IN TO THE FOLLOWING TELEPHONE NUMBER: +1 510-210-0967,545539741#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, Chief Medical Officer – Alameda Alliance* *Nora Tomassian, PharmD MBA, Interim Pharmacy Director – Alameda Alliance* • New P&T member: Dr. Charles Raynard – Alameda Behavioral Health, Director of Pharmacy Services • D-SNP P&P updates • Recruitment for permanent director of pharmacy services • Optum Pharmacy network inclusion starting 1/1/2025 • Electronic prescriptions on provider portal update	15 min	-
III)	**Pharmacy Utilization Reports (Quarter 3, 2024)** *Nora Tomassian, PharmD MBA, Interim Pharmacy Director – Alameda Alliance* • Top 50 Drugs by Cost • Top 50 PA Reviewed Drugs	2 min	-
	ADJOURN TO CLOSED SESSION *(Pursuant to California Government Code Title 5, §54954.5(h))* ***Discussion will Concern:*** *Review and Recommendations to changes to the AAH Formulary and utilization management for selected drug classes* ***Estimated Date of Public Disclosure: 12/17/2024*** *(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

TBD, PharmD, Senior Pharmacy Director – Alameda Alliance
Benita Ochoa, CPhT, Lead Pharmacy Technician – Alameda Alliance
(All matters listed on the Consent Calendar are to be approved with one motion unless a member of the P&T Committee removes an item for separate action. Any consent calendar item for which separate action is requested shall be heard as the next Agenda item in closedsession.)

Monographs/Class Reviews	Changes
Blood Glucose Test Strips class review	• No changes
Calcium and Vitamin D class review	• No changes
Osteoporosis Agents class review	• No changes
Pulmonary Arterial Hypertension Agents class review	• No changes
Urinary Tract Antispasmodics class review	• No changes
Medication Request Guidelines	**Changes**
Oral and Injectable Oncology Medications	• No changes
Non-Formulary/Prior Authorization Required Medications	• No changes
Step Therapy Exception	• No changes
Prior Authorization Exception	• No changes
Urinary Incontinence Agents	• Naming change to reflect generic availability of Myrbetriq as mirabegron
Blood Glucose Testing Supplies	• No changes
Butorphanol (Stadol NS)	• No changes
Corticotropin	• Remove duplicate specialist prescriber restriction
Endari	• No changes
Diclofenac sodium (Solaraze) 3% gel	• No changes
Growth Hormone	• Remove discontinued drug SaizenPrep
Rapid-Acting Insulin	• No changes
Long-Acting Basal Insulin	• No changes
Isotretinoin capsules	• Remove discontinued drug Myorisan
Gonadotropin Releasing Hormone (GNRH) Agonists	• No changes

10 min EV

Self-administered Disease Modifying Therapies (DMTs) for Multiple Sclerosis	• No changes
dalfampridine (Ampyra)	• No changes
Ophthalmic Anti-Inflammatory Agents	• No changes
Fentanyl Citrate	• No changes
Proton Pump Inhibitors (PPIs)	• No changes
Ranolazine (Ranexa, Aspruzyo)	• No changes
Temazepam (Restoril)	• No changes
Testosterone Agents	• No changes
Thalomid (thalidomide)	• No changes
Topical Diclofenac	• No changes
Oral Anti-Fungals	• Change naming convention of Noxafil to reflect its generic availability
Gattex (teduglutide)	• No changes
Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors	• No changes
Otezla (apremilast) for Behcet Disease	• No changes
Rayaldee (calcifediol ER)	• No changes
Korlym (mifepristone)	• No changes
Tetracycline Antibiotics	• No changes
Agents for graft versus host disease	• No changes
Janus Kinase Inhibitors for Nonsegmental Vitiligo	• No changes
Budesonide Nebulization Solution (Pulmicort Respules)	• No changes
Lodoco	• No changes
Sohonos	• No changes
Physician Administered Drug (PAD) Guidelines	**Changes**
Injectable/Specialty Medications	• No changes
Oral and Injectable Oncology Medications	• No changes
Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple	• No changes

Viltepso	• No changes
Veopoz	• No changes
Lantidra	• No changes
Bleeding Disorder Products	• No changes
Interim Formulary Updates	
See p. 188 in packet	
Summary of Physician Administered Drug (PAD) Updates	
• None	
Pharmacy Policy & Procedure Updates	
• RX-004 Formulary Management	
D-SNP P&Ps (11, clean versions)	
• Medicare Medication Coverage under Part A, Part B or Part D	• Claim Adjudication
• Part D Coverage Determinations	• Drug Utilization Management
• Medicare Part D Daily Rejected Claims Review	• Medicare Part D End Stage Renal Disease (ESRD)
• Part D Appeals (Redeterminations)	• Part D Formulary Development and Management
• Pharmacy and Therapeutics (P&T) Committee Delegation Oversight and Monitoring	• Prescription Drugs Event (PDE) Submission, Rejection, Monitoring and Resolution
• Part D Transition Process	
ED Oversight	
• **None**	
90 Day Maintenance List updates	
• **NA**	
P&T Meeting Minutes	
• P&T Meeting Minutes Q3 September 24, 2024	

V) New Business

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

- **Medical Benefit PAD recalls P&P** (RX-015)

New MRG

- Ohtuvayre
- Nemluvio
- Yorvipath
- Ileal bile acid transporter inhibitors (IBATs)

New PAD

- Kisunla
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) Agents

V

VI) Class Reviews, Monographs, and Recommendations

Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Topical Agents for Actinic Keratosis Class Review
2. Cobenfy Monograph
    a. New MRG: Cobenfy
3. Tecelra Monograph
    a. New PAD: Tecelra

VII) Medication Request Guidelines

Rahel Negash, PharmD, Pharmacist – Alameda Alliance

1. Injectable Methotrexate
2. Immunizations
3. Botulinum Toxins A&B
4. Jesduvroq
5. Ocaliva
6. Vigabatrin (Sabril)
7. Oxbryta (voxelotor)

VIII) Physician Administered Drug (PAD) Policies

Iryna Makukh, PharmD, Pharmacist – PerformRx

1. Complement Inhibitors
2. Neuromyelitis Optica Spectrum Disorder (NMOSD) Agents
3. Botulinum Toxins A&B
4. Myasthenia Gravis Agents
5. Gene therapy for sickle cell disease

10 min — V

IX) Informational Updates on New Developments in Pharmacy

Iryna Makukh, PharmD, Pharmacist – PerformRx

- New Product Review

2 min — -

X) Old Business

Rahel Negash, PharmD, Pharmacist – Alameda Alliance

- Pharmacists to prescribe Naloxone at POS

2 min — V

RECONVENE IN OPEN SESSION

XI) Public Comment

XII) Adjournment

PHARMACY & THERAPEUTICS COMMITTEE

Tuesday, December 17th, 2024
5:00pm – 7:00pm

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

FUTURE P&T MEETINGS	
NEXT MEETING	**2025 P&T MEETINGS**
March 18, 2025	June 17, 2025 September 16, 2025 December 16, 2025

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

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

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

636 IHSS Top 50 Drugs by Cost for 3rd Quarter 2024

- The top 50 drugs accounted for **1,425 claims** for **834 members** and cost **$1,691,221,** which is an increase of $248,849 in spend from the previous quarter.
- Biktarvy remains at number one, claims having gone up by 4, and there is one less member since the previous quarter.
- Ozempic is at numbers 2, 7 and 8, with 268 total claims for 117 members. There was an increase of 59 claims and of 14 members from the previous quarter.
- Zejula is down to number 3 with 3 claims for 1 member. This medication is managed via the Oral and Injectable Oncology Medications MRG.
- Rezurock is up to number 4 with 3 claims for 1 member. This medication is managed via the Agents for graft versus host disease MRG.
- Paxlovid is up at number 5 with 65 claims for 65 members. There was an increase of 37 claims and of 37 members from the previous quarter.

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
1	201625	Biktarvy Oral Tablet 50-200-25 MG	35	11	$134,504.62
2	221271	Ozempic (0.25 or 0.5 MG/DOSE) Subcutaneous Solution Pen-injector 2 MG/3ML	123	56	$114,472.19
3	223302	Zejula Oral Tablet 100 MG	3	1	$106,178.85
4	215662	Rezurock Oral Tablet 200 MG	3	1	$105,491.01
5	219459	Paxlovid (300/100) Oral Tablet Therapy Pack 20 x 150 MG & 10 x 100MG	65	65	$92,436.96
6	195609	Vemlidy Oral Tablet 25 MG	52	20	$83,765.78
7	218338	Ozempic (2 MG/DOSE) Subcutaneous Solution Pen-injector 8 MG/3ML	80	32	$74,638.21
8	209911	Ozempic (1 MG/DOSE) Subcutaneous Solution Pen-injector 4 MG/3ML	65	29	$60,451.99
9	197146	Cosentyx Sensoready (300 MG) Subcutaneous Solution Auto-injector 150 MG/ML	7	2	$50,927.94
10	120505	Sprycel Oral Tablet 20 MG	3	1	$44,782.98
11	214809	Skyrizi Pen Subcutaneous Solution Auto-injector 150 MG/ML	2	2	$41,332.16
12	219135	Skyrizi Subcutaneous Solution Cartridge 360 MG/2.4ML	2	1	$41,332.16

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
13	122702	Januvia Oral Tablet 100 MG	72	28	$39,541.33
14	207961	Rybelsus Oral Tablet 7 MG	41	20	$38,160.74
15	177191	Eliquis Oral Tablet 5 MG	65	31	$36,839.89
16	217445	Tarpeyo Oral Capsule Delayed Release 4 MG	2	1	$31,936.26
17	190802	Genvoya Oral Tablet 150-150-200-10 MG	8	3	$31,157.18
18	202548	Humira (2 Syringe) Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	2	1	$26,885.14
19	170343	Jakafi Oral Tablet 5 MG	2	1	$24,974.70
20	184849	Jardiance Oral Tablet 25 MG	42	18	$24,102.03
21	193380	Sofosbuvir-Velpatasvir Oral Tablet 400-100 MG	3	1	$23,154.00
22	229056	Dupixent Subcutaneous Solution Auto-injector 300 MG/2ML	6	2	$22,637.94
23	207962	Rybelsus Oral Tablet 14 MG	24	10	$22,389.36
24	198848	Nerlynx Oral Tablet 40 MG	4	1	$21,739.60
25	229051	Trulicity Subcutaneous Solution Auto-injector 1.5 MG/0.5ML	23	9	$21,665.18
26	223809	Cosentyx UnoReady Subcutaneous Solution Auto-injector 300 MG/2ML	3	1	$21,559.53
27	201117	Steglatro Oral Tablet 15 MG	60	26	$20,072.80
28	184848	Jardiance Oral Tablet 10 MG	34	16	$19,828.83
29	201116	Steglatro Oral Tablet 5 MG	46	21	$19,147.26
30	193034	Ocaliva Oral Tablet 5 MG	2	1	$18,889.02
31	218736	Radicava ORS Starter Kit Oral Suspension 105 MG/5ML	1	1	$18,682.26
32	182336	Farxiga Oral Tablet 10 MG	33	16	$18,245.20

Rank	DDID	Label Name	Claims	Unique Members	Total Cost
33	224365	Comirnaty Intramuscular Suspension Prefilled Syringe 30 MCG/0.3ML	103	103	$17,994.60
34	182488	Glatiramer Acetate Subcutaneous Solution Prefilled Syringe 40 MG/ML	3	1	$16,013.49
35	190947	Tagrisso Oral Tablet 80 MG	1	1	$15,706.50
36	215134	Wegovy Subcutaneous Solution Auto-injector 0.5 MG/0.5ML	12	9	$15,687.42
37	229072	Mounjaro Subcutaneous Solution Auto-injector 5 MG/0.5ML	14	7	$14,407.84
38	215135	Wegovy Subcutaneous Solution Auto-injector 0.25 MG/0.5ML	11	10	$14,382.44
39	204204	Shingrix Intramuscular Suspension Reconstituted 50 MCG/0.5ML	61	59	$13,043.17
40	212379	Cabenuva Intramuscular Suspension Extended Release 600 & 900 MG/3ML	2	2	$13,025.31
41	215132	Wegovy Subcutaneous Solution Auto-injector 1 MG/0.5ML	10	9	$12,973.30
42	199152	Mavyret Oral Tablet 100-40 MG	1	1	$12,688.68
43	224366	Spikevax Intramuscular Suspension Prefilled Syringe 50 MCG/0.5ML	69	69	$12,335.94
44	182335	Farxiga Oral Tablet 5 MG	22	9	$12,152.52
45	170142	Xarelto Oral Tablet 20 MG	20	8	$11,759.25
46	215133	Wegovy Subcutaneous Solution Auto-injector 2.4 MG/0.75ML	9	5	$11,639.09
47	217440	Apretude Intramuscular Suspension Extended Release 600 MG/3ML	3	2	$11,507.61
48	127437	FreeStyle Lite Test In Vitro Strip	150	101	$11,426.66
49	197463	Dupixent Subcutaneous Solution Prefilled Syringe 300 MG/2ML	3	1	$11,318.97
50	189098	Entresto Oral Tablet 24-26 MG	18	8	$11,234.70
TOTAL			**1,425**	**834**	**$1,691,220.59**

Medi-Cal Top 50 Drugs by Cost for 3rd Quarter 2024

- The top 50 drugs accounted for **37,181 claims** for **31,766 members** and cost **$56,322,079.64,** which is an increase of $**3,282,412** in spend from the previous quarter.
- **Biktravy** remains at the number 1 spot with **912** claims for **690** members. An increase of **28** claims from last quarter.
- **Ozempic** also remains at the number 2 spot, with **2,141** claims for **1,673** members. This is an increase of **26** claims from last quarter.
- **Jardiance** is still at number 3 for the 25 mg strength with **1812** claims for **1673** members, but also at number 4 for the 10mg strength with **1855** claims for **1681** members. Total Jardiance claims for the 25mg strength has increased by **135** claims from last quarter and the total Jardiance claims for the 10mg strength has increased by **100** claims. This increased utilization reflects the expanded indication for Jardiance (Type 2 diabetes, prophylaxis heart failure in diabetes and non diabetes patients and reduction of risk of GFR decline in ESRD patients).
- **Skyrizi** is at the number 5 spot down from number 5, with 102 claims in 92 members, an increase of 3 claims from last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	44426	BIKTARVY 50-200-25 MG TABLET	912	690	$6,121,036.89
2	53536	OZEMPIC 0.25-0.5 MG/DOSE PEN	2141	1673	$3,046,903.62
3	36723	JARDIANCE 25 MG TABLET	1812	1673	$2,462,547.93
4	36716	JARDIANCE 10 MG TABLET	1855	1681	$2,424,863.18
5	49591	SKYRIZI 150 MG/ML PEN	102	92	$2,225,297.49
6	48208	OZEMPIC 1 MG/DOSE (4 MG/3 ML)	1204	995	$2,114,555.92
7	43506	HUMIRA(CF) PEN 40 MG/0.4 ML	125	101	$2,039,621.08
8	52125	OZEMPIC 2 MG/DOSE (8 MG/3 ML)	853	690	$1,589,559.28
9	48277	DUPIXENT 300 MG/2 ML PEN	183	155	$1,449,526.06
10	49748	WEGOVY 0.25 MG/0.5 ML PEN	986	881	$1,435,147.72
11	42624	VEMLIDY 25 MG TABLET	423	353	$1,335,022.09
12	51742	PAXLOVID 300-100 MG DOSE PACK	888	882	$1,238,062.81

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
13	97400	JANUVIA 100 MG TABLET	854	783	$1,236,157.31
14	33935	ELIQUIS 5 MG TABLET	1080	874	$1,206,062.61
15	28159	STELARA 90 MG/ML SYRINGE	33	29	$1,202,199.45
16	40133	TAGRISSO 80 MG TABLET	40	26	$1,183,751.93
17	49754	WEGOVY 2.4 MG/0.75 ML PEN	551	433	$1,174,972.54
18	49749	WEGOVY 0.5 MG/0.5 ML PEN	773	674	$1,141,682.06
19	49099	CABENUVA ER 600 MG-900 MG SUSP	140	127	$1,141,087.86
20	49752	WEGOVY 1 MG/0.5 ML PEN	699	618	$1,094,537.22
21	27418	INVEGA SUSTENNA 234 MG/1.5 ML	179	131	$1,051,781.12
22	97724	ENBREL 50 MG/ML SURECLICK	73	63	$965,701.95
23	34394	FARXIGA 10 MG TABLET	680	613	$933,416.91
24	40953	DESCOVY 200-25 MG TABLET	260	195	$905,224.02
25	46965	RYBELSUS 7 MG TABLET	424	389	$895,571.21
26	49753	WEGOVY 1.7 MG/0.75 ML PEN	530	434	$891,853.23
27	46966	RYBELSUS 14 MG TABLET	354	317	$792,340.03
28	43968	SYMTUZA 800-150-200-10 MG TAB	102	85	$790,112.67
29	25200	FREESTYLE LITE TEST STRIP	4421	4206	$782,998.75
30	98637	BASAGLAR 100 UNIT/ML KWIKPEN	1498	1243	$744,067.57
31	47136	TRIKAFTA 100-50-75 MG/150 MG	18	10	$689,593.68
32	97005	HUMIRA PEN 40 MG/0.8 ML	45	38	$687,542.78
33	44014	HUMIRA(CF) PEN 80 MG/0.8 ML	18	14	$671,811.56

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
34	38702	INVEGA TRINZA 819 MG/2.63 ML	63	60	$662,667.85
35	40092	GENVOYA TABLET	95	72	$633,641.91
36	54456	FERRIPROX 1,000 MG TAB(2X/DAY)	11	8	$558,598.25
37	37682	ABILIFY MAINTENA ER 400 MG SYR	109	81	$555,255.38
38	37169	TRULICITY 0.75 MG/0.5 ML PEN	341	294	$538,215.99
39	22913	ALBUTEROL HFA 90 MCG INHALER	10967	8957	$534,660.86
40	49468	COSENTYX UNOREADY 300 MG PEN	26	19	$518,588.28
41	49487	APRETUDE ER 600 MG/3 ML VIAL	106	95	$511,279.83
42	37171	TRULICITY 1.5 MG/0.5 ML PEN	295	244	$493,300.08
43	37789	COSENTYX SNRDY 300MG DOSE-2PEN	35	28	$481,270.70
44	43222	DUPIXENT 300 MG/2 ML SYRINGE	60	55	$473,040.66
45	37788	COSENTYX 300 MG DOSE-2 SYRINGE	23	18	$472,351.88
46	44106	HEMLIBRA 105 MG/0.7 ML VIAL	7	5	$466,927.35
47	30819	XARELTO 20 MG TABLET	398	333	$448,905.98
48	37633	ODEFSEY TABLET	78	56	$446,808.09
49	43924	ENBREL 50 MG/ML MINI CARTRIDGE	34	25	$442,523.71
50	97399	JANUVIA 50 MG TABLET	277	248	$429,432.31
TOTAL			**37,181**	**31,766**	**$56,322,079.64**

636 IHSS Top 50 Prior Authorization Requests by Volume for 3rd Quarter 2024

- Top 50 PA requests = 179. There were 287 total PA requests for quarter 3.
  - 75 requests (42%) were approved. This approval rate is the same as it was observed last quarter.
  - 104 requests (58%) were denied or partially approved.
- Wegovy is at numbers 1 and 9 with 31 total requests and 10 approvals (32%).
  - Wegovy to reduce excess body weight requires a diagnosis of obesity or BMI ≥27 and at least one weight-related comorbidity (diabetes, hypertension, hyperlipidemia) or history of heart attack, despite diet and exercise, and trial and failure or inability to use Qsymia and Contrave.
  - Wegovy to reduce the risk of major adverse cardiovascular events requires a documentation that the patient is obese or has BMI ≥27, has an established cardiovascular disease (prior myocardial infarction, stroke or symptomatic peripheral arterial disease), patient is on standard of care treatment for CVD and does not have diabetes.
- Jardiance is at numbers 2 & 8 with 19 total requests and 14 approvals (73%).
  - Jardiance requires trial and failure of one of the following: metformin, branded/generic drug containing metformin, branded angiotensin receptor/neprilysin inhibitor (ARNi), generic angiotensin-converting enzyme inhibitor (ACEi), generic angiotensin receptor blocker (ARB), generic mineralocorticoid receptor antagonist (MRA), or generic beta blocker.
- Lidocaine 5% patch is at number 3 with 14 requests and 3 approvals (21%).
  - 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 0.25-0.5 mg/dose is at number 4 with 10 requests and 3 approvals (30%).
  - Ozempic requires a trial and failure of metformin.
- Vemlidy is at number 5 with 9 requests. There were 3 approvals (33%).
  - Vemlidy requires a diagnosis of Hepatitis B, and trial and failure of, intolerance to, or inability to use entecavir tablets.

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
1	Wegovy Subcutaneous Solution Auto-injector 0.25 MG/0.5ML	26	8	30.77%	17	65.38%	1	3.85%
2	Jardiance Oral Tablet 10 MG	14	11	78.57%	1	7.14%	2	14.29%
3	Lidocaine External Patch 5 %	14	3	21.43%	10	71.43%	1	7.14%
4	Ozempic (0.25 or 0.5 MG/DOSE) Subcutaneous Solution Pen-injector 2 MG/3ML	10	3	30.0%	5	50.0%	2	20.0%
5	Vemlidy Oral Tablet 25 MG	9	3	33.33%	6	66.67%	0	0.0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
6	cycloSPORINE Ophthalmic Emulsion 0.05 %	6	3	50.0%	3	50.0%	0	0.0%
7	Tretinoin External Cream 0.025 %	6	1	16.67%	5	83.33%	0	0.0%
8	Jardiance Oral Tablet 25 MG	5	3	60.0%	1	20.0%	1	20.0%
9	Wegovy Subcutaneous Solution Auto-injector 0.5 MG/0.5ML	5	2	40.0%	3	60.0%	0	0.0%
10	Cequa Ophthalmic Solution 0.09 %	4	3	75.0%	1	25.0%	0	0.0%
11	Tacrolimus External Ointment 0.1 %	4	2	50.0%	1	25.0%	1	25.0%
12	Zepbound Subcutaneous Solution Auto-injector 7.5 MG/0.5ML	4	1	25.0%	3	75.0%	0	0.0%
13	Adbry Subcutaneous Solution Prefilled Syringe 150 MG/ML	3	0	0.0%	3	100.0%	0	0.0%
14	Atovaquone-Proguanil HCl Oral Tablet 250-100 MG	3	2	66.67%	1	33.33%	0	0.0%
15	Linzess Oral Capsule 145 MCG	3	1	33.33%	2	66.67%	0	0.0%
16	Ozempic (1 MG/DOSE) Subcutaneous Solution Pen-injector 4 MG/3ML	3	2	66.67%	1	33.33%	0	0.0%
17	Phentermine HCl Oral Tablet 37.5 MG	3	2	66.67%	0	0.0%	1	33.33%
18	Synjardy XR Oral Tablet Extended Release 24 Hour 12.5-1000 MG	3	1	33.33%	2	66.67%	0	0.0%
19	Tretinoin External Cream 0.05 %	3	0	0.0%	3	100.0%	0	0.0%
20	Xiidra Ophthalmic Solution 5 %	3	0	0.0%	3	100.0%	0	0.0%
21	Zepbound Subcutaneous Solution Auto-injector 2.5 MG/0.5ML	3	1	33.33%	2	66.67%	0	0.0%
22	Ciclopirox External Gel 0.77 %	2	0	0.0%	2	100.0%	0	0.0%
23	Dupixent Subcutaneous Solution Pen-injector 300 MG/2ML	2	1	50.0%	0	0.0%	1	50.0%
24	HYDROcodone-Acetaminophen Oral Tablet 10-325 MG	2	2	100.0%	0	0.0%	0	0.0%
25	Methadone HCl Oral Tablet 10 MG	2	2	100.0%	0	0.0%	0	0.0%
26	Nexletol Oral Tablet 180 MG	2	0	0.0%	1	50.0%	1	50.0%
27	Ondansetron HCl Oral Tablet 8 MG	2	2	100.0%	0	0.0%	0	0.0%
28	Opzelura External Cream 1.5 %	2	0	0.0%	2	100.0%	0	0.0%
29	Pitavastatin Calcium Oral Tablet 1 MG	2	0	0.0%	2	100.0%	0	0.0%
30	Sofosbuvir-Velpatasvir 400-100MG Tablet	2	1	50.0%	1	50.0%	0	0.0%
31	Sublocade Subcutaneous Solution Prefilled Syringe 300 MG/1.5ML	2	2	100.0%	0	0.0%	0	0.0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
32	Suflave Oral Solution Reconstituted 178.7 GM	2	1	50.0%	1	50.0%	0	0.0%
33	Talicia Oral Capsule Delayed Release 250-12.5-10MG	2	2	100.0%	0	0.0%	0	0.0%
34	Trelegy Ellipta Inhalation Aerosol Powder Breath Activated 200-62.5-25 MCG/ACT	2	1	50.0%	1	50.0%	0	0.0%
35	Tretinoin External Cream 0.1 %	2	0	0.0%	1	50.0%	1	50.0%
36	Ubrelvy Oral Tablet 50 MG	2	1	50.0%	1	50.0%	0	0.0%
37	Xifaxan Oral Tablet 550 MG	2	2	100.0%	0	0.0%	0	0.0%
38	Abiraterone Acetate Oral Tablet 250 MG	1	0	0.0%	0	0.0%	1	100.0%
39	Adalimumab-adaz Subcutaneous Solution Auto-injector 40 MG/0.4ML	1	0	0.0%	1	100.0%	0	0.0%
40	Adapalene External Gel 0.1 %	1	1	100.0%	0	0.0%	0	0.0%
41	Admelog SoloStar Subcutaneous Solution Pen-injector 100 UNIT/ML	1	0	0.0%	0	0.0%	1	100.0%
42	Advair Diskus Inhalation Aerosol Powder Breath Activated 500-50 MCG/ACT	1	1	100.0%	0	0.0%	0	0.0%
43	Advair HFA Inhalation Aerosol 115-21 MCG/ACT	1	1	100.0%	0	0.0%	0	0.0%
44	Ajovy Subcutaneous Solution Auto-injector 225 MG/1.5ML	1	0	0.0%	1	100.0%	0	0.0%
45	Allegra-D Allergy & Congestion Oral Tablet Extended Release 24 Hour 180-240 MG	1	1	100.0%	0	0.0%	0	0.0%
46	Allopurinol Oral Tablet 200 MG	1	1	100.0%	0	0.0%	0	0.0%
47	Alogliptin Benzoate Oral Tablet 25 MG	1	0	0.0%	0	0.0%	1	100.0%
48	ALPRAZolam Oral Tablet 0.25 MG	1	0	0.0%	1	100.0%	0	0.0%
49	Amjevita Subcutaneous Solution Auto-injector 40 MG/0.4ML	1	0	0.0%	1	100.0%	0	0.0%
50	Amnesteem Oral Capsule 40 MG	1	1	100.0%	0	0.0%	0	0.0%
TOTAL		**179**	**75**	**42%**	**89**	**50%**	**15**	**8%**

Medi-Cal Top 50 Claims by Volume for 3rd Quarter 2024

- The top 50 drugs accounted for **207,454 claims** for **185,206members** and cost of **$4,993,622.41.** This is a **decrease of 7,094** claims from last quarter but an increase of **$284,558** compared to last quarter.
- Albuterol remains at the number 1 spot with **10,967** claims for **8,957** members. This is a **decrease of 2,371** claims from last quarter.
- Ibuprofen is at number 2, with **9,755** claims for **8,746** members .This is an increase of 364 claims compared to the previous quarter. Ibuprofen was at number 3 last quarter.
- Aspirin has risen from 4th spot last month to 3rd spot with **9,074** claims and **8,382** unique members. This is a decrease of 115 claims compared to last quarter.
- Fluticasone has dropped from the number 2 to the number 4 spot with **8,363** claims for **7,443** members. There was a **decrease of 2,570** claims from last quarter.
- Diclofenac gel has risen from 7th spot to number 5 with **7,650** claims for **6,651** members. This is an increase of **612** claims compared to last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	22913	ALBUTEROL HFA 90 MCG INHALER	10967	8957	$534,660.86
2	35742	IBUPROFEN 600 MG TABLET	9755	8746	$141,094.25
3	00161	ASPIRIN EC 81 MG TABLET	9074	8382	$101,742.49
4	62263	FLUTICASONE PROP 50 MCG SPRAY	8363	7443	$187,501.87
5	45680	DICLOFENAC SODIUM 1% GEL	7650	6651	$239,191.41
6	16965	ACETAMINOPHEN 500 MG CAPLET	7352	6610	$98,949.09
7	49291	CETIRIZINE HCL 10 MG TABLET	6558	5990	$109,622.31
8	60563	LORATADINE 10 MG TABLET	6289	5638	$101,253.71
9	43722	ATORVASTATIN 40 MG TABLET	5701	5216	$94,550.25
10	02683	AMLODIPINE BESYLATE 5 MG TAB	5515	4980	$78,122.49
11	02682	AMLODIPINE BESYLATE 10 MG TAB	5120	4611	$75,220.39
12	10857	METFORMIN HCL 1,000 MG TABLET	5032	4622	$84,169.99
13	43721	ATORVASTATIN 20 MG TABLET	4902	4566	$76,164.06

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
14	10810	METFORMIN HCL 500 MG TABLET	4474	3973	$71,481.02
15	25200	FREESTYLE LITE TEST STRIP	4421	4206	$782,998.75
16	86212	POLYETHYLENE GLYCOL 3350 POWD	4374	4030	$110,766.56
17	46430	FAMOTIDINE 20 MG TABLET	4329	3830	$64,316.54
18	04348	OMEPRAZOLE DR 20 MG CAPSULE	4253	3675	$68,050.18
19	00781	GABAPENTIN 300 MG CAPSULE	4122	3396	$75,635.09
20	00223	VITAMIN D3 25 MCG TABLET	3825	3609	$47,304.24
21	99882	VITAMIN D3 50 MCG SOFTGEL	3704	3575	$47,525.44
22	43720	ATORVASTATIN 10 MG TABLET	3608	3340	$55,003.74
23	94444	MONTELUKAST SOD 10 MG TABLET	3552	3282	$57,285.95
24	40120	PANTOPRAZOLE SOD DR 40 MG TAB	3467	2933	$55,321.39
25	94422	VITAMIN D2 1.25MG(50,000 UNIT)	3454	3162	$52,508.98
26	09101	DOCUSATE SODIUM 100 MG SOFTGEL	3453	3067	$47,263.45
27	16965	ACETAMINOPHEN 500 MG TABLET	3396	3098	$33,887.19
28	20045	ONDANSETRON ODT 4 MG TABLET	3298	3000	$49,443.06
29	97503	FERROUS GLUCONATE 324 MG TAB	3074	2817	$44,555.91
30	39661	AMOXICILLIN 500 MG CAPSULE	3045	2810	$42,753.93
31	14851	LOSARTAN POTASSIUM 50 MG TAB	3018	2710	$46,777.43
32	35793	NAPROXEN 500 MG TABLET	2934	2597	$48,326.29
33	94781	FOLIC ACID 1 MG TABLET	2892	2469	$48,054.44

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
34	48191	TAMSULOSIN HCL 0.4 MG CAPSULE	2723	2367	$47,171.04
35	39802	CEPHALEXIN 500 MG CAPSULE	2696	2534	$39,958.54
36	35744	IBUPROFEN 800 MG TABLET	2683	2316	$42,614.94
37	70330	HYDROCODONE-ACETAMIN 10-325 MG	2629	1128	$52,565.42
38	16964	ACETAMINOPHEN 325 MG TABLET	2611	2450	$26,868.31
39	29189	SYSTANE BALANCE 0.6% EYE DROP	2603	2467	$92,639.42
40	94200	FREESTYLE 28G LANCETS	2582	2522	$47,197.23
41	14850	LOSARTAN POTASSIUM 25 MG TAB	2533	2279	$35,419.75
42	16391	TRAZODONE 50 MG TABLET	2532	2000	$41,685.00
43	13943	HYDROXYZINE HCL 25 MG TABLET	2514	1985	$41,432.00
44	30370	CLOTRIMAZOLE 1% TOPICAL CREAM	2476	2264	$39,902.15
45	34824	HYDROCHLOROTHIAZIDE 25 MG TAB	2451	2207	$35,843.40
46	31242	TRIAMCINOLONE 0.1% OINTMENT	2366	2183	$47,333.37
47	35741	IBUPROFEN 400 MG TABLET	2291	2180	$31,891.11
48	14853	LOSARTAN POTASSIUM 100 MG TAB	2287	2090	$37,765.71
49	50272	LIDOCAINE 5% PATCH	2280	2017	$168,426.77
50	56163	COMIRNATY 2024-25(12Y UP) SYRG	2226	2226	$393,445.50
TOTAL			**207,454**	**185,206**	**$4,993,622.41**

Diagnostic Agents, Blood Glucose Test Strips

Executive Summary

CLASS OVERVIEW

This review includes diagnostic test strips for blood glucose. Blood glucose test strips are primarily used in patient self-management of diabetes to guide the need for glucose or insulin therapy. Blood glucose trends can also be used by providers to guide changes to treatment regimens. All products contained within this review are classified as devices and available over-the-counter.

The American Diabetes Association Standards of Medical Care in Diabetes has been updated for 2024. It is worth noting that while continuous glucose monitoring (CGM) devices are more commonly available and used, there remains a need for testing with test strips, even for patients who use CGM devices, for calibration and to confirm readings discordant with symptoms.

UTILIZATION FINDINGS

There were 154 claims for 104 members, for a total cost of $14,012.14 and an average cost per claim of $90.99. The most highly utilized medication was Freestyle Lite test strips, with 151 claims, followed by Precision Xtra test strips with 2 claims. There were 2 prior authorizations with 2 approvals (100%).

RECOMMENDATIONS

- No changes

CLINICAL SUMMARY

This review includes diagnostic test strips for blood glucose. Blood glucose test strips are primarily used in patient self-management of diabetes to guide the need for glucose or insulin therapy. Blood glucose trends can also be used by providers to guide changes to treatment regimens. All products contained within this review are classified as devices and available over-the-counter.

The American Diabetes Association Standards of Medical Care in Diabetes has been updated for 2024. It is worth noting that while continuous glucose monitoring (CGM) devices are more commonly available and used, there remains a need for testing with test strips, even for patients who use CGM devices, for calibration and to confirm readings discordant with symptoms.

PRACTICE GUIDELINES

American Diabetes Association Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S111-S125.

Statement on Glycemic Assessment by Blood Glucose Monitoring (BGM)

- For many people with diabetes, glucose monitoring, either using BGM by capillary (finger-stick) devices or CGM in addition to regular A1C testing, is key for achieving glycemic goals.
- Major clinical trials of insulin-treated individuals have included BGM as part of multifactorial interventions to demonstrate the benefit of intensive glycemic control on diabetes complications.
- An integral component of effective therapy for individuals taking insulin is BGM; people with diabetes should be provided with BGM devices as indicated by their circumstances, preferences, and treatment.

Recommendations for Continuous Glucose Monitoring (CGM)

- In recent years, CGM has become a standard method for glucose monitoring for most people with type 1 diabetes; both approaches to glucose monitoring allow people with diabetes to evaluate individual responses to therapy and assess whether glycemic goals are being safely achieved.
- The specific needs and goals of individuals with diabetes should dictate BGM frequency and timing and people using CGM devices must also have access to BGM at all times. A
- People who are taking insulin and using BGM should be encouraged to check their blood glucose levels when appropriate based on their insulin therapy which may include checking when fasting, prior to meals and snacks, after meals, at bedtime, in the middle of the night, prior to, during, and after exercise, when hypoglycemia is suspected, after treating low blood glucose levels until they are normoglycemic, when hyperglycemia is suspected, and prior to and while performing critical tasks such as driving. B
- Health care professionals should be aware of the differences in accuracy among blood glucose meters; only meters approved by the U.S. Food and Drug Administration (FDA) (or comparable regulatory agencies for other geographical locations) with proven accuracy should be used, with unexpired test strips purchased from a pharmacy or licensed distributor and properly stored. E
- Although BGM in people on noninsulin therapies has not consistently shown clinically significant reductions in A1C levels, it may be helpful when altering meal plans, physical activity plans, and/or medications (particularly medications that can cause hypoglycemia) in conjunction with a treatment adjustment program. E
- Health care professionals should be aware of medications and other factors that can interfere with glucose meter accuracy and provide clinical management as indicated. E

Recommendation Definitions

Level of Evidence	Definition
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence-Based Medicine at the University of Oxford Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including • Evidence from a well-conducted trial at one or more institutions • Evidence from a meta-analysis that incorporated quality ratings in the analysis

Level of Evidence	Definition
B	Supportive evidence from well-conducted cohort studies • Evidence from a well-conducted prospective cohort study or registry • Evidence from a well-conducted meta-analysis of cohort studies Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (07-01-2024 to 09-30-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Accu-Chek Aviva Plus Test Strp	0	0	0	0	0	0 (0%)	NF	No change
Accu-Chek Guide Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Accu-Chek Smartview Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Accutrend Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Advance Micro-Draw Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Advance Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Cvs Advanced Glucose Test Str	0	0	0	0	0	0 (0%)	NF	No change
Cvs Advanced Glucose Test Str	0	0	0	0	0	0 (0%)	NF	No change
Cvs Advanced Glucose Test Str	0	0	0	0	0	0 (0%)	NF	No change
Advocate Redi-Code Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Advocate Redi-Code+ Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Advocate Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Agamatrix Amp Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Assure 3 Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Assure 4 Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Assure Ii Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Assure Platinum Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Assure Prism Multi Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Assure Pro Test Strips	0	0	0	0	0	0 (0%	NF	No change
Bioscanner Glucose Strips	0	0	0	0	0	0 (0%)	NF	No change
Gs Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Careone Blood Glucose Tst Strp	0	0	0	0	0	0 (0%)	NF	No change
Rexall Blood Glucose Test Strp	0	0	0	0	0	0 (0%)	NF	No change
Up & Up Blood Glucose Tst Strp	0	0	0	0	0	0 (0%)	NF	No change
Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Ght Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Eq Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Blulink Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Caresens N Test Strips	0	0	0	0	0	0 (0%)	NF	No change

Caretouch Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Clever Choice Micro Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Clever Choice Pro Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Clever Choice Talk Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Clever Choice Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Clever Choice Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Clever Choice Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Clever Choice Voice+ Tst Strip	0	0	0	0	0	0 (0%)	NF	No change
Contour Next Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Contour Plus Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Contour Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Cool Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Diatrue Plus Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Duo-Care Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Easy Plus Ii Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easy Pro Plus Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Easy Step Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Easy Talk Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easy Talk Plus Ii Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easy Touch Blulink Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easy Touch Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Gnp Easy Touch Gluc Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easy Touch Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easy Trak Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easy Trak Ii Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easygluco Plus Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Easygluco Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Easymax Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Easymax 15 Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Easypro Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Element Compact Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Element Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Embrace Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Embrace Evo Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Embrace Pro Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Embrace Pro Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Embrace Talk Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Embrace Talk Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Evencare Glucose Tst Strips	0	0	0	0	0	0 (0%)	NF	No change

Evencare Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Evencare G2 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Evencare G3 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Evencare Mini Glucose Test Str	0	0	0	0	0	0 (0%)	NF	No change
Evencare Proview Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Evolution Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Exactech Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Exactech Rsg Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Fifty50 Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora 6 Connect Glucose Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora 6conn-Gtel-Tn'g Adv Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora D15g Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Fora D20 Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Fora D40-G31 Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Fora G20 Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Fora G30-Premium V10 Test Strp	0	0	0	0	0	0 (0%)	NF	No change
Fora Gd50 Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Fora Gtel Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora Tn'g Advan Pro Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora Tn'g Voice Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Fora V10 Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora V10-V12-D10-D20 Strips	0	0	0	0	0	0 (0%)	NF	No change
Fora V12 Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Fora V20 Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Foracare Gd20 Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Foracare Gd40 Glucose Strips	0	0	0	0	0	0 (0%)	NF	No change
Fortiscare G1 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Fortiscare Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Freestyle Insulinx Strip Nfrs	0	0	0	0	0	0 (0%)	F-QL 200/30 Members over 21 years on a prenatal vitamin or insulin: 200 strips/30 days; other members allowed 100 strips/30 days; Members 0-21 years on a prenatal vitamin: 200 strips/30 days.	No change
Freestyle Lite Test Strip Nfrs	151	102	$13,724.57	$90.89	1	1 (100%)	F-QL 200/30 Members over 21 years on a prenatal vitamin or insulin: 200 strips/30 days; other members allowed 100 strips/30	No change

							days; Members 0-21 years on a prenatal vitamin: 200 strips/30 days.	
Freestyle Prec Neo Test Strips	1	1	$11.59	$11.59	1	1 (100%)	NF	No change
Freestyle Test Strips	0	0	0	0	0	0 (0%)	F-QL 200/30 Members over 21 years on a prenatal vitamin or insulin: 200 strips/30 days; other members allowed 100 strips/30 days; Members 0-21 years on a prenatal vitamin: 200 strips/30 days.	No change
Ge100 Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Ge333 Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Gluco Navii Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Glucocard 01 Sensor Plus Strip	0	0	0	0	0	0 (0%)	NF	No change
Glucocard Expression Test Strp	0	0	0	0	0	0 (0%)	NF	No change
Glucocard Shine Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Glucocard Vital Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Glucocard X-Sensor Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Glucocom Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Blood Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Blood Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Gojji Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Harmony Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Healthpro Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Iglucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Infinity Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Infinity Voice Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Keynote Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Liberty Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Relion Micro Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Microdot Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Myglucohealth Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Neutek 2tek Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Nova Max Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
On Call Express Test Strip	0	0	0	0	0	0 (0%)	NF	No change
On Call Plus Test Strip	0	0	0	0	0	0 (0%)	NF	No change
On Call Vivid Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Onetouch Ultra Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Onetouch Ultra Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Onetouch Verio Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Optium Test Strip	0	0	0	0	0	0 (0%)	NF	No change

Optium Ez Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Optumrx Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Pharmacist Choice Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Pip Blood Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Pocketchem Ez Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Precision Pcx Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Precision Pcx Plus Test Str	0	0	0	0	0	0 (0%)	NF	No change
Precision Point Of Care Str	0	0	0	0	0	0 (0%)	NF	No change
Precision Q-I-D Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Precision Sof-Tact Test Str	0	0	0	0	0	0 (0%)	NF	No change
Precision Xtra Test Strips	2	1	$275.98	$137.99	0	0 (0%)	F-QL 200/30 Members over 21 years on a prenatal vitamin or insulin: 200 strips/30 days; other members allowed 100 strips/30 days; Members 0-21 years on a prenatal vitamin: 200 strips/30 days.	No change
Relion Premier Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Relion Premier Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Premium Blood Glucose Test Str	0	0	0	0	0	0 (0%)	NF	No change
Premium Blood Glucose Tst Strp	0	0	0	0	0	0 (0%)	NF	No change
Kro Premium Blood Glucose Test	0	0	0	0	0	0 (0%)	NF	No change
Premium V10 Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Pro Voice V8-V9 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Prodigy No Coding Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Pts Panels Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Quicktek Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Quintet Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Quintet Ac Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Refuah Plus Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Relion Prime Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Reveal Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Rightest Gs100 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Rightest Gs300 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Rightest Gs550 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Rightest Gt333 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Rightest Gt333 Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Smart Sense Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Smart Sense Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Smartest Test Strips	0	0	0	0	0	0 (0%)	NF	No change

Solus V2 Audible Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Supreme Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Sure Edge Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Sure-Test Easyplus Mini Strip	0	0	0	0	0	0 (0%)	NF	No change
Surechek Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Telcare Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Test N'go Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Pharmacist Choice Test Strips	0	0	0	0	0	0 (0%)	NF	No change
True Metrix Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Relion True Metrix Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Gnp True Metrix Test Strip	0	0	0	0	0	0 (0%)	NF	No change
True Metrix Pro Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Truetest Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Truetrack Glucose Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Gnp Truetrack Glucose Test Str	0	0	0	0	0	0 (0%)	NF	No change
Relion Ultima Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Ultratrak Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Ultratrak Ultimate Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Unistrip1 Glucose Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Verasens Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Vivaguard Ino Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Vocal Point Test Strip	0	0	0	0	0	0 (0%)	NF	No change
Wavesense Jazz Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Wavesense Presto Test Strips	0	0	0	0	0	0 (0%)	NF	No change
Accu-Chek Compact Plus Strips	0	0	0	0	0	0 (0%)	NF	No change
Total	**154**	**104**	**$14,012.14**	**$90.99**	**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

Recommendation: No changes

Blood Glucose Testing Supplies	
Therapeutic Classes (AHFS)	Diabetes mellitus
Medications	Formulary with quantity limits: Members over 21 years on a prenatal vitamin or insulin are allowed 200 strips/30 days, other members allowed 100 strips/30days. Members 0-21 years on a prenatal vitamin are allowed 200 strips/30 days. All other members 0-21, bill CCS **(Check AAH active CCS cases for members < 21 years of age)** FreeStyle InsuLinx Test Strips- 100ct FreeStyle InsuLinx Test Strips- 50ct FreeStyle Lite Test Strips- 100ct FreeStyle Lite Test Strips- 50ct FreeStyle Test Strips- 100ct FreeStyle Test Strips- 50ct Precision Xtra Test Strips- 100ct Precision Xtra Test Strips- 50ct Formulary, limited to 1 meter per 365 days FreeStyle Freedom Lite Meter FreeStyle InsuLinx Meter FreeStyle Lite Meter Precision Xtra Meter ALAMEDA ALLIANCE FOR HEALTH PREFERS USE OF PRECISION OR FREESTYLE BLOOD GLUCOSE TESTING PRODUCTS (MANUFACTURED BY ABBOTT).
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 for members who are not pregnant
Prescriber Restrictions	N/A
Coverage Duration	See "PA Review Criteria". If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For requests for **Precision or Freestyle preferred test strips**, approve up to 200 strips/30 days for up to 12 months if: • Member is > 21 years of age AND insulin dependent (claims evidence for insulin or documentation from physician if new to plan) OR • Member is any age AND pregnant • For requests for a non-preferred product, documentation or inability to use preferred test strips must be provided. Please consider the preferred alternatives, Precision or Freestyle test strips (with quantity limits). For requests for **Precision or Freestyle preferred test strips**, approve up to a quantity of 100 strips/30 days for up to 12 months if: • Member is > 21 years of age AND no documentation of insulin-dependence or pregnancy • For requests for a non-preferred product, documentation or inability to use preferred test strips must be provided. Please consider the preferred alternatives, Precision or Freestyle test strips (with quantity limits).

Blood Glucose Testing Supplies	
	If member is 0-21 years of age AND no documentation of pregnancy, do not approve. Member is covered by CCS. Check AAH active CCS cases for members < 21 years of age For requests for **Freestyle or Precision Blood Glucose meters**: • Member is allowed 1 meter per year • If request is for a non-preferred product, documentation or inability to use preferred test strips must be provided. Please consider the preferred alternative Freestyle or Precision meters (within fill limits).
Criteria Statement	Freestyle and Precision test strips over a quantity of 100 strips for 30 days are reserved for members who are over 21 years old and insulin dependent OR for members of any age who are pregnant.
Last P&T Review Date	~~12/2023~~12/2024

REFERENCES

1. American Diabetes Association Professional Practice Committee. 6. Glycemic Goals and Hypoglycemia: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S111-S125.

Calcium and Vitamin D

Executive Summary

CLASS OVERVIEW

Calcium and vitamin D [25-hydroxyvitamin D or 25(OH)D] are essential for bone health. Although part of a balanced diet, the average American adult only consumes about half of the recommended daily calcium intake, increasing the risk of osteoporosis, falls, and bone fractures. Vitamin D exists in two forms: Ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Vitamin D2 originates from plants or fortified foods while Vitamin D3 originates from animals. The most active metabolite of vitamin D, calcitriol, leads to the increase in intestinal absorption of calcium, increased bone resorption, and decreased renal calcium and phosphate excretion, ultimately promoting bone formation. Foods rich in calcium and vitamin D include dairy, nuts, orange juice, salmon, green vegetables, and fortified cereals.

Calcium and vitamin D requirements are both age-specific and dependent on risk factors and comorbidities. The Institute of Medicine Dietary Reference Nutrient Intake suggests that postmenopausal women with osteoporosis consume 1200 mg of calcium per day and 800 international units (IU) of vitamin D daily. In healthy adults, 1000 mg of calcium and 600 IU of vitamin D daily are generally recommended. Recommended intake values for calcium and vitamin D can vary slightly between different organizations.

Calcium carbonate, calcium citrate, and calcium gluconate may be used as calcium supplementation and are available over the counter. Vitamin D is also available over the counter in its D2 and D3 formulations. High dose vitamin D3 (ergocalciferol) 50,000 IU, however, is only available by prescription. Calcium and vitamin D combination formulations are also available to improve adherence and ease of use. Calcitriol is available in an oral formulation but is only indicated for the treatment of hypocalcemia in patients with chronic kidney disease on dialysis, due to the risk of developing hypercalcemia. The focus of this class review will be calcium and vitamin D supplementation associated with osteoporosis.

UTILIZATION FINDINGS

There were 266 claims for 234 members, for a total cost of $1,068.38 and an average cost per claim of $4.02. The most highly utilized medication was Cholecalciferol capsule, with 103 claims, followed by Cholecalciferol tablet with 82 claims. There was 1 prior authorization with 1 approval (100%).

RECOMMENDATIONS

- No changes

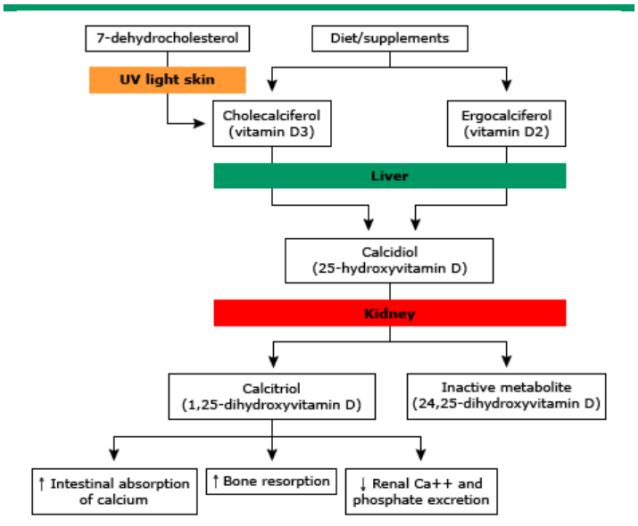
CLINICAL SUMMARY

Osteoporosis is characterized by low bone mineral density (BMD) and subsequent micro-architectural disruption and skeletal fragility. Reduced BMD is responsible for vertebral, hip, or other fractures that may result in falls and lead to morbidity and mortality. A T-score of <= -2.5 or a fragility fracture are diagnostic for osteoporosis. The majority of postmenopausal women have BMD reduction due to reduced estrogen levels. Calcium supplementation is essential for this patient population to combat low serum calcium levels and improve bone mineralization.

Calcium is an essential component in bone mineral formation and proper intracellular communication. It can be consumed exogenously or resorbed from bone into the body in response to reduced serum levels. Vitamin D is responsible for the increase in intestinal absorption of calcium and is also associated with improved muscle performance, balance, and immune function. It can be consumed through the diet or produced by the body in response to ultraviolet (UV) light in the skin. Vitamin D exists in two forms: Ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Vitamin D2 originates from plants or fortified foods while Vitamin D3 originates from animals. Foods rich in calcium include dairy, nuts, orange juice, salmon, green vegetables, and fortified cereals.

Direct UV light leads to the conversion of 7-dehydrocholesterol in the skin to vitamin D3. Vitamins D2 and D3 are converted by the liver to their active form, 25-hydroxyvitaminD (calcidol), which the kidneys convert to the most active metabolite, 1, 25-dihydroxyvitamin D (calcitriol). Calcitriol leads to the increase in intestinal absorption of calcium, increased bone resorption, and decreased renal calcium and phosphate excretion, promoting bone formation. Calcitriol is available in an oral capsule but is only indicated for the treatment of hypocalcemia in patients with chronic kidney disease on dialysis, due to the risk of developing hypercalcemia.

Pathways of vitamin D synthesis



Metabolic activation of vitamin D to calcitriol and its effects on calcium and phosphate homeostasis. The result is an increase in the serum calcium and phosphate concentrations.

UV: ultraviolet.

When serum 25(OH)D levels fall, less calcium is absorbed in the intestines, leading to an increase in parathyroid hormone concentrations. This feedback loop results in the conversion of calcidol to calcitriol, restoring adequate calcium absorption and subsequently, normalizing serum calcium levels. Although the optimal 25(OH)D concentration for skeletal health is controversial, clinical consensus recommends maintaining serum levels between 30 and 40 ng/mL.

Calcium and vitamin D requirements are both age-specific and dependent on risk factors and comorbidities. The Institute of Medicine Dietary Reference Nutrient Intake suggests that postmenopausal women with osteoporosis

consume 1200 mg of calcium per day and 800 international units (IU) daily. In healthy adults, 1000 mg of calcium and 600 IU of vitamin D daily are generally recommended. Recommended intake values for calcium and vitamin D can vary slightly between different organizations.

Calcium carbonate, calcium citrate, and calcium gluconate may be used as calcium supplementation and are available over the counter. Vitamin D is also available over the counter in its D2 and D3 formulations. High dose vitamin D3 (ergocalciferol) 50,000 IU, however, is only available by prescription. Calcium and vitamin D combination formulations are also available to improve adherence and ease of use.

2020 AACC/ACE Postmenopausal Osteoporosis Guidelines
Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 Update. Endocr Pract. 2020 May;26(Suppl 1):1-46. doi: 10.4158/GL-2020-0524SUPPL. PMID: 32427503.

R10. Measure serum 25-hydroxyvitamin D (25[OH]D) in patients who are at risk for vitamin D insufficiency, particularly those with osteoporosis (Grade B; BEL 2).

R11. Maintain serum 25-hydroxyvitamin D (25[OH]D) ≥ 30 ng/mL in patients with osteoporosis (preferable range, 30 to 50 ng/mL) (Grade A; BEL 1).

R12. Supplement with vitamin D3 if needed, with a daily dose of 1,000 to 2,000 international units (IU) typically required to maintain an optimal serum 25(OH)D level (Grade A; BEL 1).

R13. Higher doses of vitamin D3 may be necessary in patients with present factors such as obesity, malabsorption, and older age (Grade A; BEL 1).

R14. Counsel patients to maintain adequate dietary intake of calcium, to a total intake (including diet plus supplement, if needed) of 1,200 mg/day for women age ≥ 50 years (Grade B; BEL 1, downgraded due to limited evidence).

Table 13
Recommended Dietary Allowance for Calcium

Age	Sex	Recommended dietary allowance (mg/d)
0-6 mo	M + F	200
6-12 mo	M + F	260
1-3 y	M + F	700
4-8 y	M + F	1,000
9-18 y	M + F	1,300
19-50 y	M + F	1,000
51-70 y	M	1,000
51-70 y	F	1,200
71+ y	M + F	1,200

From Ross et al (77 [EL 4; consensus NE]). Reproduced with permission.

Table 4. 2017 AACE Protocol for Production of Clinical Practice Guidelines Revised and Detail Mapping Protocol (Step IV: Creating Initial Recommendation Grades)aa

Best Evidence Level	Predominantly Negative SF and/or RQ	Predominantly Positive SF and/or RQ	Consensus for Recommendation and for Grade	EL to Grade Mapping	Map to Final Recommendation Grade
1	No	No	>66%	Direct	1 → A
Any[b]	No	No	>100%	Rule	Any → A (new)
2	No	Yes	>66%	Adjust up	2 → A
2	No	No	>66%	Direct	2 → B
1	Yes	No	>66%	Adjust down	1 → B
3	No	Yes	>66%	Adjust up	3 → B
3	No	No	>66%	Direct	3 → C
2	Yes	No	>66%	Adjust down	2 → C
4	No	Yes	>66%	Adjust up	4 → C
4	No	No	>66%	Direct	4 → D
3	Yes	No	>66%	Adjust down	3 → D
Any[b]	Yes/no	Yes/no	>66%	Rule	Any → AD (new)

Abbreviations: AACE = American Association of Clinical Endocrinologists; BEL = best evidence level; EL = evidence level; RQ = recommendation qualifiers; SF = subjective factors.

a Recommendation Grade A = "Very Strong"; B = "Strong"; C = "Not Strong"; D = "Primarily Based on Expert Opinion." Mappings are provided in online supplementary material from (1).

b Rule-based adjustment wherein any recommendation can be a "Very Strong" Grade A if there is 100% consensus to use this designation. Similarly, if >66% consensus is not reached, even with some degree of scientific substantiation, a "Primarily Based on Expert Opinion" Grade D designation is assigned. The reasons for downgrading to D may be an inconclusive or inconsistent evidence base or simply failure of the expert writing committee to sufficiently agree. Note that any formulated recommendation is omitted from the document if sufficiently flawed, so any Grade D recommendation in the final document must be deemed sufficiently important.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (07-01-2024 to 09-30-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Calcium								
Calcium carbonate tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium carbonate chewable tablet/wafer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium carbonate powder	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate oral granules	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium gluconate capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium acetate tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium lactate tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Vitamin D								
Ergocalciferol capsule	80	65	$556.38	$6.95	0	0 (0%)	Ergocalciferol Cap 50 MCG (2000 Unit)- NF Ergocalciferol Cap 1.25 MG (50000 Unit) 1.25mg - F	No change
Ergocalciferol tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Ergocalciferol solution	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Cholecalciferol capsule	103	94	$368.57	$3.58	0	0 (0%)	Cholecalciferol Cap 10 MCG (400 Unit) - **NF** Cholecalciferol Cap 25 MCG (1000 Unit)- **F** Cholecalciferol Cap 50 MCG (2000 Unit)- **F** Cholecalciferol Cap 62.5 MCG (2500 Unit) -**NF** Cholecalciferol Cap 100 MCG (4000 Unit)- **NF** Cholecalciferol Cap 125 MCG (5000 Unit) - **F** Cholecalciferol Cap 250 MCG (10000 Unit) **- F** Cholecalciferol Cap 325 MCG (13000 Unit)- **NF** Cholecalciferol Cap 350 MCG (14000 Unit) - **NF** Cholecalciferol Cap 625 MCG (25000 Unit) - **NF** Cholecalciferol Cap 1.25 MG (50000 Unit) - **F**	No change

Cholecalciferol tablet	82	74	$142.37	$1.74	0	0 (0%)	Cholecalciferol Tab 10 MCG (400 Unit) -**F** Cholecalciferol Tab 20 MCG (800 Unit) - **NF** Cholecalciferol Tab 25 MCG (1000 Unit) - **F** Cholecalciferol Tab 50 MCG (2000 Unit) - **F** Cholecalciferol Tab 75 MCG (3000 Unit) - **NF** Cholecalciferol Tab 100 MCG (4000 Unit) **- NF** Cholecalciferol Tab 125 MCG (5000 Unit) - **F** Cholecalciferol Tab 250 MCG (10000 Unit) - **NF** Cholecalciferol Tab 1.25 MG (50000 Unit) - **F**	No change
Cholecalciferol chewable tablet	0	0	$0.00	$0.00	0	0 (0%)	Cholecalciferol Chew Tab 10 MCG (400 Unit) - **NF** Cholecalciferol Chew Tab 25 MCG (1000 Unit) - **F** Cholecalciferol Chew Tab 50 MCG (2000 Unit) - **NF** Cholecalciferol Chew Tab 62.5 MCG (2500 Unit) - **NF** Cholecalciferol Chew Tab 125 MCG (5000 Unit) - **NF**	No change
Cholecalciferol oral liquid	0	0	$0.00	$0.00	0	0 (0%)	Cholecalciferol Oral Liquid 30 MCG/15ML (1200 Unit/15ML) - **NF** Cholecalciferol Oral Liquid 417 MCG/ML (16667 Unit/ML) - **NF** Cholecalciferol Oral Liquid 25 MCG/10ML (1000 Unit/10ML) - **NF** Cholecalciferol Oral Liquid 10 MCG/ML (400 Unit/ML) - **F** Cholecalciferol Oral Liquid 125 MCG/0.5ML (5000 Unit/0.5ML) - **NF** Vitamin D Liquid 12.5 MCG/0.25ML (500 Unit/0.25ML) - **NF**	No change
Cholecalciferol drops	0	0	$0.00	$0.00	0	0 (0%)	Cholecalciferol Drops 125 MCG/ML (5000 Unit/ML) - **NF** Cholecalciferol Drops 10 MCG/0.03ML (400 Unit/0.03ML) - **NF** Cholecalciferol Drops 10 MCG/0.04ML (400 Unit/0.04ML) - **NF** Cholecalciferol Drops 10 MCG/0.028ML (400 Unit/0.028ML) - **NF** Cholecalciferol Drops 10 MCG/0.036ML (400 Unit/0.036ML) - **NF** Cholecalciferol Drops 10 MCG/0.025ML (400 Unit/0.025ML)- **NF** Cholecalciferol Drops 15 MCG/0.028ML (600 Unit/0.028ML) - **NF** Cholecalciferol Drops 25 MCG/0.03ML (1000 Unit/0.03ML) - **NF** Cholecalciferol Drops 25 MCG/0.028ML (1000 Unit/0.028ML) - **NF** Cholecalciferol Drops 25 MCG/0.04ML (1000 Unit/0.04ML) - **NF** Cholecalciferol Drops 50 MCG/0.03ML (2000 Unit/0.03ML - **N**F Cholecalciferol Drops 50 MCG/0.04ML (2000 Unit/0.04ML) - **NF** Cholecalciferol Drops 50 MCG/0.028ML (2000 Unit/0.028ML) **- NF**	No change
Cholecalciferol chewable wafer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Cholecalciferol orally disintegrating tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium + Vitamin D Combinations								
Calcium carbonate-calcium gluconate-ergocalciferol tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium carbonate-vitamin D capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

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Calcium carbonate-vitamin D tablet	1	1	$1.06	$1.06	1	1 (100%)	NF	No change
Calcium carbonate-vitamin D chewable tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium carbonate-vitamin D liquid	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate-vitamin D tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate-vitamin D chewable tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate-vitamin D liquid	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate-vitamin D powder	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium citrate maleate-cholecalciferol tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium phosphate-cholecalciferol chewable tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Total	**266**	**234**	**$1,068.38**	**$4.02**	**1**	**1 (100%)**		

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

REFERENCES

1. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on 5/14/2018.
2. "DailyMed." DailyMed. N.p., n.d. Web. 26 May 2016. Available at https://dailymed.nlm.nih.gov/dailymed/
3. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020 Update. Endocr Pract. 2020 May;26(Suppl 1):1-46. doi: 10.4158/GL-2020-0524SUPPL. PMID: 32427503.

Osteoporosis
Executive Summary

CLASS OVERVIEW

Osteoporosis is a bone disease that develops when bone mineral density (BMD) and bone mass decreases, or when the structure and strength of bone changes. This can lead to a decrease in bone strength that can increase the risk of fractures. Many patients with osteoporsis do not exibit symptoms until they break a bone. Osteoporosis is the major cause of fractures in postmenopausal women and in older men. According to the National Osteoporosis Foundation, 1 in 2 women and 1 in 4 men over 50 years of age will break a bone due to osteoporosis. It is estimated that over 50 million Americans have osteoporis or another form of low bone mass. Although fractures can occur in any bone, breaks most often occur in the bones of the hip, vertebrae in the spine, and wrist. Factors that may increase the risk of osteoporosis include sex, age, body size, race, family history, changes to hormones, and diet.

Treatment options for osteoporosis include bisphosphonates, estrogen/progestin, selective estrogen receptor modulators (SERMs), calcitonin, parathyroid hormones, sclerostin inhibitors, and bone modifying agents. This class review will focus primarily on agents for postmenopausal women and men age 50 and over, since this is the population with the highest incidence of disease/risk. The American College of Physicians and American Association of Clinical Endocrinologists (AACE/ACE) and the American College of Endocrinology (ACP) recommend using oral bisphosphonates (eg. alendronate, risedronate, zoledronic acid, etc.) as first line treatment due to efficacy, cost, and long-term safety data. Denosumab is also an appropriate first line treatment option especially in patients who are unable to use oral therapy, have impaired renal function, or are at very high risk for fracture. The parathyroid hormones, abaloparatide and teriparatide, may be considered as first line therapy for patients with very high fracture risk. However, their treatment is limited to 24 months.

Systematic reviews of bone resorption inhibitors and parathyroid hormones reveal that no single agent is significantly more effective than the other. However, agents differ in their cost-saving opportunities. Evenity, a sclerostin inhibitor monoclonal antibody, is the newest drug for the treatment of osteoporosis with approval in April 2019. Wyost (biosimilar to Xgeva) and Jubbonit (biosimilar to Prolia), were approved in March 2024 and expected to launch in 2025. Oral bisphosphonates will likely continue to servce as the mainstay of prevention and treatment due to efficacy, favorable cost, generic availability, and long-term safety data.

UTILIZATION FINDINGS

There were 106 claims for 78 members, for a total cost of $12,895.69 and an average cost per claim of $121.66. The most highly utilized medication was Alendronate, with 89 claims, followed by Ibandronate with 13 claims. There were no prior authorization requests.

RECOMMENDATIONS

- No changes

CLINICAL SUMMARY

Osteoporosis is a bone disease that develops when BMD and bone mass decreases, or when the structure and strength of bone changes. This can lead to a decrease in bone strength that can increase the risk of fractures. Many patients with osteoporsis do not exibit symptoms until they break a bone. Osteoporosis is the major cause of fractures in postmenopausal women and in older men. According to the National Osteoporosis Foundation, 1 in 2 women and 1 in 4 men over 50 years of age will break a bone due to osteoporosis. It is estimated that over 50 million Americans have osteoporis or another form of low bone mass. Although fractures can occur in any bone, breaks most often occur in the bones of the hip, vertebrae in the spine, and wrist. Factors that may increase the risk of osteoporosis include sex, age, body size, race, family history, changes to hormones, and diet.

Osteoporosis is diagnosed most commonly utilizing a dual energy x-ray absorptiometry (DEXA or DXA) scan or Fracture Risk Assessment Tool (FRAX). DEXA scans produce a "T-score" to determine the number of standard deviations (SD) an individual falls above or below the young adult mean. FRAX determines a persons 10-year probability of a major osteoporotic fracture. Using the DXA score and FRAX probability, clinicians determine when to initiate pharmacotherapy.

World Health Organization Criteria for Classification of Osteopenia and Osteoporosis	
Category	**T-score**
Normal	−1.0 or above
Osteopenia	Between −1.0 and −2.5
Osteoporosis	−2.5 or below
Severe or established osteoporosis	−2.5 or below with fragility fracture

Source: Kanis JA, et al. *J Bone Miner Res.* 1994;9(8):1137-1141

Treatment options for osteoporosis include bisphosphonates, estrogen/progestin, selective estrogen receptor modulators (SERMs), calcitonin, parathyroid hormones, sclerostin inhibitors, and bone modifying agents. This class review will focus primarily on agents for postmenopausal women and men age 50 and over, since this is the population with the highest incidence of disease/risk. The American College of Physicians and American Association of Clinical Endocrinologists (AACE/ACE) and the American College of Endocrinology (ACP) recommend using oral bisphosphonates (eg. alendronate, risedronate, zoledronic acid, etc.) as first line treatment due to efficacy, cost, and long-term safety data. Denosumab is also an appropriate first line treatment option especially in patients who are unable to use oral therapy, have impaired renal function, or are at very high risk for fracture. The parathyroid hormones, abaloparatide and teriparatide, may be considered as first line therapy for patients with very high fracture risk. However, their treatment is limited to 24 months.

It is unlikely first-line treatment selections will have significant changes in the next several years, but newer approvals have changed formularly management and utilization for the second and third line treatment options. The 2017 approval of Tymlos (abaloparatide) represented the first meaningful competition to Eli Lilly's long-standing market leader, Forteo (teriparatide). In 2022 Tymlos received an expanded approval to increase bone density in men with osteoporosis at high risk of fracture or in patients who have failed or are intolerant to other available osteoporosis therapy. Tymlos was originally approved for the treatment of postmenopausal women with osteoporosis at high risk of fracture. In 2019, Evenity (romosozumab-aqqg) was approved as first and only sclerostin inhibitor. This treatment category has started to shift with the 2023 approval of generic Forteo. Additionally, the FDA approved two interchanagle biosiimlars in March 2024. Wyost (biosimilar to Xgeva) and Jubbonit (biosimilar to Prolia) are expected to launch in 2025.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
alendronate (Fosamax®, Binosto®)	• Osteoporosis (treatment and prevention in females ; treatment in males) • Glucocorticoid-induced osteoporosis • Paget disease (Fosamax only)	• Osteoporosis in females, prophylaxis: 5 mg once daily or 35 mg one weekly • Osteoporosis in females, treatment: 10 mg once daily or 70 mg once weekly • Osteoporosis in males, treatment: 10 mg once daily or 70 mg once weekly • Glucocorticoid-induced osteoporosis in males and females, treatment: 5 mg once daily; 10 mg one daily in postmenopausal females not receiving estrogen • Paget disease: 40 mg once daily for 6 months
Fosamax® Plus D (alendronate-vitamin D3)	• Osteoporosis (treatment in postmenopausal women) • Treatment to increase bone mass (men with osteoporosis)	• Oral: One tablet (alendronate 70 mg/cholecalciferol 2,800 units or alendronate 70 mg/cholecalciferol 5,600 units) once weekly.
ibandronate	• Osteoporosis (treatment and prevention in females)	• Osteoporosis in females, treatment: oral 150 mg once monthly; IV: 3mg every 3 months • Osteoporosis in females, prevention: oral: 150 mg once monthly
pamidronate	• Hypercalcemia of malignancy • Osteolytic bone metastases of breast cancer • Osteolytic lesions of multiple myeloma • Paget disease	• Hypercalcemia of malignancy, moderate: 60-90 mg IV as a single dose over 2-24 hours (corrected serum calcium 12-13.5 mg/dL) • Hypercalcemia of malignancy, severe: 90 mg IV as a single dose over 2-24 hours (corrected serum calcium >13.5 mg/dL) • Breast cancer, osteolytic bone metastases: IV: 90 mg over 2 hours once every 3-4 weeks • Multiple myeloma, osteolytic bone lesions: IV: 90 mg over 4 hours once monthly; Lytic bone disease: 90 mg over at least 2 hours once every 3 to 4 weeks for up to 2 years • Paget disease (moderate-to-severe): IV: 30 mg over 4 hours once daily for 3 consecutive days (total dose = 90 mg)
Prolia ® (denosumab)	• Glucocorticoid-induced osteoporosis • Osteoporosis/bone loss (treatment in females and in males)	• Glucocorticoid-induced osteoporosis, treatment: SubQ: 60 mg as a single dose, once every 6 months • Androgen deprivation-induced bone loss in male with prostate cancer, treatment: SubQ: 60 mg as a single dose, once every 6 months • Aromatase inhibitor-induced bone loss in female with breast cancer, treatment: SubQ: 60 mg as a single dose, once every 6 months • Osteoporosis in men or postmenopausal female, treatment : SubQ: 60 mg as a single dose, once every 6 months
Xgeva ® (denosumab)	• Bone metastases from solid tumors (prevention of skeletal-related events) • Multiple myeloma (prevention of skeletal-related events) • Giant cell tumor of bone • Hypercalcemia of malignancy	• Bone metastases from solid tumors (prevention of skeletal-related events): SubQ: 120 mg every 4 weeks • Multiple myeloma (prevention of skeletal-related events): SubQ: 120 mg every 4 weeks • Giant cell tumor of bone: SubQ: 120 mg once every 4 weeks; during first month, give an additional 120 mg on days 8 and 15 • Hypercalcemia of malignancy: SubQ: 120 mg every 4 weeks; during first month, give an additional 120 mg on days 8 and 15

Medication	Indications	Dosing/Administration
Calcitonin (Miacalcin®)	• Osteoporosis (Intranasal or Injection) • Paget disease (Injection) • Hypercalcemia (Injection)	• Osteoporosis in female: IM, SubQ: 100 units daily; • Intranasal: 200 units (1 spray) in one nostril once daily • Paget disease, symptomatic: IM, SubQ: 100 units daily • Hypercalcemia: IM, SubQ: 4 units/kg every 12 hours; if response is unsatisfactory after 24-48 hours, may increase to 8 units/kg every 12 hours; if response remains unsatisfactory after an additional 48 hours, may increase to a maximum dose of 8 units/kg every 6 hours.
raloxifene (Evista ®)	• Osteoporosis (treatment and prevention in females) • Risk reduction for invasive breast cancer	• Osteoporosis: Oral: 60 mg once daily • Risk reduction for invasive breast cancer (postmenopausal): Oral: 60 mg once daily. • Duration of therapy for breast cancer risk reduction: 5 years; may be used longer than 5 years in women with osteoporosis where breast cancer risk reduction is a secondary benefit.
risedronate (Actonel®, Atelvia®)	• Osteoporosis (treatment and prevention in females ; treatment in males) • Glucocorticoid-induced osteoporosis • Paget disease (Actonel only)	• Osteoporosis in females: IR tablet, prevention and treatment: 5 mg once daily or 35 mg once weekly or 150 mg once monthly; • DR tablet, treatment: 35 mg once weekly • Osteoporosis in males, treatment: IR tablet: 35 mg once weekly • Glucocorticoid-induced osteoporosis, prevention and treatment: IR tablet: 5 mg once daily • Paget disease: IR tablet: 30 mg once daily for 2 months
zoledronic acid (Reclast®)	• Osteoporosis (treatment and prevention in females ; treatment in males) • Glucocorticoid-induced osteoporosis • Paget disease	• Osteoporosis in females, prevention: 5 mg IV once every 2 years • Osteoporosis in males or females, treatment: 5 mg IV once a year • Paget disease: 5 mg IV as a single dose • Glucocorticoid-induced osteoporosis , prevention and treatment: IV 5mg once a year
zoledronic acid	• Bone metastases from solid tumors • Multiple myeloma osteolytic lesions • Hypercalcemia of malignancy	• Bone metastases from solid tumors: IV: 4 mg once every 3-4 weeks • Multiple myeloma osteolytic lesions IV: 4 mg once every 3-4 weeks • Hypercalcemia of malignancy: IV: 4 mg (maximum) given as a single dose. Wait at least 7 days before considering re-treatment. (albumin-corrected serum calcium ≥12 mg/dL)
Forteo® (teriparatide)	• Osteoporosis (treatment in female and male) • Glucocorticoid-induced osteoporosis	• Osteoporosis in male, female, glucocorticoid-induced: SubQ: 20 mcg once daily for up to 2 years
Tymlos® (abaloparatide)	• Osteoporosis (treatment in femaleand male)	• Osteoporosis in females: SubQ: 80 mcg once daily (duration of therapy not to exceed 2 years)
Evenity® (romosozumab)	• Osteoporosis in postmenopausal women at high risk for fracture	• 210 mg subcutaneously once every month for 12 doses in the abdomen, thigh, or upper arm. Two separate subcutaneous injections are needed to administer the total dose of 210 mg. Inject two syringes, one after the other.

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
alendronate (Fosamax®, Fosamax® Plus D, Binosto®) risedronate (Actonel®, Atelvia®)	None	• Hypersensitivity to medication or any component of the formulation • Hypocalcemia • Abnormalities of the esophagus which delay esophageal emptying (eg. stricture, achalasia) • Patient unable to stand or sit upright for at least 30 minutes • Patients with increased risk of aspiration (only with Alendronate effervescent tablets or oral solution)
ibandronate	None	• Hypersensitivity to medication or any component of the formulation • Hypocalcemia • Abnormalities of the esophagus which delay esophageal emptying (eg. stricture, achalasia) • Patient unable to stand or sit upright for at least 60 minutes
pamidronate	None	• Hypersensitivity to medication or any component of the formulation
Prolia ® (denosumab) Xgeva ® (denosumab)	Prolia: risk of severe hypocalecmia in patients with advanced kidney disease	• Hypersensitivity to medication or any component of the formulation • Preexisting hypocalcemia • Pregnancy (Prolia only)
Calcitonin (Miacalcin®)	None	• Hypersensitivity to calcitonin salmon or any component of the formulation
raloxifene (Evista ®)	Increased risk of VTE: females with active or past history of VTE should not take raloxifene. Cardiovascular disease: Increased risk of death due to stroke noted in trial in postmenopausal female with documented coronary heart disease or increased risk for major coronary events.	• History of or current venous thromboembolic disorders (including DVT, PE and retinal vein thrombosis) • Pregnancy
zoledronic acid (Reclast®)	None	• Hypersensitivity to medication or any component of the formulation • Hypocalcemia (Reclast only) • Patient with CrCl <35 mL/minute and acute renal impairment (Reclast only)
Forteo® (teriparatide)	None	• Hypersensitivity to medication or any component of the formulation
Tymlos® (abaloparatide)	Abaloparatide caused a dose-dependent increase in the incidence of osteosarcoma; avoid in patients at increased risk	None
Evenity® (romosozumab)	Evenity may increase the risk of myocardial infarction, stroke and cardiovascular death	Hypocalcemia Hypersensitivity to component of the formulation

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
alendronate (Fosamax®, Fosamax® Plus D, Binosto®)	• Bone fractures: atypical femur fractures have been reported • Bone/joint/muscle pain

Medication	Warnings/Precautions
	• Gastrointestinal mucosa irritation: esophagitis, dysphagia, esophageal ulcers, esophageal erosions, and esophageal stricture have been reported • Hypocalcemia: correct for hypocalcemia prior to initiation and (for Fosamax®, Binosto®): ensure adequate calcium/vitamin D intake • Osteonecrosis of the jaw: risk increase with invasive dental procedures, cancer diagnosis, concomitant therapy, poor oral hygiene, ill-fitting dentures and comorbid disorders • Renal impairment: use is not recommended in patients with CrCl <35 mL/minute • Ocular effects: conjunctivitis, uveitis, episcleritis, and scleritis have been reported • Effervescent tablet: contains 650 mg of sodium; use with caution in patients with sodium-restricted diet
risedronate (Actonel®, Atelvia®)	• Glucocorticoid-induced osteoporosis: evaluate sex steroid hormonal status prior to initiation • Bone fractures: atypical femur fractures have been reported • Bone/joint/muscle pain • Gastrointestinal mucosa irritation: esophagitis, dysphagia, esophageal ulcers, esophageal erosions, and esophageal stricture have been reported • Hypocalcemia: correct for hypocalcemia prior to initiation and ensure adequate calcium/vitamin D intake • Osteonecrosis of the jaw: risk increase with invasive dental procedures, cancer diagnosis, concomitant therapy, poor oral hygiene, ill-fitting dentures and comorbid disorders • Renal impairment: use is not recommended in patients with CrCl <35 mL/minute
ibandronate	• Hypersensitivity • Bone fractures: atypical femur fractures have been reported • Bone/joint/muscle pain • Gastrointestinal mucosa irritation: esophagitis, dysphagia, esophageal ulcers, esophageal erosions, and esophageal stricture have been reported • Hypocalcemia: correct for hypocalcemia prior to initiation and ensure adequate calcium/vitamin D intake • Osteonecrosis of the jaw**:** risk increase with invasive dental procedures, cancer diagnosis, concomitant therapy, poor oral hygiene, ill-fitting dentures and comorbid disorders • Renal impairment: use is not recommended in patients with CrCl <35 mL/minute • Injection: may cause renal toxicity and transient decreases in serum calcium
pamidronate	• Renal deterioration: glomerulosclerosis and renal failure have been reported; single dose should not exceed 90 mg. Withhold treatments in patients with renal deterioration. Longer infusion times (>2 hours) may reduce the risk for renal toxicity. • Electrolyte abnormalities: includes hypophosphatemia, hypokalemia, hypomagnesemia, and hypocalcemia • Myelosuppression: closely monitor patients with preexisting anemia, leukopenia, or thrombocytopenia during the first 2 weeks of treatment • Patient with hypoparathyroidism are predisposed to pamidronate-related hypocalcemia • Bone fractures: atypical femur fractures have been reported • Bone/joint/muscle pain • Osteonecrosis of the jaw: risk increase with invasive dental procedures, cancer diagnosis, concomitant therapy, poor oral hygiene, ill-fitting dentures and comorbid disorders • Adequate hydration is required during treatment of multiple myeloma and hypercalcemia of malignancy (urine output about 2 L/day); avoid overhydration • Renal impairment: evaluate serum creatinine prior to initiation; patient with serum creatinine >3 mg/dL were not studied in clinical trials and limited data are available in patients with CrCl <30 mL/minute.

Medication	Warnings/Precautions
Prolia ® (denosumab) Xgeva ® (denosumab)	• Hypersensitivity • Dermatologic reactions: dermatitis, eczema, and rash have been reported • Bone fractures: atypical femur fractures have been reported • Bone/joint/muscle pain • Osteonecrosis of the jaw: risk increase with invasive dental procedures, cancer diagnosis, concomitant therapy, poor oral hygiene, ill-fitting dentures and comorbid disorders • Hypercalcemia: may occur in patients with growing skeletons weeks to months following discontinuation • Hypocalcemia: may result in fatalities; risk increase in patients with inadequate/no calcium supplementation, renal dysfunction (CrCl <30 mL/minute) and on dialysis. Correct for hypocalcemia prior to initiation and ensure adequate calcium/vitamin D intake • Infection: endocarditis, serious skin infections, abdominal, urinary, ear, or periodontal infections have been reported. Use with caution in patients with impaired immune systems or using concomitant immunosuppressive therapy • Renal impairment: risk of hypocalcemia increases; use with caution in patient with CrCl <30 mL/minute or on dialysis. Dose adjustment is not needed for Prolia when given at 60 mg every 6 months. For Xgeva, once-monthly dosing has not been evaluated in patients with renal impairment. • Long-term therapy cause significant suppression of bone turnover • Packaging may contain natural latex rubber • Do not administer Prolia and Xgeva to the same patient for different indications
Calcitonin (Miacalcin®)	• Hypersensitivity to salmon-derived product; perform a skin test prior to initiation in patient with suspected sensitivity • Malignancy: increased risk of cancer with long-term use of calcitonin • Antibody formation to calcitonin-salmon has been reported with injection and nasal spray • Hypocalcemia: tetany and seizure activity have been reported. Correct for hypocalcemia prior to initiation and ensure adequate calcium/vitamin D intake • Urinary sediment abnormalities: coarse granular casts and casts containing renal tubular epithelial cells were observed • Nasal spray: rhinitis, epistaxis and mucosal alterations may occur. Perform nasal examinations prior to initiation, during therapy and anytime nasal symptoms occur. Withdraw use temporarily if ulceration of nasal mucosa occurs. Discontinue for severe ulcerations (>1.5 mm), those that penetrate below the mucosa or those associated with heavy bleeding. Patients >65 years of age may experience a higher incidence of nasal adverse events with calcitonin nasal spray. • Fracture reduction efficacy has not been demonstrated; reserve use for patients not suitable for alternative treatments
raloxifene (Evista ®)	• Thromboembolic events: increased risk of DVT and PE; avoid in patient with history of VTE • Hypertriglyceridemia • Uterine bleeding • Not indicated for use in men • Not recommended for use in premenopausal women • Use has not been studied in women with breast cancer history • Use with caution in hepatic impairment and renal impairment • Concurrent use with systemic estrogen therapy is not recommended • Discontinue raloxifene at least 72 hours prior to and during prolonged immobilization; restart only once patient fully ambulatory. Advise patients to move periodically during prolonged travel
zoledronic acid (Reclast®)	• Hypersensitivity • Bone/joint/muscle pain

Medication	Warnings/Precautions
	• Bone fractures: atypical femur fractures have been reported • Ocular infection: conjunctivitis, uveitis, episcleritis, and scleritis have been reported • Use with caution in patient with aspirin-sensitive asthma; may cause bronchoconstriction • Hypocalcemia: QTc prolongation, cardiac arrhythmias, neurologic events and fatalities have been reported. Use with caution in patients with calcium and mineral metabolism disturbances. Correct for hypocalcemia prior to initiation and ensure adequate calcium/vitamin D intake. • Osteonecrosis of the jaw: risk increase with invasive dental procedures, cancer diagnosis, concomitant therapy, poor oral hygiene, ill-fitting dentures and comorbid disorders • Renal impairment: increase risk preexisting renal compromise, severe dehydration, concurrent use with diuretics or nephrotoxic drugs. Single and multiple infusions have been associated with renal deterioration, resulting in renal failure and dialysis. Adequate hydration is required during treatment (urine output about 2 L/day); avoid overhydration.
Forteo® (teriparatide)	• Osteosarcoma: increased incidence of osteosarcoma was reported in rats; avoid in patients at increased risk of osteosarcoma • Orthostatic hypotension: occurs within 4 hours of dosing and within the first several doses • Urolithiasis: risk of exacerbation can occur in patients with active or recent urolithiasis • Multiple-dose injection pens: do not use pen-shaped injection for more than one person due to risk of infections
Tymlos® (abaloparatide)	• Use for > 2 years is not recommended • Hypercalcemia: use is not recommended in patients with preexisting hypercalcemia or underlying hypercalcemic disorder • Osteosarcoma: increased incidence of osteosarcoma was reported in rats; avoid in patients at increased risk of osteosarcoma • Orthostatic hypotension: occurs within 4 hours of dosing • Urolithiasis: risk of exacerbation can occur in patients with active or recent urolithiasis
Evenity® (romosozumab)	• Major Adverse Cardiac Events (MACE): monitor for symptoms of MI and stroke and seek prompt medical attention if symptoms occur • Hypersensitivity: hypersensitivity reactions, including angioedema, erythema multiforme, dermatitis, rash, and urticaria • Hypocalcemia: adequately supplement calcium and vitamin D during treatment • Osteonecrosis of the Jaw: monitor for symptoms. Consider discontinuation of therapy based on benefit-risk assessment • Atypical Femoral Fracture: evaluate new or unusual thigh, hip, or groin pain to rule out an incomplete femur fracture

PRACTICE GUIDELINES

American College of Physicians (ACP) (2017)
Qaseem A, Forciea MA, McLean RM, Denberg TD, for the Clinical Guidelines Committee of the American College of Physicians. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update From the American College of Physicians. Ann Intern Med. 2017;166:818–839. doi: 10.7326/M15-1361.

- Recommendation 1: ACP recommends that clinicians offer pharmacologic treatment with alendronate, risedronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis. (Grade: strong recommendation; high-quality evidence)
- Recommendation 2: ACP recommends that clinicians treat osteoporotic women with pharmacologic therapy for 5 years. (Grade: weak recommendation; low-quality evidence)
- Recommendation 3: ACP recommends that clinicians offer pharmacologic treatment with bisphosphonates to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis. (Grade: weak recommendation; low-quality evidence)
- Recommendation 4: ACP recommends against bone density monitoring during the 5-year pharmacologic treatment period for osteoporosis in women. (Grade: weak recommendation; low-quality evidence)
- Recommendation 5: ACP recommends against using menopausal estrogen therapy or menopausal estrogen plus progestogen therapy or raloxifene for the treatment of osteoporosis in women. (Grade: strong recommendation; moderate-quality evidence)
- Recommendation 6: ACP recommends that clinicians should make the decision whether to treat osteopenic women 65 years of age or older who are at a high risk for fracture based on a discussion of patient preferences, fracture risk profile, and benefits, harms, and costs of medications. (Grade: weak recommendation; low-quality evidence)

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) 2020 Camacho P, Petak S, Binkley N, et al. Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis. Endocr Pract. 2020;26 (Suppl 1). Available at: https://www.endocrinepractice.org/article/S1530-891X(20)42827-7/fulltext#secst0045

- Candidates for pharmacologic therapy:
  - Pharmacologic therapy is strongly recommended for patients with osteopenia or low bone mass and a history of fragility fracture of the hip or spine **(Grade A; best evidence level (BEL) 1)**.
  - Pharmacologic therapy is strongly recommended for patients with a T-score of −2.5 or lower in the spine, femoral neck, total hip, or 1/3 radius **(Grade A; BEL 1)**.
  - Pharmacologic therapy is strongly recommended for patients with a T-score between −1.0 and −2.5 if the FRAX® (fracture risk assessment tool) (or if available, trabecular bone score [TBS]-adjusted FRAX®) 10-year probability for major osteoporotic fracture is ≥20% or the 10-year probability of hip fracture is ≥3% in the U.S. or above the country-specific threshold in other countries or regions **(Grade A; BEL 1)**.
  - Consider patients with a recent fracture (e.g., within the past 12 months), fractures while on approved osteoporosis therapy, multiple fractures, fractures while on drugs causing skeletal harm (e.g., long-term

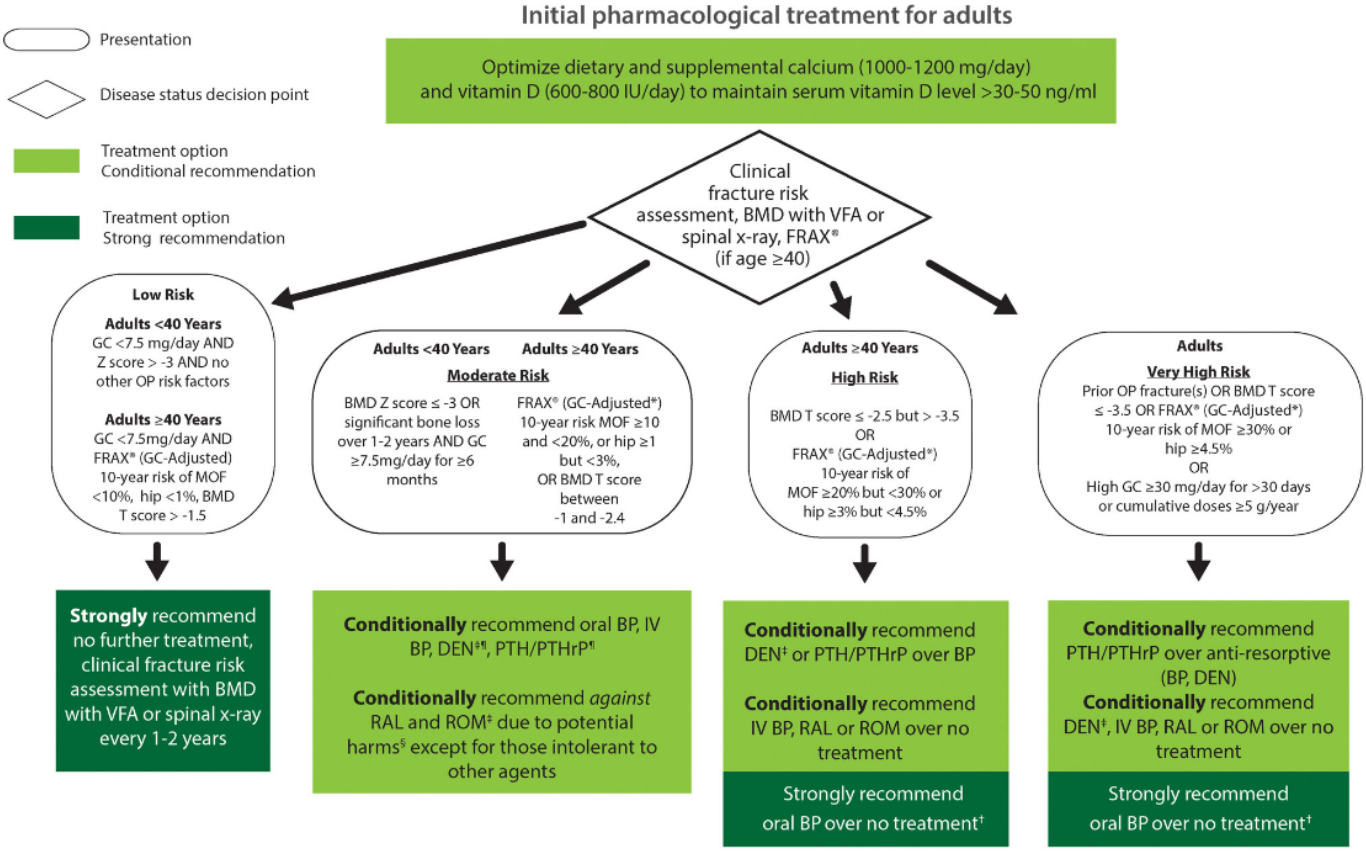
glucocorticoids), very low T-score (e.g., less than −3.0), high risk for falls or history of injurious falls, and very high fracture probability by FRAX® (fracture risk assessment tool) (e.g., major osteoporosis fracture >30%, hip fracture >4.5%) or other validated fracture risk algorithm to be at very high fracture risk. Consider patients who have been diagnosed with osteoporosis but are not at very high fracture risk, as defined above, to be high risk **(Grade B; BEL 1; downgraded due to limited evidence)**.

- Pharmacological treatments includes:
  - Approved agents with efficacy to reduce hip, nonvertebral, and spine fractures including alendronate, denosumab, risedronate, and zoledronate are appropriate as initial therapy for most osteoporotic patients with high fracture risk, as defined in R23 **(Grade A; BEL 1)**.
  - Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate should be considered for patients unable to use oral therapy and as initial therapy for patients at very high fracture risk, as defined in R23 **(Grade A; BEL 1)**.
  - Ibandronate or raloxifene may be appropriate initial therapy in some cases for patients requiring drugs with spine-specific efficacy **(Grade B; BEL 1, downgraded due to limited evidence)**.

Recommendation grade	Description
A	Homogeneous evidence from multiple, well-designed, randomized, controlled trials with sufficient statistical power Homogeneous evidence from multiple, well-designed, cohort-controlled trials with sufficient statistical power ≥1 conclusive level 1 publications demonstrating benefit >> risk
B	Evidence from ≥1 well-designed clinical trial, cohort- or case-controlled analytic study, or meta-analysis No conclusive level 1 publications; ≥1 conclusive level 2 publications demonstrating benefit >> risk
C	Evidence based on clinical experience, descriptive studies, or expert consensus opinion No conclusive level 1 or 2 publications; ≥1 conclusive level 3 publications demonstrating benefit >> risk No conclusive risk at all and no conclusive benefit demonstrated by evidence
D	Not rated No conclusive level 1, 2, or 3 publications demonstrating benefit >> risk Conclusive level 1, 2, or 3 publications demonstrating risk >> benefit
Best Evidence level	**Description**
1	Strong evidence
2	Intermediate evidence
3	Weak evidence
4	No evidence

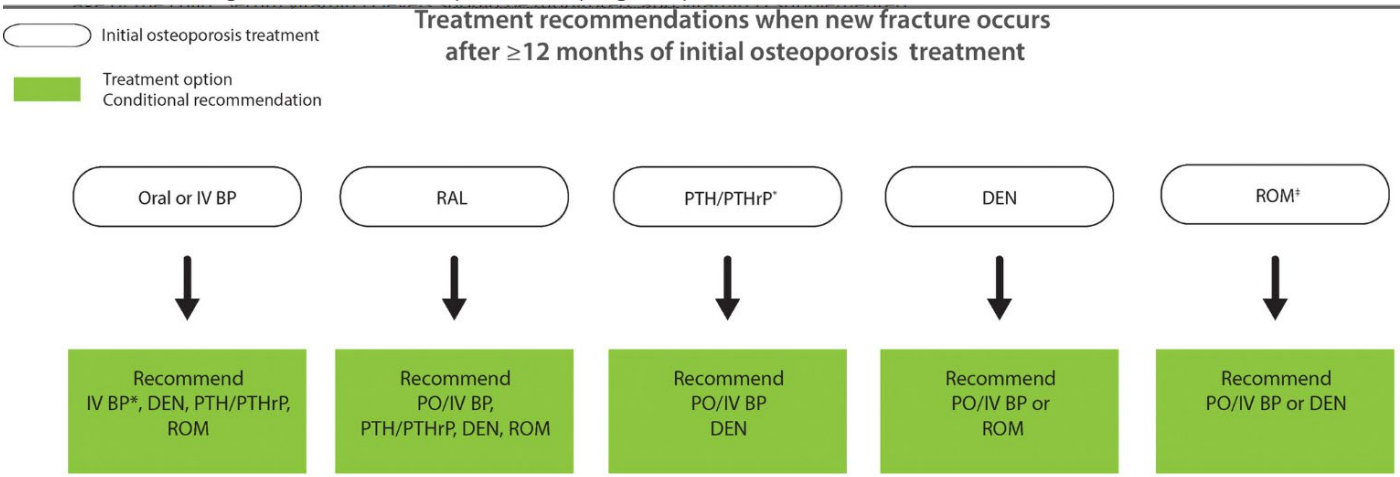
American College of Rhematology Guideline for the Prevnetion and Treatment of Glucocorticoid-Induced Osteoporosis (2022) Humphrey MB, Russell L, Danila MI, et al. 2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. Arthritis Rheumatol. 2023 Dec;75(12):2088-2102. doi: 10.1002/art.42646. Epub 2023 Oct 16. PMID: 37845798. https://www.endocrinepractice.org/article/S1530-891X(20)42827-7/fulltext#secst0045

Initial pharmacological treatment for adults



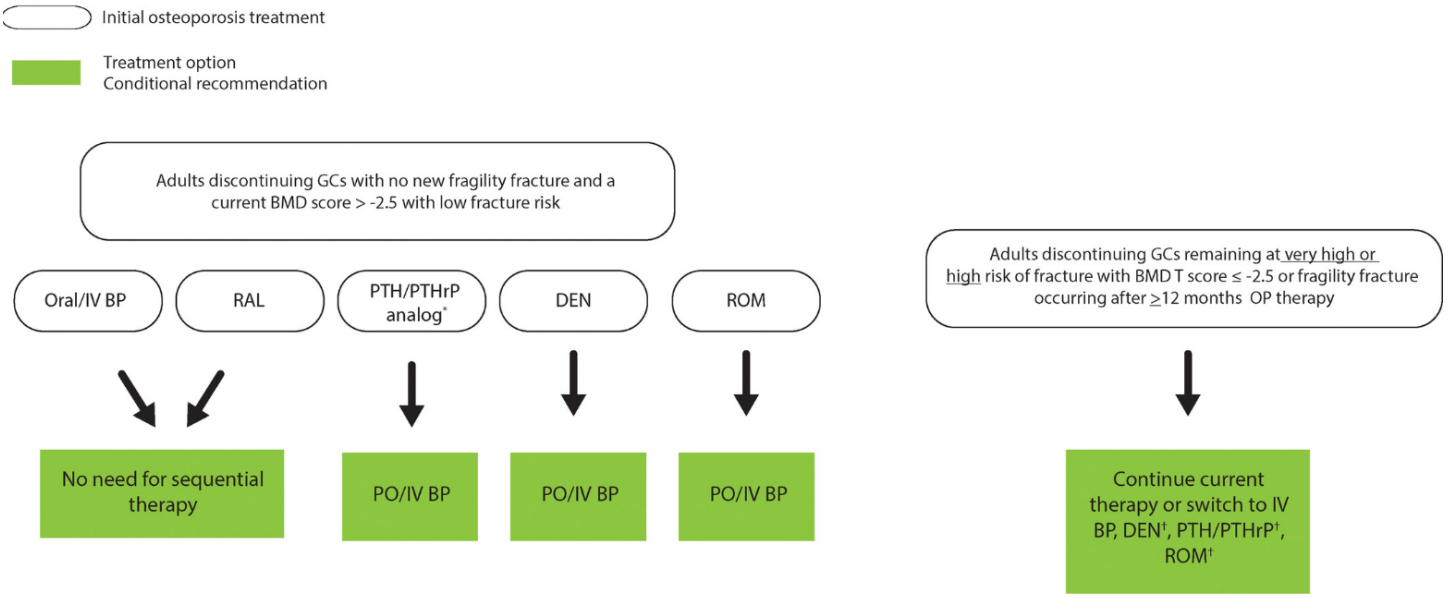
FRAX® = https//www.shef.ac.uk/FRAX/Tool.jsp; MOF= major osteoporotic fracture; *FRAX® GC correction for GC ≥7.5 mg/day example: if hip fracture risk is 2.0% multiply by 1.2 for adjusted risk = 2.4%, BP = bisphosphonate, IV = intravenous, PO = oral, PTH/PTHrP = parathyroid hormone/ parathyroid hormone related protein, DEN = denosumab, RAL = raloxifene, ROM = romosozumab, †Based on fracture data in GIOP, ‡Women who may become pregnant need birth control and avoid pregnancy until >5 months after last dose; §RAL(PE, DVT, fatal stroke); ROM (myocardial infarction, stroke and death; conditionally recommend RAL/ROM use in the highest risk patients unable to tolerate other agents; ¶Use with caution in persons with open growth plates

Treatment recommendations when new fracture occurs after ≥12 months of initial osteoporosis treatment



BP = bisphosphonate, IV = intravenous, PO = oral, DEN = denosumab, ROM = romosozumab, PTH = parathyroid hormone, PTHrP = PTH related peptide, RAL = raloxifene, OP = osteoporosis. BMD = bone mineral density, *If oral BP absorption or adherence a concern, †Bone loss may be gradual and anti-fracture efficacy may last 18 months but should be followed by anti-resorptive, ‡ROM is used for 12 months only

Sequential osteoporosis treatment recommendation when initial therapy and GC are discontinued



BP = bisphosphonate, IV = intravenous, PO = oral, DEN = denosumab, ROM = romosozumab, PTH = parathyroid hormone, PTHrP = PTH related peptide, RAL = raloxifene, OP = osteoporosis; *Bone loss may be gradual and anti-fracture efficacy maintained 18 months but antiresorptive is recommended; †Will require sequential therapy with BP

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Saag KG, Petersen J, Brandi ML, et al. Romosozumab or Alendronate for Fracture Prevention in Women with Osteoporosis (ARCH). N Engl J Med. 2017 Oct 12;377(15):1417-1427. doi: 10.1056/NEJMoa1708322. Epub 2017 Sep 11. PMID: 28892457.	N = 4,093 • Phase 3, multicenter, international, randomized, double-blind trial • Arms: monthly subcutaneous romosozumab (210 mg) or weekly oral alendronate (70 mg) for 12 months **Inclusion Criteria:** • Postmenopausal women with osteoporosis, defined as low bone mineral density (BMD T-score at the total hip or femoral neck of ≤ -2.50) **Exclusion Criteria:** • BMD T-score of ≤ -3.50 at the total hip or femoral neck • History of hip fracture • Any severe or more than 2 moderate vertebral fractures, as assessed by the central imaging based on lateral spine x-rays	Primary Endpoint: Percentage of participants with new vertebral fractures at 24 months; Percentage of participants with a clinical fracture at the primary analysis (after clinical fractures had been confirmed in ≥330 patients)
Results: Fracture risk reductions with romosozumab versus alendronate were apparent at 12 months: new vertebral fracture incidence was reduced by 37% (*P* = .003) and nonvertebral fracture incidence reduced by 26% (*P* = .06). At 24 months, new vertebral fracture risk was reduced by 48% (*P* <0.001) in patients treated with romosozumab followed by alendronate. Similarly, at primary analysis (end of study), nonvertebral fractures were reduced by 19% (*P* <0.04) and hip fractures reduced by 38% (*P* <0.02) in patients who received romosozumab first followed by alendronate, compared to those who received alendronate only. **Conclusion**: In postmenopausal women with osteoporosis who were at high risk for fracture, romosozumab treatment for 12 months followed by alendronate resulted in a significantly lower risk of fracture than alendronate alone.		
Citation	**Design**	**Endpoints**
Miller PD, Hattersley G, Riis BJ, et al. Effect of Abaloparatide vs Placebo on New Vertebral Fractures in Postmenopausal Women With Osteoporosis: A Randomized Clinical Trial. JAMA. 2016;316(7):722-733.	N= 2463 • Randomized, international, placebo- and active-controlled, phase 3 trial • Participants were either blinded and received daily subcutaneous injections of placebo, or abaloparatide 80 mcg, or open-label teriparatide 20 mcg for 18 months. Inclusion Criteria: • Postmenopausal female aged 49-86 years with bone mineral density (BMD) T-score ≤ -2.5 and > -5.0 at the lumbar spine or femoral neck measured by dual energy x-ray absorptiometry (DXA) and with radiologic evidence of at least 2 mild vertebral fractures or 1	Primary Endpoint: Percentage of participants with new vertebral fracture with abaloparatide vs placebo Secondary endpoints: • Percentage of change in BMD at total hip with abaloparatide vs placebo • Percentage of change in BMD at femoral neck

	moderate vertebral fracture or with history of a low-trauma fracture of the forearm, humerus, sacrum, pelvis, hip, femur, or tibia within the past 5 years • Female > 65 years who met fracture criteria but had a T-score ≤−2.0 and > -5.0 were eligible • Female > 65 years were eligible without fracture criteria if T-score ≤−3.0 and > -5.0 • Normal values for serum calcium, intact parathyroid hormone, phosphorus and alkaline phosphatase and 25-hydroxyvitamin D > 15 ng/mL (37.5 nmol/L) Exclusion Criteria: • History of 4 mild, moderate, or any severe vertebral fractures and fewer than 2 evaluable lumbar vertebrae, or if hip BMD was unevaluable • History of osteosarcoma • Evidence of metabolic bone disease or malabsorption or concurrent use of medications that would interfere with bone metabolism • Use bisphosphonates for more than 3 months in the past 5 years or denosumab within the past year	• Percentage of change in BMD at lumbar spine • Time to first incident nonvertebral fracture with abaloparatide vs placebo

Results:

- New vertebral fracture occurred in 0.58% of participants in the abaloparatide group and in 4.22% in placebo. Risk difference (RD) vs placebo, −3.64 [95% CI, −5.42 to −2.10]; relative risk (RR), 0.14 [95% CI, 0.05 to 0.39]; p < 0.001
- New vertebral fracture occurred in 0.84% of participants in the teriparatide group (RD vs placebo, −3.38 [95% CI, −5.18 to −1.80]; RR, 0.20 [95% CI, 0.08 to 0.47]; p < 0.001)
- Change from baseline BMD at total hip in abaloparatide group vs placebo: 4.18% vs −0.10%; treatment difference, 4.25% [95% CI, 3.90% to 4.59%]; p < 0.001
- Change in BMD at femoral neck: 3.60% vs −0.43%; treatment difference, 4.01% [95% CI, 3.58% to 4.45%]; p < 0.001
- Change in BMD at lumbar spine: 11.20% vs 0.63%; treatment difference, 10.37% [95% CI, 9.75% to 10.98%]; p < 0.001
- Event rate for nonvertebral fracture was 2.7% in the abaloparatide group vs 4.7% in the placebo group: RD, −2.01 [95% CI, −4.02 to −0.00]; hazard ratio [HR], 0.57 [95% CI, 0.32 to 1.00]; p = .049
- BMD increases at total hip were greater in the abaloparatide group vs teriparatide group: 2.32% vs 1.44%; treatment difference, 0.83% [95% CI, 0.58% to 1.08%]; p < 0.001
- BMD increases at femoral neck were greater in abaloparatide group vs teriparatide group: 1.72% vs 0.87%; treatment difference, 0.81% [95% CI, 0.49% to 1.12%]; p <0 .001
- BMD increases at lumbar spine in abaloparatide group vs teriparatide group: 6.58% vs 5.25%; treatment difference, 1.32 [95% CI, 0.86 to 1.79]; p < 0.001;
- Event rate for nonvertebral fracture: 2.7% in abaloparatide group vs 3.3% in teriparatide group: RD, −0.55 [95% CI, −2.34 to 1.24]; HR, 0.79 [95% CI, 0.43 to 1.45]; p = 0.44

Conclusion: The use of abaloparatide reduces the risk of new vertebral and nonvertebral fractures over 18 months when compared to placebo.

Citation	Design	Endpoints

Saag KG, Wagman RB, Geusens P, et al. Denosumab versus risedronate in glucocorticoid-induced osteoporosis: a multicentre, randomised, double-blind, active-controlled, double-dummy, non-inferiority study. Lancet Diabetes Endocrinol. 2018 Jun;6(6):445-454.	N= 795 • Multicenter, randomized, double-blind, active-controlled, double-dummy, non-inferiority study • Participants received either denosumab 60 mg subcutaneous every 6 months and oral placebo daily for 24 months or risedronate 5 mg oral daily and subcutaneous placebo every 6 months for 24 months. Inclusion criteria • Male or female 18 years and older taking glucocorticoids (≥7.5 mg prednisone daily or equivalent) for at least 3 months (glucocorticoid continuing) or less than 3 months (glucocorticoid initiating) • Male or female less than 50 years with a history of osteoporosis-related fracture • Male or female 50 years old and older who are glucocorticoid continuing patients with a lumbar spine, total hip or femoral neck BMD T-score ≤ -2. 0 or ≤ -1.0, if had a history of osteoporosis-related fracture	Primary Endpoint: Non-inferiority of denosumab to risedronate in terms of percentage change from baseline in lumbar spine bone mineral density at 12 months Secondary endpoints: Superiority
Results: • For glucocorticoid-continuing patient, denosumab change in BMD at lumbar spine was 4·4% [95% CI 3.8-5·0] vs risedronate 2.3% [95% CI 1.7-2·9]; p<0.0001 • For glucocorticoid-initiating, patient denosumab change in BMD at lumbar spine was 3.8% [95% CI 3.1-4.5] vs risedronate 0.8% [0·2-1·5]; p<0·0001 • Side effects included back pain (5% with denosumab vs 4% with risedronate) and arthralgia (4% with denosumab vs 5% with risedronate) • Serious infections were reported (4% with denosumab and 4% with risedronate) **Conclusion**: • Denosumab was non-inferior and superior to risedronate for effects on BMD at lumbar spine at 12 months and could be useful for both glucocorticoid-continuing and glucocorticoid-initiating patients		
Citation	**Design**	**Endpoints**
Stevenson M, Jones ML, De Nigris E, et al. A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis. Health Technol Assess. 2005 Jun;9(22):1-160.	Systematic review N= 90 RTCs • The 5 interventions included alendronate, etidronate, risedronate, raloxifene and teriparatide • The 5 comparators included calcium, calcium plus vitamin D, calcitriol, hormone replacement therapy • The studies also involved groups with placebo or no treatment Inclusion criteria • Open-label studies for which fracture was an end-point of interest	Objective: to evaluate the clinical and cost-effectiveness of alendronate, etidronate, risedronate, raloxifene or teriparatide to reduce the risk of osteoporotic fracture in postmenopausal women

	• Studies reporting fracture incidence in terms of number of patients suffering fractures • Studies that defined fractures as resulting in a 20% or greater reduction in anterior, middle or posterior vertebral height	

Results:

- All 5 drugs reduced the risk of vertebral fracture in women with severe osteoporosis and who are taking calcium adequately
- Alendronate and raloxifene reduced the risk of vertebral fracture in women taking calcium or vitamin D adequately and who have osteoporosis without fracture
- Only risedronate and teriparatide reduced the risk of non-vertebral fracture in women with severe osteoporosis and adequate calcium intakes
- Intervention costs of treating 100 osteoporotic females for 5 years were £900-1500 million ($1,200-$2,000) for alendronate, etidronate, risedronate and raloxifene. Costs for teriparatide was not calculated because it had a much higher acquisition cost and was used in a small subset of the population.
- For women with severe osteoporosis at the threshold of osteoporosis:
  - At 50 years of age, no treatment had a cost per quality-adjusted life-years (QALYs) below £35,000 ($46,000)
  - At 60 years of age, raloxifene's cost per QALY was £26,000 ($34,000), assuming no effect on hip fracture and was £31,000 ($41,000), assuming adverse effects. No other interventions had a cost per QALY below £35,000 ($46,000).
  - At 70 years of age, the cost per QALY for alendronate was £10,000 ($13,000), for risedronate was £15,000 ($20,000), for etidronate was £28,000 ($37,000) and for raloxifene was £24,000 ($31,500), assuming no effect on hip fracture.
- Assuming fracture risk were doubled at each site:
  - The cost per QALY for alendronate and risedronate was below £30,000 ($40,000) at all ages
  - The cost per QALY for etidronate was below £30,000 ($40,000) only at 70 years of age and above
  - The cost per QALY for raloxifene was below £30,000 ($40,000), assuming no effect on hip fracture at all ages
- For women at the threshold of osteoporosis and without a prior fracture:
  - The cost of per QALY of alendronate, etidronate, risedronate was between £34,000 ($45,000) to £41,000 ($54,000) at 70 years of age
  - The cost per QALY for raloxifene was £23,000 ($30,000), assuming no effect on hip fracture at 70 years of age
- The assumed efficacy of all interventions has not been proven in women 80 years of age

Conclusion:

- None of these drugs were found to be significantly more effective than the other
- All 5 interventions achieved gains in quality-adjusted life-years compared with no treatment in women taking calcium and vitamin D adequately
- The cost per QALYs ratios decreased with age for all scenarios
- The net costs were different by age and some interventions showed cost-saving opportunities at higher age ranges in patients with a prior fracture

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (07-01-2024 to 09-30-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Bisphosphonates								
Alendronate 70mg/75ml oral solution	0	0	$0.00	$0.00	0	0 (0%)	F-QL (300ml/30)	No change
Alendronate (Fosamax®) 5mg, 10mg, 35mg, 70mg oral tablet	89	71	$2,209.52	$24.83	0	0 (0%)	F-QL 5mg, 10mg (30/30) F-35mg , 70mg	No change
Binosto® (alendronate) 70 mg effervescent oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
ibandronate 3mg/3ml intravaneous solution	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
ibandronate 150mg oral tablet	13	6	$124.85	$9.60	0	0 (0%)	F	No change
pamidronate 30mg/10ml, 60mg/10ml, 90mg/10ml, 30mg, 90mg vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
risendronate (Actonel®) 5mg, 30mg, 35mg, 150mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
risendronate (Atelvia®) 35mg delayed release oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
zoledronic acid-mannitol-water (Reclast®) 4mg/100ml, 5mg/100ml intravaneous solution	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
zoledronic acid 4 mg/ 5mL vial	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Bisphosphonate and Vitamin D Combinations								
Fosamax® Plus D (alendronate-vitamin D3) 70 mg-2,800 mg, 70 mg-5,600 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Bone-Modifying Agents								
Prolia® (denosumab) 60 mg/ml syringe	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Xgeva® (denosumab) 120 mg/1.7 ml vial	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
SERMs								

raloxifene (Evista®) 60 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	F-QL (30/30)	No change
Calcitonin								
calcitonin (salmon) 200 units/actuation nasal solution	0	0	$0.00	$0.00	0	0 (0%)	F	No change
calcitonin (salmon) (Miacalcin®) 200 units/mL vial	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Parathyroid Hormone								
Tymlos® (abaloparatide) 80 mcg/dose pen injector	4	$1.00	$10,561.32	$2,640.33	0	0 (0%)	F-PA-SP	No change
teriparatide (Forteo®) 600 mcg/2.4 ml, 620 mcg/2.48 ml pen injector	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Sclerostin Inhibitor								
Evenity® (romosozumab) 105 mg/1.17 ml syringe	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	**106**	**78**	**$12,895.69**	**$121.66**	**0**	**0 (0%)**		

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

PRIOR AUTHORIZATION CRITERIA

No changes

Injectable/Infusible Agents for Osteoporosis and Paget's Disease	
Therapeutic Classes (AHFS)	Bone resorption inhibitors; Parathyroid agents
Medications	ibandronate (Boniva) injection zoledronic acid (Reclast) Prolia (denosumab) teriparatide (Forteo)--PREFERRED Tymlos (abaloparatide)--PREFERRED Evenity (romosozumab-aqqg) pamidronate
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. ***FORTEO/TERIPARATIDE/TYMLOS REQUESTS WILL ONLY BE APPROVED FOR A TOTAL DURATION OF 24 MONTHS*** *** EVENITY WILL ONLY BE APPROVED FOR A TOTAL OF 12 MONTHS*** If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	**CRITERIA FOR APPROVAL FOR ALL REQUESTS:** • Documentation (by either attestation or claims data) the member is taking adequate calcium and vitamin D supplementation • The member has a documented (consistent with pharmacy claims) adequate trial of an oral bisphosphonate or has a medical reason (e.g. intolerance, hypersensitivity, contraindication, etc.) for not using an oral bisphosphonate **POSTMENOPAUSAL OR MALE OSTEOPOROSIS:** • If the request is for **very high risk** postmenopausal osteoporosis or postmenopausal osteoporosis, with prior fractures, a documented trial and failure of an oral bisphosphonate will not be required. o Very high risk is defined as having one or more of the following: ▪ History of fracture in the past 12 months ▪ Multiple fractures ▪ Fractures while on drugs causing skeletal harm (e.g. long-term glucocorticoids) ▪ Very low T scores (< -3.0) ▪ High risk for falls ▪ History of injurious falls ▪ Very high fracture probability as determined by fracture risk assessment tool (FRAX) (e.g. major osteoporosis fracture >30%, hip fracture > 4.5%) • Documentation was submitted indicating the member is a postmenopausal woman or a male over 50 years of age and one of the following:

	○ A bone mineral density (BMD) value consistent with osteoporosis (i.e., T-scores equal to or less than –2.5) ○ Has had an osteoporotic fracture ○ A T-score between -1 and -2.5 at the femoral neck or spine and a 10 year hip fracture probability >3% or a 10 year major osteoporosis-related fracture probability >20% based on the US-adapted WHO absolute fracture risk model. • If the request is for Forteo (teriparatide), Teriparatide, Evenity (romosozumab), or Tymlos (abaloparatide), one of the following applies to the member: ○ Documented trial and failure of ibandronate (Boniva) or zoledronic acid (Reclast) AND Prolia (denosumab) or has a medical reason (e.g. intolerance, contraindication, etc.) why these therapies are not suitable to be used ○ Has severe osteoporosis (T-Score -3.5 or below, or T-Score of -2.5 or below plus a fragility fracture) • If the request is for Forteo or Evenity, a medical reason why the member is unable to use Tymlos or teriparatide, if appropriate, based on the diagnosis. ○ Requests for brand Forteo (teriparatide) also require a medical reason why the member is unable to use Teriparatide • If the request is for Evenity, the member does not have a history of a heart attack or stroke within the preceding year **GLUCOCORTICOID-INDUCED OSTEOPOROSIS:** • For members ≥ 40 years of age on long-term glucocorticoid therapy: ○ Documentation that the member is currently utilizing glucocorticoid therapy for a minimum of 3 months ○ Dosage of the glucocorticoid therapy is greater than 2.5 mg of prednisone daily or its equivalent ○ Member has a moderate to very high risk of fracture based on ONE of the following: ▪ History of osteoporotic fracture ▪ BMD less than or equal to -1 at the hip or spine ▪ FRAX 10-year probability of hip or combined major osteoporotic fracture of ≥1 and 10 percent (with glucocorticoid adjustment), respectively • For adult members (all ages) receiving HIGH dose glucocorticoid therapy: ○ Member has a moderate to very high risk of fracture based on ONE of the following: ▪ History of prior fracture ▪ Glucocorticoid dose ≥ 30 mg/day or cumulative ≥ 5 grams/year of prednisone or its equivalent ▪ Continuing glucocorticoid treatment ≥ 7.5 mg/day of prednisone or its equivalent for ≥ 6 months AND BMD Z score < -3 OR significant BMD loss (> least significant change of DXA) • If the request is for Forteo (teriparatide), Teriparatide or Tymlos (abaloparatide), the member has a documented trial and failure of zoledronic acid (Reclast) or Prolia (denosumab) or a medical reason (e.g. intolerance, contraindication, etc.) as to why the member is unable to use these medications is provided: ○ Requests for brand Forteo (teriparatide) also require a medical reason why the member is unable to use Teriparatide **PAGET'S DISEASE:** • Documentation of a confirmed diagnosis of Paget's disease. • Documentation (from within 60 days of the request) that the member has a serum alkaline phosphatase level of ≥ two times the upper limit of normal OR

	the member is symptomatic OR the member is at risk for complication from Paget's disease **CRITERIA FOR REAPPROVAL:** • The member has documentation of clinical benefit from the medication
Criteria Statement	Ibandronate (Boniva) Injection, Prolia, or zoledronic acid (Reclast) are reserved for members with a diagnosis of postmenopausal or male osteoporosis who have used (or cannot/should not use) oral bisphosphonates, unless the member has very high risk osteoporosis, an oral bisphosphonate is not required. Forteo, teriparatide, Evenity, or Tymlos are reserved for members with a diagnosis of postmenopausal or male osteoporosis who have used (or cannot/should not use) ibandronate (Boniva) or zoledronic acid (Reclast) AND Prolia. Additionally, Forteo and Evenity are reserved for members who have used (or cannot/should not use) Tymlos or teriparatide. Forteo is reserved for members who have used (or cannot/should not use) teriparatide. Tymlos, Forteo, Teriparatide, Prolia or zoledronic acid (Reclast) are reserved for members with glucocorticoid-induced osteoporosis who are 40 years of age or older on long-term glucocorticoid therapy or are on high dose glucocorticoid therapy regardless of age,and have a moderate to very high risk of fracture, and have used (or cannot/should not use) oral bisphosphonates. Forteo, Teriparatide, or Tymlos are reserved for members with glucocorticoid-induced osteoporosis who have used (or cannot/should not use) zoledronic acid (Reclast) or Prolia. Additionally, Forteo is reserved for members who have used (or cannot/should not use) Teriparatide, Zoledronic acid (Reclast) and pamidronate are reserved for members with Paget's disease who have used (or cannot/should not use) oral bisphosphonates.
Last P&T Review Date	9/2024

Injectable/Infusible Bone-Modifying Agents for Oncology Indications	
Therapeutic Classes (AHFS)	Bone resorption inhibitors
Medications	**Preferred Agent, prior authorization required** Pamidronate disodium: 3mg/ml, 6 mg/ml, 9 mg/ml liquid in10 ml vials, 30 mg, 90 mg vials Zoledronic Acid 4 mg/5 ml vial **Non-preferred Agents, prior authorization required** Xgeva (denosumab) Prolia (denosumab)
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 an oncologist or endocrinologist
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to for 6 months or as recommended per FDA approved indications and/or as defined by the medical compendium as defined above and/or per the NCCN, ASCO, NOF or NIH standard of care guidelines; if all of the above criteria are not met then, the request is referred to Clinical Reviewer for medical necessity review.

PA Review Criteria	**CRITERIA FOR APPROVAL:**
	• Prescribed dosing of medication is within FDA approved indications or is supported by the medical compendium as defined by the Social Security Act or per the NCCN, ASCO, or NIH standard of care guidelines.
	• If the request is for Xgeva (denosumab) for any of the indications below, the patient must have a documented trial and failure of pamidronate OR zoledronic acid or has a documented medical reason (intolerance, hypersensitivity, contraindication, renal insufficiency, etc) for not utilizing one of these agents to manage the medical condition
	  ○ bone metastases from solid tumors
	  ○ hypercalcemia of malignancy
	  ○ multiple myeloma osteolytic lesions
	• If the medication request if for Xgeva (denosumab) for treating **Giant Cell Tumor of Bone**, the patient has documentation submitted that the giant cell tumor of bone is unresectable, that surgical resection is likely to result in severe morbidity (e.g. denosumab is being used to aid in resection by shrinking the tumor), or that disease has recurred.
	• If the request is for Prolia (denosumab) for breast cancer, the patient has a documented trial and failure of pamidronate OR zoledronic acid that is consistent with claims history, or has a documented medical reason (intolerance, hypersensitivity, contraindication, etc) for not utilizing one of these agents to manage their medical condition
	• If the request is for Prolia (denosumab) for prostate cancer, approve.

Criteria Statement	Xgeva is reserved for treating Giant Cell Tumor of Bone in members who are not able to have surgery or who are not candidates for surgery, or in members where disease has recurred. Xgeva is reserved for members with cancer indications who have used (or cannot/should not use) pamidronate or zoledronic acid. Prolia is reserved for members with cancer indications who have used (or cannot/should not use) pamidronate or zoledronic acid.
Last P&T Review Date	9/2024

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Pulmonary Arterial Hypertension

Executive Summary

CLASS OVERVIEW

Pulmonary arterial hypertension (PAH) is characterized by an elevated pulmonary arterial pressure and increased pulmonary vascular resistance, leading to right-sided heart failure. The prevalence of PAH is estimated to be 15 cases/million adults. The disease has a poor prognosis and an approximate mortality rate of 15% within one year on therapy. The World Health Organization (WHO) classifies pulmonary hypertension into five groups based on etiology. Group 1 PAH includes patients with PAH due to hereditary or idiopathic origin, or due to certain diseases or drug use, and pharmacologic therapies for this group will be the focus of this review. Additionally, a patient's disease severity is described based on the WHO and New York Heart Association (NYHA) functional classes which assess impact on limitations on physical activity ranging from little (class I) to significant (class IV).

Treatment for pulmonary hypertension of all WHO groups can be divided into primary (which targets the underlying cause of disease) and advanced (which targets the pulmonary hypertension itself) therapies. There are now six classes of medications FDA-approved for the treatment of PAH: prostanoids, endothelin receptor antagonists (ERAs), phosphodiesterase-5 inhibitors (PDE5i), soluble guanylate cyclase stimulators, non-prostanoid IP prostacyclin receptor agonists, and activin signaling inhibitors.

Agent selection for advanced therapy is multifactorial, and includes contemplation of variables including WHO functional class, patient preferences and characteristics, hemodynamics, right ventricular function, and vasoreactivity test results. There has been a shift in recent years to prefer dual agent therapy initially vs. starting with a single agent and adding additional over time as symptoms require. Most recent guidelines from the American College of Chest Physicians (CHEST) and the European Society of Cardiology/European Respiratory Society (ESC/ERS) were examined for the purposes of this review. The newest update to CHEST guidelines for 2019 are notable for addition of the specific recommendation for combination therapy with tadalafil and ambrisentan as first line therapy in functional class II and III treatment naïve PAH patients, and currently stable or symptomatic patients already using ambrisentan monotherapy, to improve 6 minute walk distance. If these patients are unable or unwilling to initiate combination therapy with these agents, then monotherapy recommendations with a currently approved ERA, a PDE5i, or the soluble guanylate cyclase stimulator riociguat as outlined in the 2014 guidelines are suggested. The 2022 ESC/ERS guidelines recommend treatment decisions be made based the presence or absence of cardiopulmonary comorbidities and by disease severity assessed via risk stratification models. Initial combination therapy (dual ERA/PDE5i) with treatment escalation if needed based on outcomes is the standard for non-vasoreactive patients without cardiopulmonary comorbidities. Overall, there is not a general consensus regarding the "best" drug agents for the treatment of Group 1 PAH due to lack of head-to-head comparative data. Guidelines tend to make grade and evidence level recommendations or general consensus statements, some for specific agents or combinations of agents, and other times per drug class based on patient clinical status.

Multiple-source generic options are already available for many PAH agents, especially within the "backbone" therapy classes ERAs and PDE5is. Short term potential generic launches include Tracleer dispersible tablet in 2024-2025, and Opsumit in late 2025.

Several PAH products have newly available dosage forms. Liqrev is a new oral liquid formulation of sildenafil, approved via the 505(b)(2) pathway referencing clinical data from Revatio to support approval. Due to regulatory exclusivity patents on Revatio, Liqrev is not labeled for use in pediatric patients. Another new approval the first fixed-dose combination oral product Opsynvi, containing macitentan and tadalafil. Both macitentan and tadalafil are commonly used first-line treatment options in PAH, and the convenience of single-tablet dosing may be appealing to some patients and providers.

Inhaled prostanoid Ventavis is now unavailable for new starts due to the discontinuation of the I-neb AAD device by its manufacturer, and limited amounts of Ventavis are being made available to existing users. While Remodulin is available generically, subcutaneous administration of the generic product continues to be challenged by a lack of available administration devices. Currently the Remunity pump is only approved for use with brand Remodulin in adults. The single other available pump device used for generic treprostinil via subcutaneous route of administration has been discontinued and is being serviced for existing users until 2025. An alternative delivery device has been announced as in development, but providers and patients may experience challenges in receiving continuity of care and need to explore alternative options. Teva pharmaceuticals have also discontinued their generic version of Flolan, leaving only brand Flolan available on the market to date.

Winrevair (sotatercept) is a recently approved therapy with a novel mechanism of action for PAH treatment. Sotatercept is an activin receptor type IIA fusion protein that targets the underlying signaling pathways to modulate vascular proliferation. Winrevair was studied in WHO functional class II or III patients, added to their current background therapies in the phase 3 STELLAR trial. Results at 24 weeks showed improvement of 41 meters in 6-minute walk distance and 84% lower risk of all-cause death and nonfatal clinical worsening compared to patients on placebo. It is the first PAH treatment to market to have the potential to be disease modifying, but longer-term outcomes data is needed to confirm. Winrevair's place in therapy is not well determined due to limited experience, but currently it is thought it will likely be utilized most as add-on therapy for patients on dual therapy or triple therapy with vasodilator PAH agents. There are no new drug candidates for PAH currently under FDA review.

UTILIZATION FINDINGS

There were no claims and no prior authorization requests.

RECOMMENDATIONS

- No changes to formulary
- Remove 6-month timeframe for trial and failure of combination therapy before Winrevair in the criteria.

CLINICAL SUMMARY

Pulmonary arterial hypertension (PAH) is characterized by an elevated pulmonary arterial pressure and increased pulmonary vascular resistance, leading to right-sided heart failure. The prevalence of PAH is estimated to be 15 cases/million adults. The disease has a poor prognosis and an approximate mortality rate of 15% within one year on therapy. The World Health Organization (WHO) classifies pulmonary hypertension into five groups based on etiology. Group 1 PAH includes patients with PAH due to hereditary or idiopathic origin, or due to certain diseases or drug use, and pharmacologic therapies for this group will be the focus of this review. Additionally, a patient's disease severity is described based on the WHO and New York Heart Association (NYHA) functional classes which assess impact on limitations on physical activity ranging from little (class I) to significant (class IV).

Treatment for pulmonary hypertension of all WHO groups can be divided into primary (which targets the underlying cause of disease) and advanced (which targets the pulmonary hypertension itself) therapies. Advanced therapy for Group 1 PAH is usually needed. Additionally, so-called conventional or supportive therapies, which include diuretics, supplemental oxygen, and oral anticoagulants, may have a place in therapy for PAH patients, depending on patient-specific variables and most current clinical research.

There are now six classes of medications FDA-approved for the treatment of WHO Group I PAH: prostanoids, endothelin receptor antagonists (ERAs), phosphodiesterase-5 inhibitors (PDE5i), soluble guanylate cyclase stimulators, non-prostanoid IP prostacyclin receptor agonists, and activin signaling inhibitors. Calcium channel blockers are recommended for consideration in certain individuals if vasoreactivity testing shows the patient is a viable candidate for therapy, but are not FDA approved for treatment of PAH, and therefore are not covered in this review. Current advanced treatments for PAH work to reduce the increased vascular pressure via multiple mechanisms: reduction of cell proliferation and remodeling of the endothelium (which leads to decreased elasticity of the arteries) or by decreasing vasoconstriction. A high-level overview of the mechanisms of these agents is described below.

Prostacyclin pathway agents (prostanoids and non-prostanoid IP prostacyclin receptor agonists) exert their effect on the pulmonary vasculature by essentially increasing circulating prostacyclin in the body or mimicking its effects on end receptors. Prostacyclin is a potent vasodilator and can have anti-proliferative effects as well as inhibit platelet aggregation. Endothelin receptor antagonists block endogenous endothelin, known to be elevated in PAH patients, from exerting its remodeling, proliferative and vasoconstrictive effects on the endothelium and vascular smooth muscle. PDE5i and sGC stimulators work via mechanisms that ultimately result in increased production of nitric oxide in the body, a potent vasodilator and inhibitor of cell proliferation of which PAH patients have reduced levels.

Winrevair (sotatercept) is a recently approved therapy with a novel mechanism of action for PAH treatment. Sotatercept is an activin receptor type IIA fusion protein that targets the underlying signaling pathways to modulate vascular proliferation. Rat models demonstrated cellular changes in the vasculature that were associated with thinner vessel walls, partial reversal of right ventricular remodeling, and improved hemodynamics. It is the first PAH treatment to market to have the potential to be disease modifying, though longer term outcomes data is needed to confirm.

Agent selection for advanced therapy of PAH patients is multifactorial, and includes contemplation of variables including WHO functional class, patient preferences and characteristics, hemodynamics, right ventricular function, and vasoreactivity test results. Most recent guidelines from the American College of Chest Physicians (CHEST) and the European Society of Cardiology/European Respiratory Society (ESC/ERS) were examined for the purposes of this review. Overall, there is not a general consensus regarding the "best" drug therapies (in reference to advanced therapy agents) for the treatment of Group 1 PAH due to lack of head-to-head comparative data. Guidelines tend to make grade and evidence level recommendations or general consensus statements, some for specific agents or combinations of agents, and other times per drug class based on patient clinical status.

According to CHEST guidelines, symptomatic, treatment-naïve patients in WHO functional Class I do not require pharmacologic therapy but rather should be closely monitored and adopt lifestyle management practices which reduce the risk of disease progression. For patients in class II and III, recommendations from the 2019 CHEST guidelines suggest combination therapy with tadalafil and ambrisentan as first-line therapy in treatment naïve PAH patients to improve 6-minute walk distance, and currently stable or symptomatic patients already using ambrisentan monotherapy should

have tadalafil added to their regimen. If this is not feasible for the patient, then monotherapy recommendations with highest grades/evidence levels typically include ERAs, PDE5i and riociguat. Use of additional agents from other pharmacotherapeutic classes are recommended when current treatments fail or the response is inadequate, and it is not uncommon for patients to be on multiple agents (vs. switching) as disease progression occurs. Starting in class III use of a prostanoid agent is advised in certain circumstances, such as evidence of rapid progression of disease or other markers of poor clinical progress. For class IV patients, treatment with a parenteral prostanoid should be initiated. Most consider intravenous epoprostenol to be the preferred agent.

The 2022 ESC/ERS guidelines recommend treatment decisions be made based the presence or absence of cardiopulmonary comorbidities and by disease severity assessed via risk stratification models. Initial combination therapy (dual ERA/PDE5i) with treatment escalation if needed based on outcomes is the standard in non-vasoreactive patients with low to intermediate risk. High risk patients should have an IV or SC prostacyclin agonist added to this regimen. Initial oral monotherapy with a PDE5i or an ERA is recommended for non-vasoreactive patients with cardiopulmonary comorbidities. Treatment escalation at follow up for sub-optimal response is tailored to each patient's clinical situation.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Sildenafil (Revatio®)	• The treatment of pulmonary arterial hypertension (PAH) (WHO Group I) in adults to improve exercise ability and delay clinical worsening. • Indicated in pediatric patients 1 to 17 years old for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise ability and, in pediatric patients too young to perform standard exercise testing, pulmonary hemodynamics thought to underly improvements in exercise.	Adults: • 20 mg three times a day Dose may be increased based on symptoms and tolerability. Pediatric patients • ≤20 kg: 10 mg three times a day • 20 kg to 45 kg: 20 mg three times a day • >45 kg: 20 mg three times a day. Dose may be increased based on symptoms and tolerability. Injection (Adults): • 10 mg three times a day administered as an intravenous bolus injection.
Liqrev® (sildenafil)	For the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group I) in adults to improve exercise ability and delay clinical worsening.	Adults: 20 mg orally three times a day.
Tadalafil (Adcirca®) Tadliq® (tadalafil)	The treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).	Tablets: • 40 mg once daily, with or without food. • Dividing the dose (40 mg) over the course of the day is not recommended. • Use with ritonavir requires dosage adjustments. Oral suspension: • 40 mg (10 mL) once daily, with or without food. • Use with ritonavir requires dosage adjustments.
ambrisentan (Letairis®)	The treatment of pulmonary arterial hypertension (PAH) (WHO Group 1): • To improve exercise ability and delay clinical worsening. • In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability. Studies establishing effectiveness included trials predominantly in patients with WHO Functional Class II–III symptoms and etiologies of idiopathic or heritable PAH (60%) or PAH associated with connective tissue diseases (34%).	Initiate treatment at 5 mg once daily. • May be started with tadalafil. • Titrate at 4-week intervals as needed and tolerated. • Do not split, crush, or chew tablets.
Opsumit® (macitentan)	The treatment of pulmonary arterial hypertension (PAH, WHO Group I) to reduce the risks of disease progression and hospitalizations for PAH.	10 mg once daily. Doses higher than 10 mg once daily have not been studied in patients with PAH and are not recommended.

<table>
<tr><th>Medication</th><th>Indications</th><th>Dosing/Administration</th></tr>
<tr><td></td><td>Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%)</td><td></td></tr>
<tr><td>Bosentan (Tracleer®) tablets
Tracleer® (bosentan) tablets for oral suspension</td><td>The treatment of pulmonary arterial hypertension (PAH) (WHO Group 1):
• in adults to improve exercise ability and to decrease clinical worsening. Studies establishing effectiveness included predominantly patients with WHO Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital heart disease with left-to-right shunts (18%).
• in pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability.</td><td>Patients older than 12 years of age: initiate at 62.5 mg orally twice daily; for patients weighing greater than 40 kg, increase to 125 mg orally twice daily after 4 weeks.

Patients 12 years of age and younger: dosage is based on weight, see Table 1.
<table>
<tr><th></th><th>Initial 4 weeks</th><th>Maintenance (after 4 weeks)</th></tr>
<tr><td>Patients >12 years of age and >40 kg</td><td>62.5 mg twice daily</td><td>125 mg twice daily</td></tr>
<tr><td>Patients >12 years of age and <40 kg</td><td>62.5 mg twice daily</td><td>62.5 mg twice daily</td></tr>
<tr><td>Patients ≤12 years of age</td><td></td><td></td></tr>
<tr><td>≥4-8 kg</td><td>16 mg twice daily</td><td>16 mg twice daily</td></tr>
<tr><td>>8-16 kg</td><td>32 mg twice daily</td><td>32 mg twice daily</td></tr>
<tr><td>>16-24 kg</td><td>48 mg twice daily</td><td>48 mg twice daily</td></tr>
<tr><td>>24-40 kg</td><td>64 mg twice daily</td><td>64 mg twice daily</td></tr>
</table>
Reduce the dose and closely monitor patients developing aminotransferase elevations more than 3 × Upper Limit of Normal (ULN).</td></tr>
<tr><td>Epoprostenol sodium (glycine) (Flolan®)</td><td>The treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly (97%) patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (49%) or PAH associated with connective tissue diseases (51%).</td><td>• Initiate intravenous infusion through a central venous catheter at 2 ng/kg/min.
• Change dose in 1-to 2-ng/kg/min increments at intervals of at least 15 minutes based on clinical response.
• Avoid sudden large dose reductions.</td></tr>
<tr><td>Epoprostenol sodium (arginine) (Veletri®)</td><td>The treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and</td><td>Dosage:
Infusion should be initiated at 2 ng/kg/min and increased in increments of 2 ng/kg/min every 15 minutes or longer until dose-limiting pharmacologic effects are elicited or until a tolerance limit to the drug is established.</td></tr>
</table>

Medication	Indications	Dosing/Administration
	etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.	If symptoms of pulmonary hypertension persist or recur after improving - the infusion should be increased by 1- to 2-ng/kg/min increments at intervals sufficient to allow assessment of clinical response; these intervals should be at least 15 minutes. Administration: Veletri® is administered by continuous intravenous infusion via a central venous catheter using an ambulatory infusion pump. Do not mix with any other parenteral medications or solutions prior to or during administration.
Ventavis® (iloprost tromethamine)	The treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration. Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (65%) or PAH associated with connective tissue diseases (23%).	• Do not initiate therapy in patients with systolic blood pressure below 85 mmHg. • Initial, 2.5 mcg inhaled using the I-neb(R) ADD(R) System; if tolerated, increase dose to 5 mcg inhaled 6 to 9 times per day (no more than every 2 hours) during waking hours; MAX daily dose was 45 mcg (5 mcg 9 times per day).
Uptravi® (selexipag)	The treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH. Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), PAH associated with congenital heart disease with repaired shunts (10%)	Tablets: • Starting dose: 200 mcg twice daily. • Increase the dose by 200 mcg twice daily at weekly intervals to the highest tolerated dose up to 1600 mcg twice daily. • Maintenance dose is determined by tolerability. • Moderate hepatic impairment: Starting dose 200 mcg once daily, increase the dose by 200 mcg once daily at weekly intervals to the highest tolerated dose up to 1600 mcg. For Injection: • Dose is determined by the patient's current dose of Uptravi tablets. Administer Uptravi for injection by intravenous infusion, twice daily.
treprostinil sodium (Remodulin®)	Indicated for: • Treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary	PAH WHO Group 1 in patients with NYHA Class II-IV symptoms: • Initial dose for patients new to prostacyclin infusion therapy: 1.25 ng/kg/min; increase based on clinical response (increments of 1.25 ng/kg/min per week for the first 4 weeks of treatment, later 2.5 ng/kg/min per week). Avoid abrupt cessation. • Mild to moderate hepatic insufficiency: Decrease initial dose to 0.625 ng/kg/min.

Medication	Indications	Dosing/Administration
	shunts (23%), or PAH associated with connective tissue diseases (19%). • Pulmonary Arterial Hypertension in patients who require transition from epoprostenol, to reduce the rate of clinical deterioration. The risks and benefits of each drug should be carefully considered prior to transition.	• Severe hepatic insufficiency: No studies performed. Transition from Epoprostenol: • Increase the Remodulin® dose gradually as the epoprostenol dose is decreased, based on constant observation of response. Administration: • Continuous subcutaneous infusion is the preferred mode. Use intravenous (IV) infusion if subcutaneous infusion is not tolerated.
Tyvaso® (treprostinil)	Indicated for the treatment of: • Pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability. Studies with Tyvaso establishing effectiveness predominately included patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%). • Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. The study with Tyvaso establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%), and WHO Group 3 connective tissue disease (22%).	• Use only with the Tyvaso® Inhalation System. • Administer undiluted, as supplied. A single breath of Tyvaso® delivers approximately 6 mcg of treprostinil. • Administer in 4 separate treatment sessions each day approximately four hours apart, during waking hours. • Initial dosage: 3 breaths (18 mcg) per treatment session. If 3 breaths are not tolerated, reduce to 1 or 2 breaths. • Dosage should be increased by an additional 3 breaths per session at approximately 1-2 week intervals, if tolerated. • Titrate to target maintenance doses of 9 to 12 breaths per treatment session, 4 times daily
Tyvaso® DPI (treprostinil)		• Use only with the Tyvaso DPI Inhaler. • Administer using a single inhalation per cartridge. • Administer in 4 separate treatment sessions each day approximately 4 hours apart, during waking hours. • Initial dosage: one 16 mcg cartridge per treatment session. • Dosage should be increased by an additional 16 mcg per treatment session at approximately 1- to 2-week intervals, if tolerated. • Titrate to target maintenance doses of 48 mcg to 64 mcg per treatment session, 4 times daily.
Orenitram® (treprostinil diolamine)	Indicated for: • Treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to delay disease progression and improve exercise capacity. The study that established effectiveness included	• Give with food. Swallow tablets whole; use only intact tablets. • Starting dose: 0.25 mg BID or 0.125 mg TID.

Medication	Indications	Dosing/Administration
	predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (66%) or PAH associated with connective tissue disease (26%).	• Titrate by 0.25 mg or 0.5 mg BID or 0.125 mg TID, not more than every 3 to 4 days as tolerated. • If transitioning from intravenous (IV) or subcutaneous (SC) Remodulin®, the Orenitram® dose should be increased while simultaneously decreasing the IV/SC infusion rate. • Mild hepatic impairment (Child Pugh Class A): Initiate at 0.125 mg BID. Increment at 0.125 mg BID every 3 to 4 days. • Avoid use in patients with moderate hepatic impairment.
Adempas® (riociguat)	The treatment of adults with: • Persistent/recurrent Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class. • Pulmonary Arterial Hypertension (PAH) (WHO Group 1) to improve exercise capacity, improve WHO functional class and to delay clinical worsening. Efficacy was shown in patients on Adempas monotherapy or in combination with endothelin receptor antagonists or prostanoids. Studies establishing effectiveness included predominately patients with WHO functional class II–III and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (25%).	• Initiate treatment at 1 mg taken three times a day. • For patients who may not tolerate the hypotensive effect of Adempas®, consider a starting dose of 0.5 mg, three times a day. • Increase dosage by 0.5 mg at intervals of no sooner than 2-weeks as tolerated to a maximum of 2.5 mg three times a day. • Tablets may be crushed and mixed with water or soft foods for patients who have difficulty swallowing.
Opsynvi® (macitentan-tadalafil)	For the chronic treatment of pulmonary arterial hypertension (PAH, WHO Group I) in adult patients of WHO functional class (FC) II–III. Individually, macitentan reduces the risk of clinical worsening events and hospitalization, and tadalafil improves exercise ability.	For patients who are treatment-naïve to any PAH specific therapy or transitioning from ERA monotherapy • The recommended starting dose of Opsynvi is one 10 mg/20 mg tablet taken orally once daily with or without food for one week. If tolerated, up titrate Opsynvi to one 10 mg/40 mg tablet taken orally once daily with or without food as the maintenance dose. For patients transitioning from PDE5 inhibitor monotherapy or PDE5 inhibitor and ERA therapy in combination • The recommended dose of Opsynvi is one 10 mg/40 mg tablet taken orally once daily.

Medication	Indications	Dosing/Administration
Winrevair® (sotatercept-csrk)	For the treatment of adults with pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to increase exercise capacity, improve WHO functional class (FC), and reduce the risk of clinical worsening events.	• The recommended starting dose is 0.3 mg/kg by subcutaneous injection. • The recommended target dose is 0.7 mg/kg every 3 weeks by subcutaneous injection. • Dosage modifications due to increased hemoglobin (Hgb) and decreased platelets may be necessary. Check Hgb and platelets before each dose for the first 5 doses, or longer if values are unstable, and monitor periodically thereafter. • See full prescribing information for preparation and administration instructions.

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Sildenafil (Revatio®)	None.	• Use with organic nitrates or riociguat. • History of hypersensitivity reaction to sildenafil or any component of the tablet, injection, or oral suspension.
Liqrev® (sildenafil)	None.	• Use with organic nitrates or riociguat. • History of hypersensitivity reaction to sildenafil or any component of the oral suspension.
Tadalafil (Adcirca®) Tadliq® (tadalafil)	None.	• Concomitant organic nitrates. • Concomitant Guanylate Cyclase (GC) Stimulators. • History of known serious hypersensitivity reaction to Tadliq ®, Adcirca® or Cialis®.
ambrisentan (Letairis®)	Embryo-fetal toxicity.	• Pregnancy. • Idiopathic pulmonary fibrosis.
Opsumit® (macitentan)	Embryo-fetal toxicity.	• Pregnancy. • Hypersensitivity.
Tracleer® (bosentan)	Risks of hepatotoxicity, embryo-fetal toxicity.	• Pregnancy. • Use with Cyclosporine A. • Use with Glyburide. • Hypersensitivity.
Epoprostenol sodium (glycine) (Flolan®)	None.	• Heart failure with reduced ejection fraction. • Hypersensitivity to Flolan® or any of its ingredients.
Epoprostenol sodium (arginine) (Veletri®)	None.	• Congestive heart failure due to severe left ventricular systolic dysfunction. • Pulmonary edema.

Medication	Boxed Warnings	Contraindications
		• Hypersensitivity to the drug or to structurally related compounds.
Ventavis® (iloprost tromethamine)	None.	None.
Uptravi® (selexipag)	None.	Concomitant use with strong CYP2C8 inhibitors.
treprostinil sodium (Remodulin®)	None.	None.
Tyvaso® (treprostinil) Tyvaso DPI® (treprostinil)	None.	None.
Orenitram® (treprostinil diolamine)	None.	Severe hepatic impairment (Child Pugh Class C).
Adempas® (riociguat)	Embryo-fetal toxicity.	• Pregnancy. • Use with nitrates or nitric oxide donors in any form. • Use with PDE inhibitors. • Patients with concomitant use of other soluble guanylate cyclase (sGC) • stimulators • Pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP).
Opsynvi® (macitentan-tadalafil)	Embryo-fetal toxicity.	• Pregnancy • Hypersensitivity • Concomitant organic nitrates • Concomitant guanylate cyclase stimulators
Winrevair® (sotatercept-csrk)	None.	• None.

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Sildenafil (Revatio®)	• Increased mortality with increasing doses in pediatric patients. Not recommended for use in pediatric patients. • Vasodilation effects may be more common in patients with hypotension or on antihypertensive therapy. • Use in pulmonary veno-occlusive disease may cause pulmonary edema and is not recommended. • Hearing or visual impairment: Seek medical attention if sudden decrease or loss of vision or hearing occurs. • Pulmonary hypertension secondary to sickle cell disease: Revatio® may cause serious vaso-occlusive crises.
Liqrev® (sildenafil)	• Vasodilation effects may be more common in patients with hypotension or on antihypertensive therapy. • Use in pulmonary veno-occlusive disease (PVOD) may cause pulmonary edema and is not recommended. • Hearing or visual impairment: Seek medical attention if sudden decrease or loss of vision or hearing occurs. • Pulmonary hypertension (PH) secondary to sickle cell disease: Liqrev may cause serious vaso-occlusive crises.

Medication	Warnings/Precautions
Tadalafil (Adcirca®) Tadliq® (tadalafil)	• Hypotension: Carefully consider whether patients with certain underlying cardiovascular disease could be adversely affected by vasodilatory effects of Adcirca/Tadliq. Not recommended in patients with pulmonary venoocclusive disease. • Effects on the eye: Sudden loss of vision could be a sign of non-arteritic ischemic optic neuropathy (NAION) and may be permanent. • Hearing impairment: Cases of sudden decrease or loss of hearing have been reported with tadalafil. • Concomitant PDE5 inhibitors: Avoid use with Cialis, Adcirca or other PDE5 inhibitors. • Prolonged erection: Advise patients to seek emergency treatment if an erection lasts >4 hours.
ambrisentan (Letairis®)	• Fluid retention may require intervention. • If patients develop acute pulmonary edema during initiation of therapy with Letairis®, consider underlying pulmonary veno-occlusive disease and discontinue treatment if necessary. • Decreases in sperm count have been observed in patients taking endothelin receptor antagonists. • Decreases in hemoglobin have been observed within the first few weeks; measure hemoglobin at initiation, at 1 month, and periodically thereafter.
Opsumit® (macitentan)	• ERAs cause hepatotoxicity and liver failure. Obtain baseline liver enzymes and monitor as clinically indicated. • Fluid retention may require intervention. • Decreases in hemoglobin. • Pulmonary edema in patients with pulmonary veno-occlusive disease. If confirmed, discontinue treatment. • Decreases in sperm count have been observed in patients taking ERAs.
Tracleer® (bosentan)	• Fluid retention: May require intervention. • Pulmonary veno-occlusive disease (PVOD): If signs of pulmonary edema occur, consider the diagnosis of associated PVOD and consider discontinuing Tracleer®. • Decreased sperm counts. • Decreases in hemoglobin and hematocrit: Monitor hemoglobin levels after 1 and 3 months of treatment, then every 3 months thereafter.
Epoprostenol sodium (glycine) (Flolan®)	• Pulmonary edema: Discontinue therapy if pulmonary edema occurs. • Rebound pulmonary hypertension: Do not abruptly discontinue or decrease the dose. • Vasodilation reactions: Monitor blood pressure and symptoms regularly during initiation and after dose change. • Increased risk for bleeding: Increased risk for hemorrhagic complications, particularly for patients with other risk factors for bleeding.
Epoprostenol sodium (arginine) (Veletri®)	• Do not abruptly lower the dose or withdraw dosing. All dosing initiation and changes should be closely monitored.
Ventavis® (iloprost tromethamine)	• Hypotension leading to syncope has been observed. Ventavis® should not be administered in patients with systolic blood pressure below 85 mmHg. • Pulmonary venous hypertension: Discontinue if pulmonary edema is present. • May cause bronchospasm: Patients with a history of hyperreactive airway disease may be more sensitive.
Uptravi® (selexipag)	• Pulmonary edema in patients with pulmonary veno-occlusive disease. If confirmed, discontinue treatment.
treprostinil sodium (Remodulin®)	• Chronic intravenous infusions delivered using an external infusion pump with an indwelling central venous catheter are associated with the risk of blood stream infections (BSIs) and sepsis, which may be fatal.

Medication	Warnings/Precautions
	• Do not abruptly lower the dose or withdraw dosing. • Remodulin® may cause symptomatic hypotension. • Remodulin® inhibits platelet aggregation and increases the risk of bleeding.
Tyvaso® (treprostinil) Tyvaso DPI® (treprostinil)	• May cause symptomatic hypotension. • Inhibits platelet aggregation and increases the risk of bleeding. • Dosage adjustments may be necessary if inhibitors or inducers of CYP2C8 are added or withdrawn. • May cause bronchospasm: Patients with a history of hyperreactive airway disease may be more sensitive
Orenitram® (treprostinil diolamine)	• Do not abruptly discontinue dosing. • In patients with diverticulosis Orenitram® tablets can become lodged in a diverticulum.
Adempas® (riociguat)	• Symptomatic hypotension. • Bleeding. • Pulmonary edema in patients with pulmonary veno-occlusive disease. If confirmed, discontinue treatment.
Opsynvi® (macitentan-tadalafil)	• Hepatotoxicity, obtain baseline liver enzymes and monitor as clinically indicated • Hypotension • Hemoglobin decrease • Worsening Pulmonary Veno-Occlusive Disease: If pulmonary edema is confirmed, discontinue treatment. • Visual loss (non-arteritic ischemic optic neuropathy) • Hearing impairment or loss • Fluid retention: may require intervention • Avoid use with other PDE5 inhibitors • Decreased sperm count • Prolonged erection: seek emergency treatment if longer than 4 hours
Winrevair® (sotatercept-csrk)	• Erythrocytosis: If severe, may increase the risk of thromboembolic events and hyperviscosity syndrome. Monitor Hgb before each dose for the first 5 doses, or longer if values are unstable, and periodically thereafter to determine if dose adjustments are required. • Severe Thrombocytopenia: May increase the risk of bleeding. Monitor platelets before each dose for the first 5 doses, or longer if values are unstable, and periodically thereafter to determine if dose adjustments are required. • Serious Bleeding: Serious bleeding events were reported and were more likely with concomitant prostacyclin and/or antithrombotic agents, or with low platelet counts. Do not administer Winrevair if the patient is experiencing serious bleeding. • Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use of effective contraception. • Impaired Fertility: May impair female and male fertility.

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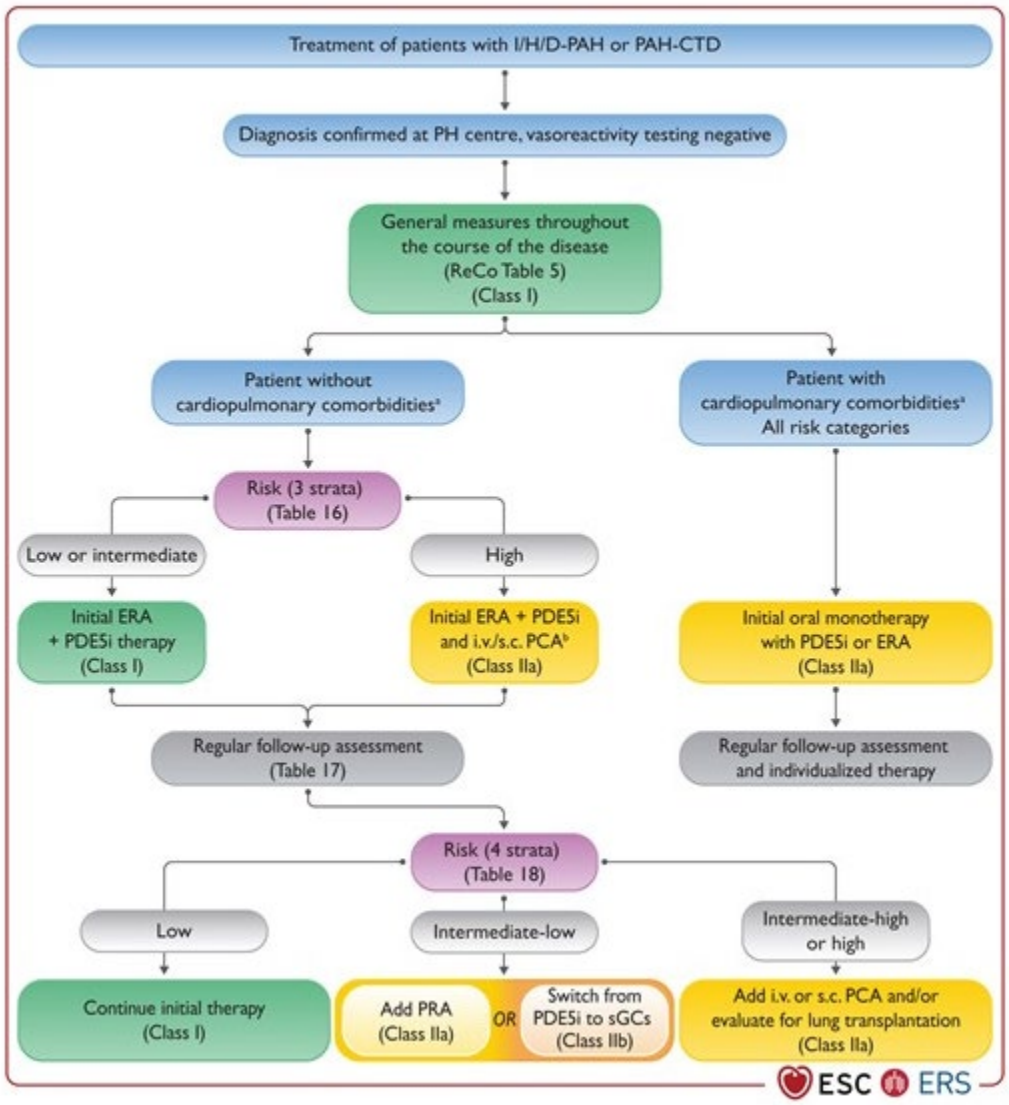

Recommendation Table 7 Recommendations for the treatment of vasoreactive patients with idiopathic, heritable, or drug-associated pulmonary arterial hypertension

Recommendations	Class[a]	Level[b]
High doses of CCBs are recommended in patients with IPAH, HPAH, or DPAH who are responders to acute vasoreactivity testing	I	C
Close follow-up with complete reassessment after 3–4 months of therapy (including RHC) is recommended in patients with IPAH, HPAH, or DPAH treated with high doses of CCBs	I	C
Continuing high doses of CCBs is recommended in patients with IPAH, HPAH, or DPAH in WHO-FC I or II with marked haemodynamic improvement (mPAP <30 mmHg and PVR <4 WU)	I	C
Initiating PAH therapy is recommended in patients who remain in WHO-FC III or IV or those without marked haemodynamic improvement after high doses of CCBs	I	C
In patients with a positive vasoreactivity test but insufficient long-term response to CCBs who require additional PAH therapy, continuation of CCB therapy should be considered	IIa	C
CCBs are not recommended in patients without a vasoreactivity study or non-responders, unless prescribed for other indications (e.g. Raynaud's phenomenon)	III	C

CCB, calcium channel blocker; DPAH, drug-associated pulmonary arterial hypertension; HPAH, heritable pulmonary arterial hypertension; IPAH, idiopathic pulmonary arterial hypertension; mPAP, mean pulmonary arterial pressure; PAH, pulmonary arterial hypertension; PVR, pulmonary vascular resistance; RHC, right heart catheterization; WHO-FC, World Health Organization functional class; WU, Wood units.

a Class of recommendation.

b Level of evidence.

Recommendation Table 8 Recommendations for the treatment of non-vasoreactive patients with idiopathic, heritable, or drug-associated pulmonary arterial hypertension who present without cardiopulmonary comorbidities[a]

Recommendation Table 8A		
Recommendations	**Class**[b]	**Level**[c]
Recommendations for initial therapy		
In patients with IPAH/HPAH/DPAH who present at high risk of death, initial combination therapy with a PDE5i, an ERA, and i.v./s.c. prostacyclin analogues should be considered[d]	**IIa**	**C**
Recommendations for treatment decisions during follow-up		
In patients with IPAH/HPAH/DPAH who present at intermediate–low risk of death while receiving ERA/PDE5i therapy, the addition of selexipag should be considered[419]	**IIa**	**B**
In patients with IPAH/HPAH/DPAH who present at intermediate–high or high risk of death while receiving ERA/PDE5i therapy, the addition of i.v./s.c. prostacyclin analogues and referral for LTx evaluation should be considered	**IIa**	**C**
In patients with IPAH/HPAH/DPAH who present at intermediate–low risk of death while receiving ERA/PDE5i therapy, switching from PDE5i to riociguat may be considered[429]	**IIb**	**B**

Recommendation Table 8B				
	GRADE			
Recommendations	**Quality of evidence**	**Strength of recommendation**	**Class**[a]	**Level**[b]
Recommendations for initial therapy				
In patients with IPAH/HPAH/DPAH who present at low or intermediate risk of death, initial combination therapy with a PDE5i and an ERA is recommended[166]	Low	Conditional	**I**	**B**

CI, cardiac index; DLCO, Lung diffusion capacity for carbon monoxide; DPAH, drug-associated pulmonary arterial hypertension; ERA, endothelin receptor antagonist; HFpEF, heart failure with preserved ejection fraction; HPAH, heritable pulmonary arterial hypertension; IPAH, idiopathic pulmonary arterial hypertension; i.v., intravenous; LTx, lung transplantation; PAH, pulmonary arterial hypertension; PDE5i, phosphodiesterase 5 inhibitor; PVR, pulmonary vascular resistance; RAP, right atrial pressure; s.c., subcutaneous; SVI, stroke volume index; WU, Wood units.

a Cardiopulmonary comorbidities are predominantly encountered in elderly patients and include risk factors for HFpEF such as obesity, diabetes, coronary heart disease, a history of hypertension, and/or a low DLCO.

b Class of recommendation.

c Level of evidence.

d Initial triple-combination therapy including i.v./s.c. prostacyclin analogues may also be considered in patients presenting at intermediate risk but severe haemodynamic impairment (e.g. RAP ≥20 mmHg, CI <2.0 L/min/m^2, SVI <31 mL/m^2, and/or PVR ≥12 WU).

Recommendation Table 9 Recommendations for initial oral drug combination therapy for patients with idiopathic, heritable, or drug-associated pulmonary arterial hypertension without cardiopulmonary comorbidities

Recommendations	Class[a]	Level[b]
Initial combination therapy with ambrisentan and tadalafil is recommended[166,420,423]	I	B
Initial combination therapy with macitentan and tadalafil is recommended[421,430]	I	B
Initial combination therapy with other ERAs and PDE5is should be considered[303]	IIa	B
Initial combination therapy with macitentan, tadalafil, and selexipag is not recommended[421]	III	B

Recommendation Table 10 Recommendations for sequential drug combination therapy for patients with idiopathic, heritable, or drug-associated pulmonary arterial hypertension

Recommendations	Class[a]	Level[b]
General recommendation for sequential combination therapy		
It is recommended to base treatment escalations on risk assessment and general treatment strategies (see *Figure 9*)	I	C
Evidence from studies with a composite morbidity/mortality endpoint as the primary outcome measure		
The addition of macitentan to PDE5is or oral/inhaled prostacyclin analogues is recommended to reduce the risk of morbidity/mortality events[167,168,437]	I	B
The addition of selexipag to ERAs[c] and/or PDE5is is recommended to reduce the risk of morbidity/mortality events[418,419]	I	B
The addition of oral treprostinil to ERA or PDE5i/riociguat monotherapy is recommended to reduce the risk of morbidity/mortality events[412,413,415]	I	B
The addition of bosentan to sildenafil is not recommended to reduce the risk of morbidity/mortality events[419]	III	B

Evidence from studies with change in 6MWD as the primary outcome measure		
The addition of sildenafil to epoprostenol is recommended to improve exercise capacity[392,438]	I	B
The addition of inhaled treprostinil to sildenafil or bosentan monotherapy should be considered to improve exercise capacity[411,439]	IIa	B
The addition of riociguat to bosentan should be considered to improve exercise capacity[395,440]	IIa	B
The addition of tadalafil to bosentan may be considered to improve exercise capacity[393]	IIb	C
The addition of inhaled iloprost to bosentan may be considered to improve exercise capacity[441,442]	IIb	B
The addition of ambrisentan to sildenafil may be considered to improve exercise capacity[443]	IIb	C
The addition of bosentan to sildenafil may be considered to improve exercise capacity[419,444]	IIb	C
The addition of sildenafil to bosentan may be considered to improve exercise capacity[444–446]	IIb	C
Other sequential double- or triple-combination therapies may be considered to improve exercise capacity and/or alleviate PH symptoms	IIb	C
Evidence from studies with safety of combination therapy as the primary outcome measure		
Combining riociguat and PDE5is is not recommended[d389]	III	B

6MWD, 6-minute walking distance; ERA, endothelin receptor antagonist; PDE5i, phosphodiesterase 5 inhibitor; PH, pulmonary hypertension.

6MWD, 6-minute walking distance; ERA, endothelin receptor antagonist; PDE5i, phosphodiesterase 5 inhibitor; PH, pulmonary hypertension.

a Class of recommendation.

b Level of evidence.

c ERAs used in the GRIPHON study were bosentan and ambrisentan.

d The PATENT plus study investigated the combination of sildenafil and riociguat; however, combining riociguat with any PDE5i is contraindicated.

Recommendation Table 11 Recommendations for the treatment of non-vasoreactive patients with idiopathic, heritable, or drug-associated pulmonary arterial hypertension who present with cardiopulmonary comorbidities[a]

Recommendations	Class[b]	Level[c]
Recommendations for initial therapy		
In patients with IPAH/HPAH/DPAH and cardiopulmonary comorbidities, initial monotherapy with a PDE5i or an ERA should be considered	**IIa**	**C**
Recommendations for treatment decisions during follow-up		
In patients with IPAH/HPAH/DPAH with cardiopulmonary comorbidities who present at intermediate or high risk of death while receiving PDE5i or ERA monotherapy, additional PAH medication may be considered on an individual basis	**IIb**	**C**

DPAH, drug-associated pulmonary arterial hypertension; ERA, endothelin receptor antagonist; HPAH, heritable pulmonary arterial hypertension; IPAH, idiopathic pulmonary arterial hypertension; PAH, pulmonary arterial hypertension; PDE5i, phosphodiesterase 5 inhibitor.

a Cardiopulmonary comorbidities are predominantly encountered in elderly patients and include risk factors for HFpEF such as obesity, diabetes, coronary heart disease, a history of hypertension, and/or a low DLCO.

Recommendation Table 15 Recommendations for pulmonary arterial hypertension associated with connective tissue disease

Recommendations	Class[a]	Level[b]
In patients with PAH associated with CTD, treatment of the underlying condition according to current guidelines is recommended[166,167,419,524]	**I**	**A**
In patients with PAH associated with CTD, the same treatment algorithm as for patients with IPAH is recommended	**I**	**C**

PAH-CTD, pulmonary arterial hypertension associated with connective tissue disease; IPAH, idiopathic pulmonary arterial hypertension.

Recommendation Table 16 Recommendations for pulmonary arterial hypertension associated with human immunodeficiency virus infection

Recommendations	Class[a]	Level[b]
In patients with PAH associated with HIV infection, antiretroviral treatment according to current guidelines is recommended[541,542]	I	A
In patients with PAH associated with HIV infection, initial monotherapy should be considered, followed by sequential combination if necessary, taking into consideration comorbidities and drug–drug interactions	IIa	C

HIV, Human immunodeficiency virus; PAH, pulmonary arterial hypertension.

Recommendation Table 17 Recommendations for pulmonary arterial hypertension associated with portal hypertension

Recommendations	Class[a]	Level[b]
Echocardiography is recommended in patients with liver disease or portal hypertension with signs or symptoms suggestive of PH, and as a screening tool in patients evaluated for liver transplantation or transjugular portosystemic shunt	I	C
It is recommended that patients with PAH associated with portal hypertension are referred to centres with expertise in managing both conditions	I	C
In patients with PAH associated with portal hypertension, initial monotherapy should be considered, followed by sequential combination if necessary, taking into consideration the underlying liver disease and indication for liver transplantation	IIa	C
Liver transplantation should be considered on an individual basis in patients with PAH associated with portal hypertension, as long as PVR is normal or near normal with PAH therapy	IIa	C
Drugs approved for PAH are not recommended for patients with portal hypertension and unclassified PH (i.e. elevated mPAP, high CO, and a normal PVR)	III	C

mPAP, mean pulmonary arterial pressure; CO, cardiac output; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; PVR, pulmonary vascular resistance.

Recommendation Table 19 Recommendations for pulmonary arterial hypertension associated with adult congenital heart disease

Recommendations	Class[a]	Level[b]
Risk assessment		
Risk assessment is recommended for patients with persistent PAH after defect closure	I	C
Risk assessment should be considered in patients with Eisenmenger syndrome	IIa	C
Treatment		
Bosentan is recommended in symptomatic patients with Eisenmenger syndrome to improve exercise capacity[574]	I	B
In patients with Eisenmenger syndrome, the use of supplemental oxygen therapy should be considered in cases where it consistently increases arterial oxygen saturation and reduces symptoms	IIa	C
Supplemental iron treatment should be considered in patients with iron deficiency	IIa	C
In patients with adult CHD, including Eisenmenger syndrome, other ERAs, PDE5is, riociguat, prostacyclin analogues, and prostacyclin receptor agonists should be considered	IIa	C
In patients with PAH after corrected adult CHD, initial oral combination therapy with drugs approved for PAH should be considered for patients at low and intermediate risk, while initial combination therapy including i.v./s.c. prostacyclin analogues should be considered for patients at high risk	IIa	C[c]
In patients with adult CHD, including Eisenmenger syndrome, sequential combination therapy should be considered if patients do not meet treatment goals	IIa	C

In the absence of significant haemoptysis, oral anticoagulant treatment may be considered in patients with Eisenmenger syndrome with pulmonary artery thrombosis	IIb	C
In women with Eisenmenger syndrome, pregnancy is not recommended	III	C
In patients with Eisenmenger syndrome, routine phlebotomy to lower elevated haematocrit is not recommended	III	C

CHD, congenital heart disease; ERA, endothelin receptor antagonist; i.v., intravenous; PAH, pulmonary arterial hypertension; PDE5i, phosphodiesterase 5 inhibitor; s.c., subcutaneous.

Level of Evidence	Definition
Level A	Data derived from multiple randomized trial or meta-analyses.
Level B	Data derived from a single randomized clinical trial or large nonrandomized studies.
Level C	Consensus option of the experts and/or small studies, retrospective studies, registries.

Class of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended, Is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	Should be considered
Class IIa	Weight of evidence/opinion is in favor of usefulness/efficacy.	
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/ effective, and in some cases may be harmful.	Is not recommended

Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guideline and Expert Panel Report (2019).

- *Updates have been made to the CHEST treatment guidelines in relation to pharmacotherapy for PAH since the 2014 edition.*
    - *For treatment naive PAH patients with WHO FC II and III, **we suggest** initial combination therapy with ambrisentan and tadalafil to improve 6MWD (weak recommendation, moderate quality evidence)*
    - *For stable or symptomatic PAH patients on background therapy with ambrisentan, we suggest the addition of tadalafil to improve 6MWD (weak recommendation, low quality evidence)*

Treatment Naive PAH Patients Without Symptoms (WHO FC I) and Patients at Increased Risk for the Development of PAH

4. For treatment-naive PAH patients with WHO FC I symptoms, we suggest continued monitoring for the development of symptoms that would signal disease progression and warrant the initiation of pharmacotherapy (Ungraded consensus-based statement).
5. We suggest that patients at increased risk for the development of PAH be monitored for the development of symptoms of PAH (Ungraded consensus-based statement).
6. We suggest also that contributing causes of PH (eg, sleep apnea and systemic hypertension) in patients with PAH be treated aggressively (Ungraded consensus-based statement).

Symptomatic Patients With PAH

Vasoreactivity Testing and Use of Calcium Channel Blockers (CCBs)

7. We suggest that patients with PAH, in the absence of contraindications, should undergo acute vasoreactivity testing using a short-acting agent at a center with experience in the performance and interpretation of vasoreactivity testing (Ungraded consensus-based statement).
8. We suggest that patients with PAH who, in the absence of right-sided heart failure or contraindications to CCB therapy, demonstrate acute vasoreactivity according to consensus definition, should be considered candidates for a trial of therapy with an oral CCB (Ungraded consensus-based statement).
9. We suggest that CCBs should not be used empirically to treat PAH in the absence of demonstrated acute vasoreactivity (Ungraded consensus-based statement).

PAH-Specific Pharmacotherapies

10. For treatment naive PAH patients with WHO FC II and III, we suggest initial combination therapy with ambrisentan and tadalafil to improve 6MWD (weak recommendation, moderate quality evidence).

Patients With WHO FC II Symptoms

For treatment-naive patients with PAH with WHO FC II symptoms who are not candidates for, or who have failed, CCB therapy, we advise that therapy be initiated with a combination of ambrisentan and tadalafil as stated in Recommendation #10. For patients who are unwilling or unable to tolerate combination therapy, we advise monotherapy with a currently approved ERA, PDE5 inhibitor, or the soluble guanylate cyclase stimulator riociguat as outlined in the 2014 guidelines. More specifically in these patients:
11. We recommend ambrisentan to improve 6MWD (strong recommendation, low quality evidence).
12-13. We suggest bosentan to delay time to clinical worsening (Ungraded Consensus-Based Statement).
14. We suggest macitentan to delay the time to clinical worsening (Ungraded Consensus-Based Statement).
15. We recommend sildenafil to improve 6MWD (strong recommendation, low quality evidence).
16. We suggest tadalafil to improve 6MWD (Ungraded Consensus-Based Statement).
17-20. We suggest riociguat to improve 6MWD (Ungraded Consensus-Based Statement), improve WHO FC (Ungraded Consensus-Based Statement), delay the time to clinical worsening (Ungraded Consensus-Based Statement).

21. We suggest that parenteral or inhaled prostanoids not be chosen as initial therapy for treatment naive PAH patients with WHO FC II symptoms or as second line agents for PAH patients with WHO FC II symptoms who have not met their treatment goals (Ungraded Consensus-Based Statement).

Patients With WHO FC III Symptoms

For treatment-naive PAH patients with WHO FC III symptoms who are not candidates for, or who have failed CCB therapy, we advise that therapy be initiated with a combination of ambrisentan and tadalafil as stated in Recommendation #10. For patients who are unwilling or unable to tolerate combination therapy, we advise monotherapy with a currently approved ERA, a PDE5I, or the soluble guanylate cyclase stimulator riociguat. More specifically in these patients:

22. We recommend the use of bosentan to improve 6MWD (strong recommendation, moderate quality evidence).
23-24. We suggest the use of bosentan to decrease hospitalizations related to PAH in the short-term (weak recommendation, low quality evidence).
25. We recommend the use of ambrisentan to improve 6MWD (strong recommendation, low quality evidence).
26-27. We suggest macitentan to improve WHO FC (Ungraded Consensus-Based Statement) and delay the time to clinical worsening (Ungraded Consensus-Based Statement).
28-30. We recommend the use of sildenafil to improve 6MWD (strong recommendation, low quality evidence), to improve WHO FC (Ungraded Consensus-Based Statement).
31-34. We suggest the use of tadalafil to improve 6MWD (Ungraded Consensus-Based Statement), to improve WHO FC (Ungraded Consensus-Based Statement), to delay time to clinical worsening (Ungraded Consensus-Based Statement).
35-38. We suggest riociguat to improve 6MWD (Ungraded Consensus-Based Statement), improve WHO FC (Ungraded Consensus-Based Statement), delay the time to clinical worsening (Ungraded Consensus-Based Statement).

For treatment naive PAH patients with WHO FC III symptoms who have evidence of rapid progression of their disease, or other markers of a poor clinical prognosis, we advise consideration of initial treatment with a parenteral prostanoid. More specifically in these patients:

39-41. We suggest continuous IV epoprostenol to improve FC (Ungraded Consensus-Based Statement), improve 6MWD (Ungraded Consensus-Based Statement).
42. We suggest continuous IV treprostinil to improve 6MWD (Ungraded Consensus-Based Statement).
43-44. We suggest continuous subcutaneous treprostinil to improve 6MWD (Ungraded Consensus-Based Statement).

For PAH patients in WHO FC III who have evidence of progression of their disease, and/or markers of poor clinical prognosis despite treatment with one or two classes of oral agents, we advise consideration of the addition of a parenteral or inhaled prostanoid. More specifically in these patients:

45-47. We suggest IV epoprostenol to improve WHO FC (Ungraded Consensus-Based Statement), improve 6MWD (Ungraded Consensus-Based Statement).
48-49. We suggest IV treprostinil to improve 6MWD (Ungraded Consensus-Based Statement).
50. In patients with PAH who remain symptomatic on stable and appropriate doses of an ERA or a PDE5I, we suggest the addition of inhaled treprostinil to improve 6MWD (weak recommendation, low quality evidence).
51-52. In patients with PAH who remain symptomatic on stable and appropriate doses of an ERA or a PDE5I, we suggest the addition of inhaled iloprost to improve WHO FC (Ungraded Consensus-Based Statement) and delay the time to clinical worsening (Ungraded Consensus-Based Statement).

Patients With WHO FC IV Symptoms

For treatment naive PAH patients in WHO FC IV, we advise initiation of therapy with a parenteral prostanoid agent. More specifically in these patients:

53-55. We suggest continuous IV epoprostenol to improve WHO FC (Ungraded Consensus-Based Statement), improve 6MWD (Ungraded Consensus-Based Statement).
56. We suggest continuous IV treprostinil to improve 6MWD (Ungraded Consensus-Based Statement).
57-58. We suggest continuous subcutaneous treprostinil to improve 6MWD (Ungraded Consensus-Based Statement).

59. For treatment naive PAH patients in WHO FC IV who are unable or do not desire to manage parenteral prostanoid therapy, we advise treatment with an inhaled prostanoid in combination with an oral PDE5I and an ERA (Ungraded Consensus-Based Statement).

PAH Patients on Established PAH-Specific Therapy

60. In patients with PAH initiating therapy with IV epoprostenol, we suggest against the routine simultaneous initiation of bosentan (Ungraded Consensus-Based Statement).

For WHO FC III or IV PAH patients with unacceptable clinical status despite established PAH specific monotherapy, we advise addition of a second class of PAH therapy to improve exercise capacity. Such patients are ideally evaluated at centers with expertise in the evaluation and treatment of patients with PAH. More specifically:

61. In patients with PAH who remain symptomatic on stable doses of an ERA or a PDE5I, we suggest the addition of inhaled iloprost to improve 6MWD (Ungraded Consensus-Based Statement).

62. In patients with PAH who remain symptomatic on stable doses of an ERA or a PDE5I, we recommend the addition of inhaled treprostinil to improve 6MWD (strong recommendation, low quality evidence).

63. In patients with PAH who remain symptomatic on stable doses of established IV epoprostenol, we suggest the addition of sildenafil or up titration of epoprostenol to improve 6MWD (Ungraded Consensus-Based Statement).

64-66. In patients with PAH who remain symptomatic on stable doses of bosentan, ambrisentan or an inhaled prostanoid, we suggest the addition of the soluble guanylate cyclase stimulator riociguat to improve 6MWD (Ungraded Consensus-Based Statement), WHO FC (Ungraded Consensus-Based Statement) and to delay the time to clinical worsening (Ungraded Consensus-Based Statement).

67-69. In patients with PAH who remain symptomatic on stable doses of a PDE5I or an inhaled prostanoid we suggest macitentan to improve 6MWD (Ungraded Consensus-Based Statement), WHO FC (Ungraded Consensus-Based Statement) and to delay the time to clinical worsening (Ungraded Consensus-Based Statement).

70. For WHO FC III or IV PAH patients with unacceptable or deteriorating clinical status despite established PAH-specific therapy with two classes of PAH pharmacotherapy, we suggest addition of a third class of PAH therapy (Ungraded Consensus-Based Statement).

Combination Studies of Endothelin Receptor Antagonists and Phosphodiesterase Inhibitors

71. For stable or symptomatic PAH patients on background therapy with ambrisentan, we suggest the addition of tadalafil to improve 6MWD (weak recommendation, low quality evidence).

Grade of Recommendation	Definition
1A	Strong recommendation, high quality evidence (benefit clearly outweighs risk or vice versa).
1B	Strong recommendation, moderate quality evidence (benefit clearly outweighs risk or vice versa).
1C	Strong recommendation, low or very low quality evidence (benefit clearly outweighs risk or vice versa).
2A	Weak recommendation, high quality evidence (benefit closely balanced with risk).
2B	Weak recommendation, moderate quality evidence (benefit closely balanced with risk).
2C	Weak recommendation, low or very low quality of evidence (uncertainty of benefits and risks).
CB	Consensus-based recommendation (uncertainty due to lack of evidence, expert opinion that benefit outweighs risk or vice versa).

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Hoeper MM, Badesch DB, Ghofrani HA, et al. Phase 3 Trial of Sotatercept for Treatment of Pulmonary Arterial Hypertension. *N Engl J Med*. 2023;388(16):1478-1490. doi:10.1056/NEJMoa2213558	A phase 3, double-blind, placebo-controlled, multicenter, parallel-group clinical trial in 323 patients with PAH (WHO Group 1 FC II or III). Subjects were randomized 1:1 to receive either of the following administered subcutaneously once every 3 weeks: • Winrevair (target dose 0.7 mg/kg) (n=163) • placebo (n=160) All the patients were receiving stable background therapy for pulmonary arterial hypertension for at least 90 days before enrollment and continued receiving background therapy throughout the trial. Background treatments consisted of monotherapy, double therapy, or triple therapy with currently available medications for pulmonary arterial hypertension.	Primary: • Change from baseline at Week 24 in 6-Minute Walk Distance (6 MWD). Secondary, tested hierarchically in the following order: • Multicomponent improvement (improvement in 6-minute walk distance [increase of ≥30 m], improvement in NT-proBNP level [decrease of ≥30%] or maintenance or achievement of an NT-proBNP level of <300 pg per milliliter, and improvement in WHO functional class [class III to II or I, or II to I] or maintenance of class II) • Change in pulmonary vascular resistance • Change in N-terminal pro–B-type natriuretic peptide level • Improvement in WHO functional class • Time to death or clinical worsening • French risk score • Changes in the Pulmonary Arterial Hypertension–Symptoms and Impact (PAH-SYMPACT) Physical Impacts, Cardiopulmonary Symptoms, and Cognitive/Emotional Impacts domain scores
Results: Primary: • In the Winrevair group, the placebo-adjusted median increase in 6 MWD was 41 meters (95% CI: 28, 54; p<0.001). Secondary:		

- The first eight secondary end points were significantly improved with sotatercept as compared with placebo, whereas the PAH-SYMPACT Cognitive/Emotional Impacts domain score was not. Notably:
    - The number of patients who met all three criteria of the multicomponent improvement end point at week 24 was 63 of 162 (38.9%) in the sotatercept group and 16 of 159 (10.1%) in the placebo group (P<0.001).
    - Treatment with Winrevair led to an improvement from baseline by at least 1 WHO FC at Week 24 in 29% of patients compared to 14% of patients treated with placebo (p<0.001).
    - Treatment with Winrevair resulted in an 84% reduction in the occurrence of death from any cause or PAH clinical worsening events compared to placebo.

Adverse Events/Safety:

- The most common adverse events of interest included bleeding events (in 35 patients [21.5%] in the sotatercept group and 20 [12.5%] in the placebo group; mostly nonserious epistaxis and gingival bleeding) and thrombocytopenia (in 10 patients [6.1%] in the sotatercept group and 4 [2.5%] in the placebo group).
- The mean platelet count decreased by 15.9×10^9 per liter in the sotatercept group and increased by 1.1×10^9 per liter in the placebo group at week 24.
- A total of 17 patients (10.4%) in the sotatercept group and 5 patients (3.1%) in the placebo group had telangiectasia, a predefined adverse event of special interest. None of these events were severe or serious.

Conclusion: The authors concluded in patients with pulmonary arterial hypertension who were receiving stable background therapy, sotatercept resulted in a greater improvement in exercise capacity (as assessed by the 6-minute walk test) than placebo.

Citation	Design	Endpoints
Chin KM, Sitbon O, Doelberg M, et al. Three- Versus Two-Drug Therapy for Patients With Newly Diagnosed Pulmonary Arterial Hypertension (TRITON). *J Am Coll Cardiol*. 2021;78(14):1393-1403. doi:10.1016/j.jacc.2021.07.057	A double-blind, randomized phase 3b trial evaluating initial triple versus initial double oral therapy in newly diagnosed, treatment-naive patients with PAH. Treatment arms included: • macitentan, tadalafil, and selexipag (n=123) vs • macitentan, tadalafil, and placebo (n=124) Inclusion criteria: • 18-75 years of age • group 1 pulmonary hypertension (including idiopathic, heritable, or drug- and toxin-induced PAH, or PAH associated with connective tissue disease, human immunodeficiency virus infection, or corrected congenital heart disease) • 6-minute walk distance (6MWD) ≥50 m and pulmonary vascular resistance (PVR) ≥6 WU Excluded: those previously treated with PAH therapy	• Primary endpoint: change in pulmonary vascular resistance (PVR) at week 26 • Secondary endpoints: change in 6-minute walk distance (6MWD), N-terminal pro-brain natriuretic peptide, and risk of disease progression (assessed at week 26)

Results: At week 26, both treatment strategies reduced PVR compared with baseline (by 54% and 52%), with no significant difference between groups (ratio of geometric means: 0.96; 95% confidence interval: 0.86-1.07; P = 0.42). Six-minute walk distance and N-terminal pro-brain natriuretic peptide improved by week 26, with no difference between groups. Risk for disease progression (to end of main observation period) was reduced with initial triple versus initial double therapy (hazard ratio: 0.59; 95% confidence interval: 0.32-1.09). Most common adverse events with initial triple therapy included headache, diarrhea, and nausea. By the end of the main observation period, 2 patients in the initial triple and 9 in the initial double therapy groups had died.

Conclusion: The authors concluded in patients with newly diagnosed PAH, both treatment strategies markedly reduced PVR by week 26, with no significant difference between groups (primary endpoint not met). Exploratory analyses suggested a possible signal for improved long-term outcomes with initial triple versus initial double oral therapy.

Citation	Design	Endpoints
Petrovič M, Locatelli I. A Bayesian Network Meta-analysis of Add-on Drug Therapies Specific for Pulmonary Arterial Hypertension. Ann Pharmacother. 2020 May;54(5):423-433. doi: 10.1177/1060028019888760. Epub 2019 Nov 18.	A Bayesian network meta-analysis (NMA) examining PAH-specific drug treatments used as add-on (sequential) therapy for treatment of PAH in patients already using another PAH-specific drug. Trials included only RCT design, patients with WHO group 1 PAH, mostly adults and follow up was 8 weeks at minimum. Articles where comparator was another PAH-specific drug, placebo, or conventional therapy were included. Patients were mostly treatment experienced. Analysis included 16 RCTs and 4,112 patients. Abbreviations: Background therapy (BT); 6-minute walk distance (6MWD); adverse events (AE); nonintravenous formulations of prostacyclin analogue (PCA); endothelin receptor antagonist (ERA); phosphodiesterase type 5 inhibitor (PDE5i);	• Efficacy outcomes: change from baseline in 6MWD, mortality • Safety outcome: discontinuation due to adverse events

Results:

6MWD: BT was most often an ERA or PDE5i. Combination therapy with ERA + tadalafil and ERA + inhaled treprostinil showed statistically significant improvements in 6MWD vs. ERA alone. ERA + tadalafil also performed better with significance vs ERA + oral treprostinil. Based on the ERA-focused NMA model for 6MWD, PAH treatments can be rank ordered as follows: ERA+tadalafil > ERA+riociguat = ERA+inhaled treprostinil > ERA+iloprost > ERA+oral treprostinil > ERA+sildenafil = ERA alone. When PDE5i was BT, PDE5i+macitentan or bosentan performed statistically significantly better. Based on this NMA model for 6MWD, PAH treatments can be rank ordered as follows: PDE5i+macitentan = PDE5i+bosentan > PDE5i+oral treprostinil > PDE5i. In the epoprostenol-focused NMA model, epoprostenol+PDE5i demonstrated statistically significant improvement of 6MWD when compared with epoprostenol. In the NMA model comparing a mixture of BTs (MIX 1) as ERA or PDE5i or ERA&PDE5i with selexipag as add-on therapy, the latter performed statistically significantly better. Similarly, the combination of PCA+riociguat demonstrated significantly greater effect size of the riociguat as add-on therapy compared with the PCA monotherapy.

All-cause mortality and discontinuation to AEs: Not statistically significant for either the mortality or the AE/discontinuation outcome.

Conclusion: Adding on tadalafil, riociguat, or inhaled treprostinil to an ERA, or macitentan or bosentan added to PDE5i improved the 6MWD. Among these, BT ERA+tadalafil and BT PDE5i+macitentan ranked as most effective. The mortality and discontinuation/AE outcomes were not significant. The authors felt their findings were consistent with guidelines on treatment of PAH in patients on established PAH-specific drug therapy.

Citation	Design	Endpoints
Kirtania L, Maiti R, Srinivasan A, Mishra A. Effect of Combination Therapy of Endothelin Receptor Antagonist and Phosphodiesterase-5 Inhibitor on Clinical Outcome and Pulmonary Haemodynamics in Patients with Pulmonary Arterial Hypertension: A Meta-Analysis. Clin Drug Investig. 2019	This was a meta-analysis aimed at evaluating the effect of combination ERA-PDE5i therapy in treatment of PAH. Studies could include RCTs or retrospective studies of Group 1 PAH only that included the relevant outcomes being examined, ages 12 and up. Experimental intervention: dual therapy for 12 weeks minimum of an ERA+PDE5i. Control/comparator intervention: monotherapy with either class of agent with or without placebo. MA included 7 relevant articles published between 2009 and 2017 (6 RCTs and 1 retrospective analysis).	• Primary: change in 6MWD • Secondary: Clinical worsening, change from baseline to trial endpoint in Pulmonary vascular resistance (PVR) and N-terminal pro-brain natriuretic peptide (NT-proBNP)

Nov;39(11):1031-1044. doi: 10.1007/s40261-019-00841-1.		

Results:

- For clinical worsening, combination therapy had a superior benefit vs monotherapy, with an odds ratio of 0.56 [95% confidence interval (CI) 0.41–0.76; p = 0.0002].
- Exercise capacity was significantly improved with combination therapy vs monotherapy, with a mean difference of 15.64 (95% CI 2.67–28.61; p = 0.02) for 6MWD.
- Change of effect on PVR was not significant between monotherapy and combination therapy, with a mean difference of − 1.66 (95% CI − 3.82 to 0.50; p = 0.13).
- Change of NT-proBNP from baseline for combination therapy vs monotherapy significantly favored combination therapy, with a mean difference of − 21.04 (95% CI − 26.87 to − 15.22; p < 0.00001).
- The meta-regression showed no statistically significant association between the dose and duration of treatment and outcomes (odds ratio of clinical worsening and mean difference of 6-minute walking distance).

Conclusion: Outcomes for 6MWD, clinical worsening, and NT-proBNP were improved with combination ERA-PDE5i combination therapy vs monotherapy. PVR was not improved with the combination therapy vs monotherapy.

Citation	Design	Endpoints
Simonneau G, Rubin LJ, Galie N, et al. Long –term sildenafil added to intravenous epoprostenol in patients with pulmonary arterial hypertension. The Journal of Heart and Lung Transplantation. Vol 33, No 7, July 2014. http://jhltonline.org.	In the PACES-1 Study (a 16-week randomized, placebo-controlled trial) of patients with PAH, adding oral sildenafil to IV epoprostenol improved 6-minute walk distance (6MWD) and hemodynamics. Therapy also delayed time to clinical worsening. Patients completing PACES-1 could receive sildenafil in an open-label extension study (PACES-2) for ≥ 3 years and additional therapy was added at discretion of investigator's clinical judgment.	• 6MWD and WHO functional class.

Results: 6MWD improved or maintained in patients at 1, 2, and 3 years in 59%, 44% and 33% of patients, respectively. 73%, 59%, and 46% of patients improved or maintained their functional class status.
Conclusion: A long-term RCT is required to definitively assess safety and efficacy. However the combination of sildenafil with IV epoprostenol seems to be generally well tolerated.

Citation	Design	Endpoints
Galiè N, Barberà JA, Frost AE, et al. Initial Use of Ambrisentan plus Tadalafil in Pulmonary Arterial Hypertension (AMBITION). N Engl J Med 2015; 373:834. DOI: 10.1056/NEJMoa1413687.	Double-blind, randomized controlled trial in which study participants were assigned in a 2:1:1 ration to receive initial combination therapy with ambrisentan 10 mg plus tadalafil 40 mg, ambrisentan 10 mg plus placebo, or tadalafil 40 mg plus placebo. Participants were required to have WHO functional class II or III symptoms of PAH and had not previously received any treatment.	• The primary end point in this trial, which was event-driven, was the first event of clinical failure defined as first occurrence of composite of death, hospitalization for worsening PAH, disease progression, or unsatisfactory long-term clinical response.

Results: A primary endpoint occurred in 18% of combination group participants, 34% of ambrisentan monotherapy group, and 28% of tadalafil monotherapy group. At week 24, the combination therapy group had statistically significant greater improvement in 6MWD. The rate of satisfactory clinical response (reduction in symptoms to, or maintenance of, WHO functional class I or II with improved exercise capacity and an absence of clinical events) was significantly higher in the combination-therapy group than in the pooled-monotherapy group but was not significantly higher in the combination-therapy group than in ambrisentan-monotherapy group.
Some adverse events occurred more frequently in the combination therapy group and included peripheral edema, headache, nasal congestion, and anemia.
Conclusion: Overall, this study demonstrated a significantly lower risk of clinical-failure events with initial combination therapy versus monotherapy.

Citation	Design	Endpoints
Sitbon O, Channick R, Chin K, et al. Selexipag for the Treatment of Pulmonary Arterial Hypertension (GRIPHON). N Engl J Med 2015;373:2522-33. DOI: 10.1056/NEJMoa1503184.	Double-blind, placebo-controlled, parallel group, event-drive study of 1,156 patients with symptomatic PAH. Majority of patients were WHO Functional Class III (53%) and II (46%). Study participants were randomized to receive placebo or selexipag. Selexipag dose was increased in 200 mcg increments to the maximum tolerated, 1600 mcg twice daily. Use of phosphodiesterase type 5 inhibitors and/or endothelin receptor antagonists was allowed during study. At initiation, most patients were being treated with an endothelin receptor antagonist, a PDE5i, or both.	• Time to first occurrence of event: death, hospitalization for PAH, PAH worsening requiring lung transplant, septostomy, initiation of parenteral prostanoid therapy or chronic oxygen therapy, or disease progression based on 15% decrease from baseline 6MWD plus worsening functional class or need for additional PAH specific treatment.
Results: The selexipag treatment group resulted in a statistically significant 40% reduction in occurrence of primary endpoint events compared to placebo treatment group. This was primarily due to reduction in hospitalization and in other disease progression events. There was no significant difference in mortality between the study groups. The observed benefit was similar regardless of the dose achieved when patients were titrated to their highest tolerated dose. **Conclusion:** Selexipag therapy showed a significantly lower risk of PAH complication or death vs placebo, with no difference in mortality.		
Citation	Design	Endpoints
Liu H, Chen X, Li J, et al. Efficacy and Safety of Pulmonary Arterial Hypertension-specific Therapy in Pulmonary Arterial Hypertension: A Meta-analysis of Randomized Controlled Trials. Chest. 2016 Aug;150(2):353-66. doi: 10.1016/j.chest.2016.03.031.	A meta-analysis (MA) examining randomized, controlled trials in the treatment of PAH evaluating any PAH-specific medications. 35 RCTs with 6,702 patients were included.	• To compare trials of PAH monotherapies vs trials of PAH combination therapies.
Results: In monotherapy vs placebo/conventional therapy, significance was obtained in mortality reduction, 6-min walk test, New York Heart Association/World Health Organization functional class, and hemodynamic status. In combination therapy vs monotherapy, significance was reached for the 6-min walk test (mean difference, 19.96 m [95% CI, 15.35 to 24.57]; P < .00001), functional class (OR, 1.65 [95% CI, 1.20 to 2.28]; P = .002), hemodynamic status, and incidence of withdrawal due to adverse effects (OR, 2.01 [95% CI, 1.54 to 2.61]; P < .00001) but not for mortality reduction (OR, 0.98 [95% CI, 0.57 to 1.68]; P = .94). **Conclusion:** PAH-specific monotherapy could improve mortality, exercise capacity, functional class, and hemodynamic status compared with placebo or conventional therapy. Exercise capacity, functional class, and hemodynamic status were further improved compared with monotherapy, but no effect was shown on mortality. Patients on combination therapy were much more likely to withdraw from therapy due to adverse events vs patients on monotherapy.		
Citation	Design	Endpoints
Duo-Ji M, Long Z. Comparative efficacy and acceptability of endothelin receptor antagonists for pulmonary arterial hypertension: A network meta-analysis. Int J Cardiol. 2017 May 1;234:90-98. DOI: 10.1016/j.ijcard.2016.12.092.	This was a network meta-analysis comparing endothelin receptor agonists ambrisentan, sitaxsentan (not available in US) bosentan, and macitentan for PAH. Ten (10) studies including 2,172 patients were analyzed.	• Efficacy outcomes compared were 6MWD and clinical worsening. Acceptability outcomes were serious adverse events and all-cause discontinuation.

Results: All of the ERA therapies significantly increased 6MWD compared to placebo (P<0.05). There was a significant decrease in the risk of clinical worsening compared to placebo with bosentan and ambrisentan. Ambrisentan was significantly less likely for all-cause discontinuation when compared to placebo. No significant differences in efficacy or acceptability was found between ERA agents. **Conclusion:** Ambrisentan in PAH treatment appears to have an advantage over other in-class agents in terms of risk of clinical worsening and tolerability.		
Citation	Design	Endpoints
Zhang H, Xiaobing L, Huang J, Hongying L, Su Z, Wang J. Comparative Efficacy and Safety of Prostacyclin Analogs for Pulmonary Arterial Hypertension. Medicine (Baltimore). 2016 Jan; 95(4): e2575. DOI: [10.1097/MD.0000000000002575].	This pairwise and network meta-analysis examined comparative efficacy and safety between agents epoprostenol, treprostinil, iloprost, and beraprost (not available in the US). Fourteen RCTs were selected including 2,511 subjects; all trials were placebo-controlled. There were no-head-to-head trials.	• Efficacy was assessed as defined by 6MWD, mortality, functional class amelioration, and patient discontinuation of the drug.
Results: Patients taking epoprostenol were anticipated to demonstrate more expedient 6-MWD than those taking placebo in both the network meta-analysis and the pairwise meta-analysis. Treprostinil had similar advantage in 6MWD over placebo in the pairwise MA, but these results were not replicated in NMA. For FC amelioration, the superiority of epoprostenol over placebo in the NMA could not be confirmed by pairwise meta-analysis. In the NMA, epoprostenol appears to result in remarkably favorable FC amelioration comparing to other regimens. **Conclusion:** The authors concluded epoprostenol to be the most favorable choice of treatment for moderate/advanced PAH patients when taking mortality, functional class amelioration, discontinuation, and 6MWH into consideration.		

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (07-01-2024 to 09-30-2024)

UTILIZATION HISTORY			COST			PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Cost/ Month^**	**Total**	**Approved (%)**	**Current**	**Recommend**
Phosphodiesterase Type 5 Inhibitors (PDE5i)									
Sildenafil (Revatio®) 20 mg tablet; 10 mg/mL oral suspension	0	0	0	$0.00	$0.00	0	0 (0%)	F- PA-SP *AL 20mg tabs (>21yrs)	No change
Sildenafil (Revatio®)10 mg/12.5 mL IV solution	0	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Liqrev® (sildenafil) 10 mg/mL oral suspension	0	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Tadalafil (Adcirca®) 20 mg tablet	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP-AL (>21yrs)	No change
Tadliq® (tadalafil) 20 mg/5 mL (4 mg/mL) oral suspension	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Endothelin Receptor Antagonists (ERAs)									
Bosentan (Tracleer®) 62.5 mg, 125 mg tablet	0	0	0	$0.00	$0.00	0	0 (0%)	F-SP-AL (>21yrs)	No change
Tracleer® (bosentan) 32 mg tablet for suspension	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Opsumit® (macitentan) 10 mg tablet	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Ambrisentan (Letairis®) 5mg, 10 mg tablet	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Prostanoids									
Treprostinil sodium (Remodulin®) 1 mg/mL, 2.5 mg/mL, 5 mg/mL, 10 mg/mL injection solution	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Ventavis® (iloprost tromethamine) 10 mcg/mL, 20 mcg/mL solution for nebulization	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Tyvaso® (treprostinil) 1.74 mg/2.9 mL solution for nebulization; inhalation starter kit; institutional starter kit, inhalation refill kit	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP-AL (>21yrs)	No change

Tyvaso® (treprostinil) DPI 16 mcg, 32 mcg, 48 mcg, 64 mcg cartridge with inhaler; 16 (112)-32 (112)-48 (28) mcg cartridge with inhaler	0	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Epoprostenol sodium (Veletri®) Flolan® (epoprostenol sodium) 0.5 mg, 1 mg vial for IV solution	0	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Orenitram® (treprostinil diolamine) 0.125 mg, 0.25 mg, 1 mg, 2.5 mg, 5 mg extended-release tablet, titration kit	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Soluble Guanylate Cyclase (sGC) Stimulators									
Adempas® (riociguat) 0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg tablet	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Non-Prostanoid IP Prostacyclin Receptor Agonists									
Uptravi® (selexipag) 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,000 mcg, 1,200 mcg, 1,400 mcg, 1,600 mcg tablet; 200-800 mcg titration pack; 1800 mcg IV solution	0	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP NF-1,800 mcg IV Sol	No change
Activin Signaling Inhibitors									
Winrevair® (sotatercept-csrk) 45 mg, 60 mg SC injection kit	0	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Combination Products									
Opsynvi® (macitentan-tadalafil) 10-20 mg, 10-40 mg tablet	0	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	**0**	**0**	**0**	**$0.00**	**$0.00**	**0**	**0 (0%)**		

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

PRIOR AUTHORIZATION CRITERIA

Recommendation: Remove timeframe of trial and failure for combination therapy for Winrevair because guidelines do not specify an appropriate t/f timeframe for combination therapy. Also, the majority of other plans do not have t/f timeframe or have 90 days at most. Winrevair has the potential to be curative, no clinical reason to have a 6-month timeframe for trial and failure.

Pulmonary Hypertension (PH) Agents	
Therapeutic Classes (AHFS)	Vasodilating agents (respiratory tract); phosphodiesterase type 5 inhibitors
Medications	**PDE-5 Inhibitors:** Formulary, prior authorization required tadalafil (Adcirca/Tadliq), sildenafil (Revatio) tablet Non-Formulary sildenafil (Revatio/Liqrev) oral suspension **Endothelin Receptor Antagonists (ERA)**: Formulary, prior authorization required ambrisentan (Letairis) tablet, bosentan (Tracleer) tablet, Tracleer (bosentan) tablet for suspension, Opsumit (macitentan) **ERA and Phosphodiesterase-5 (PDE-5) Inhibitor Combinations:** Non-Formulary Opsynvi (macitentan and tadalafil) **Prostaglandin Vasodilators**: Formulary, prior authorization required Orenitram (treprostinil diolamine), treprostinil sodium (Remodulin), Ventavis (iloprost), Tyvaso/Tyvaso DPI (treprostinil) Non-Formulary Flolan (epoprostenol), epoprostenol (Veletri) **Soluble Guanylate Cyclase (sCG) Stimulators:** Formulary, prior authorization required Adempas (riociguat) **Prostacyclin Receptor Agonists**: Formulary, prior authorization required Uptravi (selexipag) **Transforming Growth Factor-beta (TGF-beta) Signaling Modulator:** Non-Formulary Winrevair (sotatercept-csrk) **and any other newly marketed PAH 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	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be pulmonologist or cardiologist.
Coverage Duration	**Approval** Orenitram, Tyvaso, Adempas, Ventavis: 3 months for initial request Opsynvi: 4 months for initial request

Pulmonary Hypertension (PH) Agents	
	Uptravi: Request will be approved for the titration pack for 28 days until the highest tolerated dose (maintenance dose) is achieved. Once the member has achieved maintenance dosing, further refills can be approved for a 6 month duration. For all others, if all of the conditions are met, the initial request will be approved for a 6 month duration. All reauthorization requests will be approved for a 6 month duration. If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**PA CRITERIA FOR INITIAL APPROVAL:**
	• Member has a confirmed diagnosis and request is appropriate for member (e.g. functional class) as indicated in package labeling or standard of care guidelines
	• Documentation of the patient's current weight, dosing, and titration scheduled is provided (if applicable)
	• For Uptravi, Orenitram, Tyvaso/Tyvaso DPI, Ventavis, Remodulin, Adempas, ONE of the following:
	  ○ Documented trial and failure of one PDE-5 inhibitor (e.g. sildenafil, tadalafil) AND one Endothelin Receptor Antagonist [bosentan (Tracleer), ambrisentan (Letairis), or Opsumit]
	  ○ Diagnosis of WHO Group 1 FC III with evidence of rapid disease progression or FC IV (Uptravi, Orenitram, Tyvaso, Ventavis, Remodulin ONLY)
	  ○ Diagnosis of persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) WHO Group 4 after surgical treatment, or inoperable CTEPH (Adempas ONLY)
	  ○ Diagnosis of pulmonary hypertension associated with interstitial lung disease (PH-ILD) WHO Group 3 (Tyvaso ONLY)
	• If the request is for Opsumit the patient must have a documented trial and failure or intolerance to ambrisentan and bosentan, or provide a medical reason why these therapies are not appropriate
	• If the request is for sildenafil oral suspension, Liqrev (sildenafil) oral suspension, Tracleer (bosentan) tablet for suspension, or Tadliq (tadalafil) oral suspension, documentation has been submitted as to why patient is unable to use the same ingredient in a tablet dosage form (e.g. difficulty swallowing)
	• If the request is for Opsynvi, BOTH of the following:
	  ○ Patient has been stable for at least 6 months on combination therapy consisting of a PDE-5 inhibitor AND an ERA
	  ○ Documentation is provided as to why patient is unable to take individual pills for combination therapy (e.g. adherence due to pill burden)
	• If the request is for Winrevair, ALL of the following:
	  ○ Documented trial and failure of, or contraindication to~~, at least 6 months of~~ combination therapy including one PDE-5 inhibitor AND one ERA OR Opsynvi
	  ○ Documentation of platelet count of $\geq$ 50,000/mm^3
	
	PA CRITERIA FOR REAUTHORIZATION:
	• Documentation has been submitted indicating the clinical benefit of therapy (e.g. improvement in functional class, improvement in 6-minute walk test, exercise capacity, or hemodynamics).
	• Documentation of the patient's current weight, dosing, and titration schedule is provided (if applicable).

Pulmonary Hypertension (PH) Agents	
	• Request is appropriate for member (e.g. functional class) as indicated in package labeling or standard of care guidelines
Criteria Statement	Opsumit is reserved for members who have used (or cannot/should not use) bosentan (Tracleer) tablets and ambrisentan (Letairis) tablets. Sildenafil oral suspension, Liqrev (sildenafil) oral suspension, Tracleer (bosentan) tablet for suspension, or Tadliq (tadalafil) oral suspension are reserved for members who have used (or cannot/should not use) the same ingredients in an oral tablet dosage form. Opsynvi is reserved for members that have been stable on combination therapy: a phosphodiesterase 5 enzyme inhibitor (PDE-5) and an endothelin receptor antagonist (ERA) and documentation as to why the member is unable to be treated with individual pills for combination therapy. Winrevair is reserved for members who have documented trial and failure, or contraindication to ~~at least 6 months of~~ combination therapy (PDE-5 inhibitor and ERA or Opsynvi) and have platelet count of ≥ 50,000/mm^3.
Last P&T Review Date	~~9/2024~~12/2024

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PERFORMRx℠

Urinary Tract Antispasmodics
Executive Summary

CLASS OVERVIEW

Overactive bladder (OAB), which may occur with or without incontinence, and urinary incontinence (UI), are underdiagnosed and undertreated and can significantly impact quality of life. Urinary incontinence, in particular, is associated with increased rates of depression and altered activities of daily living as a coping mechanism. Urinary tract antispasmodics are used in the treatment of OAB and urge urinary incontinence (UUI) in both men and women, adults and children. Antispasmodic agents can be categorized by mechanism of action into two types: antimuscarinics and β-3 agonists. Antimuscarinics act by antagonizing the effects of acetylcholine on muscarinic receptors reducing smooth muscle tone, increasing bladder capacity and decreasing detrusor overactivity. Antimuscarinics include oxybutynin (Oxytrol®, Gelnique®), darifenacin, fesoterodine (Toviaz®), solifenacin (Vesicare®), tolterodine (Detrol®/Detrol® LA), trospium and flavoxate. The marketed β-3 agonists Gemtesa® (vibegron) and mirabegron (Myrbetriq®) act by activating β-3 adrenergic receptors in the bladder thereby relaxing the detrusor smooth muscle and increasing bladder capacity. Due to anticholinergic properties, antimuscarinics tend to have more side effects compared to β-3 agonists; this is a factor to be considered when selecting an appropriate therapeutic agent.

Various United States guidelines are available for the treatment of OAB/urge incontinence, most directed toward the treatment in women. Notably, the American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) published updated guidelines pertaining to treatment of idiopathic OAB in 2024. This guideline eliminated the concept of "step therapy," and instead emphasized the importance of shared decision-making to select the best therapy or therapies, regardless of invasiveness, based on the patient's needs, desires, and side effect tolerance. The American College of Physicians (ACP) published Nonsurgical Management of Urinary Incontinence in Women: A Clinical Practice Guideline from the American College of Physicians in 2014. Annals of Internal Medicine International guidelines pertaining to the treatment of UI, pelvic organ prolapse (POP), and fecal incontinence were published by the Sixth International Consultation on Incontinence Recommendations of the International Scientific Committee in 2018 and put forth recommendations for both non-neurogenic and neurogenic UI. Specific guideline recommendations are presented later in this review.

UTILIZATION FINDINGS

There were 50 claims for 28 members, for a total cost of $2,957.84 and an average cost per claim of $59.16. The most highly utilized medication was Oxybutynin ER tablet, with 18 claims, followed by Tolterodine tablet and Solifenacin tablet with 8 claims each. There was 1 prior authorization with 1 approval (50%).

RECOMMENDATIONS

- No changes

CLINICAL SUMMARY

OAB, which may occur with or without incontinence, and UI, are underdiagnosed and undertreated and can significantly impact quality of life. A clinical diagnosis of OAB, as defined by the International Continence Society, includes "urinary urgency, usually accompanied by frequency and nocturia, with or without urinary incontinence, in the absence of urinary tract infection or other obvious pathology. Because diagnosis of OAB is based on symptom assessment, the quality of life impact of OAB is a critical component in seeking treatment. Urinary incontinence, in particular, is associated with increased rates of depression and altered activities of daily living as a coping mechanism. In population-based studies, the prevalence of OAB ranges from 7% to 27% in men and 9% to 43% in women, with symptoms of OAB worsening with age. UUI is consistently more common in women than men. Risk factors for OAB include age over 40 years, current smoking, obesity, diabetes, and prior vaginal delivery.

Urinary tract antispasmodics are used in the treatment of OAB and urinary urge incontinence in both men and women, adults and children. Antispasmodic agents can be categorized by mechanism of action into two types: antimuscarinics and β-3 agonists. Antimuscarinics act by antagonizing the effects of acetylcholine on muscarinic receptors reducing smooth muscle tone, increasing bladder capacity and decreasing detrusor overactivity. Antimuscarinics include oxybutynin (Oxytrol®, Gelnique®), darifenacin, fesoterodine (Toviaz®), solifenacin (Vesicare®), tolterodine (Detrol®/Detrol® LA), trospium and flavoxate. The marketed β-3 agonists Gemtesa® (vibegron) and mirabegron (Myrbetriq®) act by activating β-3 adrenergic receptors in the bladder thereby relaxing the detrusor smooth muscle and increasing bladder capacity. Due to anticholinergic properties, antimuscarinics tend to have more side effects compared to β-3 agonists; this is a factor to be considered when selecting an appropriate therapeutic agent. There are no drugs to treat OAB or UI in the pipeline and slated for approval in the coming year.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Oxybutynin (Gelnique®, Oxytrol®)	OAB with symptoms of urinary urge incontinence, urgency, frequency, urinary leakage, dysuria	Oral: – Immediate release (IR): 5 mg 2 to 3 times daily, adjust dose as needed in 5 mg increments every 2 weeks; max dose: 5 mg 4 times daily – Extended release (ER): 5 to 10 mg once daily, adjust dose as needed in 5 mg increments at weekly intervals; max dose: 30 mg once daily Topical gel: 1 sachet (100 mg/g) once daily Transdermal (TDS): One patch (3.9 mg) twice weekly (every 3 to 4 days); change on the same 2 days each week OTC labeling (*Oxytrol*® only): One patch (3.9 mg) every 4 days
	OAB symptoms due to a neurological condition (e.g., spina bifida) in patients ≥ 6 years (*ER tablets* only)	
Fesoterodine (Toviaz®)	OAB with symptoms of urinary urge incontinence, urgency, or frequency	4 mg orally once daily; may increase to max dose of 8 mg once daily based on response/tolerability
	Neurogenic detrusor overactivity (NDO) in pediatric patients ≥ 6 years of age and weighing > 25 kg	– Patients > 25 kg to ≤ 35 kg: 4 mg orally once daily; may increase to 8 mg once daily based on response/tolerability – Patients > 35 kg: 4 mg orally once daily; after 1 week increase to 8 mg once daily; max dose: 8 mg/day
Tolterodine (Detrol®, Detrol® LA)	OAB with symptoms of urinary urge incontinence, urgency, or frequency	IR: 1 mg orally twice daily; may increase to 2 mg twice daily after 2 to 6 weeks based on response and tolerability ER: 2 mg orally once daily; may increase to 4 mg once daily after 2 to 6 weeks based on response and tolerability
Darifenacin		7.5 mg orally once daily, may be increased to 15 mg once daily after a minimum of 2 weeks
Trospium		IR: 20 mg orally twice daily ER: 60 mg orally once daily in the morning
Flavoxate	Symptomatic relief of dysuria, nocturia, suprapubic pain, urgency, frequency, and incontinence in patients with cystitis, urethritis, urethrocystitis, urethrotrigonitis, and prostatitis	100 to 200 mg orally 3 to 4 times daily; reduce the dose when symptoms improve
Solifenacin (Vesicare®, Vesicare LS™)	OAB with symptoms of urinary urge incontinence, urgency, or frequency (*Vesicare*® only)	5 mg orally once daily, may increase to 10 mg once daily
	NDO in pediatric patients ≥ 2 years of age (*Vesicare LS*™ only)	– 9 to 15 kg: 2 mg orally once daily, may titrate every 3 weeks to lowest effective dose; max dose: 4 mg/day – 15 kg to 30 kg: 3 mg orally once daily, may titrate every 3 weeks to lowest effective dose; max dose: 5 mg/day

Medication	Indications	Dosing/Administration
		– 30 kg to 45 kg: 3 mg orally once daily, may titrate every 3 weeks to lowest effective dose; max dose: 6 mg/day – 45 kg to 60 kg: 4 mg orally once daily, may titrate every 3 weeks to lowest effective dose; max dose: 8 mg/day – > 60 kg: 5 mg orally once daily, may titrate every 3 weeks to lowest effective dose; max dose: 10 mg/day
Myrbetriq® (mirabegron)	OAB in adults with symptoms of UI, urgency, or frequency, as monotherapy or in combination with an antimuscarinic agent *(tablets* only)	25 mg orally once daily, may increase to 50 mg once daily after 4 to 8 weeks based on response/tolerability
	NDO in pediatric patients ≥ 3 years of age	Tablets (≥35 kg only): 25 mg orally once daily; after 4 to 8 weeks, the dose may be increased to 50 mg orally once daily Granules: 3 ml (24 mg) to 6 ml (48 mg) orally once daily depending on patient weight; after 4 to 8 weeks, the dose may be increased if needed up to a max dose of 10 ml (80 mg) once daily
Gemtesa® (vibegron)	OAB in adults with symptoms of urge UI, urgency, and frequency	75 mg orally once daily

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BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Oxybutynin (Gelnique®, Oxytrol®)	None	Hypersensitivity to oxybutynin or any component of the formulation; patients with or at risk for uncontrolled narrow-angle glaucoma, urinary retention, gastric retention, or conditions with severely decreased GI motility OTC labeling (*Oxytrol®* only): Do not use in the following settings – if experiencing symptoms of urinary tract infection (UTI) such as dysuria, fever or chills, hematuria, unexplained lower back or side pain, pyuria, or foul-smelling urine – in male patients – < 18 years of age – stress incontinence – urinary, gastric retention – glaucoma – hypersensitivity to oxybutynin
Fesoterodine (Toviaz®) Tolterodine (Detrol®, Detrol® LA) Darifenacin Trospium Solifenacin (Vesicare®, Vesicare LS™)		Hypersensitivity to the active ingredient or any component of the formulation; patients with or at risk for uncontrolled narrow-angle glaucoma, urinary retention, or gastric retention *Tolterodine and fesoterodine* only*:* Hypersensitivity to either drug (both are metabolized to 5-hydroxymethyl tolterodine [HMT]) *Trospium ER* only: severe renal impairment (CrCl < 30 mL/min)
Flavoxate		Pyloric or duodenal obstruction; gastrointestinal hemorrhage; obstructive intestinal lesions; ileus; achalasia; obstructive uropathies of lower urinary tract (e.g., benign prostatic hypertrophy [BPH])
Myrbetriq® (mirabegron)		Hypersensitivity to the active ingredient or any component of the formulation
Gemtesa® (vibegron)		

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WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Oxybutynin (Gelnique®, Oxytrol®) Fesoterodine (Toviaz®) Tolterodine (Detrol®, Detrol® LA) Darifenacin Trospium Solifenacin (Vesicare®, Vesicare LS™)	Concerns related to adverse effects: – Angioedema: Of the face, lips, tongue, and/or larynx has been reported – CNS effects: Anticholinergic effects may impair physical or mental abilities – Heat prostration: May occur in the presence of increased environmental temperature – QT prolongation: Caution in patients with a history of QT prolongation or those receiving QT interval prolonging medications (*tolterodine* and *solifenacin* only); prolongation may be more likely in CYP2D6 poor metabolizers or in the presence of inhibitors of CYP2D6 and CYP3A4 (*tolterodine* only) Disease-related concerns: – Alzheimer disease (AD): Anticholinergics may adversely affect the clinical course of AD in patients receiving cholinesterase inhibitors – Bladder outlet obstruction (BOO): Increased risk of urinary retention in patients with BOO – GI obstructive disorders: Increased risk of gastric retention in patients with decreased GI motility or gastrointestinal obstructive disorders – Glaucoma: May exacerbate angle-closure glaucoma – Myasthenia gravis: May exacerbate condition – *Oxybutynin* only ○ Hiatal hernia: Use with caution ○ Hyperthyroidism: May exacerbate hyperthyroidism ○ Parkinson disease: May aggravate symptoms ○ Caution due to limited experience in hepatic/renal impairment – *Tolterodine* only: Dose adjustment required in hepatic/renal impairment – *Fesoterodine* only: Not recommended in severe hepatic impairment; dose adjust in severe renal impairment (CrCl <30 mL/min) – *Darifenacin* only: Dose adjust in moderate hepatic impairment, not recommended in severe hepatic impairment – *Trospium* only: Caution in moderate or severe hepatic impairment; dose adjust IR formulation in renal impairment – *Solifenacin* only: Dose adjust in moderate hepatic impairment, not recommended in severe hepatic impairment; dose adjust in severe (CrCl <30 mL/minute) renal impairment Concurrent drug therapy issues: – Drug-drug interactions: ○ *Tolterodine* only: Lower dose when used concomitantly with CYP3A4 inhibitors ○ *Trospium* only: Use caution with other medications that are eliminated by active tubular secretion Dosage form specific issues: – *Oxybutynin* only ○ ER formulation: Drug is contained within a nondeformable matrix, the use of which has been rarely associated with obstruction in patients with stricture/narrowing of the GI tract ○ Topical gel: Cover the treated area with clothing after gel has dried to prevent unintended exposure; skin irritation may occur; contains ethanol, do not expose to open flame or smoking until dry ○ TD patch: May contain conducting metal (e.g., aluminum), remove prior to MRI – *Trospium* only ○ ER formulation: Ethanol should not be ingested within 2 hours of the administration of the ER formulation; may increase incidence of drowsiness – *Solifenacin* only ○ Propylene glycol: Some dosage forms may contain propylene glycol; use caution as large amounts are potentially toxic

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Medication	Warnings/Precautions
Flavoxate	Concerns related to adverse effects: – CNS effects: Anticholinergic effects may impair physical or mental abilities Disease-related concerns: – Glaucoma: Use with caution Concurrent drug therapy issues: – Sedatives: Use with other sedative drugs or ethanol may potentiate CNS effects
Myrbetriq® (mirabegron)	Concerns related to adverse effects: – Angioedema: Of the face, lips, tongue, and/or larynx has been reported Disease-related concerns: – Hepatic impairment: Use with caution in mild to moderate hepatic impairment; dose adjust in moderate hepatic impairment; use is not recommended in severe hepatic impairment – Hypertension (HTN): Use with caution in patients with controlled and less severe HTN; use is not recommended in patients with uncontrolled HTN – Renal impairment: Use with caution; dose adjust in patients with severe renal impairment; use is not recommended in end-stage renal disease (ESRD) (eGFR < 15 mL/min/1.73 m^2 with or without hemodialysis) Dosage form specific issues: – Product interchangeability: ER granules and ER tablets are not interchangeable; products should not be combined to achieve a total dose; select appropriate product based on patient's indication and weight; granules are not approved for adult use
Gemtesa® (vibegron)	Disease-related concerns: – BOO: Increased risk of urinary retention in patients with BOO and in patients using concomitant muscarinic antagonists – Hepatic impairment: Not recommended in severe hepatic impairment – Renal impairment: Not recommended for use in patients with ESRD (eGFR < 15 mL/min/1.73 m^2 with or without hemodialysis)

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PRACTICE GUIDELINES

Cameron AP, Chung DE, Dielubanza EJ, et al. The AUA/SUFU Guideline on the Diagnosis and Treatment of Idiopathic Overactive Bladder. J Urol. 2024;212(1):11-20.

None-Invasive Therapies:

- Clinicians should discuss incontinence management strategies (e.g., pads, diapering, barrier creams) with all patients who have urgency urinary incontinence. (Expert Opinion)
- Clinicians should offer bladder training to all patients with OAB (Strong Recommendation; Evidence Level: Grade A)
- Clinicians should offer behavioral therapies to all patients with OAB. (Clinical Principle)
- Clinicians may offer select non-invasive therapies to all patients with OAB. (Clinical Principle)
- In patients with OAB whose symptoms do not adequately respond to monotherapy, clinicians may combine one or more of the following: behavioral therapy, non-invasive therapy, pharmacotherapy, and/or minimally invasive therapies. (Expert Opinion)

Pharmacotherapy

- Clinicians should offer antimuscarinic medications or beta-3 agonists to patients with OAB to improve urinary urgency, frequency, and/or urgency urinary incontinence. (Strong Recommendation; Evidence Level: Grade A).
- Clinicians should counsel patients with OAB on the side effects of all oral medication options; treatment should be chosen based on side effect profiles and in the context of shared decision-making. (Clinical Principle)
- Clinicians should discuss the potential risk for developing dementia and cognitive impairment with patients with OAB who are taking, or who are prescribed, antimuscarinic medications. (Clinical Principle)
- Clinicians should use antimuscarinic medications with extreme caution in patients with OAB who have narrow-angle glaucoma, impaired gastric emptying, or a history of urinary retention. (Clinical Principle).
- Clinicians should assess patients with OAB who have initiated pharmacotherapy for efficacy and for onset of treatment side effects. (Expert Opinion)
- In patients with OAB who experience intolerable side effects or who do not achieve adequate improvement with an OAB medication, clinicians may offer a different medication in the same class or a different class of medication to obtain greater tolerability and/or efficacy. (Clinical Principle).
- In patients with OAB who do not achieve adequate improvement with a single OAB medication, clinicians may offer combination therapy with a medication from a different class. (Conditional Recommendation; Evidence Level: Grade B)

Minimally Invasive Therapies

- Clinicians may offer minimally invasive procedures to patients with OAB who are unable or unwilling to undergo behavioral, non-invasive, or pharmacologic therapies. (Clinical Principle)
- Clinicians may offer patients with OAB, in the context of shared decision-making, minimally invasive therapies without requiring trials of behavioral, non-invasive, or pharmacologic management. (Expert Opinion)
- In patients with OAB who have an inadequate response to, or have experienced intolerable side effects from, pharmacotherapy or behavioral therapy, clinicians should offer sacral neuromodulation, tibial nerve stimulation, and/or intradetrusor botulinum toxin injection. (Moderate Recommendation; Evidence Level: Grade A)

Recommendation Definitions

Recommendation Type	Definition
Strong	Benefits are greater than risks/burdens (or vice versa). Net benefit (or net harm) is substantial.
Moderate	Benefits are greater than risks/burdens (or vice versa). Net benefit (or net harm) is moderate.
Conditional	Balance between benefits and risks/burdens are unclear. Best action depends on individual patient circumstances.
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.

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Recommendation Type	Definition
Expert Opinion	A statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there is no evidence.

Evidence Level	Definition
Grade A	Well-conducted randomized controlled trials (RCT) or exceptionally strong observational studies.
Grade B	RCTs with some weaknesses of procedure or generalizability or generally strong observational studies.
Grade C	Observational studies that are inconsistent, have small sample sizes or have other problems that potentially confound interpretation of data.

Abrams P, Andersson KE, Apostolidis A, et al. Sixth International Consultation on Incontinence Recommendations of the International Scientific Committee: Evaluation and treatment of urinary incontinence, pelvic organ prolapse, and fecal incontinence. Neurourol Urodyn. 2018 Sep;37(7):2271-2272.

Children

Initial management

- Initial treatment for mono-symptomatic nocturnal enuresis should include:
  - Parental and child counseling and motivation
  - Review of bladder diary with attention to night-time polyuria
  - Age-appropriate education and demystification or explanation
- A choice between either bed wetting alarm (Grade A) or anti-diuretic hormone analogues of desmopressin (Grade A). It may be a parental and child choice if advantages and disadvantages are well explained.
- Daytime incontinence should be managed holistically including:
  - Counselling, timed voiding, behavior modification and bowel management when necessary (Grade B)
  - Antimuscarinics may be used if the child has OAB symptoms (Grade A)

Specialized management

- The treatment of incontinence associated with urinary tract anomalies is complex and cannot easily be dealt with in an algorithm. In many children more than one pathology demands treatment. If there are complex congenital abnormalities present, the treatment is mostly surgical and it should be individualized according to the type and severity of the problem.
- Initial treatment should be non-surgical:
  - For stress urinary incontinence (SUI): Pelvic floor muscle training (Grade C)
  - For OAB symptoms: Fluid/voiding regimens and antimuscarinics (Grade A)
  - For voiding dysfunction: Timed voiding, voiding re-education, pelvic floor muscle relaxation (+/- biofeedback), α-blocker therapy, and intermittent catheterization (when post-void residual [PVR] >30% of bladder capacity) (Grade A/B)
  - For bowel dysfunction: High fiber diet and laxatives as appropriate, and transanal irrigation in severe cases (Grade A)

Men

Initial management

- For men with stress, urgency or mixed urgency/stress incontinence, initial treatment should include appropriate lifestyle advice, pelvic floor muscle training, scheduled voiding regimes, behavioral therapies and medication. In particular:
  - Antimuscarinic/β3-adrenoceptor agonists drugs for OAB symptoms with or without urgency incontinence (Grade B) if the patient has no evidence of significant post-void residual urine
  - α-blockers can be added if itis thought that there may also be BOO (Grade C)

Specialized management

- When basic management has been unsuccessful and if the patient's incontinence markedly disrupts his quality of life, then invasive therapies should be considered:
  - For sphincter incompetence the recommended option is the artificial urinary sphincter (Grade B). Other options, such as a male sling, may be considered (Grade C)

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- For refractory idiopathic detrusor overactivity, (with intractable OAB symptoms) the recommended therapies are: Botulinum toxin A (Grade B), and SNS (Grade C)
- If incontinence is associated with BOO, then consideration should be given to surgical treatment to relieve obstruction (Grade B). α-blockers and/or 5α-reductase inhibitors would be an optional treatment (Grade C)
- There is increased evidence for the safety of antimuscarinics for OAB symptoms in men, chiefly in combination with an α-blocker (Grade B)

Women

Initial management

- For women with stress, urgency or mixed urinary incontinence, initial treatment should include appropriate lifestyle advice, pelvic floor muscle training (PFMT), scheduled voiding regimes, behavioral therapies and medication. In particular:
  - If estrogen deficiency and/or UTI is found, the patient should be treated at initial assessment and then reassessed after using vaginal estrogens for a suitable period (Grade B)
  - Antimuscarinics/β3-adrenoceptor agonists for OAB symptoms with or without urgency incontinence (Grade A); duloxetine* may be considered for SUI (Grade B)

Specialized management

- Antimuscarinics/β3-adrenoceptor agonists for OAB symptoms with or without urgency incontinence (Grade A); duloxetine* may be considered for SUI (Grade B)
- Refractory urgency incontinence (OAB) secondary to idiopathic detrusor overactivity may be treated by botulinum toxin A (Grade A), sacral nerve stimulation (Grade B) or bladder augmentation/intestinal cystoplasty (Grade D)

Neurogenic Urinary Incontinence

Initial management

- Initial treatment for patients with incontinence due to suprapontine pathology, like stroke, need to be assessed for degree of mobility and ability to cooperate. Initial recommended treatments are behavioral therapy (Grade C) and anti-muscarinic drugs for presumed detrusor overactivity (Grade A). If incontinence persists and if operative procedures are not indicated, then continence products (Grade B) or catheters (Grade C) may be necessary on a long-term basis. These can also be necessary in non-cooperative or less mobile patients.
- Pharmacological detrusor relaxation and/or antibiotics may be useful in cases of persistent bypass leakage and/or recurrent UTI (patients with continuous drainage)

Specialized management

- Antimuscarinics (Grade A)
- α-1 blockers (Grade C)
- Oral cannabinoid agonists (multiple sclerosis) (Grade C)
- β3-adrenoceptor agonist alone or as an add-on to antimuscarinic (Grade D)

Frail Older Men and Women

Initial management

- For the select cognitively intact older person with UI or fecal incontinence, pelvic floor muscle therapy can be considered, but there are few studies (Grade C). Antimuscarinics may be added to conservative therapy of UUI (Grade A-C, depending on agent)
- α-blockers may be cautiously considered in frail men with suspected prostatic obstruction (Grade C). All drugs should be started at the lowest dose and titrated with regular review until either care goals are met or adverse effects are intolerable

**Duloxetine is not approved for use in United States. In Europe it is approved for use in severe stress incontinence (see committee report on pharmacological management for information regarding efficacy, adverse events (AEs), and 'black box' warning by the Food and Drug Administration of the United States).*

Recommendation Definitions

Evidence Grade	Definition
Grade A	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect
Grade B	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Grade C	Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
Grade D	Any estimate of effect is very uncertain.

Qaseem A, Dallas P, Forciea MA, et al. Nonsurgical Management of Urinary Incontinence in Women: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med. 2014 Sep 16;161(6):429-40.

- ACP recommends first-line treatment with pelvic floor muscle training in women with SUI (Grade: Strong recommendation, high-quality evidence)
- ACP recommends bladder training in women with UUI (Grade: Strong recommendation, moderate-quality evidence)
- ACP recommends pelvic floor muscle training with bladder training in women with mixed UI (Grade: Strong recommendation, moderate-quality evidence)
- ACP recommends against treatment with systemic pharmacologic therapy for stress UI (Grade: Strong recommendation, low-quality evidence)
- ACP recommends pharmacologic treatment in women with UUI if bladder training was unsuccessful. Clinicians should base the choice of pharmacologic agents on tolerability, adverse effect profile, ease of use, and cost of medication (Grade: Strong recommendation, high-quality evidence)
- ACP recommends weight loss and exercise for obese women with UI (Grade: Strong recommendation, moderate-quality evidence)

Recommendation Definitions

Strength of Recommendation	Definition
Strong	Benefits clearly outweigh risks and burden OR risks and burden clearly outweigh benefits.
Weak	Benefits finely balanced with risks and burden.

Evidence Grade	Definition
High	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low	Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
Insufficient	Evidence either is unavailable or does not permit a conclusion.

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CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Maman K, Aballea S, Nazir J, et al. Comparative efficacy and safety of medical treatments for the management of overactive bladder: a systematic literature review and mixed treatment comparison. Eur Urol. 2014 Apr;65(4):755-65. doi: 10.1016/j.eururo.2013.11.010.	Systematic review (as per Centre for Reviews and Dissemination [CRD] and Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines) and Bayesian mixed treatment comparison to evaluate the relative safety and efficacy of OAB medications N=44 RCTs; 27,309 participants	Efficacy: micturition frequency, incontinence episodes, UUI (all per 24 hours) Safety: incidence of dry mouth, constipation, blurred vision

Results:

Efficacy:

- Micturition frequency: Mirabegron was found to be as effective as antimuscarinics except solifenacin 10 mg which was found to be more effective (mean difference vs mirabegron 50 mg of −0.584 [95% CrI*, −0.837 to −0.332]).
- Incontinence: Mirabegron was found to be as effective as antimuscarinics; solifenacin (5 mg and 10 mg) were 97% more probable to be effective compared to mirabegron.
- UUI: Mirabegron was found to be as effective as antimuscarinics; solifenacin 10 mg was significantly more efficacious compared to mirabegron (mean difference vs mirabegron 50 mg of −0.422 urgency incontinence episodes per day [95% CrI, −0.786 to −0.060]).

Safety: Antimuscarinics were associated with higher rates of dry mouth and constipation compared to mirabegron and solifenacin had a significantly higher risk of constipation compared to mirabegron with OR ranging from 1.914 (95% CrI, 1.135–3.032) to 7.603 (95% CrI, 2.076–22.660).

Conclusion: The authors concluded that mirabegron had similar efficacy compared to most antimuscarinics and lower rates of dry mouth. A significant strength of this study is that it met the CRD Database of Abstracts of Reviews of Effects (DARE) scientific quality criteria for systematic reviews. This adds to the credibility and reliability of the results and conclusions.

**CrI – Credibility interval*

Citation	Design	Endpoints
Nalliah S, Wg P, Masten Singh PK, Naidu P, Lim V, Ahamed AA. Comparison of efficacy and tolerability of pharmacological treatment for the overactive bladder in women: A network meta-analysis. Aust Fam Physician. 2017 Mar;46(3):139-144.	Systematic review and network meta-analysis (NMA) of RCTs and prospective cohort studies of "commonly prescribed pharmacological agents" for the treatment of OAB sourced from PubMed and Cochrane between July 31, 2000 and July 31, 2015. N=5 studies; 5356 participants	Efficacy: Relative efficacy as measured by OR Safety: Number of AEs (e.g., dry mouth, dry eyes, blurred vision and constipation)

Results:

Efficacy: Solifenacin 10 mg was the most effective followed by oxybutynin 3 mg TDS > solifenacin 5 mg QD > darifenacin 15 mg QD > fesoterodine 8 mg QD > darifenacin 7.5 mg QD > tolterodine 4 mg QD.

Safety: Darifenacin 7.5 mg QD had the fewest AEs, whereas solifenacin 10 mg QD caused the most AEs when compared with every other intervention except oxybutynin 3 mg TDS.

Conclusion: The authors concluded that, considering effectiveness, adverse effects, and cost, solifenacin 5 mg is the drug of choice. This study included relatively few RCTs, and it did not include an assessment of the relative effectiveness or safety of the β3 agonist mirabegron. It was conducted in Australia; it is possible mirabegron was not available in Australia during the search timeframe.

Citation	Design	Endpoints
Kelleher C, Hakimi Z, Zur R, et al. Efficacy and Tolerability of Mirabegron Compared with Antimuscarinic Monotherapy or Combination Therapies for Overactive Bladder: A Systematic Review and Network Meta-analysis. Eur Urol. 2018 Sep;74(3):324-333. doi: 10.1016/j.eururo.2018.03.020. Epub 2018 Apr 23.	A systematic review and NMA of RCTs from 2000 to 2017 assessing mirabegron and antimuscarinics monotherapies and combination therapies for OAB N=64 studies; 46,666 participants	Efficacy: Mean change from baseline for micturition frequency, UUI episodes, and incontinence episodes (all per 24 hours) Safety: Dry mouth, constipation, blurred vision, HTN, urinary retention, UTI, tachycardia, withdrawal for any reason, and withdrawal due to lack of efficacy

Results:

Efficacy:

- Micturition frequency: Efficacy of mirabegron 50 mg did not differ significantly from the other active treatments, except for solifenacin 10 mg monotherapy and solifenacin 5 mg + mirabegron 50 mg (combination), both of which were more efficacious than mirabegron 50 mg (mean change: –0.37 [95% CrI: –0.62, –0.13] and –0.59 [95% CrI: –0.87, –0.30], respectively)
- UUI episodes: Efficacy of mirabegron 50 mg did not differ significantly from the other active treatments, except for solifenacin 5 mg + mirabegron 25 or 50 mg (combinations) and fesoterodine 8 mg, all of which were more efficacious than mirabegron 50 mg monotherapy
- Incontinence episodes: Mirabegron was significantly more efficacious than placebo; no significant differences were observed versus other comparators except for solifenacin 5 and 10 mg monotherapy and solifenacin/mirabegron combinations (all of which were more efficacious than mirabegron)

Safety:

- Dry mouth: The risk with mirabegron 50 mg was similar to that with placebo (OR: 0.82 [95% CrI: 0.65, 1.03]) and significantly lower compared with all other active treatments except for oxybutynin IR 5 mg (OR: 2.99 [95% CrI: 0.68, 13.75])
- Constipation: The risk was significantly lower for mirabegron 50 mg compared with nine active treatments (darifenacin 7.5 and 15 mg, fesoterodine 8 mg, propiverine 20 mg, solifenacin 5 mg + mirabegron 25 or 50 mg, solifenacin 5 and 10 mg, and trospium 60 mg)
- HTN: The risk for mirabegron 50 mg was similar to that for placebo (OR: 0.97 [95% CrI: 0.76, 1.25]) and all other treatments
- Urinary retention: Mirabegron 50 mg had a significantly lower frequency of urinary retention compared with seven active treatments (fesoterodine 4 and 8 mg, oxybutynin IR 9 mg, solifenacin 10 mg, solifenacin 5 mg combined with mirabegron 25 or 50 mg, and trospium 60 mg). No significant differences were seen versus mirabegron 50 mg for the remaining four comparators (placebo, propiverine 20 mg, solifenacin 5 mg, and tolterodine ER 4 mg)
- Blurred vision, UTI, Tachycardia: There were no significant differences
- Withdrawal for any reason: Mirabegron was significantly better tolerated compared with oxybutynin IR (OR: 2.14 [95% CrI: 1.36, 3.37])
- Withdrawal due to lack of efficacy: Mirabegron was significantly better tolerated compared with placebo (OR: 1.95 [95% CrI: 1.21, 3.24])

Conclusion: The authors concluded that "relief of key OAB symptoms produced by mirabegron 50 mg is significantly better than placebo, and similar to a range of common antimuscarinics, with the benefit of significantly fewer bothersome anticholinergic side effects such as dry mouth." Additionally, combination treatment of solifenacin + mirabegron was found to improve efficacy although with additional anticholinergic side effects.

Citation	Design	Endpoints
Lozano-Ortega G, Walker DR, Johnston K, et al. Comparative safety and efficacy of treatments for overactive bladder among older adults: a network meta-analysis. Drugs Aging. 2020;37(11):801-816.	Systematic review and NMA of RCTs among older adults with OAB that reported the safety and efficacy outcomes associated with the use of mirabegron and/or antimuscarinics sourced from PubMed and Cochrane between January 1, 2000 and August 21, 2018. N=21 studies	Efficacy: Incontinence episodes per 24 hours, UUI episodes per 24 hours, micturitions per 24 hours, volume voided per micturition, and urgency episodes per 24 hours

		Safety: Urinary retention, dry mouth, constipation, overall treatment-emergent AEs, and AE-related treatment discontinuations

Results:

Efficacy:

- A similar treatment effect was observed across all efficacy endpoints between mirabegron and antimuscarinics.

Safety:

- Mirabegron was not associated with an increased odds of dry mouth (OR: 0.76 [95% CrI: 0.26, 2.37]) or constipation (OR: 1.08 [95% CrI: 0.39, 3.02]) relative to placebo, whereas antimuscarinics were strongly associated with these events (OR range: 3.78 to 7.85 and 2.12 to 4.66, respectively)
- Mirabegron was associated with similar odds of experiencing AE-related treatment discontinuations relative to placebo (OR: 0.99 [95% CrI: 0.57, 1.70]), while the odds of experiencing an AE-related treatment discontinuation for antimuscarinics had a range of 1.14–3.03 (in most cases, the association was mild)
- No increased odds of experiencing overall treatment-emergent AEs was observed for mirabegron or antimuscarinics (OR range: 1.25 to 1.55), apart from fesoterodine (OR: 2.23 [95% CrI: 1.37, 3.37])

Conclusion: The authors concluded that the safety and efficacy profile of mirabegron remains favorable compared with antimuscarinics among older adults. This includes safety outcomes typically associated with anticholinergic burden, which were less frequently observed in patients treated with mirabegron.

Citation	Design	Endpoints
Su S, Liang L, Lin J, Liu L, Chen Z, Gao Y. Systematic review and meta-analysis of the efficacy and safety of vibegron vs antimuscarinic monotherapy for overactive bladder. Medicine (Baltimore). 2021;100(5):e23171.	Systematic review and NMA of RCTs of vibegron vs. antimuscarinic monotherapy for OAB sourced from PubMed and Cochrane to March 2020. N=3 studies; 1751 participants	Efficacy: Mean number of micturitions episodes per day, mean number of urgency episodes per day, mean number of UUI episodes per day, mean number of incontinence episodes per day, and mean volume voided/micturition Safety: Dry mouth, drug related treatment-emergent AEs, serious AEs, and discontinuations due to AEs

Results:

Efficacy:

- The mean number of micturitions episodes per day (p= 0.16), the mean number of urgency episodes per day (p=0.05), mean number of UUI episodes per day (p=0.11), and mean number of incontinence episodes per day (p=0.14) indicated that vibegron and antimuscarinic therapy had no significant differences in terms of OAB treatment efficacy

Safety:

- With regard to dry mouth and drug related treatment-emergent AEs, vibegron showed better tolerance than antimuscarinics. Serious AEs and discontinuations due to AE did not show a significant difference between the two groups

Conclusion: The authors concluded that the therapeutic effect of vibegron is similar to that of antimuscarinics, but vibegron does not increase the risk of AEs.

Citation	Design	Endpoints
Kennelly M, Wielage R, Shortino D, Thomas E, Mudd PN. Long-term efficacy and safety of vibegron versus mirabegron and	Systematic review and NMA of RCTs of vibegron, mirabegron, and anticholinergics for the treatment of OAB sourced from MEDLINE, Embase and Cochrane and performed on September 16, 2020	Efficacy: Change from baseline to week 48-52 in mean daily total UI episodes, mean daily

anticholinergics for overactive bladder: a systematic review and network meta-analysis. Drugs Context. 2022;11:2022-4-2.	N=6 studies; 2492 participants	micturitions, and volume voided per micturition Safety: AEs

Results:

Efficacy:

- Mean (95% credible interval) change from baseline in total UI episodes for vibegron 75 mg (–2.2; –2.9 to –1.5) showed a significantly greater reduction than mirabegron 50 mg (–1.3; –1.9 to –0.8) and tolterodine 4 mg extended release (–1.6; –2.1 to –1.1)
- No significant differences were observed between vibegron and comparators for daily micturitions or volume voided/micturition

Safety:

- The 4 most common AEs (range) for anticholinergics included dry mouth (5.2–90.0%), constipation (7.7–65.0%), blurred vision (3.8–35.0%) and hypertension (8.6–9.6%)
- The 4 most commonly reported AEs for β3-adrenergic agonists included hypertension (8.8–9.2%), urinary tract infection (5.9–6.6%), headache (5.5%) and nasopharyngitis (4.8–5.2%)

Conclusion: Vibegron was associated with significantly greater improvement in daily total UI episodes at 52 weeks than mirabegron and tolterodine. The most common AE for anticholinergics was dry mouth and for β3-adrenergic agonists was hypertension.

Citation	Design	Endpoints
He W, Zhang Y, Huang G, Tian Y, Sun Q, Liu X. Efficacy and safety of vibegron compared with mirabegron for overactive bladder: A systematic review and network meta-analysis. Low Urin Tract Symptoms. 2023;15(3):80-88.	A systematic search was performed on Pubmed, Web of Science, Embase, and the Cochrane Central Register of Controlled Trials databases to identify studies from the date of database inception to January 1, 2022. All randomized controlled trials comparing mirabegron or vibegron with tolterodine, imidafenacin, or placebo were eligible. N=11 studies; 10806 patients	Efficacy: Outcomes assessed at week 12 - Mean voided volume per micturition - Mean daily micturitions - Mean daily incontinence episodes - Urgency episodes per day - UUI episodes [er day - Nocturia Safety: AEs

Results:

Efficacy:

- All treatments resulted in a significant improvement in mean voided volume per micturition compared with placebo. Only vibegron had significantly higher values compared with mirabegron and any other group at week 12.
- All active treatments showed a statistically significant reduction versus placebo at week 12. No significant difference was found between vibegron and mirabegron in the mean number of micturitions at week 12. However, vibegron resulted in a significantly greater improvement than tolterodine, and mirabegron was similar to tolterodine.
- All five active interventions showed a significantly greater reduction compared with placebo in incontinence episodes. There was no significant difference between vibegron and mirabegron in the mean number of incontinence episodes at week 12, whereas mirabegron showed a significantly greater improvement than tolterodine, and vibegron was similar to tolterodine.
- Compared with placebo, all active treatment groups showed a significantly greater reduction in urgency episodes per day and UUI episodes per day, whereas all treatment groups except tolterodine had a significantly greater reduction than placebo in nocturia. No significant differences were observed between vibegron and mirabegron in urgency episodes per day, UUI episodes per day, and nocturia at week 12.

Safety:

- Compared with placebo, vibegron and mirabegron were not associated with an increased risk of dry mouth, constipation, hypertension, and urinary tract infection.
- Mirabegron had higher rates of nasopharyngitis and cardiovascular AEs than placebo.

Conclusion: Both vibegron and mirabegron seem to be comparable and well tolerated, particularly as direct comparisons are not available. However, vibegron may be more effective than mirabegron in reducing mean voided volume.

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FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (07-01-2024 to 09-30-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Antimuscarinics - Rx								
Tolterodine (Detrol®) 1 mg, 2 mg oral tablets	8	4	$410.74	$51.34	0	0 (0%)	F-ST (Prior use of oxybutynin IR or ER or solifenacin required. Pays at point of sale for members 65 years or older).	No change
Tolterodine (Detrol® LA) 2 mg, 4 mg ER oral capsules	5	2	$188.85	$37.77	0	0 (0%)	F-ST (Prior use of oxybutynin IR or ER or solifenacin required. Pays at point of sale for members 65 years or older).	No change
Oxybutynin 2.5 mg, 5 mg oral tablets	5	4	$212.94	$42.59	0	0 (0%)	F (5mg) NF (2.5mg)	No change
Oxybutynin 5 mg/5 mL oral syrup	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Oxybutynin 5 mg, 10 mg, 15 mg ER oral tablets	18	12	$440.45	$24.47	0	0 (0%)	F	No change
Gelnique® (oxybutynin) 10 % (100 mg/gram) transdermal gel packet	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Oxytrol® (oxybutynin) 3.9 mg/24 hr transdermal patch	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Flavoxate 100 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Trospium 20 mg oral tablet	1	1	$14.72	$14.72	1	1 (100%)	F-ST (Prior use of oxybutynin IR or ER or solifenacin required. Pays at point of sale for members 65 years or older.	No change
Trospium 60 mg ER oral capsule	0	0	$0.00	$0.00	0	0 (0%)	F-ST (Prior use of oxybutynin IR or ER or solifenacin required. Pays at point of sale for members 65 years or older.	No change
Fesoterodine (Toviaz®) 4 mg, 8 mg ER oral tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Solifenacin (Vesicare®) 5 mg, 10 mg oral tablets	8	3	$80.17	$10.02	0	0 (0%)	F	No change
Vesicare LS® (solifenacin) 1 mg/mL oral suspension	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

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Commented [MI1]: Oxybutynin 5mg $0.12 per tab; 2.5mg $2.33 per tab per WAC; oral sol-n $0.036 per ml
No utilization of 2.5 mg--keep NF

Darifenacin 7.5 mg, 15 mg ER oral tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Antimuscarinics - OTC								
Oxytrol® For Women (oxybutynin) 3.9 mg/24 hour transdermal patch	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Beta-3 Agonists								
Mirabegron (Myrbetriq®) 25 mg, 50 mg ER oral tablets	5	2	$1,609.97	$321.99	0	0 (0%)	F-PA	No change
Myrbetriq® (mirabegron) 8 mg/mL ER oral suspension	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Gemtesa® (vibegron) 75 mg oral tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	**50**	**28**	**$2,957.84**	**$59.16**	**1**	**1 (100%)**		

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

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PRIOR AUTHORIZATION CRITERIA

No changes

Urinary Incontinence Agents	
Therapeutic Classes (AHFS)	Antimuscarinics and Beta-3-Adrenergic Agonists
Medications	**Formulary, preferred:** Oxybutynin (Ditropan), Oxybutynin ER (Ditropan XL), solifenacin (Vesicare) **Formulary, step therapy required:** Tolterodine (Detrol), Tolterodine ER (Detrol LA), Trospium (Sanctura), Trospium ER (Sanctura XR) **Formulary, prior authorization required:** Darifenacin (Enablex), fesoterodine (Toviaz), flavoxate (Urispas), Myrbetriq (mirabegron) **Non-formulary:** Gemtesa (vibegron), Vesicare LS (solifenacin) oral suspension, Oxytrol (oxybutynin) patch, Gelnique (oxybutynin), Oxytrol for women OTC **Any other non-formulary agent for urinary incontinence**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Criteria for approval of **tolterodine, tolterodine ER, trospium, or trospium ER:** • Documented trial and failure, intolerance, contraindication, or inability to use oxybutynin or oxybutynin ER or solifenacin for at least 4 weeks (28 days) of therapy within the past 6 months OR • Member aged 65 years or older. Criteria for approval of: **darifenacin, Oxytrol, fesoterodine, Gelnique, flavoxate, Gemtesa, Vesicare LS, or Myrbetriq:** • Documented trial and failure, intolerance, contraindication, or inability to use oxybutynin or oxybutynin ER or solifenacin • AND tolterodine, tolterodine ER, trospium, or trospium ER for at least 4 weeks (28 days) of therapy within the past 6 months.
Criteria Statement	Tolterodine, tolterodine ER, trospium, or trospium ER are reserved for members who have used (or cannot/should not use) oxybutynin or oxybutynin ER or solifenacin or are over age 65 years. Darifenacin, Oxytrol, fesoterodine, Gelnique, flavoxate, Gemtesa, Vesicare LS or Myrbetriq are reserved for members who have used (or cannot/should not use) oxybutynin or oxybutynin ER or solifenacin AND tolterodine, tolterodine ER, trospium, or trospium ER.
Last P&T Review Date	~~12/2023~~12/2024

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Alameda MRGs for review Q4 2024 P&T Consent Agenda

Recommendation: No changes

Oral and Injectable Oncology Medications	
Therapeutic Classes (AHFS)	Antineoplastics
Medications	Oral and Injectable Oncology Medications without medication 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 Healthcare Professional (USP DI), and the Drug Package Insert, and/or per the National Comprehensive Cancer Network (NCCN)
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	N/A
Prescriber Restrictions	**Initial requests:** Prescriber must be an oncologist. **Reauthorization requests**: Prescriber must be an oncologist. An exception can be made if the prescriber is in consultation with an oncologist (see Coverage Duration section for approval duration for reauthorizations exceptions).
Coverage Duration	**Initial Approval (for new treatment or dose changes to existing treatment)**: 6 months duration with a day supply limit of up to a 15 day supply for the first fill (for medications that must be stored in the original container, a supply of up to 30 days is allowed). Subsequent fills have a day supply limit of up to 30 days **Later Approvals (with no dose change, given that at least 15 days of therapy are completed)**: Prescribed by an oncologist: 6 months with a day supply limit of up to 30 days Reauthorization exceptions: 1 month with a day supply limit of up to 30 days If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	All of the following criteria must be met: • Requested indication must be supported by NCCN category 1 or 2A level of evidence. If the request is for a category 2B recommendation then the medical documentation has been provided as to why member is unable to utilize a treatment regimen with a higher level of evidence (e.g. allergic reaction, contraindication). • Documentation provided of results of genetic testing where required per drug package insert. • Documentation provided of results of all required laboratory values and member specific information (e.g., weight, ALT/AST, creatinine kinase, etc.) when recommended/required per drug package insert. • The medication is being prescribed at a dose that is within FDA approved/NCCN guidelines. • For any medication where a biosimilar is available (Kanjinti, Zirabev etc), the member must have documented 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. • Requests for abiraterone (Zytiga) 500mg tablets should be modified into two abiraterone acetate 250mg tablets. • Requests for Lenvima must be for the most appropriate package size based on the dose requested. Requests for Lenvima should be approved for only the correct daily dosage package size (i.e. for Lenvima 20mg daily, the Lenvima 20mg Daily Dose packaging must be used, and not two packages of Lenvima 10mg Daily Dose)
Criteria Statement	Oral and injectable oncology medications without specific criteria are reserved for indications supported by NCCN category 1 or 2A level of evidence.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Non-Formulary/Prior Authorization Required Medications	
Therapeutic Classes (AHFS)	N/A
Medications	• Non-formulary/ PA Required Medications and/or specialty drugs without drug or class specific prior authorization criteria • Brand drugs and reference biologics when a therapeutic equivalent generic drug or biosimilar/interchangeable biologic is available *** The Oral and Injectable Oncology Medications prior authorization criteria will be applied to oncology drugs without drug or class 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), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	According to package insert Check AAH active CCS cases for members < 21 years of age **unless** the medication is being requested for one of the following conditions: • Asthma • Acne • Atopic Dermatitis/Eczema • Psoriasis (except disfiguring condition) • Turner's syndrome • Migraine (not as a result of a CCS coverable condition) • Autism • ADHD • Depression • Failure to thrive • Exogenous obesity • Contraception (Birth control) • Smoking cessation
Prescriber Restrictions	N/A
Coverage Duration	If all of the conditions are met, requests will be approved for up to 12 months (depending on the diagnosis and usual treatment duration).
PA Review Criteria	**If the request is for a brand name medication with a generic or biosimilar available, all requests must be reviewed by a clinical pharmacist first and then forwarded to AAH for review** ****The use of medications for cosmetic purposes is NOT a covered benefit, unless used to treat gender dysphoria, mental health, or substance use disorder. Medications for cosmetic purposes ARE a covered benefit when used to treat gender dysphoria, mental health, or substance use disorder, when other formulary alternatives are not available**** **Authorization:** • The drug is requested for an appropriate use (per the references outlined in "Covered Uses" • The dose requested is appropriate for the requested use (per the references outlined in "Covered Uses")

	• Patient meets one of the four following criteria: ○ Documented trial and failure or intolerance with up to two formulary/preferred medications appropriate for the requested use (per the references outlined in "Covered Uses" or has a medical reason why these drug(s) cannot be used (e.g. intolerance, contraindication). For medications where there is only one preferred agent, only that agent must have been ineffective or not tolerated. ○ No other preferred medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia. ○ All other preferred medications are contraindicated based on the patient's diagnosis, other medical conditions, or other medication therapy. ○ The member has tried and failed the 2 separate formulary components of the combination medication OR 2 separate therapeutic equivalents to the components of the combination medication, if available on formulary OR the provider has submitted a medical reason why the requested combination medication would be superior to the required prerequisite trial(s) with formulary drug(s) [e.g. Yosprala (aspirin/omeprazole), the 2 separate components would need to be tried and failed] **AND, if applicable**: ○ The dose should be consolidated if clinically appropriate (ex: if a request is for Trintellix 10mg tablet, take 2 tablets (=20mg) once daily, a 20mg tablet should be approved, dosed once daily.) • If the request is for a brand drug with a therapeutically equivalent (A-rated) generic drug currently available, documentation of the following: ○ The provider either verbally or in writing has submitted a medical or member specific reason why the brand name drug is required based on the member's condition or treatment history; **AND** if the member had side effects or a reaction to the generic drug, the provider has completed and submitted an FDA MedWatch form to justify the member's need to avoid these drugs. The MedWatch form must be included with the prior authorization request • If the request is for a reference biologic drug with either a biosimilar or interchangeable biologic drug currently available, documentation of one of the following: ○ The prescriber has verbally or in writing submitted a medical or member specific reason why the reference biologic is required based on the member's condition or treatment history; **AND** if the member had side effects or a reaction to all biosimilar or interchangeable biologics, the provider has completed and submitted an FDA MedWatch form to justify the member's need to avoid these drugs. The MedWatch form must be included with the prior authorization ○ The currently available biosimilar product(s) does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested
Criteria Statement	N/A
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Step Therapy Exception	
Therapeutic Classes (AHFS)	N/A
Medications	Drugs on the Alameda Alliance's formulary with a step therapy restriction which do not meet step therapy requirements
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	• The provider has demonstrated knowledge of step therapy requirements. AND • The provider verbally or in writing has submitted a medical reason why required step therapy drug(s) would be ineffective or have the potential to cause harm or deterioration of the member's condition. OR • The provider has submitted a medical reason why the requested drug would be superior to the required prerequisite trial(s) with formulary drug(s).
Criteria Statement	N/A
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Prior Authorization Exception	
Therapeutic Classes (AHFS)	N/A
Medications	Requests for exception to the drug's prior authorization criteria requirements
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	See "PA Review Criteria"
Required Clinical Information	See "PA Review Criteria"
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	• The provider either verbally or in writing has submitted a medical or member specific reason why prior authorization criteria all or in part is not applicable to the member. ○ Medical reasons may include but are not limited to: ▪ Criteria requirements are not applicable to the member based on the uniqueness of the member's condition or other physical characteristics of the member's condition. OR ○ Member specific reasons may include but are not limited to: ▪ Psychiatric, intellectual, physical, cultural, and/or linguistic characteristics of the member which may inhibit the provider from obtaining all necessary prior authorization criteria requirements.
Criteria Statement	N/A
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes, except change naming to reflect generic availability of Myrbetriq as mirabegron

Urinary Incontinence Agents	
Therapeutic Classes (AHFS)	Antimuscarinics and Beta-3-Adrenergic Agonists
Medications	**Formulary, preferred:** Oxybutynin (Ditropan), Oxybutynin ER (Ditropan XL), solifenacin (Vesicare) **Formulary, step therapy required:** Tolterodine (Detrol), Tolterodine ER (Detrol LA), Trospium (Sanctura), Trospium ER (Sanctura XR) **Formulary, prior authorization required:** Darifenacin (Enablex), fesoterodine (Toviaz), flavoxate (Urispas), ~~Myrbetriq (~~mirabegron~~)~~ (Myrbetriq) **Non-formulary:** Gemtesa (vibegron), Vesicare LS (solifenacin) oral suspension, Oxytrol (oxybutynin) patch, Gelnique (oxybutynin), Oxytrol for women OTC **Any other non-formulary agent for urinary incontinence**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Criteria for approval of **tolterodine, tolterodine ER, trospium, or trospium ER:** • Documented trial and failure, intolerance, contraindication, or inability to use oxybutynin or oxybutynin ER or solifenacin for at least 4 weeks (28 days) of therapy within the past 6 months OR • Member aged 65 years or older. Criteria for approval of: **darifenacin, Oxytrol, fesoterodine, Gelnique, flavoxate, Gemtesa, Vesicare LS, or Myrbetriq (mirabegron):** • Documented trial and failure, intolerance, contraindication, or inability to use oxybutynin or oxybutynin ER or solifenacin • AND tolterodine, tolterodine ER, trospium, or trospium ER for at least 4 weeks (28 days) of therapy within the past 6 months.
Criteria Statement	Tolterodine, tolterodine ER, trospium, or trospium ER are reserved for members who have used (or cannot/should not use) oxybutynin or oxybutynin ER or solifenacin or are over age 65 years. Darifenacin, Oxytrol, fesoterodine, Gelnique, flavoxate, Gemtesa, Vesicare LS or Myrbetriq are reserved for members who have used (or cannot/should not use) oxybutynin or oxybutynin ER or solifenacin AND tolterodine, tolterodine ER, trospium, or trospium ER.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Blood Glucose Testing Supplies	
Therapeutic Classes (AHFS)	Diabetes mellitus
Medications	Formulary with quantity limits: Members over 21 years on a prenatal vitamin or insulin are allowed 200 strips/30 days, other members allowed 100 strips/30days. Members 0-21 years on a prenatal vitamin are allowed 200 strips/30 days. All other members 0-21, bill CCS **(Check AAH active CCS cases for members < 21 years of age)** FreeStyle InsuLinx Test Strips- 100ct FreeStyle InsuLinx Test Strips- 50ct FreeStyle Lite Test Strips- 100ct FreeStyle Lite Test Strips- 50ct FreeStyle Test Strips- 100ct FreeStyle Test Strips- 50ct Precision Xtra Test Strips- 100ct Precision Xtra Test Strips- 50ct Formulary, limited to 1 meter per 365 days FreeStyle Freedom Lite Meter FreeStyle InsuLinx Meter FreeStyle Lite Meter Precision Xtra Meter ALAMEDA ALLIANCE FOR HEALTH PREFERS USE OF PRECISION OR FREESTYLE BLOOD GLUCOSE TESTING PRODUCTS (MANUFACTURED BY ABBOTT).
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 for members who are not pregnant
Prescriber Restrictions	N/A
Coverage Duration	See "PA Review Criteria". If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For requests for **Precision or Freestyle preferred test strips**, approve up to 200 strips/30 days for up to 12 months if: • Member is > 21 years of age AND insulin dependent (claims evidence for insulin or documentation from physician if new to plan) OR • Member is any age AND pregnant • For requests for a non-preferred product, documentation or inability to use preferred test strips must be provided. Please consider the preferred alternatives, Precision or Freestyle test strips (with quantity limits). For requests for **Precision or Freestyle preferred test strips**, approve up to a quantity of 100 strips/30 days for up to 12 months if: • Member is > 21 years of age AND no documentation of insulin-dependence or pregnancy • For requests for a non-preferred product, documentation or inability to use preferred test strips must be provided. Please consider the preferred alternatives, Precision or Freestyle test strips (with quantity limits).

Blood Glucose Testing Supplies	
	If member is 0-21 years of age AND no documentation of pregnancy, do not approve. Member is covered by CCS. Check AAH active CCS cases for members < 21 years of age For requests for **Freestyle or Precision Blood Glucose meters**: • Member is allowed 1 meter per year • If request is for a non-preferred product, documentation or inability to use preferred test strips must be provided. Please consider the preferred alternative Freestyle or Precision meters (within fill limits).
Criteria Statement	Freestyle and Precision test strips over a quantity of 100 strips for 30 days are reserved for members who are over 21 years old and insulin dependent OR for members of any age who are pregnant.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Butorphanol (Stadol NS)	
Therapeutic Classes (AHFS)	Opiate, partial agonists
Medications	Butorphanol (Stadol NS) 10 mg/ml nasal spray
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	Pain specialist: pain management, neurologist, headache/migraine specialist
Coverage Duration	**Initial Approval** 3 months (quantity limit of 1 bottle/30 days) **Later Approvals** 6 months (quantity limit of 1 bottle/30 days) If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	****All requests for narcotics must be reviewed by a clinical pharmacist.**** **INITIAL AUTHORIZATION FOR DIAGNOSIS OF PAIN:** 1. Diagnosis of pain. 2. Documented trial and failure with therapeutic doses or intolerance to at least three oral narcotic medications including: oxycodone, oxycodone/acetaminophen, hydromorphone, hydrocodone/acetaminophen, acetaminophen/codeine, and morphine sulfate (first line therapies) **INITIAL AUTHORIZATION FOR DIAGNOSIS OF PAIN DUE TO MIGRAINE HEADACHE** 1. Diagnosis of pain from migraine headache 2. Documented trial with therapeutic doses of at least one recommended migraine preventative therapy (i.e., topiramate, propranolol, timolol, divalproex sodium, amitriptyline, nortriptyline, Emgality, or verapamil) 3. Documented trial and failure with therapeutic doses or intolerance to at least one triptan (unless contraindicated). **REAUTHORIZATION FOR DIAGNOSIS OF PAIN AND PAIN DUE TO MIGRAINE HEADACHE** 1. Documentation submitted supporting re-evaluation of member OR medical necessity of continued use of medication
Criteria Statement	Butorphanol is reserved for members with a diagnosis of pain who have used (or cannot/should not use) at least three oral narcotic medications including: oxycodone, oxycodone/acetaminophen, hydromorphone, hydrocodone/acetaminophen, acetaminophen/codeine, and morphine sulfate. Butorphanol is reserved for members with diagnosis of migraine headache pain and who have used (or cannot/should not use) at least one recommended migraine preventative therapy (topiramate, propranolol, timolol, divalproex sodium, amitriptyline, nortriptyline, Emgality, or verapamil) and at least one triptan.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes, except remove the prescriber specialty from Indications section as it is already included in the Prescriber restrictions section

Corticotropin	
Therapeutic Classes (AHFS)	Other miscellaneous therapeutic agents
Medications	Formulary, PA required Preferred: Cortrophin (corticotropin) Non-Preferred: Acthar Gel (corticotropin)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	**Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Diagnosis by a neurologist or a specialist in the condition they are treating
Coverage Duration	**Initial Approval** 4 weeks **Later Approval** 4 weeks If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**All requests must be reviewed by a clinical pharmacist first and then forwarded to AAH for review** **Multiple Sclerosis:** • Documentation was submitted that the member is having an acute attack, with neurologic symptoms and increased disability or impairments in vision, strength or cerebellar function, and has failed therapy with IV methylprednisolone, or a medical reason has been submitted why member is unable to use IV methylprednisolone. • If the request is for a non-preferred product, trial and failure of, contraindication to or medical reason for not using the preferred product is required. **All Other FDA Approved Conditions and Indications:** • Documented trial and failure of IV AND oral corticosteroids, or documented medical reason for why the member cannot use these therapies for treatment **AND** • Documentation was provided that ALL other standard therapies have been used to treat the member's condition as described in medical compendia (Micromedex, AHFS, Drug Points, and package insert) as defined in the Social Security Act and/or per recognized standard of care guidelines OR there is a documented medical reason (i.e. medical intolerance, treatment failure, etc.) for why all other standard therapies could not be used to treat the member's condition. **AND** • ~~Prescriber is a specialist in the condition they are treating.~~ • If the request is for a non-preferred product, trial and failure of, contraindication to or medical reason for not using the preferred product is required **Appeals/Reconsiderations:** • Requests for appeals/reconsiderations will be sent out for independent medical review.

Criteria Statement	Cortrophin (corticotropin) is reserved for members with a diagnosis of an acute attack of multiple sclerosis who have used (or cannot/should not use) IV methylprednisolone Acthar is reserved for members with a diagnosis of an acute attack of multiple sclerosis who have used (or cannot/should not use) IV methylprednisolone AND Cortrophin.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Endari	
Therapeutic Classes (AHFS)	Other Miscellaneous Therapeutic Agents
Medications	Non-formulary Endari (L-Glutamine)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), and the Drug Package Insert.
Exclusion Criteria	N/A
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	**Initial/Later Approval** — **If all of the conditions are met, requests will be approved for a 12 months.** If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Initial: • Member has diagnosis of sickle cell disease • Documentation was provided that the member had 2 or more crises in the last 12 months • Documentation was provided the member has been on hydroxyurea at the maximum tolerated dose and was compliant within the last 6 months (or a medical reason was provided why member is unable to use hydroxyurea) • Request is for an FDA approved dose Reauthorization: • Prescriber attests member had reduction in number of sickle cell crises • Request is for an FDA approved dose
Criteria Statement	**Endari:** Endari is reserved for members who have unstable sickle cell disease and are taking the highest tolerated dose of hydroxyurea or cannot/should not take hydroxyurea.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Diclofenac sodium (Solaraze) 3% gel	
Therapeutic Classes (AHFS)	Antineoplastic Agents
Medications	Formulary, PA required Diclofenac sodium (Solaraze) 3% gel
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 dermatologist
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to 3 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	Criteria for approval • Diagnosis of actinic keratosis (AK) • Documented trial and failure of one formulary alternative [i.e. fluorouracil (Efudex) cream or imiquimod (Aldara) cream]
Criteria Statement	Diclofenac sodium 3% gel is reserved for members who have actinic keratosis and have used (or cannot/should not use) one formulary alternative such as fluorouracil (Efudex) or Imiquimod (Aldara) creams.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes, except remove discontinued drug SaizenPrep

Growth Hormone	
Therapeutic Classes (AHFS)	Pituitary
Medications	Formulary, Prior Authorization Required **Omnitrope – preferred agent** Non-formulary: Genotropin, GenotropinMiniQuick Humatrope Norditropin FlexPro Nutropin AQ NuSpin Saizen~~, SaizenPrep~~ Serostim Zomacton Skytrofa Ngenla Sogroya Any other newly marketed growth hormone product
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 the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), the American College of Obstetricians and Gynecologists (ACOG), or the American Academy of Pediatrics (AAP) standard of care guidelines.
Exclusion Criteria	Treatment of idiopathic short stature (ISS)-not a covered benefit and will not be approved
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber is an endocrinologist or specialist in diagnosis being treated
Coverage Duration	**Initial Approval** CO-GHD, CKD, AO-GHD, Genetic causes: 12 months HIV/AIDS-wasting syndrome: 3 months **Later Approvals** CO-GHD, CKD, AO-GHD, Genetic causes: 12 months HIV/AIDS-wasting syndrome: 3 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** **If request is not for Omnitrope, documentation of medical reason, intolerance, inability, or contraindication to use Omnitrope must be provided.** **Initial Authorization** **Childhood-onset growth hormone deficiency (CO-GHD)** • If diagnosis is childhood-onset GH deficiency (CO-GHD) ○ And member is currently **pediatric**, **all** of the following ▪ IGF-1 and insulin-like growth factor binding protein-3 (IGFBP-3) deficiency (< 0 SD below reference range for age and gender)* with prescriber attestation of growth failure ▪ Provider attests that MRI or CT has been completed to exclude possibility of a pituitary tumor

Growth Hormone	
	▪ Provider attests that member's epiphyses are open ○ And member is currently **adult, <u>one</u>** of the following ▪ If diagnosis is idiopathic isolated GHD, documentation was provided that indicates GH therapy is still medically necessary (IGF-1 retesting during the transition period after a minimum 1 month of therapy discontinuation reveals continued GH deficiency) ▪ Diagnosis is GHD associated with multiple (≥3) pituitary hormone deficiencies (MPHD), genetic defect affecting the HPA axes, or member with hypothalamic pituitary structural brain defect **<u>Growth failure due to chronic renal insufficiency (CRI)/ Chronic kidney disease (CKD):</u>** ▪ Documentation of either pretreatment height is < -1.88 standard deviations (SD) below the mean for age or a height velocity–for-age < 3rd percentile that persists beyond 3 months • Provider attests that the member's epiphysis are open **<u>Short stature associated with Prader-Willi Syndrome, Noonan Syndrome, Turner Syndrome, short stature homeobox-containing gene (SHOX) mutation, or other underlying genetic cause</u>** ▪ Documentation of confirmatory genetic test **<u>Adult-onset growth hormone deficiency (AO-GHD)</u>** • If the diagnosis is adult-onset GH deficiency (AO-GHD), documentation of **<u>one</u>** of the following: ○ Insulin Growth Factor (IGF-1) deficiency (< -2 SD below reference range for age and gender)* and multiple (≥3) pituitary hormone deficiencies (MPHD) ○ Evidence of genetic defects affecting the hypothalamic pituitary axes (HPA) (e.g. pituitary disease) ○ Evidence of hypothalamic pituitary structural brain defects (e.g. hypothalamic disease) ○ Positive results of GH stimulatory test (e.g. insulin tolerance test [ITT], glucagon, or macimorelin) **<u>HIV/AIDS-wasting syndrome (Serostim)</u>** • Member is on antiviral therapy • 10% unintentional weight loss over 12 months • Documentation of inadequate response to previous therapy including exercise training, nutritional supplements, appetite stimulants or steroid hormones such as megestrol acetate. **<u>Reauthorization</u>** • Documentation of diagnosis [Note: Idiopathic Short Stature (ISS) is not a covered benefit] • Documented IGF-1 levels do not exceed upper limit of normal (ULN) (> 2 SD above reference range for age and gender)*, or if the IGF-1 levels do not exceed ULN, the dose has been reduced • In CO-GHD, growth response (as demonstrated by length/height and calculated height velocity within previous 6 months). • For HIV/AIDs wasting syndrome: documented clinical response including increase in muscle mass and weight

Growth Hormone	
	*IGF-1 levels are highly age and gender specific. In the event the form provides a value and not the corresponding reference range, refer to published reference ranges for interpretation.
Criteria Statement	• Growth hormone other than Omnitrope is reserved for members who have used (or cannot/should not use) Omnitrope. • For childhood-onset growth deficiency where the member is currently pediatric, growth hormone is reserved for members with growth failure and the epiphysis are open. • For childhood-onset growth deficiency where the member is currently an adult, growth hormone is reserved for members where growth hormone is still medically necessary. • For growth failure due to chronic renal insufficiency, growth hormone is reserved for members with height at least -1.88 standard deviations (SD) below the normal for age and or a height velocity–for-age less than the 3rd percentile that persists beyond 3 months and epiphysis are open. • For short stature in Turner Syndrome, Prader-Willi Syndrome, Noonan Syndrome, short stature homeobox-containing gene (SHOX) mutation, or other underlying genetic cause growth hormone is reserved for members with a confirmatory genetic test. • For adult-onset growth hormone deficiency, growth hormone is reserved for members with pituitary disease and positive results of a growth hormone stimulation test. • For HIV/AIDS wasting syndrome, growth hormone is reserved for members using antiretroviral therapy and have lost at least 10% of initial weight over 12 months and have used (or cannot/should not use) exercise training, nutritional supplements, appetite stimulants or steroid hormones such as megestrol acetate.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Rapid-Acting Insulin	
Therapeutic Classes (AHFS)	Insulins
Medications	Formulary with quantity limits: Admelog U-100 vial and Admelog Solostar Insulin Lispro 100 units/ml vial, pen Non-formulary Apidra 100 units/ml vial Apidra Solostar 100 units/ml Humalog KwikPen 100 units/ml, 200 units/ml Humalog 100 units/ml vial, cartridge Novolog 100 units/ml vial Novolog FlexPen100 units/ml Fiasp vial, FlexTouch, penfill Lyumjev KwikPen (insulin lispro-aabc) 100units/ml, 200units/ml Insulin aspart 100 units/ml Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For requests for non-formulary rapid acting insulin, approve if: • Diagnosis of Type I or Type II Diabetes • Documentation of trial and failure, inability to use, intolerance, or contraindication to one of the formulary rapid acting insulins. If request is for pen formulation, documentation of trial and failure, inability to use, intolerance, or contraindication to using Admelog Solostar or Insulin Lispro 100 units/ml vial or pen must be provided.
Criteria Statement	Non-formulary rapid acting insulins are reserved for members with diabetes who have used (or cannot/should not use) Admelog vial, Admelog Solostar, Insulin Lispro 100 units/ml vial or pen.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Long-Acting Basal Insulin	
Therapeutic Classes (AHFS)	Insulins
Medications	Formulary with quantity limit (30/30): Insulin glargine-yfgn solution 100 unit/ml vial and pen injector **PREFERRED** Rezvoglar (insulin glargine-aglr) 100unit/ml KwikPen **PREFERRED** Lantus Solostar (insulin glargine) 100 unit/ml, Lantus (insulin glargine) 100 unit/ml vial **PREFERRED** Non-formulary Semglee (YFGN) (insulin glargine) 100 unit/ml vial and pen Insulin glargine (Winthrop) 100 unit/ml vial, Solostar Levemir FlexTouch (insulin detemir), Levemir (insulin detemir) vial Toujeo Solostar (insulin glargine) 300 unit/ml pen Tresiba (insulin degludec) 100 unit/ml vial and pen, 200 unit/ml pen Basaglar (insulin glargine) KwikPen 100 unit/ml Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For requests for non-formulary basal insulin, approve if: • Diagnosis of Type I or Type II Diabetes • Documentation of trial and failure, inability to use, intolerance, or contraindication to one formulary preferred long-acting insulin For requests above the quantity limit • The provider has submitted a medical reason why the plan's quantity limit will be inadequate based on the member's condition and treatment history.
Criteria Statement	Non-formulary basal insulins are reserved for members with diabetes who have used (or cannot/should not use) one preferred formulary basal insulin: insulin glargine-yfgn solution 100 unit/ml vial / pen injector, Lantus Solostar/ vial, or Rezvoglar KwikPen.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes, except remove Myorisan that was discontinued

Isotretinoin capsules	
Therapeutic Classes (AHFS)	Skin and mucous membrane agents, miscellaneous
Medications	Formulary, PA required PREFERRED • Claravis (isotretinoin) • ~~Myorisan (isotretinoin)~~ • Zenatane (isotretinoin) • Amnesteem (isotretinoin) • Accutane (isotretinoin) • Isotretinoin Formulary, PA required NON-PREFERRED • Isotretinoin (Absorica) • Absorica LD (isotretinoin) Or any newly marketed oral retinoid product
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** 6 months **Later Approvals** 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 for approval: • Diagnosis of moderate to severe recalcitrant nodular acne. • Documented treatment with a therapeutic trial and failure or intolerance to one or more first line topical therapies (e.g. topical antibiotics or topical retinoids) IN COMBINATION WITH one or more first line oral therapies (e.g. doxycycline, tetracycline, or minocycline) for at least 4 weeks (28 days) of therapy of each drug in the previous 365days • If the request is for a non-preferred drug, documentation has been provided that the member has tried and failed two preferred drugs or has a medical reason why these drugs cannot be used
Criteria Statement	Preferred generic isotretinoin medications (e.g., Claravis, ~~Myorisan,~~ Zenatane, Amnesteem, Accutane) are reserved for members with moderate to severe recalcitrant nodular acne who have used (or cannot/should not use) oral antibiotics. Isotretinoin (Absorica) or Absorica LD (isotretinoin) are reserved for members who have severe acne, who have used (or cannot/should not use) topical therapies (e.g. topical antibiotics or topical retinoids) AND oral antibiotics. Non-preferred agents are reserved for members with moderate to severe recalcitrant nodular acne who have used (or cannot/should not use) oral antibiotics. Isotretinoin (Absorica) 25mg or 35mg capsules or Absorica LD (isotretinoin) are reserved for members who have severe acne, who have used (or cannot/should not use) topical therapies (e.g. topical antibiotics or topical retinoids) AND oral antibiotics AND at least two preferred agents.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Gonadotropin Releasing Hormone (GNRH) Agonists	
Therapeutic Classes (AHFS)	Gonadotropins
Medications	**<u>Preferred GnRH Agonist(s) for their respective indications:</u>** Lupron Depot (leuprolide acetate) Lupron Depot-Ped (leuprolide acetate) Zoladex (goserelin acetate) **<u>Non-Preferred GnRH Agonist(s):</u>** Fensolvi (leuprolide acetate) Supprelin LA (histrelin acetate) Synarel (nafarelin acetate) Triptodur (triptorelin pamoate) Any newly marketed GnRH agonist
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), and the Drug Package Insert.
Exclusion Criteria	N/A
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a specialist in the field to treat the member's condition.
Coverage Duration	**Initial Approval** — For central precocious puberty: the request will be approved for up to 12 months. If all of the conditions are met, the request will be approved for up to 3-6 months as indicated below for other indications as recommended per FDA approved indications and/or as defined by the medical compendium or standard of care guidelines. **Later Approvals** — See Initial Approvals If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review
PA Review Criteria	****IF DIAGNOSIS IS CANCER, USE Oral and Injectable Oncology Medications CRITERIA**** **PEDIATRIC POPULATION** *For GID/gender dysphoria coverage, please refer to the Gender Dysphoria medication guidelines for age less than 21.* **ADULT POPULATION** *For GID/gender dysphoria coverage, please refer to the Gender Dysphoria medication guidelines for age 21 years of age or older.* **<u>INITIAL AUTHORIZATION for ALL REQUESTS:</u>** • The medication is being prescribed for an FDA approved/standard of care guideline indication and within FDA approved/standard of care dosing guidelines. AND the member meets the following for the respective diagnosis:

	Criteria for central precocious puberty:
	• Onset of secondary sexual characteristics occurred when member was aged less than 8 years for females or aged less than 9 years for males
	• Diagnosis of central precocious puberty as defined by one of the following
	  ○ Pubertal response to a GnRH stimulation test and/or measurement of gonadotropins (FSH/LH)
	  ○ Bone age advanced one year beyond the chronological age
	  ▪ Members with low or intermediate basal levels of LH should have a GnRH stimulation test to clarify the diagnosis.
	  • If basal levels of ultrasensitive LH are markedly elevated [e.g. more than 0.3ml IU/L (where IU-International units)] in a child with precocious puberty, then a diagnosis of CPP can be made without proceeding to a GnRH stimulation test.
	• Brain magnetic resonance imaging (MRI) has been performed for all boys with CPP and for girls with onset of secondary sexual characteristics before the age of six years of age to rule out a tumor.
	• If the request is for any agent other than Lupron Depot-Ped the member has had a documented trial and failure with Lupron Depot-Ped or a documented medical reason (e.g. intolerance, hypersensitivity, contraindication) was submitted why the member is not able to use Lupron Depot-Ped
	
	Endometriosis:
	• Member has a confirmed diagnosis (e.g. laparoscopy, etc.) of endometriosis
	• Documented contraindication to or trial and failure of the use of a combined oral estrogen-progestin contraceptive OR a progestin only AND non-steroidal anti-inflammatory agents.
	  ○ If one of the following drugs has been tried previously, a trial of OCPs is not required: Orilissa (elagolix), Myfembree, danazol, or aromatase inhibitors (e.g. anastrozole, letrozole)
	• Member is receiving “add back” hormonal therapy (e.g. norethindrone acetate, conjugated estrogen or progestin therapy, etc.)
	• If the request is for a non-preferred agent, the member has had a documented trial and failure with one of the preferred agents or a documented medical reason (e.g. intolerance, hypersensitivity, contraindication) was submitted why the member is not able to use these medications
	• Approval is 6 months
	
	Leiomyomata/fibroids:
	• Member has a confirmed diagnosis (e.g. pelvic examination, etc.)
	• If the request is for any agent other than Lupron Depot the member has had a documented trial and failure with Lupron Depot or a documented medical reason (e.g. intolerance, hypersensitivity, contraindication) was submitted why the member is not able to use Lupron Depot
	• Approval is 3 months
	
	Endometrial thinning
	• Documentation indicates member is scheduled for endometrial ablation for dysfunctional uterine bleeding.
	• If the request is for any agent other than Zoladex the member has had a documented trial and failure with Zoladex or a documented medical reason (e.g. intolerance, hypersensitivity, contraindication) was submitted why the member is not able to use Zoladex
	• Approval is 3 months

	REAUTHORIZATION for all requests: • The medication is being prescribed for an FDA approved indication and within FDA approved dosing guidelines. • Documentation was provided supporting continued treatment (e.g. member still has symptoms), and medication is being continued as recommended in package insert or standard of care guidelines. AND meets the following per diagnosis: Central precocious puberty (CPP) • If the medication reauthorization is for central precocious puberty, the child is male and < 12 years or female and < 11 years of age OR a documented medical reason to continue treatment was provided with request, and includes current height and bone age Endometriosis • Prescriber has evaluated member for osteoporosis (e.g. Dexascan), and member is receiving "add back" hormonal therapy (e.g. norethindrone acetate, conjugated estrogen or progestin therapy, etc., AND calcium and vitamin D supplementation. • The member has not received cumulative doses of the GnRH agonist greater than 12 months of therapy. Fibroids • The member has not received cumulative doses of the GnRH agonist greater than 6 months of therapy
Criteria Statement	**Central Precocious Puberty:** Lupron Depot-Ped is reserved for members who have met the criteria for the diagnosis and treatment of central precocious puberty. **Endometriosis**: Zoladex and Lupron Depot/Ped are reserved for members who have met the criteria for the diagnosis and treatment of endometriosis. **Uterine leiomyomas (Fibroids):** Lupron Depot is reserved for members who have met the criteria for the diagnosis and treatment of uterine leiomyomas (fibroids). **Endometrial thinning:** Zoladex is reserved for members who have met the criteria for the diagnosis and treatment of endometrial thinning. **Non-preferred agents:** <Insert agent> is reserved for members who have met the criteria for the diagnosis and treatment of <insert indication> and have used (or cannot/ should not use) the preferred agent for the diagnosis <Insert agent(s)>.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Self-administered Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	
Therapeutic Classes (AHFS)	Immunomodulatory agents
Medications	**Preferred:** **glatiramer acetate (COPAXONE)** **dimethyl fumarate (TECFIDERA)** **Non-preferred:** **GILENYA (fingolimod)** **MAYZENT (siponimod)** **AUBAGIO (teriflunomide)** **Vumerity (diroximel fumarate)** **AVONEX, REBIF (Interferon beta-1a)** **BETASERON, EXTAVIA (Interferon beta-1b)** **COPAXONE (glatiramer acetate)** **glatiramer acetate (GLATOPA)** **PLEGRIDY (Peginterferon beta-1a)** **MAVENCLAD (cladribine)** **ZEPOSIA (ozanimod)** **PONVORY (ponesimod)** **BAFIERTAM (monomethyl fumarate)** **KESIMPTA (ofatumumab)** **Any other newly marketed self-administrable DMT for MS indicated for the listed diagnoses**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Members with primary progressive MS (PPMS) Mavenclad • Clinically Isolated Syndrome (CIS)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Member must be age appropriate per prescribing information (PI) **NOTE: Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	**Initial Approval** — If all of the criteria are met, the request will be approved for 12 months for all agents except Mavenclad (cladribine). If all of the criteria for Mavenclad (cladribine) are met, the request will be approved for 1 course at a time with a lifetime maximum of 2 yearly treatment courses [1 course = (1 cycle per 30 days) two times]. **Later Approval** — 12 months: If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization** • For all requests, the medication is being prescribed at a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed literature. Clinically Isolated Syndrome (CIS) • Diagnosis of CIS

	• If the request is for glatiramer or dimethyl fumarate (Tecfidera) approve. • If the request is for a non-preferred agent, the member must have a documented trial of BOTH preferred agents or have a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing both of these therapies (exception Gilenya, see bullet below) **AND** o If the request is for Gilenya (fingolimod), documentation of the following ▪ Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination ▪ If the request if for Gilenya (fingolimod) and the member has "highly active" MS, approve <u>WITHOUT</u> requiring trial and failure of both preferred agents o If the request is for Mayzent (siponimod), documentation of the following ▪ Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination ▪ Results of CYP2C9 genotyping AND • Member does not have CYP2C9 *3/*3 (**CONTRAINDICATED)** • If member has CYP2C9 *1/*3 or *2/*3, dose does not exceed 1 mg daily o If the request is for Ponvory (ponesimod) or Zeposia (ozanimod), Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination o If the request is for Kesimpta (ofatumumab), documentation that immunizations are up-to-date. <u>Relapsing Remitting MS (RRMS) and Secondary Progressive MS (SPMS)</u> • Diagnosis of RRMS or SPMS • If the request is for glatiramer or dimethyl fumarate (Tecfidera) approve • If the request is for a non-preferred agent, then the member must have a documented trial of at BOTH preferred agents, or have a documented medical reason (e.g. contraindication, intolerance, hypersensitivity, etc.) for not utilizing both of these therapies (exception Gilenya, see bullet below) **AND** o If the request is for Gilenya (fingolimod), documentation of the following ▪ Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination ▪ If the request if for Gilenya (fingolimod) and the member has "highly active" MS approve <u>WITHOUT</u> requiring trial and failure of both preferred agents o If the request is for Mayzent (siponimod), documentation of the following ▪ Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination ▪ Results of CYP2C9 genotyping AND • Member does not have CYP2C9 *3/*3 (**CONTRAINDICATED)** • If member has CYP2C9 *1/*3 or *2/*3, dose does not exceed 1 mg daily o If the request is for Mavenclad (cladribine), documentation of the following ▪ Member's current weight

	▪ Results of VZV antibody testing and, if negative, documentation of VZV vaccination ▪ If the member has not tried at least one of the preferred therapies listed above but has a documented medical reason for not utilizing these therapies, the member has tried and failed at least one other DMT for MS ○ If the request is for Ponvory (ponesimod) or Zeposia (ozanimod), Healthcare Provider (HCP)-confirmed history of chickenpox, results of varicella zoster virus (VZV) antibody testing and, if negative, documentation of VZV vaccination ○ If the request is for Kesimpta (ofatumumab), documentation that immunizations are up-to-date. **Reauthorization** CIS • The medication is being prescribed at a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed literature • Documentation was provided that the prescriber has reviewed the risks and benefits of continuing DMT versus stopping. RRMS and SPMS • The medication is being prescribed at a dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed literature • Documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit). AND • If the request is for Mavenclad (cladribine) ○ Member's current weight ○ ****NO MORE THAN 2 COURSES IN TOTAL WILL BE APPROVED.**** **Continuation of Therapy/Grandfathering Provision:** Members with history (within the past 90 days or past 12 months for Mavenclad [cladribine]) of a non-preferred product are not required to try a preferred product prior to receiving the non-preferred product.
Criteria Statement	Dimethyl fumarate (Tecfidera) and glatiramer acetate (Copaxone) are the preferred agents for multiple sclerosis, dependent on the specific sub-type of the disease. Non-preferred agents are reserved for members who have used (or cannot/should not use) the preferred agents.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

dalfampridine (Ampyra)	
Therapeutic Classes (AHFS)	Other miscellaneous therapeutic agents
Medications	Formulary, PA required **dalfampridine (Ampyra)**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	History of seizures. Moderate or severe renal impairment (creatinine clearance ≤ 50mL/minute)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Patient must be 18 years of age or older. **NOTE: Check AAH active CCS cases for members < 21 years of age**
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	**Initial Approval** 6 months **Later Approval** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization:** • Baseline creatinine clearance (within 6 months of request) • Patient has diagnosis of multiple sclerosis (MS), patient is ambulatory (baseline 25 foot walk was submitted with request), AND patient has walking impairment • Documentation was submitted (consistent with pharmacy claims data, OR for new members to the health plan, consistent with chart notes) that patient is currently being treated for MS (e.g. immunomodulator, interferon, immunosuppressive), or documentation of a medical reason (intolerance, hypersensitivity) as to why patient is unable to use one of these agents to treat their medical condition • Drug is being requested at an FDA approved dose **Re-authorization:** • Documentation of improvement (above baseline) in 25 foot walk was submitted with request • Documentation was submitted patient is on MS treatment (e.g. immunomodulator, interferon, immunosuppressive), or documentation of a medical reason (intolerance, hypersensitivity) as to why patient is unable to use one of these agents to treat their medical condition • Drug is being requested at an FDA approved dose
Criteria Statement	**Dalfampridine (Ampyra)** is reserved for members who are ambulatory, have a walking impairment, and are using (or cannot/should not use) disease modifying oral or injectable treatment for multiple sclerosis.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Ophthalmic Anti-Inflammatory Agents	
Therapeutic Classes (AHFS)	EENT Nonsteroidal and Corticosteroid anti-inflammatory agents
Medications	Prolensa (bromfenac) 0.07% Bromsite (bromfenac) 0.075% Ketorolac (Acular LS) 0.4% Acuvail (ketorolac) 0.45% Ilevro (nepafenac) 0.3% Nevanac (nepafenac) 0.1% Bromfenac 0.09% Difluprednate (Durezol) 0.05% (quantity limit)
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-auth** If all criteria are met, approve for up to a 12 month duration with a quantity limit of 1 bottle; 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 USE: • Documentation of trial and failure, intolerance, contraindication, or inability to use TWO preferred formulary alternatives: diclofenac 0.1%, flurbiprofen 0.03%, ketorolac 0.5% drops, prednisolone 1%, or dexamethasone 0.1% eye drops for at least 30 days each within the last 12 months. • If diagnosis is uveitis: Documentation of trial and failure, intolerance, contraindication, or inability to use both preferred formulary alternatives: prednisolone 1% AND dexamethasone 0.1% eye drops
Criteria Statement	Difluprednate (Durezol), Prolensa, Bromsite, ketorolac (Acular LS), Acuvail, Ilevro, Nevanac, and Bromfenac are reserved for members who have used (or cannot/should not use) TWO preferred formulary alternatives diclofenac 0.1%, flurbiprofen 0.03%, ketorolac 0.5% drops, prednisolone 1%, or dexamethasone 0.1% eye drops for at least 30 days within the last 12 months. For uveitis patients, difluprednate (Durezol) is reserved for members who have used (or cannot/should not use) preferred formulary alternatives prednisolone 1% AND dexamethasone 0.1% eye drops
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Fentanyl Citrate	
Therapeutic Classes (AHFS)	Opiate agonists
Medications	**Non-formulary and require prior authorization:** **Fentanyl citrate (Actiq)** lozenge -PREFERRED Fentanyl citrate (**Fentora**) buccal tablet **Lazanda (fentanyl citrate)** nasal spray pump **Subsys (fentanyl citrate)** sublingual spray **Any other short-acting oral/buccal/sublingual/nasal fentanyl formulation**
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	Oncologist, hospice/palliative care physician, hematologist, or attestation that the requesting prescriber is working in consultation with one of the aforementioned specialty types.
Coverage Duration	**Initial Approval** 6 months not to exceed #120 per 30 days; Lazanda is limited to 15 bottles per 30 days Subsys is limited to 4 boxes per 30 days **Later Approvals** 6 months not to exceed #120 per 30 days; Lazanda is limited to 15 bottles per 30 days Subsys is limited to 4 boxes per 30 days If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	****All requests for narcotics must be reviewed by a clinical pharmacist.**** **<u>Authorization for Fentanyl Citrate:</u>** • A diagnosis of cancer pain AND • Member is on a maintenance dose of an around-the-clock controlled release pain medication consisting of daily doses of at least morphine 60 mg orally or daily use of an equianalgesic dose of another opioid for a week or longer [e.g. sustained relief morphine, oxycodone ER, fentanyl transdermal patches, morphine ER capsule (Kadian or Avinza)]. AND • Member is unable to swallow, has dysphagia, esophagitis, mucositis, or uncontrolled nausea/vomiting OR documentation of trial and failure of at least 2 of the following immediate-release oral pain medications: morphine sulfate, oxycodone/acetaminophen, oxycodone immediate release, hydrocodone/acetaminophen, and hydromorphone. • For requests for (fentanyl citrate) Fentora, Fentora, Subsys, and Lazanda, all criteria listed above must be met AND documentation required of trial and failure, intolerance, contraindication to fentanyl citrate (Actiq) lozenges
Criteria Statement	Fentanyl citrate (Actiq) lozenges are reserved for members with cancer pain who are on maintenance doses of controlled release opioids and who are unable to swallow or has used (or cannot/should not use) at least 2 of the following immediate-release oral pain medications: morphine sulfate, oxycodone/acetaminophen, oxycodone immediate release, hydrocodone/acetaminophen, and hydromorphone. (Fentanyl citrate) Fentora, Subsys, or Lazanda are reserved for members with cancer pain who are on maintenance doses of controlled release opioids and member is

	unable to swallow or has used (or cannot/should not use) at least 2 of the following immediate-release oral pain medications: morphine sulfate, oxycodone/acetaminophen, oxycodone immediate release, hydrocodone/acetaminophen, and hydromorphone AND fentanyl citrate (Actiq) lozenges.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Proton Pump Inhibitors (PPIs)	
Therapeutic Classes (AHFS)	Proton Pump Inhibitors
Medications	Formulary Omeprazole (Prilosec) capsule Pantoprazole (Protonix) tablet Lansoprazole (Prevacid) DR capsule Formulary, step therapy required Rabeprazole (Aciphex) tablet Esomeprazole (Nexium) capsule Formulary, PA required Dexlansoprazole (Dexilant) capsule Non-Formulary Omeprazole tablet and capsule (Prilosec OTC) Omeprazole/sodium bicarbonate (Zegerid) capsules and packets Lansoprazole (Prevacid) orally disintegrating tablets Esomeprazole (Nexium 24 HR) tablet Nexium DR (esomeprazole) oral granules packet Rabeprazole (Aciphex) sprinkle capsules Pantoprazole (Protonix) packet for oral suspension Prilosec packet for oral suspension Any other non-formulary proton pump inhibitor medication or dosage formulation
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	Criteria for approval: Rabeprazole tablets or esomeprazole capsules are approved when the following criteria is met: • Documentation of a trial and failure, or intolerance to omeprazole 40mg capsules AND pantoprazole 40 mg or lansoprazole DR capsule Dexlansoprazole (Dexilant) and non-formulary medications are approved when the following criteria are met: • Documentation of a trial and failure, or intolerance to at least 4 of the following formulary alternatives: omeprazole capsule, pantoprazole tablet, lansoprazole DR capsule, as first line; esomeprazole capsule or rabeprazole tablet as second line
Criteria Statement	Rabeprazole tablets or esomeprazole capsules are reserved for members who have used (or cannot/should not use) omeprazole 40 mg capsules AND pantoprazole 40 mg or lansoprazole DR capsules.

Proton Pump Inhibitors (PPIs)	
	Dexlansoprazole (Dexilant) and non-formulary proton pump inhibitors are reserved for members who have used (or cannot/should not use) at least 4 of the following formulary alternatives: omeprazole capsule, pantoprazole tablet, lansoprazole DR capsule, as first line; esomeprazole tablet DR or rabeprazole tablet as second line.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Ranolazine (Ranexa, Aspruzyo)	
Therapeutic Classes (AHFS)	CARDIAC DRUGS, MISCELLANEOUS
Medications	Ranolazine ER (Ranexa) Aspruzyo Sprinkle (ranolazine granules)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	CRITERIA FOR AUTHORIZATION Ranolazine ER (Ranexa): • Diagnosis of chronic angina pectoris AND • Documented trial and failure, contraindication, or intolerance to use a beta-blocker, calcium channel blocker AND long-acting nitrate. OR • Documentation member's blood pressure is too low to tolerate additional medications Aspruzyo Sprinkle (ranolazine) • All of the above criteria are met • Documented trial and failure, contraindication, or intolerance to ranolazine ER (Ranexa)
Criteria Statement	Ranolazine ER (Ranexa) is reserved for members who have used (or cannot/should not use) a beta-blocker, calcium channel blocker, and long-acting nitrate. Aspruzyo Sprinkle (ranolazine) is reserved for members who have used (or cannot/should not use) a beta-blocker, calcium channel blocker, and long-acting nitrate AND ranolazine ER (Ranexa).
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Temazepam (Restoril)	
Therapeutic Classes (AHFS)	BENZODIAZEPINES (ANXIOLYTIC,SEDATIV/HYP)
Medications	Temazepam (Restoril) 7.5, 22.5 mg
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), 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** 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	**CRITERIA FOR AUTHORIZATION**
	• Request is for 7.5 mg or 22.5 mg:
	  ○ Diagnosis of insomnia.
	  ○ Documented trial and failure, intolerance, or inability to use 3 of the following: 1) temazepam 15mg or 30mg capsules, 2) zolpidem, 3) eszopiclone, 4) zaleplon for at least 2 weeks (14 days) of therapy each.

Criteria Statement	Temazepam 7.5 mg or 22.5 mg are reserved for members who have used (or cannot/should not use) three of the following medications: temazepam 15mg or 30mg, zolpidem, eszopiclone, or zaleplon for at least 2 weeks (14 days) of therapy each
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Testosterone Agents	
Therapeutic Classes (AHFS)	Androgens
Medications	<u>Formulary (first-line)</u> • Testosterone cypionate 100mg/mL (QL #10 ml/30 days), 200mg/mL intramuscular oil (QL #5 ml/30 days) • Testosterone (Vogelxo) 1% gel pump (QL #300gm/30 days) • Testosterone (Androgel) 1.62% gel pump (QL #150gm/30 days) <u>Formulary, PA required (second-line)</u> • Testosterone (Androgel) 1% 50 mg packets • Testosterone (Androgel) 1% 25 mg packets • Testosterone (Testim) 1% gel tube • Testosterone (Axiron) 30mg/1.5ml solution pump • Testosterone enanthate 200mg/mL intramuscular oil (QL #5 ml/30 days) <u>Non-formulary</u> • Testosterone (Fortesta) 2% gel pump • Testosterone (Androgel) 1.62% gel packets • Androderm (testosterone transdermal patch) 2mg/24 hours, 4mg/24 hours • Aveed 750mg/3mL vial • Testopel pellet implant • Testosterone implant pellet • Methyltestosterone (Testred) oral capsules • Methitest (methyltestosterone) oral tablets • Testone CIK (testosterone cypionate) intramuscular injection kit • Natesto (testosterone) nasal gel pump • Xyosted (testosterone enanthate) subcutaneous auto-injector • Jatenzo (testosterone undecanoate) oral capsules • Tlando (testosterone undecanoate) oral capsules • Kyzatrex (testosterone undecanoate) oral capsules Any other newly marketed agents in this class *Requests for greater than indicated Quantity Limits will be reviewed on a case by case basis
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	See "**PA Review Criteria**" below
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	See "**PA Review Criteria**" below
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** If all conditions are met, the request will be approved for up to 3 months. 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.

Testosterone Agents	

PA Review Criteria	*For GID/gender dysphoria coverage, please refer to the Gender Dysphoria medication guidelines for age less than 21 or greater than or equal to 21 years old.*
	
	INITIAL AUTHORIZATION CRITERIA:
	• Formulary, PA required (second-line) agents are approved if:
	  ○ Diagnosis of primary hypogonadism (congenital or acquired) or hypogonadotropic hypogonadism (congenital or acquired)
	  ○ Male member
	  ○ Documented testosterone level(s) below 300ng/dL(9.8-10.4 nmol/l) on two separate occasions with levels drawn before 10:00 am
	  ○ Documented trial and failure, contraindication, or intolerance to one formulary first line injectable testosterone AND one formulary first line topical testosterone
	• Non-formulary testosterone products are approved if:
	  ○ Diagnosis of primary hypogonadism (congenital or acquired) or hypogonadotropic hypogonadism (congenital or acquired)
	  ○ Male member
	  ○ Documented testosterone level(s) below 300ng/dL(9.8-10.4 nmol/l) on two separate occasions with levels drawn before 10:00 am
	  ○ Documented trial and failure, contraindication, or intolerance to one formulary first line injectable testosterone AND one formulary first line topical testosterone AND at least one formulary, PA required (second-line) agent
	REAUTHORIZATION CRITERIA
	• Diagnosis of primary hypogonadism (congenital or acquired) or hypogonadotropic hypogonadism (congenital or acquired).
	
	<u>For requests over the quantity limit:</u>
	• The member must have a documented treatment failure with the drug prescribed at the health plan's quantity limit **OR** the member requires a dose within prescribing guidelines that exceeds the plan's quantity limit. **AND**
	• The provider has submitted a medical reason why the plan's quantity limit will be inadequate based on the member's condition and treatment history. **AND**
	• The dose requested is supported by the Medical Compendia or current treatment guidelines.

Criteria Statement	(Formulary, PA required (second-line) medications) <INSERT: testosterone packets/tube/solution pump or testosterone enanthate> are reserved for members who have previously used (or cannot/should not take) testosterone cypionate injection AND testosterone (Vogelxo) 1% gel pump or testosterone (Androgel) 1.62% gel pump. Non-formulary testosterone products are reserved for members who have used (or cannot/should not use) testosterone cypionate AND testosterone (Vogelxo) 1% gel pump or testosterone (Androgel) 1.62% gel pump AND testosterone 1% gel packets, tube, or testosterone 30mg/1.5ml solution pump or testosterone enanthate 200mg/mL intramuscular oil. Requests for quantities over the quantity or fill limit are reserved for members who have a documented medical need for quantities in excess of the limits.
Last P&T Review Date	~~12/2023~~<u>12/2024</u>

Recommendation: No changes

Thalomid (thalidomide)	
Therapeutic Classes (AHFS)	IMMUNOMODULATORY AGENTS
Medications	Thalomid (thalidomide)
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	Prescribing physician is infectious disease specialist, oncologist, nephrologist, dermatologist, or hematologist
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	Thalomid is approved if: • Diagnosis of one of the following: ○ erythema nodosum leprosum ○ multiple myeloma ○ chronic graft-versus-host disease (GVHD) in hematopoietic stem cell transplant ○ AIDS-related aphthous stomatitis ○ Waldenstrom's macroglobunemia ○ Systemic light chain amyloidosis
Criteria Statement	Thalomid is reserved for members with erythema nodosum leprosum, multiple myeloma, chronic graft-versus-host disease (GVHD) in hematopoietic stem cell transplant, AIDS-related aphthous stomatitis, Waldenstrom's macroglobunemia, systemic light chain amyloidosis
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Topical Diclofenac	
Therapeutic Classes (AHFS)	Non-steroidal Anti-Inflammatory Agents
Medications	Formulary, Prior Authorization Required Diclofenac epolamine (Flector) 1.3% patch Diclofenac (Pennsaid) 2% pump Diclofenac (Pennsaid) 1.5% solution Non-Formulary Licart (diclofenac) 1.3% 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-auth** If all criteria are met, approve diclofenac (Pennsaid) 2% pump or diclofenac (Pennsaid) 1.5% solution for up to a 12 month duration or diclofenac (Flector) patch or Licart (diclofenac) patch for up to a 3 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 approval: • Diagnosis of osteoarthritis [diclofenac (Pennsaid) 1.5% topical solution] or acute pain [diclofenac (Flector) 1.3% patch] AND one of the following conditions are met: o Member is over 65 years o Member is currently taking oral anticoagulant o Documentation (by either attestation or claims data) of trial and failure, contraindication, or intolerance to one oral NSAID medication. AND o For diclofenac (Pennsaid) 1.5% topical solution, trial and failure or contraindication to use diclofenac (Voltaren) gel. OR o For diclofenac (Pennsaid) 2% pump, trial and failure or contraindication to use diclofenac (Voltaren) gel AND diclofenac (Pennsaid) 1.5% topical solution OR o For Licart (diclofenac) 1.3% patch, trial and failure or contraindication to use diclofenac epolamine (Flector) 1.3% patch
Criteria Statement	Diclofenac (Pennsaid) 1.5% solution is reserved for members with osteoarthritis who are either 65 years of age or currently using an oral anticoagulant and who have used (or cannot/should not use) one oral NSAID AND diclofenac (Voltaren) gel. Diclofenac (Flector) patch is reserved for members with acute pain who are either 65 years of age, currently using an oral anticoagulant, or who have used (or cannot/should not use) one oral NSAID. Diclofenac (Pennsaid) 2% pump is reserved for members with osteoarthritis who are either 65 years of age or currently using an oral anticoagulant and who have used (or cannot/should not use) one oral NSAID AND who have used (or cannot/should not use) diclofenac (Voltaren) gel and diclofenac (Pennsaid) 1.5% topical solution. Licart (diclofenac) 1.3% patch is reserved for members with acute pain who are either 65 years of age or currently using an oral anticoagulant and who have used (or

	cannot/should not use) one oral NSAID AND who have used (or cannot/should not use) diclofenac epolamine (Flector) 1.3% patch.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: Change naming of Noxafil to reflect its generic availability

Oral Anti-Fungals	
Therapeutic Classes (AHFS)	Azoles; antifungals miscellaneous
Medications	Formulary fluconazole 50, 100, 150, 200 mg tablet and 10, 40 mg/ml suspension terbinafine 250 mg tablet Formulary, with age restriction: limited to members ≤ 12 years griseofulvin microsize 125 mg/5 ml suspension Formulary, step therapy griseofulvin microsized 500 mg and ultramicrosized 125, 250 mg tablet Formulary, prior authorization required /Non-formulary voriconazole (Vfend) 50, 200 mg tablet and 200 mg/5 ml suspension itraconazole 100 mg capsules and 10 mg/ml suspension posaconazole delayed release-tablet ~~Noxafil (~~posaconazole~~)~~ (Noxafil) oral suspension Cresemba (isavuconazonium) capsule Flucytosine capsule
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
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	For **voriconazole**, approve if one of the following:
	• Diagnosis of one of the following:
	  • Invasive pulmonary aspergillus infections
	  • A serious fungal infection caused by Scedosporium apiospermum or Fusarium species
	  • Treatment of invasive candidiasis in critically ill patients
	  • Primary prophylaxis for aspergillus infections for special populations such as lung transplant, acute myeloid leukemia (AML), allo-stem cell transplant with prolonged neutropenia from chemotherapy AND high risk for infection
	• For esophageal candidiasis or candidemia in nonneutropenic patients: documentation of trial and failure, intolerance, or contraindication to fluconazole or nystatin
	• For blastomycosis or histoplasmosis: documentation of trial and failure, intolerance, or contraindication to itraconazole
	
	For **itraconazole** capsules, approve if one of the following:
	• Diagnosis of aspergillosis and documentation of intolerance or disease refractory to voriconazole capsules
	• Diagnosis of blastomycosis, histoplasmosis
	• Diagnosis of coccidioidal infections and documentation of trial and failure, intolerance, contraindication, or inability to use fluconazole

Oral Anti-Fungals	
	• Diagnosis of oropharyngeal or esophageal candidiasis and the member is immunocompromised. If the member is not immunocompromised, documentation of trial and failure, intolerance, contraindication, or inability to use oral fluconazole • Diagnosis of onchomycosis and documentation of trial and failure, intolerance, contraindication, or inability to use terbinafine or fluconazole For **griseofulvin** tablets, approve if: • Diagnosis of dermatophyte infections of the skin, hair, and nails: tinea barbae, capitis, corporis, cruris, pedis, unguium (onchomycosis) and documentation of trial and failure, intolerance, inability to use, or contraindication to use terbinafine 250 mg or topical therapy (e.g. ciclopirox 8% solution, terbinafine cream, gel, or solution) • If request is for oral solution, the above criteria must be met and documentation of inability or difficulty swallowing must be provided For **posaconazole tablets**, approve if one of the following: • For prophylaxis of invasive aspergillus or candida in patients at high risk of developing invasive aspergillus or candida due to being severely immunocompromised: trial and failure or inability to use voriconazole • For the treatment of invasive aspergillosis: trial and failure or inability to use voriconazole For ~~**Noxafil**~~ **posaconazole suspension,** approve if: • For oropharyngeal candidiasis, there is documentation of trial and failure, intolerance, or contraindication to fluconazole For **Cresemba**, approve if one of the following: • Diagnosis of invasive mucormycosis in adults • For invasive aspergillosis in adults, there is documentation of trial and failure, intolerance, or contraindication to voriconazole For **flucytosine**, approve if one of the following: • Diagnosis of cryptococcal meningitis or cryptococcosis • Diagnosis of candidiasis with CNS involvement, symptomatic urinary tract infections (e.g. cystitis, pyelonephritis, or fungal masses), endocarditis or infected cardiac devices, endophthalmitis, septicemia, or pulmonary infections **Reauthorization** • Documentation is provided that the member has responded to therapy • Additional therapy is medically necessary and clinically appropriate **NOTE**: ○ Requests for itraconazole solution require a documented trial and failure, or intolerance to itraconazole oral capsules unless the oral solution is being requested for diagnosis of oropharyngeal or esophageal candidiasis. ○ Requests for voriconazole suspension require a documented trial and failure, or intolerance to voriconazole tablets ○ Requests for flucytosine require combination therapy with amphotericin B for systemic candidiasis, cryptococcal meningitis, or cryptococcosis
Criteria Statement	**Voriconazole** tablets are reserved for members who have used (or cannot/should not use) a formulary medication (i.e. fluconazole or nystatin). For blastomycosis or

Oral Anti-Fungals	
	histoplasmosis, voriconazole tablets are reserved for members who have used (or cannot/should not use) itraconazole. **Voriconazole** oral suspension is reserved for members who have used (or cannot/should not use) voriconazole tablets. **Itraconazole** capsules are reserved for members who have used (or cannot/should not use) fluconazole or terbinafine tablets, **Itraconazole** oral solution is reserved for members who have used (or cannot/should not use) itraconazole capsules unless the oral solution is being requested for diagnosis of oropharyngeal or esophageal candidiasis. **Griseofulvin** tablets are reserved for members who have used (or cannot/should not use) terbinafine 250 mg tablet or topical medications. **Griseofulvin** oral solution is reserved for members who have used (or cannot/should not use) griseofulvin tablets. **Posacoazole** tablets are reserved for members who have used (or cannot/should not use) voriconazole. ~~**Noxafil**~~ Posaconazole suspension is reserved for members who have used (or cannot/should not use) fluconazole. **Cresemba** is reserved for members who have used (or cannot/should not use) voriconazole. **Flucytosine** is reserved for members who have a diagnosis of cryptococcal meningitis or cryptococcosis, candidiasis with CNS involvement, symptomatic urinary tract infections (e.g. cystitis, pyelonephritis, or fungal masses), endocarditis or infected cardiac devices, endophthalmitis, septicemia, or pulmonary infection.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Gattex (teduglutide)	
Therapeutic Classes (AHFS)	GI DRUGS, MISCELLANEOUS
Medications	Gattex (teduglutide)
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 month duration with a quantity limit of 1 kit per 30 days **Later Approvals** 12 month duration with a quantity limit of 1 kit 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 • Diagnosis of Short Bowel Syndrome (SBS) AND • Dependent on intravenous parenteral nutrition, defined as requiring parenteral nutrition at least three times per week.
Criteria Statement	Gattex is reserved for members with short bowel syndrome and who are dependent on intravenous parenteral nutrition at least 3 times a week.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors	
Therapeutic Classes (AHFS)	Vesicular Monoamine Transport 2 Inhibitor
Medications	Non-formulary, PA required: Ingrezza (valbenazine) capsules Austedo (deutetrabenazine) tablets Tetrabenazine (Xenazine) tablets 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	Concurrent use of monoamine oxidase inhibitors (MAOIs)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be a neurologist or psychiatrist.
Coverage Duration	**Initial Approval** 6 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Initial Authorization:** • Dose is within FDA-approved limits • Prescriber attests patient will not be receiving treatment with any other VMAT2 inhibitor **For approval for use in tardive dyskinesia (TD):** • Member must have clinical diagnosis of tardive dyskinesia that has persisted for the last 90 days, with documented baseline evaluation (e.g., Abnormal Involuntary Movement Scale (AIMS), the Tardive Dyskinesia Rating Scale (TDRS), etc.) • For members on antipsychotics, the antipsychotic dose(s) must have been stable for a continuous 90 day period at some point prior to the request • Prescriber has attempted at least ONE of the following strategies to manage the patient's condition, or has provided a clinical reason why NONE of the following are possible: o Reducing the dose of the drug responsible for causing dyskinesia o Discontinuing the drug responsible for causing dyskinesia o For members on first generation antipsychotics, switching to a second generation antipsychotic o Trial of benzodiazepines • For VMAT2 inhibitors other than tetrabenazine, member has a documented medical reason (e.g., treatment failure, intolerance, hypersensitivity, contraindication) for not using tetrabenazine AND o For Austedo requests: ▪ Prescriber attests patient has no signs of hepatic impairment ▪ For patients at risk for QT prolongation, prescriber attests a baseline ECG has been obtained o For Ingrezza requests: ▪ Must be dosed at one capsule per day **For approval for use in chorea associated with Huntington's Disease (HD):** • Patient must have diagnosis of moderate to severe Huntington's with chorea, with documented baseline Total Maximal Chorea (TMC) score provided

	• For VMAT2 inhibitors other than tetrabenazine, member has a documented medical reason (e.g., treatment failure, intolerance, hypersensitivity, contraindication) for not using tetrabenazine AND
	  ○ For Austedo requests:
	  ▪ Prescriber attests patient has no signs of hepatic impairment
	  ▪ For patients at risk for QT prolongation, prescriber attests a baseline ECG has been obtained
	  ○ For Ingrezza requests:
	  ▪ Must be dosed at one capsule per day
	
	Reauthorization:
	• Documentation or provider attestation of positive clinical response (e.g., improvement from baseline in average scores on the previously submitted symptom rating scale, decrease in symptoms, etc.)
	• Dose is within FDA approved limits

Criteria Statement	For a diagnosis of chorea with Huntington's disease, Austedo and Ingrezza are reserved for members who have used (or cannot/should not use) tetrabenazine. For a diagnosis of tardive dyskinesia, Austedo and Ingrezza are reserved for members who have used (or cannot/should not use) tetrabenazine.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Otezla (apremilast) for Behcet Disease	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	Otezla (apremilast)
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	Concurrent use with a biologic DMARD or targeted synthetic DMARD
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber is a rheumatologist or a dermatologist or is working in consultation with a rheumatologist or dermatologist
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer
PA Review Criteria	Criteria for initial authorization: • Drug is being requested at an FDA approved dose. • Documentation of clinical diagnosis of Behcet disease • Documentation of at least one active oral ulcer • Member is not concurrently taking a biologic DMARD (i.e. Orencia, Humira, Stelara, etc.) or a targeted synthetic DMARD (i.e. Olumiant, Xeljanz, etc.) • Documentation that the member has had (consistent with pharmacy claims data OR for new members to the health plan consistent with medical chart history) adequate trial and failure or intolerance to at least one formulary topical steroid and colchicine. Criteria for re-authorization: • Drug is being requested at an FDA approved dose. • Documentation that condition has improved or stabilized with therapy
FCriteria Statement	Otezla (apremilast) is reserved for members who have at least one active oral ulcer associated with Behcet disease and have used (or cannot/should not use) at least one formulary topical steroid and colchicine.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Rayaldee (calcifediol ER)	
Therapeutic Classes (AHFS)	Vitamin D Analog
Medications	Non-formulary, PA required Rayaldee (calcifediol ER)
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 nephrologist or endocrinologist (or working in consultation with a nephrologist or endocrinologist)
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	The following criteria must be met for initial requests: • Drug is being requested at an FDA approved dose. • Treatment of secondary hyperparathyroidism associated with a diagnosis of stage 3 or 4 chronic kidney disease (CKD) and is not on dialysis • A serum total 25-hydroxyvitamin D level less than 30 ng/mL and a serum corrected total calcium below 9.8 mg/dL • Documented trial and failure, contraindication, or documented inability to use a preferred vitamin D analog (ex. calcitriol) The following criteria must be met for renewal requests: • Drug is being requested at an FDA approved dose. • Serum total 25-hydroxyvitamin D levels between 30 and 100 ng/mL • Intact parathyroid hormone (PTH) levels within the desired therapeutic range of 10-65 ng/L • Serum calcium (corrected for low albumin) within the normal range for member • Serum phosphorus below 5.5 mg/dL
Criteria Statement	For the treatment of secondary hyperparathyroidism associated with stage 3 or 4 chronic kidney disease (CKD), Rayaldee is reserved for members who have used (or cannot/should not use) a preferred vitamin D analog (ex. calcitriol). Members must also have a serum total 25-hydroxyvitamin D level less than 30 ng/mL and a serum corrected total calcium below 9.8 mg/dl. The request will not be approved for patients with a diagnosis of stage 5 chronic kidney disease or end-stage renal disease on dialysis.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Korlym (mifepristone)	
Therapeutic Classes (AHFS)	Cortisol receptor blocker
Medications	Non-formulary, PA required Korlym (mifepristone)
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	Pregnancy
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by or in consultation with an endocrinologist
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	The following criteria must be met for initial requests: • Diagnosis of hyperglycemia secondary to endogenous Cushing's syndrome with type 2 diabetes mellitus (T2DM) or impaired glucose tolerance (IGT) • Drug is being requested at an FDA approved dose. • Member has failed pituitary surgery or is not a candidate for pituitary surgery • Documented trial and failure of insulin and at least 2 other conventional anti-hyperglycemic medications (ex. metformin, sulfonylurea, DPP-4 inhibitor, etc.) or a documented medical reason for not utilizing these medications. • For females of reproductive age: Must have documentation of a baseline negative pregnancy test within the previous 14 days The following criteria must be met for renewal requests: • Drug is being requested at an FDA approved dose. • Documentation of an improvement in or stabilization of glucose control (ex. reduction in fasting blood glucose, oral glucose tolerance test, or Hemoglobin A1c). • For females of reproductive age: Must have documentation of a recent negative pregnancy test within the previous 14 days
Criteria Statement	Korlym is reserved for members with hyperglycemia from Cushing's syndrome with type 2 diabetes or impaired glucose tolerance who have failed surgery or are not candidates for surgery. The member should have used (or cannot/should not use) other conventional anti-diabetic medications and female members must have a negative pregnancy test.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Tetracycline Antibiotics	
Therapeutic Classes (AHFS)	Tetracycline antibiotics
Medications	Formulary Doxycycline monohydrate 50mg, 100mg capsule Doxycycline monohydrate 100mg tablet Tetracycline 250mg, 500mg capsule Formulary, step therapy required Minocycline 100mg 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	**Minocycline ST and NF Tetracyclines Approval:** 6 months **Approval to Exceed QL:** 3 months If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**ALL medications in the tetracycline class are limited to a combined total of 180 days supply per 365 days**
	
	Minocycline capsule step therapy criteria:
	• Dose is appropriate per label or supported by compendia/standard of care guidelines, and is within posted quantity limits
	• Documentation of a trial and failure or intolerance to doxycycline required.
	OR
	• Documentation of culture and sensitivity data, showing minocycline is the only treatment option.
	
	Non-formulary and formulary, prior authorization required tetracyclines
	• Appropriate diagnosis/Indication for requested non-formulary or formulary, prior authorization required medication or meets off-label criteria below AND
	  ○ Off-label criteria:
	  ▪ No other formulary preferred 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 OR
	  ▪ Requested use can be supported by at least two published peer reviewed clinical studies
	• Appropriate dose of medication based on age (i.e. pediatric and elderly populations) and indication AND
	• Documentation of a trial and failure or intolerance with 3 formulary preferred tetracyclines required

	OR • Documentation of culture and sensitivity data, showing the non-formulary/prior authorization required tetracycline is the only treatment option <u>Request for exceeding quantity limit of 180 days per 365 days</u> • The member must have a documented treatment failure with the drug prescribed at the health plan's quantity limit OR the member requires a dose within prescribing guidelines that exceeds the plan's quantity limit. AND • The provider has submitted a medical reason why the plan's quantity limit will be inadequate based on the member's condition and treatment history. AND • The dose requested is supported by the Medical Compendia or current treatment guidelines.
	Minocycline capsule is reserved for members who have used (or cannot/should not use) doxycycline. Medications in the tetracycline class that are non-formulary or formulary, prior authorization required are reserved for members who have used (or cannot/should not use) at least 3 formulary preferred tetracyclines. Medications in the tetracycline class prescribed in quantities over 180 days supply per 365 days are reserved for members who have used (or cannot/should not use) tetracyclines under the quantity limit, whose prescriber has submitted a reason why this is necessary.
Last P&T Review Date	~~12/2023~~<u>12/2024</u>

Recommendation: No changes

Agents for graft versus host disease	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS, ANTINEOPLASTIC AGENTS
Medications	Rezurock (belumosudil) Imbruvica (ibrutinib) Jakafi (ruxolitinib phosphate) Orencia (abatacept)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for Healthcare Professional (USP DI), and the Drug Package Insert, and/or per the National Comprehensive Cancer Network (NCCN)
Exclusion Criteria	N/A
Required Clinical Information	See “other criteria”
Age Restrictions	According to package insert
Prescriber Restrictions	Prescriber must be a hematologist, oncologist, or other specialist in the treatment of hematopoietic cell transplants
Coverage Duration	Jakafi, Rezurock, and Imbruvica: If all of the conditions are met, the request will be approved for up to a 3 month duration for initial requests and up to a 6 month duration for renewal requests. Orencia: If all of the conditions are met, the request will be approved for 1 month duration (4 total treatments) If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	****For oncological indications, please refer to the “Oral and Injectable Oncology Medications” policy**** **Initial Authorization:** • Imbruvica o Member has a diagnosis of chronic graft versus host disease o Member has tried and failed or cannot use a systemic corticosteroid or documentation is provided as to why a systemic corticosteroid cannot be used o The drug is prescribed at an FDA-approved dose • Jakafi o Member has a diagnosis of acute graft versus host disease or a diagnosis of chronic graft versus host disease o Member has tried and failed or cannot use a systemic corticosteroid or documentation is provided as to why a systemic corticosteroid cannot be used o The drug is prescribed at an FDA-approved dose • Rezurock o Member has a diagnosis of chronic graft versus-host disease o Member has tried and failed at least two lines of systemic immunosuppressive therapy (e.g. corticosteroids, calcineurin inhibitors, mycophenolate mofetil, ibrutinib, ruxolitinib), one of which must be a systemic corticosteroid, or documentation is provided as to why a systemic corticosteroid cannot be used o The drug is prescribed at an FDA-approved dose • Orencia

	○ Orencia is being requested for prophylaxis against acute graft versus host disease ○ Member will be undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor ○ Member will be receiving Orencia in combination with a calcineurin inhibitor (e.g., tacrolimus, cyclosporine) and methotrexate ○ Member will be receiving antiviral prophylactic treatment for Epstein-Barr virus reactivation and will continue for 6 months following HSCT ○ Attestation provider has considered prophylactic antivirals for cytomegalovirus (CMV) infection/reactivation during treatment and for 6 months following HSCT ○ The drug is prescribed at an FDA-approved dose **Re-Authorization:** • Documentation is provided that the member has achieved a clinical benefit from medication (e.g. symptom improvement, reduction in corticosteroid dose) • The drug is prescribed at an FDA-approved dose
Criteria Statement	Imbruvica is reserved for members with a diagnosis of chronic graft versus host disease who have used (or cannot /should not use) a systemic corticosteroid. Jakafi is reserved for members with a diagnosis of acute graft versus host disease or a diagnosis of chronic graft versus host disease who have used (or cannot/should not use) a systemic corticosteroid. Rezurock is reserved for members with a diagnosis of chronic graft versus-host disease who have used (or cannot /should not use) at least two lines of systemic immunosuppressive therapy (e.g. corticosteroids, calcineurin inhibitors, mycophenolate mofetil, ibrutinib, ruxolitinib), one of which must be a systemic corticosteroid. Orencia is reserved for members with a need for prophylaxis against acute graft versus host disease who will be undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor, using Orencia in combination with a calcineurin inhibitor (e.g., tacrolimus, cyclosporine) and methotrexate.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Janus Kinase Inhibitors for Nonsegmental Vitiligo	
Therapeutic Classes (AHFS)	SKIN AND MUCOUS MEMBRANE AGENTS, MISC.
Medications	Opzelura (ruxolitinib)
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	> 12 years of age
Prescriber Restrictions	Dermatologist, immunologist, or specialist experienced in the treatment of vitiligo
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 nonsegmental vitiligo ○ Documentation of depigmented lesions including measurements and locations is provided ○ Prescriber attests that the total body vitiligo area (facial and nonfacial) being treated does not exceed 10% BSA ○ Trial and failure of, or intolerance to, ALL of the following: ○ Topical corticosteroids ○ Topical calcineurin inhibitors ○ Targeted phototherapy ○ Prescriber attests that the member will not concomitantly use therapeutic biologics, other Janus kinase inhibitors, potent immunosuppressants, or phototherapy for repigmentation purposes ○ Request is for an FDA-approved dose ****A MAXIMUM OF ONE 60 GRAM TUBE OF OPZELURA PER WEEK OR ONE 100 GRAM TUBE EVERY TWO WEEKS MAY BE APPROVED**** **Reauthorization** ○ Prescriber attests that the member has experienced a clinical benefit (e.g. reduction in size or quantity of or stabilization of existing depigmented lesions; absence of new depigmented lesions) ○ Request is for an FDA-approved dose
Criteria Statement	Opzelura is reserved for members with a diagnosis of nonsegmental vitiligo, with the total body vitiligo area (facial and nonfacial) being treated not exceeding 10% body surface area (BSA), who have used (or cannot/should not use) all of the following: topical corticosteroids, topical calcineurin inhibitors, and targeted phototherapy
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Budesonide Nebulization Solution (Pulmicort Respules)	
Therapeutic Classes (AHFS)	ORALLY INHALED PREPARATIONS (STEROIDS)
Medications	Budesonide nebulization solution (Pulmicort Respules)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “other criteria”
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	○ Documentation as to why the member cannot use a preferred formulary corticosteroid via inhaler ○ Total daily dose should not exceed 2 mg. Doses beyond 2 mg/day should be reviewed for medical necessity.
Criteria Statement	Budesonide nebulization solution (Pulmicort Respules) are reserved for members who have used (or cannot/should not use) a preferred formulary corticosteroid via inhaler at doses that do not exceed 2mg per day.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Lodoco	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS
Medications	Lodoco (colchicine) tablets
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a cardiologist
Coverage Duration	If all the criteria are met, the initial request will be approved for 12 months.

PA Review Criteria	**Initial Authorization**:
	• Patient has established atherosclerotic disease or multiple risk factors for cardiovascular disease
	• Patient is currently receiving statin therapy, or documentation has been provided that the member has a medical reason statin therapy is not appropriate
	• Documentation is provided that guideline directed medical therapies targeted to patient's specific risk factors are being maximized, such as medications targeted at reduction in cholesterol, blood pressure, antiplatelet therapies, and diabetes
	• Patient does not have pre-existing blood dyscrasias (ex. leukopenia, thrombocytopenia)
	• Patient does not have renal failure (CrCl less than 15 ml/min) or severe hepatic impairment
	• Patient is not currently taking medications contraindicated for concurrent use with Lodoco
	  ○ Strong CYP3A4 inhibitors (ex. atazanavir, clarithromycin, darunavir/ritonavir, indinavir, itraconazole, ketoconazole, lopinavir/ritonavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, tipranavir/ritonavir)
	  ○ P-glycoprotein inhibitors (ex. cyclosporine, ranolazine)

Criteria Statement	Lodoco is reserved for members with a diagnosis of established atherosclerotic disease or multiple risk factors for cardiovascular disease who are currently taking a statin (or cannot/should not take a statin) and does not have pre-existing blood dyscrasias or renal failure (CrCl less than 15 ml/min) or severe hepatic impairment.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: No changes

Sohonos	
Therapeutic Classes (AHFS)	Other Miscellaneous Therapeutic Agents
Medications	Sohonos (palovarotene)
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	• Pregnancy • Use in patients younger than 8 years of age for females and 10 years of age for males
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age Per package insert
Prescriber Restrictions	Prescribed by an orthopedic specialist or provider who specializes in rare connective tissue diseases
Coverage Duration	If all of the criteria are met, the initial or reauthorization request will be approved for up to 6 months taking into account patient specific scenarios
PA Review Criteria	**Initial Authorization:** • Documented diagnosis of fibrodysplasia ossificans progressiva (FOP) • Documented genetic testing of ACVR1 R206H mutation • Attestation that patient is not pregnant and appropriate contraception methods will be used at least 1 month before treatment, during treatment, and 1 month after the last dose (if applicable) • Documentation of weight for patients younger than 14 years old • Medication is prescribed at an FDA approved dose **Re-Authorization:** • Documentation or provider attestation of clinical benefit (i.e. volume reduction of heterotopic ossification) or worsening (i.e. flare-up presence and/or worsening of flare-ups) • Attestation that patient is not pregnant and appropriate contraception methods will be used at least 1 month before treatment, during treatment, and 1 month after the last dose (if applicable) • Documentation of weight for patients younger than 14 years old • Medication is prescribed at an FDA approved dose
Criteria Statement	Sohonos is reserved for members with a diagnosis of fibrodysplasia ossificans progressiva (FOP) with documented genetic testing of ACVR1 R206H mutation, who is not pregnant and appropriate contraception methods will be used at least 1 month before treatment, during treatment, and 1 month after the last dose (if applicable), with a weight documentation for those members younger than 14 years old.
Last P&T Review Date	~~12/2023~~12/2024

Alameda PADs for review Q4 2024 P&T Consent Agenda

Recommendation: No changes

Injectable/Specialty Medications	
Medications	INJECTABLE/SPECIALTY MEDICATIONS WITH NO OTHER DRUG-SPECIFIC OR DIAGNOSIS-SPECIFIC CRITERIA *** The Oral and Injectable Oncology Medications Physician Administered Drug (PAD) medication request guideline will be applied to oncology drugs without drug or class 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), 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	Up to a 12 month duration depending upon the diagnosis and usual treatment therapies
Maximum Billable Units	Variable
Other Criteria	**Initial Approval** 1. The request for the medication is for an FDA approved indication, and/or is used for a medical condition that is supported by the medical compendium (Micromedex, American Hospital Formulary Service, Drug Points, and Drug Package Insert) as defined in the Social Security Act 1927 and/or per recognized standard of care guidelines. 2. Prescribed dosing of medication is within FDA approved indications and/or is supported by the medical compendium as defined above and/or per recognized standard of care guidelines. 3. For any medication where a biosimilar is available, when indicated, the member must have documented 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. 4. If all of the above conditions are met, the request will be approved for up to 12 months or as recommended per FDA approved indications and/or as defined by the medical compendium as defined above and/or per recognized 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. **Reauthorization of Medication** 1. The prescribing physician has provided documentation as to the clinical benefits of the medication supporting continued treatment, **OR** the medication is being continued in accordance with the recommended time as defined by FDA drug package insert, and/or per recommendations of the medical compendium as described above, and/or per recognized standard of care guidelines. 2. Prescribed dosing of medication is within FDA approved indications or per supported by the medical compendium as defined above and/or per recognized standard of care guidelines.

	3. For any medication where a biosimilar is available, when indicated, the member must have documented 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. 4. If all of the above conditions are met, the request will be approved for up to 12 months or as recommended per FDA approved indications and/or as defined by medical compendium as defined above and/or per recognized 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	~~12/2023~~12/2024

Recommendation: No changes

Oral and Injectable Oncology Medications	
Medications	Oral and Injectable Oncology Medications without medication-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 Healthcare Professional (USP DI), and the Drug Package Insert, and/or per the National Comprehensive Cancer Network (NCCN)
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	Prescriber must be an oncologist
Coverage Duration	Up to a 6 month duration depending upon the diagnosis and usual treatment therapies
Maximum Billable Units	Variable
Other Criteria	All of the following criteria must be met: • Requested indication must be supported by NCCN category 1 or 2A level of evidence. If the request is for a category 2B recommendation then the medical documentation has been provided as to why member is unable to utilize a treatment regimen with a higher level of evidence (e.g. allergic reaction, contraindication). • Documentation provided of results of genetic testing where required per drug package insert. • Documentation provided of results of all required laboratory values and member specific information (e.g., weight, ALT/AST, creatinine kinase, etc.) when recommended/required per drug package insert. • The medication is being prescribed at a dose that is within FDA approved/NCCN guidelines. • For any medication where a biosimilar is available, when indicated, the member must have documented 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. • For requests for IV medications: attestation medication is administered by a healthcare professional (Medi-Cal only). If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~12/2023~~12/2024

Recommendation: No changes

Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	
Medications	**Ocrevus (ocrelizumab)** **Ruxience (rituximab-pvvr) - biosimilar** **Truxima (rituximab-abbs) - biosimilar** **Rituxan (rituximab)** **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 "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	For requests for Tysabri for the indication of Crohn's disease, please see the Injectable/Specialty Medications policy **** When the biosimilar is indicated, the member must have documented dates of trial and failure, intolerance, inability to use, or contraindication to the biosimilar medication prior to the brand medication approval, OR the currently available biosimilar product does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested, in addition to meeting all applicable criteria below.** **Initial Authorization** Clinically Isolated Syndrome (CIS), Relapsing Remitting MS (RRMS), Secondary Progressive MS (SPMS) ○ Diagnosis of CIS, RRMS, or SPMS ○ The medication is being prescribed at a dose consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature ○ 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 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	~~12/2023~~12/2024

Recommendation: No changes

Viltepso	
Medications	Viltepso (viltolarsen)
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 with another antisense oligonucleotide (e.g. Vyondys 53)
Required Clinical Information	See "other criteria"
Age Restrictions	Age ≤ 20 years Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a neurologist, or a provider who specializes in the treatment of DMD
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:** • Member has a confirmed diagnosis of Duchenne's Muscular Dystropy (DMD) and lab test was submitted confirming the mutation of dystrophin gene amenable to exon 53 skipping • Member is ambulatory • Member has stable pulmonary and cardiac function • Attestation of renal function monitoring is provided with request • Baseline dystrophin levels AND results of motor function tests are provided [e.g. 6-Minute Walk Test (6MWT), Time to Stand Test (TTSTAND), Time to Run/Walk Test (TTRW), North Star Ambulatory Assessment (NSAA), Time to Climb 4 Steps Test (TTCLIMB)] • Member must be on a stable corticosteroid regimen for at least 3 months • The request is for an FDA approved dose **Reauthorization:** • Documentation is provided that the member had an increase in dystrophin levels from baseline • Documentation is provided that the member had a positive clinical response (e.g. improvement, stabilization, or reduction of deterioration in 6MWT, TTSTAND, TTRW, NSAA, or TTCLIMB) • Member is ambulatory • Attestation of renal function monitoring is provided with request • 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	~~12/2023~~12/2024

Recommendation: No changes

Veopoz	
Medications	Veopoz (pozelimab-bbfg)
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 unresolved Neisseria meningitidis infection • Concurrent use of another complement inhibitor (i.e. Soliris)
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must have experience in treating complement related disorders (i.e., gastroenterologist, immunologist, cardiologist, etc.)
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 12 months.
Other Criteria	**Initial Authorization:** • Medication is prescribed at an FDA approved dose • Diagnosis of CD55-deficient protein-losing enteropathy (PLE), also known as CHAPLE disease • Documentation of hypoalbuminemia (serum albumin <3.5 g/dL) • Documentation of patient weight **Re-Authorization:** • Documentation or provider attestation of positive clinical response (i.e. symptom improvement, normalization of labs such as serum albumin (3.5-5.5 g/dL) and IgG concentrations, reduced hospitalizations and severe adverse events, increased quality of life, etc.) • Documentation of patient weight • 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	~~12/2023~~12/2024

Recommendation: No changes

Lantidra	
Medications	Lantidra (donislecel)
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 18 years of age and older
Prescriber Restrictions	Prescriber must be an endocrinologist
Coverage Duration	If all criteria are met, the request will be approved for one infusion. A member may only receive a maximum of 3 infusions per lifetime as there is no data regarding the efficacy or safety for treatment with more than 3 infusions.

Other Criteria	**Initial Authorization**
	• Documentation of Type 1 Diabetes diagnosis for more than 5 years
	• Documentation of blood glycated hemoglobin (HbA1c) above target goal
	• Documentation of intensive insulin management efforts (i.e., adjusting insulin regimen to multiple daily injections, frequently monitoring blood glucose levels daily, the use of devices such as a continuous glucose monitor, etc.)
	• Member has at least one of the following, despite intensive insulin management efforts:
	  ○ Inability to sense hypoglycemia until the blood glucose falls to less than 54 mg/dL
	  ○ At least 1 or more episodes of severe hypoglycemia (blood glucose below 50 mg/dL) in the past 3 years
	• Provider must confirm the following:
	  ○ Blood glycosylated hemoglobin (HbA1c) is not higher than 12%
	  ○ Member has an insulin requirement of no more than 0.7 International Units (IU)/kilogram/day
	  ○ Member has a Body Mass Index (BMI) less than 27 kg/m^2
	  ○ Member is not diagnosed with a psychiatric disorder (i.e., schizophrenia, bipolar disorder, or major depression)
	  ○ Member does not have severe cardiac disease as defined by: Recent myocardial infarction within the past 6 months, angiographic evidence of non-correctable coronary artery disease, or evidence of ischemia on a functional cardiac exam
	• Provider attests that member will be receiving concomitant immunosuppression therapy
	• Drug is being requested at an FDA-approved dose
	• Member's weight
	
	Reauthorization
	• Member has not achieved independence from exogenous insulin within one year of infusion OR member has lost independence from exogenous insulin within one year after a previous infusion
	• Provider attests that member will be receiving concomitant immunosuppression therapy

	• Drug is being requested at an FDA-approved dose • Member's weight 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	~~12/2023~~12/2024

Recommendation: No changes

Bleeding Disorder Products	
Therapeutic Classes (AHFS)	Hemostatics
Medications	Advate, Adynovate, Afstyla, Alphanate, Alphanine SD, Alprolix, Altuviiio, Benefix, Eloctate, Esperoct, Hemlibra, Hemofil M, Humate-P, Idelvion, Ixinity, Jivi, Koate, Koate-DVI, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Profilnine, Rebinyn, Recombinate, Rixubis, Wilate, Xyntha, Xyntha Solofuse, Obizur, Vonvendi, Coagadex, Corifact, Feiba, NovoSeven RT, Tretten, Sevenfact, Fibryga RiaStap, and any newly marketed blood product indicated for a bleeding 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 "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age Patient must be age appropriate per package insert
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	If all of the criteria are met, the request will be approved for 1 month. If the provider states that the requested medication is for a chronic or long-term condition for which the medication may be necessary for the life of the patient, the request will be approved for 12 months.
Other Criteria	• Patient has a diagnosis of a bleeding disorder and the type of deficiency has been provided • Product is being used for an FDA-approved indication at an FDA approved dose or the indication/dose are otherwise supported by treatment guidelines or compendia 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	~~12/2023~~12/2024

Alameda Alliance for Health (IHSS)

Q4 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
Zepbound Subcutaneous Solution 2.5 MG/0.5ML	NF to F-PA
Zepbound Subcutaneous Solution 5 MG/0.5ML	NF to F-PA
Otezla Oral Tablet 20 MG	NF to F-PA
Otezla Oral Tablet Therapy Pack 4 x 10 & 51 x20 MG	NF to F-PA
Novavax COVID-19 Vaccine Intramuscular Suspension Prefilled Syringe 5 MCG/0.5ML	NF to F
Comirnaty Intramuscular Suspension 30 MCG/0.3ML	F to NF
Comirnaty Intramuscular Suspension Prefilled Syringe 30 MCG/0.3ML	F to NF
Novavax COVID-19 Vaccine Intramuscular Suspension 5 MCG/0.5ML	F to NF
Spikevax Intramuscular Suspension 50 MCG/0.5ML	F to NF
Spikevax Intramuscular Suspension Prefilled Syringe 50 MCG/0.5ML	NF to F
Comirnaty Intramuscular Suspension Prefilled Syringe 30 MCG/0.3ML	NF to F
Potassium Chloride ER Oral Tablet Extended Release 15 MEQ	NF to F
Dasatinib Oral Tablet 20 MG	NF to F-PA
Dasatinib Oral Tablet 50 MG	NF to F-PA
Dasatinib Oral Tablet 70 MG	NF to F-PA
Dasatinib Oral Tablet 100 MG	NF to F-PA
Dasatinib Oral Tablet 80 MG	NF to F-PA
Dasatinib Oral Tablet 140 MG	NF to F-PA
OXcarbazepine ER Oral Tablet Extended Release 24 Hour 300 MG	NF to F
OXcarbazepine ER Oral Tablet Extended Release 24 Hour 600 MG	NF to F
Sprycel Oral Tablet 20 mg	F-PA to NF
Sprycel Oral Tablet 50 mg	F-PA to NF
Sprycel Oral Tablet 70 mg	F-PA to NF
Sprycel Oral Tablet 100 mg	F-PA to NF
Sprycel Oral Tablet 80 mg	F-PA to NF
Sprycel Oral Tablet 140 mg	F-PA to NF
Oxtellar XR Oral Tablet Extended Release 24 Hour 300 MG	F to NF

Medication	Formulary Change
Oxtellar XR Oral Tablet Extended Release 24 Hour 600 MG	F to NF

POLICY AND PROCEDURE TEMPLATE

Policy Number	RX-004
Policy Name	Formulary Management
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	IHSS
Effective Date	10/01/2007
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	TBD~~3/19/2024~~
Compliance Committee Approval Date	TBD~~4/10/2024~~

POLICY STATEMENT

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

PROCEDURE

A. Formulary

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

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

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

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

~~1.~~ The P&T Committee's voting membership is as described in RX-005 P&T Committee Roles and Scope.~~consists of the Alliance's Chief Medical Officer or designee, the Alliance Senior Director of Pharmacy Services or designee,~~

1. ~~(4) four licensed practicing physicians and practicing community pharmacists contracted with Alliance (not to exceed 1/3 of the voting membership of the committee or three pharmacists, whichever is greater). The non-voting membership may include a clinical pharmacist from the Alliance's Pharmacy Benefit Manager (PBM), a representative from the Alliance's Quality Improvement Unit, Alliance Operations Unit, and practicing physicians representing a medical specialty as needed in accordance with the agenda and the specific medications or subjects being reviewed.~~

2. Per the P&T Charter, the P&T Committee is responsible for the following:
   a. Develop and implement effective drug utilization review treatment outcome systems to optimize the quality of the pharmacy services
   b. Review the formulary on a quarterly basis
   c. Ensuring that the formulary review considers all drugs approved by the Federal Drug Administration (FDA)
   d. Ensuring that deletions from the formulary are documented and justified.
3. The following are considered by the P&T Committee when reviewing the formulary:
   a. Alliance Provider recommendations for additions or deletion of drugs to the formulary
   b. Bioavailability data
   c. Cost comparisons against other drugs available to treat the same medical condition(s)
   d. Current therapeutic guidelines
   e. Dosage ranges by route and age
   f. Findings from the following agencies: governmental agencies, medical and pharmaceutical associations, the National Institute of Health, and regulatory body publications
   g. Medical literature and clinical trials
   h. Off-label uses
   i. Patient risk factors relative to contraindications, warnings, and precautions
   j. Patient utilization and experience
   k. Pharmacokinetic data
   l. Pharmacologic considerations (e.g. drug class, similarity to existing drugs, side effect profile, mechanism of action, therapeutic indication, drug-to-drug interaction potential, and clinical advantages over other products in the specific drug class)
   m. Risks versus benefits regarding clinical efficacy and safety of a particular drug relative to other drugs with the same indication
   n. Special monitoring or medication administration requirements

C. Notification of Formulary Changes to Providers and Members

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

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

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

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

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

D. Content Management of Formulary Changes

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

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

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

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

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

DEFINITIONS / ACRONYMS

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

AFFECTED DEPARTMENTS/PARTIES

Utilization Management
Pharmacy Services
Member Services
Provider Relations

Communications and Outreach

RELATED POLICIES AND PROCEDURES

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

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

Attachment 1: Request for Formulary Review

REVISION HISTORY

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

REFERENCES

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

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

This policy will be reviewed annually to ensure effectiveness.

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POLICY AND PROCEDURE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Medicare Medication Coverage under Part A, Part B or Part D
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCARE
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance) follows the regulations and guidelines established by the Centers for Medicare & Medicaid Services (CMS) that governs for determining if a medication is eligible for payment under Medicare Part A or B vs. Part D. The purpose of this policy is to describe the guidelines the Alliance utilizes to determine if the medication requested can be covered under Part A or B or Part D. Most medications are covered under Part D, but there are some medications that can be covered under both Part B or Part D depending on what the drug is used for and how it is administered.

Regulatory Background: Medicare Managed Care Manual Part D Benefits Chapter 6 Section 20.2.2 (Rev. 18 -15-16)

20.2.2 - Part D Sponsor Due Diligence in Prior Authorization of Part A or B Versus Part D Coverage Determination (Rev. 18, Issued: 01-15-16, Effective: 01-15-16; Implementation: 01-15-16) A drug approved or denied through prior authorization constitutes a coverage determination, subject to all applicable coverage determination standards, timelines, and requirements. However, Part D sponsors should rely upon (1) information included by the physician with the prescription, (2) information communicated by the pharmacist or included with the submitted claim, such as diagnosis information (e.g., to determine whether the prescription is related to a Medicare covered transplant), (3)

information captured by the plan sponsor previously, such as diagnosis information from previous PAs, and (4) location of administration (e.g., to determine if the prescription is being dispensed for a beneficiary in a nursing home) when available to avoid the need for a separate coverage determination request to obtain the needed information whenever possible. Assuming the available information is sufficient to correctly assign payment to Part A or B or Part D, there is no need in such cases to require additional information to be obtained from the physician.

To the extent that the Part D sponsor requires its contracted pharmacies to report the information provided on the prescription to assist in the determination of Part A or B versus Part D coverage, the sponsor should rely on the pharmacist's report of appropriate information to appropriately adjudicate the claim under Part D. For example, for cases in which prednisone is prescribed for a condition other than immunosuppression secondary to a Medicare-covered transplant, and this is either documented on the prescription, or evident based on the prescriber's specialty, a known diagnosis, or concomitant therapies, a sponsor may cover the drug under Part D without seeking further information from the prescribing physician.

This clarification should not be construed to indicate that a Part D sponsor may not impose prior authorization or other procedures to ensure appropriate coverage under the Medicare drug benefit. Part D sponsors may apply prior authorization to establish appropriate payment under Part A or B or Part D, even if the beneficiary is currently taking the drug. However, CMS believes that the sponsor will have met appropriate due diligence standards without further contacting a physician if necessary and sufficient information is available, and the contracted pharmacy is able to communicate this information to the sponsor in order to make the coverage determination. Refer to section 30.2.2.3 for additional guidance on the application of PAs. For more information on Coverage Determination requirements, see Medicare Prescription Drug Benefit Manual, chapter 18, available at **https://www.cms.gov/Medicare/Appeals-andGrievances/MedPrescriptDrugApplGriev/Downloads/Chapter18.zip**.

Best practice for B v D resolution (CMS Best Practice Memo, dated August 27, 2014):

Sponsor initiated an internal review process to aggressively resolve Part B vs. Part D rejections from the previous day by reviewing all rejections and proactively beginning a coverage determination if one had not already begun. The process included researching information, such as call logs and claims history, and performing outreach to pharmacies and prescribers to determine the appropriate coverage in each case. This proactive approach ensured that beneficiaries did not experience more than a one day delay in access to medication as a result of Part B vs. Part D system rejections.

PROCEDURE

1.1 The Alliance may rely upon physician information included with the prescription, such as diagnosis information or the location where the medication will be administered to authorize coverage at Point of Sale (POS). Network pharmacists may utilize the call-center to request prescription authorization/override edits if the required information is available. If there is not evidence to determine coverage under Part A or Part B or Part D at POS a coverage determination must be submitted by either the prescriber or the member or the member's authorized representative.

1.1.1 If a coverage determination is submitted to determine Medicare A vs B vs D coverage, the CMS requirements for coverage determination timelines, clinical decisions and member/provider

notification apply and are described in Policy XXXXX.

1.1.2 The Alliance reviews daily rejected Part D claims to ensure appropriate member outreach and expeditious treatment for all rejected claims with NCPDP codes A3, A4, A5 or A6 (insert specific MI codes utilized) xxxx.

1.2 The following tables provide information for the most commonly utilized Part A vs Part B vs Part D determinations. Additional information may be found in Appendix C **Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements** *(Rev. 18, 01-15-16)*

Medications	Part B	Part D
Erythropoieten (Epoetin Alpha or Epogen)	If patient has End-Stage Renal Disease (ESRD), is receiving dialysis and needs medication to treat anemia. It may be administered by doctor, ESRD facility, or home therapy program. It is also covered for conditions other than ESRD if administered by a doctor.	If patient has a condition other than ESRD and the medication is purchased at the pharmacy.
Immunosuppressive medications for transplant patients	Transplant occurred in a Medicare certified facility and member was enrolled in Medicare Part A.	Transplant was not paid for by Medicare or was in a non-Medicare certified facility
Infusion medications	Medications administered by an implantable infusion pump, or an external infusion pump used at home.	Medications administered by an infusion pump outside of the home (i.e., skilled nursing facility or hospital) and the stay is not covered by Part A. Drugs administered by an external infusion pump that is used in the home but the DME contractor does not covered them for Part B use in the home.
Medications	**Part B**	**Part D**
Inhalation medications with nebulizer	Inhalation medications used with a nebulizer in the home.	Inhalation medications used with a nebulizer in a skilled nursing facility or as in inpatient in the hospital and the stay is not covered by Part A.
Injectable Medications	The medication generally cannot be self-administered and the doctor provides and administers the medication.	The medication is purchased at the pharmacy and is administered by the doctor or the patient.

Injectable Osteoporosis Medications (women who meet certain conditions)	Patient receives Medicare home health benefits and has a bone fracture related to post-menopausal osteoporosis. The Medicare home health agency provides and administers the medication.	Patient does not receive Medicare home health benefits or meets the requirements for Part B coverage, but obtains the medication directly from the pharmacy.
Intravenous Immunoglobulin (IVIG)	If used to treat immune deficiency disease and it is used in the home.	If used to treat conditions others than immune deficiency disease and it is used in the home.
Oral Anti-Cancer Medications	An oral anti-cancer drug that was once available only in an injectable form that was covered by Medicare. It must be used to treat cancer and can be administered by the patient or a doctor.	The medication is used to treat a condition other than cancer.
Medications	**Part B**	**Part D**
Oral Anti-Nausea Medications (Anti-Emetics)	Must be related to cancer and used a full replacement for IV treatment. Must also be administered within 48hrs of cancer treatment. It can be administered by the patient or a doctor.	The medication is used for conditions other than cancer. It may also be used more than 48hrs after cancer treatment or is not a full replacement for IV treatment.
Parenteral Nutrition (administered by infusion)	If patient cannot absorb nutrition through the intestines.	If used for reasons other than a digestive track that does not work.
Vaccines	Flu, pneumonia and Hepatitis B	All other commercially available vaccines, including the shingles vaccine.

DEFINITIONS / ACRONYMS

Centers for Medicare and Medicaid Services (CMS)

The division of the federal Department of Health and Human Services responsible for the administration and oversight of the Medicare program and works in partnership with state governments to administer various Medicaid programs at the State level.

Coverage Determination

Any decision made by or on behalf of the Alliance regarding payment or benefits to which an Enrollee believes he or she is entitled.

Enrollee

A Part D eligible individual who has elected a Part D plan offered by The Alliance or an Alliance client.

ESRD

End-stage Renal Disease; permanent kidney failure that requires a regular course of dialysis or a kidney transplant.

Hospice

Care designed to give supportive care to the final stage of terminal illness and focuses on comfort and quality rather than cure.

Part D

Any outpatient medication benefit for anyone with Medicare. A Medicare member must have either Medicare Part A or Medicare Part B to be eligible for Medicare Part D.

Part B

The Medicare outpatient benefit that cover's most doctor's services, durable medical equipment, ambulance and other services.

Point of Sale (POS)

A capability of retail pharmacies to electronically access plan design and eligibility information to process and transmit drug claims data at the time of purchase.

Prior Authorization (PA)

A process whereby certain designated preferred drugs must meet established criteria before the prescription can be covered.

Redetermination

The first level of the appeal process, which involves a Part D plan sponsor reevaluating an adverse Coverage Determination, the findings upon which it was based, and any other evidence submitted or obtained.

Representative

An individual either appointed by an Enrollee or authorized under State or other applicable law to act on behalf of an Enrollee in filing a Grievance, requesting a Coverage Determination, or in dealing with any of the levels of the Appeals process. Unless otherwise stated in part 423, subpart M of the Medicare Part D regulations, the Representative has all the rights and responsibilities of an Enrollee in obtaining a Coverage Determination or in dealing with any of the levels of the Appeals process, subject to the rules described in part 422, subpart M of the Medicare Part C regulations.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

42 CFR §422.112(b)(7); *Centers for Medicare and Medicaid, Prescription Drug Benefit Manual, Chapter 6, Sec. 20.2, Appendices B and C; and Centers for Medicare and Medicaid, Prescription Drug Benefit Manual, Chapter 18, Sec. 30-70; HPMS Memo – Common Conditions, Improvement Strategies, and Best Practices based on 2013 Program Audit Reviews, August 27, 2014.*

MONITORING

1.1 In addition to daily rejected claims review, the Alliance staff supervisors will perform quarterly sample reviews to ensure compliance with CMS regulations and the Alliance policies and procedures. The results of these quarterly internal audits will be provided to the Alliance Compliance Department.

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POLICY AND PROCEDURE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Claim Adjudication
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCARE
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

The Alameda Alliance for Health (the "Alliance) general policy on claims processing and timeframes as well as other processing standards applicable to Medicare Part D claims submitted by pharmacies, beneficiaries and by State Medicaid agencies for purposes of subrogation. To establish an oversight process for the Medicare claim processing performed by the delegated entity that includes assurance of compliance with CMS requirements per the Prescription Drug Benefit Manual chapters 5, 6 and 13.

PROCEDURE

The Alliance assures claims are adjudicated under the Medicare benefit in accordance with Centers for Medicare and Medicaid (CMS) policy. Currently the Alliance Claim processing function is a delegated function of the contracted PBM.

1. Claim processing (see PBM Claims Processing Policy XXXX)

   A. HIPAA Compliance and Pharmacy Certification Status: Medicare Part D claims are edited to ensure that the pharmacy has submitted a compliant transaction according to both HIPAA and NCPDP transaction standards and that the submitter of the transaction has been certified to submit production claims to XXXXX PBM.

1. Verification of Eligibility: The following items are validated to process the claim. Eligibility edit checks are performed to determine that:
    a. The group in which the beneficiary is enrolled is valid and eligible.
    b. The beneficiary for whom the prescription was written is eligible in that group on the date of service as well as ensuring the claim is submitted in the proper order when a beneficiary has multiple coverages.
    c. The pharmacy is a contracted network pharmacy with XXXXX PBM and the type of contract in place (long term care, home infusion, retail, etc.) for the patient location indicated is compliant with CMS regulations. The National Drug Code (NDC) for the claim submitted is valid.

B. Verification of Prescriber status:
    1. Pharmacy claims access prescriber files to determine that the prescriber ID has been provided and is not on the CMS excluded list. See XXX PBM Medicare Policy XXXX - Excluded Prescriber Policy

C. Verification of Pharmacy Network status:
    1. The pharmacy dispensing the drug is verified for participation in the beneficiary's network. If the pharmacy is out of network then:
        a. Pharmacy claims are rejected as out of network
        b. Direct claims require that the beneficiary indicate whether the situation was due to an emergency or not

D. Verification of drug coverage:
    1. The drug file identifies the components of the drug (brand, generic, Medicare B/D status, and other classification pertinent to the drug. The drug will also be checked against the CMS non-matched manufacturer list.
    2. The drug is then verified against the overall benefit plan in terms of coverage and other specific limitations and requirements including:
        a. If the drug is included or excluded under the benefit Plan limitations in terms of refills, quantities and days supply, etc;
        b. If the drug is a Medicare covered, excluded, enhanced, or B drug;
        c. Whether a drug requires prior authorization or not;
    3. The drug is then reviewed against any approvals for or exceptions to including any transition rules that may apply against any prior authorization records in existence for this beneficiary/drug combination and timeframe.
    4. The formulary status of the drug is validated and when not formulary, transition rules are applied as appropriate (see transition policy).
    5. Compound and vaccine rules are applied per CMS guidelines

E. Verification of clinical rules and health and safety protocols:
    1. Concurrent Drug Utilization Review (CDUR) checks are performed using the beneficiary's historical record where the following protocols are applied:
        a. For drug interactions, concomitant therapy, refill too soon, and other contraindications; and
        b. Dosing, quantity limitations and step therapy protocols.

F. Duplicate claim check:
    1. Claim history is checked to ensure that the submitted claim is not a duplicate of an already paid claim in the beneficiary's history.

G. Verification failures from above steps:

1. Claims that fail any of the above verification or duplicate claim checks will result in:
    a. A rejected response to the pharmacy at point of sale using NCPDP reject codes and additional messaging when applicable; or
    b. A rejected response to the beneficiary via a rejection status notification with information related to the appeal process; or
    c. A rejected response to the Medicaid Agency using applicable rejection codes and messaging where applicable.

Additional messages to the pharmacy are provided for most rejections in order to provide as much information as possible for the rejection reason as well as any additional action that can be taken. Examples of such messaging are:

a. When a dual eligible LICS beneficiary incurs a drug not covered rejection, a message to bill Medicaid is provided.
b. When a drug is Medicare Part B, a message indicating to bill Medicare Part B is provided when the plan is a PDP group. This message is not returned when the plan is MAPD.
c. When the drug is not a Medicare covered drug, an additional message is provided that the drug is not covered under Medicare Part D law.

H. Claim overrides and exception processing:

1. Prior authorizations are the most common way to provide exception processing due to appeals or medical necessity.
2. In very limited circumstances, a pharmacy may override for a limited number of reject reasons such as:
    a. Refill too soon, when on a vacation, lost prescription or changes in therapy apply.
3. When transitional supplies are warranted and the days supply has been reduced to the acceptable amount.
4. When a maximum daily dose alert has been reviewed and deemed appropriate.
5. When a long term care pharmacy has identified the fill is due to an emergency.
6. After manual review, direct claims can be authorized to process with certain overrides related to coverage, pricing and cost share.
7. Claim adjustments that are made after the original claim is processed have the ability to apply certain exemptions for pricing and cost share outcomes depending upon the reason for the adjustment. (see adjustment policy XXX)

I. Claims that pass the verification steps above are then priced based on the applicable pricing rules:

1. The following components are used to determine how the claim is priced for pharmacy claims:
    a. Pharmacy contract
    b. Submitted amounts (ingredient cost, Usual & Customary, etc.)
    c. Lesser of pricing components (MAC, WAC, AWP, ACQ, etc.)
    d. Patient location (long term care, home infusion, etc.) (see long term care and home infusion policies)
    e. Rebates if applicable
    f. Sales tax if applicable
    g. Dispensing fee

h. Vaccine administration fee

Medicare secondary payer (MSP) rules when Part D is the secondary payer for identified beneficiaries (see COB policy XXX)

j. Client custom rules where applicable

k. Direct claims, separate reimbursement formulas exist which can include all of the above components plus:

- Out of network pricing rules (see directs 3K)
- Out of network pricing does not occur as these claims reject

J. Beneficiary cost share is calculated:

1. When the drug is determined to be a Medicare covered drug (i.e. Drug classification code 'C'), the claims are processed using the current accumulator dollars at time of claim processing.
2. Pharmacy submitted claims determine cost share based on the following rules:
   a. The starting benefit stage based on currently accumulated drug spend and troop dollars.
   b. The defined cost share / copay rule that applies to this claim, this drug, for the adjudicated benefit stage(s).
   c. Lessor of drug cost or calculated member cost sharing is applied.
   d. The applicable discount for applicable medications in the coverage gap.
   e. There is one cost share rule for claims adjudicated in a single stage.
   f. There are multiple cost share rules for claims that straddle across two or more benefit stages dependent on the benefit structure.
   g. If the beneficiary is identified as LICS, lesser of logic is used against the LICS cost share rules and what the beneficiary would have paid under the non-LICS benefit.
      - When LICS cost share is less, then the beneficiary is charged the LICS cost sharing and LICS subsidy is calculated as the difference between the two cost shares.
      - When LICS is higher than the standard benefit, then the beneficiary is charged the standard cost share and no LICS subsidy applies.
   h. If the beneficiary has multiple coverages and Part D is the secondary payer, then CMS defined MSP logic will be used to determine beneficiary cost share (see COB policy XXX).
   i. Vaccine administration fee rules are applied.
   j. Penalties such as brand/generic differences may be applied based on the benefit and cost share rules utilized For Part D.
   k. Plans whose cost share rules include an SPAP relationship where the beneficiary's cost share is reduced in one or more benefit stages or based on specific drugs, then the cost share for the applicable beneficiaries will be reduced by the SPAP's cost share agreements.
      - In these situations, the Part D plan is covering the full amount paid to the pharmacy and is responsible for recouping any SPAP dollars paid from the SPAP directly. See PBM XXX Medicare Part D

3. Direct claims utilize the same rules as above including the following:
    a. Penalties for using an out of network pharmacy
    b. When the drug is determined to NOT be a Medicare covered drug (i.e. not Drug classification code 'C').
4. Pharmacy submitted claims determine cost share based on the following rules:
    - The defined cost share / copay rule that applies to this claim, this drug.
    - If the beneficiary has multiple coverages and the enhanced or MAPD plan is the secondary payer, than CMS defined MSP logic will be used to determine beneficiary cost share.
    - Non Part D Vaccine administration fee rules may be applied.
    - Penalties such as brand/generic differences may be applied.
    - Direct claims utilize the same rules as above including the following:

    i. Penalties for using an out of network pharmacy

K. Accumulators are updated:
1. When the drug is determined to be a Medicare covered drug (i.e. Drug classification code 'C') then the drug spend and troop accumulators are updated as defined in Troop Policy 3E:
    a. For pharmacy claims:
        - The final claim pricing that results from the pricing step and defined as (ingredient cost + dispensing fee + sales tax + vaccine admin fee) = the amount that is applied to drug spend
        - The full amount that the beneficiary is expected to pay at point of sale is applied to the troop accumulator until the catastrophic limit. For LICS beneficiaries:
            i. When the LICS cost share is less than the standard benefit, troop is also updated with the LICS subsidy, or the difference between the LICS and standard cost share amounts.
            ii. When the LICS cost share is more than the standard benefit, then the standard benefit applies to Troop, and no additional subsidy is applied.
    b. Direct claims utilize the same rules above including the following:
        - Out of network penalties for LICS beneficiaries will credit both drug spend and troop accumulations

L. Responses are returned to the submitter, indicating the pricing used and the cost share due as follows:
1. For pharmacy claims, the pricing breakdowns are communicated on the pharmacy response as:
    a. Ingredient cost paid;
    b. Dispensing fee paid;

c. Sales tax paid when applicable;
d. Vaccine admin fee paid when applicable;
e. Other amount paid by primary payer (when an MSP claim)

2. Total amount to collect from beneficiary which breaks down as:
   a. Amount beneficiary is paying that is sales tax;
   b. Amount beneficiary is paying that is brand/generic penalty;
   c. Amount beneficiary is paying related to copay/cost share.
3. Total amount paid to the pharmacy;
4. From an information only perspective, for Multi-source brand drugs with a DAW 2 (beneficiary requests the brand) claims, the estimated savings is calculated for the purposes of messaging the pharmacy with this savings and the expectation that it is passed onto the beneficiary should they choose to utilize a generic drug instead.
5. When beneficiaries are identified as having multiple coverages, any OHI (other health information) available for the beneficiary will be returned to the pharmacy to ease in submission to the next payer in line.
6. For direct claims, the beneficiary receives an explanation of benefits (EOB) along with a reimbursement check, if applicable as:
   a. Amount Submitted by the beneficiary;
   b. Amount Approved (including any messages explaining the reasons for when amounts are reduced from what was submitted);
   c. Cost share Applied;
   d. Amount paid by other payer (when MSP claim);
   e. Adjusted Amount (Difference between amount submitted and Amount Approved);
   f. Vaccine admin fee approved;
   g. Total Payable – the amount to be reimbursed to the beneficiary;
   h. Amount beneficiary is paying related to copay/cost share.

M. Claims are stored for audit, reporting, inquiry, billing and payment:

7. Paid and rejected claims are immediately available to customer and pharmacy services to manage any calls or inquiries;
8. Paid claims are billed and reimbursed on a standard schedule;
9. Paid claims are available for PDE reporting;
10. Paid and rejected claims are retained for reporting and audit;
11. All claims are retained in accordance with the CMS retention policy (see that policy)

Performance Requirements

A. Alliance PBM's on-line claims processing system XXXX processes and adjudicates claims in real time according to the following standards:
   1. 98% of all claims submitted online are adjudicated within 4 seconds.
   2. 99% of all claims paid are paid with no errors.
   3. Alliance PBM's adjudication system will be available 99% percent of the time.
   4. Non-Participating Pharmacy Submission will reject and the beneficiary must submit a direct claim form for reimbursement. (See Direct Claims Policy XXX)
   5. The claim submission window is 90 days from the date of service.
   6. There is no claim submission window for Medicaid Subrogation claims.

Oversight/Monitoring

A. Alliance performs rejected and paid claim review on a daily basis during the first 90 days (or until no new issues identified whichever is later) of the plan year. This rejected claim review includes;

a. Transition of Care eligible member claim review to ensure all edits for non-formulary and utilization management (UM) are appropriately being overridden by the automated system in accordance with Alliance's transition policy (see transition policy) and CMS guidelines
b. Claims are reviewed for adherence to the CMS approved Alliance formulary ensuring beneficiary access to drugs at point of sale including UM edits
c. Paid claims are reviewed for member appropriate cost sharing, adherence to the CMS approved benefit and claim calculations according to processing guidance.
d. Any issues identified are promptly resolved in partnership with the PBM and members notified and made whole in the case of a reprocessing event.

B. After the first 90 days the claim review outlined above is performed on a monthly basis except for daily review of Part B vs Part D claim rejects.
C. Alliance reviews claims processing performance statistics monthly to ensure adherence to CMS standards
D. Quarterly, a full review of a sample of paid and rejected claims is performed to ensure adherence to all procedures outlined in section I Claim Processing outlines above.

IV. Record Retention

Alliance will maintain all books, documents, papers and/or records relating to Medicare members for up to ten (10) years from the final date of the contract period or ten (10) years from the date of any audit if later. Alliance agrees to permit CMS, the U.S. Department of Health and Human Services, and the Comptroller General, or their designees the right to inspect any pertinent information related to the contract during the contract term, for up to ten (10) years from the final date of the contract period, and in certain instances described in the Medicare Advantage regulation(s), periods in excess of ten (10) years, as appropriate, (ten (10) years from the date of any audit, if later.)

DEFINITIONS / ACRONYMS

4RX data – Provided by the Part D plan to CMS on the enrollment file that identifies the RX Bin, RX PCN, RX group, RX cardholder id that matches the 4RX data listed on the beneficiary's ID card. The 4RX data is also what the pharmacy uses to route and submit claims to XXXXX PBM for adjudication.

Contracted network pharmacy means a pharmacy (Retail, Mail, Home Infusion, LTC, ITA, HIS, etc.) contracted with the Alliance to be a participating pharmacy in the respective the Alliance Medicare Part D Pharmacy Network.

Direct claim means a paper claim submitted by the beneficiary.

HIPAA – (Health Insurance Portability and Accountability Act)

Medicare ID card – Refers to the CMS required data included for any Medicare D beneficiary. The ID card contains the corresponding 4RX data identifiers that were reported to CMS by the Part D plan as part of the enrollment process.

NCPDP – defines the National Council for Prescription Drug Programs, which creates industry standards for the billing of pharmacy claims to payers and processors and which is a HIPAA named standard.

POS “Point-of-Sale” means electronic adjudication that occurs in real time between a Network Contracted Pharmacy and XXXXX PBM via the XXXXX system

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

[List references such as regulatory citations]

MONITORING

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

ALAMEDA Alliance FOR HEALTH

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

POLICY AND PROCEDURE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Part D Coverage Determinations
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCARE
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

The purpose of this document is to describe the Medicare Part D coverage determination and exceptions policy and procedures for Alameda Alliance for Health (the "Alliance") Pharmacy Operations staff to help ensure compliance with all applicable federal and state laws and CMS requirements.

This is the policy of The Alliance that the Medicare Part D coverage determination and exceptions process adheres to specific CMS requirements to ensure the protection of Medicare beneficiary rights and establish a standard for fully addressing and responding timely to these coverage determination requests.

PROCEDURE

The Alliance and/or its contracted PBM has established and maintains procedures for accepting oral, written, faxed and email coverage determination requests; review, processing, provider outreach, appropriate decision making and member/provider notification in accordance with current CMS requirements.

1. Types of coverage determinations (CDs):

    a. A decision about whether to provide or pay for a drug, including a decision related to:

        i. A medication that is not on the Alliance/PBM formulary (non-formulary);

        ii. A medication determined not to be medically necessary;

        iii. A medication furnished by an out-of-network pharmacy (reimbursement request); or

    b. A decision on cost share for a drug (tiering request);

    c. Failure to provide a CD in a timely manner (expedited vs. standard) when a delay would adversely affect the health of the enrollee;

    d. Decision regarding satisfaction of utilization management (UM) requirements including prior authorization (PA), step-therapy (ST), or quantity limits (QL);

    e. Exception requests are when the enrollee requests the plan waive requirements. If the Alliance/PBM does outreach and is unable to determine if an enrollee or prescriber is asking for an exception to criteria (unresponsive), treat the case as an attempt to satisfy UM criteria. Types of exception requests include:

        i. A decision regarding a tiering exception request;

        ii. A decision regarding a formulary exception request.

        iii. A decision regarding a UM exception request.

2. Who can make a request for a coverage determination?

    a. An enrollee;

    b. A prescribing physician (or other prescriber); or

    c. An enrollee's appointed representative;

3. The duration of the approval for an exception is one year from the decision date and the duration of approval of satisfying a UM requirement is dictated by the duration submitted to CMS. Will an exception approval be for one year from the date of the approval or the end of the plan year?

4. Once an adverse coverage determination has been made, the appeals (redetermination) process may be triggered. If a Part D member disputes an adverse coverage determination, the case is handled according to the Medicare appeals process. If a member complains about any other aspect of the Alliance operations

(e.g., the manner in which a benefit was provided), the Alliance addresses the issue through the grievance process.

5. When the Alliance/PBM decides not to provide or pay for a requested benefit, in whole or in part, the decision is an adverse coverage determination. If the Alliance makes an adverse coverage determination, a written denial notice that includes appeal rights must be provided to the member.

6. The Alliance does not treat the presentation of a prescription at the pharmacy counter as a request for a coverage determination. The Alliance/PBM will never extend the applicable adjudication timeframe by dispensing a temporary supply of the requested medication. For example, if the Alliance receives a request outside of its normal business hours, it cannot approve a temporary 72-hour supply of the requested medication and defer issuing a decision for 72 hours; a determination will always be made within the appropriate timeframe.

7. The Alliance/PBM has a process to accept coverage determination requests from members and prescribers 24 hours a day, 7 days a week, including holidays. Confirm the Alliance/PBM Coverage Determination hours vs after hours process. Example below :

    a. **Process for business hour Monday-Friday 8:00-5:00**
        - Coverage determination requests are sent to the Pharmacy Operations team to handle via the normal process.

    b. **Process for after hours and holidays (when turn-around-time is before business hours)**
        - ASAP the coverage determination case shall be entered into the PBM system with criteria attached and sent for Clinical Review. If a coverage determination request is taken after hours or during holidays, how will that be communicated to the Pharmacy Operations team?

        - The coverage determination case will be decisioned in the PBM system and the on call staff member will complete the effectuation and notification steps including the letter review and any process necessary in keeping the case compliant.

10. If a department other than the Member Call Center or Pharmacy Operations receives the request for coverage determinations on a prescription drug or a non-prescription drug for a Medicare member, the phone call or written documentation will be transferred to the Member Call Center on the designated telephone line. Include phone line.

9. The Alliance does not generally maintain prior authorization criteria that requires trial and failure of more than two formulary alternatives in advance of providing access to the prescribed drug. Any exceptions are supported by clinical literature, such as situations where drugs are third or fourth line therapy.

4.1 PROCEDURES FOR STANDARD COVERAGE DETERMINATION

1. The turnaround timeframe for a standard coverage determination is 72 hours beginning with the date and time the coverage determination request is received by the Alliance/PBM. The Alliance Pharmacy Operations/PBM works within this time frame for a standard coverage determination. Procedures and timeframes related to coverage determinations for direct member reimbursement are discussed in Section 4.4 Procedures for Reimbursement Requests.

2. The Alliance Pharmacy Operations/PBM will make a total of three (3) attempts within the first 48 hrs hours from the time the request was received from the member, provider or other prescriber, by phone or facsimile, to collect additional information needed to make a decision from the prescriber; each outreach is entered in (PBM Coverage Determination-CD system). The Alliance/PBM may use a CMS model request form to request the information.

3. Requests- A member, member's authorized representative, or member's prescribing physician or other prescriber may request a standard coverage determination by phone or in writing. If the drug has a UM edit, the coverage determination request for the drug needs medical documentation to support the request. Request should include:

    a. Member information, such as name, member ID, and date of birth;

    b. Requesting prescriber name, telephone and fax numbers;

    c. The pharmacy where the claim was denied: pharmacy name, telephone and fax numbers;

    d. Drug(s) requested with dispensing information, dosage and frequency, drug strength, quantity, duration, and number of refills if needed; and

    e. Diagnosis and history including formulary medications tried and medical justification for the use of drug(s) requested.

4. The Alliance/PBM makes available on its website a medication request form should the prescriber choose to use it for a coverage determination request; however, the Alliance/PBM does not require a coverage determination request to be made on a specific form. Members calling into the Alliance/PBM member call center will have their request for a coverage determination documented as to time and date.

5. Upon receipt of the request by the Alliance Pharmacy Operations/PBM, a pharmacist or pharmacy technician reviews the submitted information and attempts to collect necessary information if the submitted information is insufficient for a coverage determination. The pharmacist or pharmacy technician adheres to the timeline for a standard coverage determination beginning with the date and timestamp when the request was initially received.

6. The Alliance will place at least one outbound call to members or a member's appointed representative, if applicable, when a decision is made for a coverage determination, whether adverse or favorable. Outbound calls to members or member's appointed representative by a pharmacy technician (RPhT) or a pharmacist

(RPh) are documented in the PBM system with date and timestamp and a brief description of the call content.

7. Notification Considered Delivered by health plan

    a. Verbal notification is considered delivered on the date and time an Alliance/PBM representative speaks to or leaves a voicemail for the enrollee or their representative.

    b. If verbal notification was successfully provided, the plan must send written notification within three (3) calendar days of the verbal notice. If unable to provide verbal notification, then written notice must be provided within the standard timeframe of 72 hrs. from receipt of request.

        i. Written notification is also sent via fax to the prescriber concurrently with the member written notification.

8. Approvals-All favorable coverage determinations are entered into PBM claims system) with an override and duration of therapy to effectuate the approval.

    a. An approval letter is generated and sent to the member within the coverage determination timeframe. Outbound calls to members are placed to ensure compliance with the timeframe for a standard coverage determination. A test claim should be run to ensure the approved medication will process as expected.

    b. The Alliance/PBM uses the CMS approved coverage determination notice. The approval letter clearly informs the member of the duration of therapy, conditions of the approval, if any, and coverage rules pertaining to subsequent refills, if applicable. The letter is written in understandable language.

    c. The approval letter is addressed to the member with a facsimile copy provided to his/her appointed representative and the prescriber requesting the coverage determination.

9. Denials-All adverse or denied coverage determination decisions are entered into PBM claims adjudication system for documentation.

    a. A denial letter is generated and sent to the member within the coverage determination timeframe. The Alliance/PBM uses the CMS approved model letter for denial. Outbound calls to members are placed within the 72 hour timeframes to ensure compliance.

    b. The denial letter is sent to both the member or his/her authorized representative and the requesting prescriber.

    c. The denial letter includes:

        i. The specific reason for the denial taking into account the member's present medical condition, disabilities, and special language requirements, if any;

ii. Information regarding the right to appeal or appoint a representative to file an appeal on the member's behalf.

iii. A description of any applicable Medicare coverage rule or any other applicable Part D plan policy upon which the denial decision was based, including any specific formulary criteria that must be satisfied for approval.

iv. A description of both the standard and expedited redetermination processes and time frames, including conditions for obtaining an expedited reconsideration, and the rest of the appeals process.

d. All communications related to coverage determination should be documented with dates and times in PBM CD system.

4.2 PROCEDURES FOR EXPEDITED COVERAGE DETERMINATION

1. The turnaround timeframe for an expedited coverage determination is 24 hours beginning with the time the request for coverage determination is received by the Alliance/PBM.

2. To meet the timeframe, the Alliance Pharmacy Operations/PBM places at least one (1) outbound call to the requesting prescriber if additional information is needed to make a decision.

3. Outbound calls to prescribers by a pharmacist or a pharmacy technician are documented with date and timestamp and a brief description of the call content.

    a. A member, member's authorized representative, or member's prescribing physician or other prescriber may request an expedited coverage determination by phone or in writing.

4. The Alliance/PBM treats any request marked as "urgent, stat, ASAP or expedited" as an expedited coverage determination or the member or prescriber indicates, either orally or in writing, that applying the standard time for making a determination may seriously jeopardize the life or health of the member or the member's ability to regain maximum function.

5. If the Alliance/PBM denies the request to expedite, the request becomes a standard coverage determination. The member, member's representative, if applicable, and his or her prescriber, if involved, will be given prompt oral notice of the denial to expedite, which includes the member's rights described below, and subsequently deliver (i.e., mail) to the member, within 3 calendar days, a written letter of the member's right to appeal or appoint a representative to file an appeal on the member's behalf. May not be applicable if the Alliance opts to treat all expedited requests as expedited without additional deliberation.

6. Notification Considered Delivered by health plan for expedited coverage determinations

a. Verbal notification is considered delivered on the date and time an Alliance/PBM representative speaks to or leaves a voicemail for the enrollee or their representative.

b. If verbal notification was successfully provided, the plan must send written notification within three (3) calendar days of the verbal notice. If unable to provide verbal notification, then written notice must be provided within the expedited timeframe of 24 hrs. from receipt of request.

    i. Written notification is also sent via fax to the prescriber concurrently with the member written notification.

7. Approvals-All favorable expedited coverage determinations are entered in PBM claims adjudication system with an override and duration of therapy to effectuate the approval.

8. An approval letter is generated and sent to the member within the coverage determination timeframe. Outbound calls to members are placed to ensure compliance with the 24 hour timeframe for an expedited coverage determination.

9. The Alliance uses the CMS approved coverage determination notice. The approval letter clearly informs the member of the duration of therapy, conditions of the approval, if any, and coverage rules pertaining to subsequent refills, if applicable. The letter is written in understandable language.

10. The approval letter is addressed to the member with a facsimile copy provided to his/her appointed representative and the prescriber requesting the PA.

11. Denials-All adverse or denied expedited coverage determination decisions are entered into PBM CD system for documentation.

    a. A denial letter is generated and sent to the member within the coverage determination timeframe. The Alliance/PBM uses the CMS approved model letter for denial. Outbound calls to members are placed within the 24 hour timeframes to ensure compliance.

    b. The denial notice is sent to both the member or his/her authorized representative and the requesting prescriber.

    c. The denial notice includes:

        i. The specific reason for the denial taking into account the member's present medical condition, disabilities, and special language requirements, if any;

        ii. Information regarding the right to appeal or appoint a representative to file an appeal on the member's behalf;

        iii. A description of any applicable Medicare coverage rule or any other applicable Part D plan policy upon which the denial decision was based, including any specific formulary criteria that must be satisfied for approval

iv. A description of both the standard and expedited redetermination processes and time frames, including conditions for obtaining an expedited reconsideration, and the rest of the appeals process

d. All communications related to coverage determination should be documented with dates and times in PBM CD system.

4.3 PROCEDURES FOR EXCEPTION REQUESTS

1. Exception requests are coverage determination requests for non-formulary medication, tiering exceptions, and requests for exceptions to utilization management (UM) criteria.

    a. A tiering exception is prohibited for a non-formulary drug approved under the formulary exception process.

    b. However, an approved UM exception request for a medication may also have a tiering exception request because it is for a formulary medication.

2. Exception requests can be either standard (decision and notification within 72 hours) or expedited (decision and notification within 24 hours).

    a. The adjudication timeframe may be tolled up to 14 (fourteen) days pending receipt of the prescriber's supporting statement. Upon receiving the initial supporting statement the Alliance/PBM must obtain any additional information, make its decision, and notify the enrollee and prescriber, as appropriate within the following timeframes:

        i. If prescriber's supporting statement is received, the plan must make notification 24 (expedited) or 72 (standard) hours after receipt of the prescriber's supporting statement or 14 calendar days after receipt of the request, whichever occurs first. *Refer to 40.5.4 Adjudication Timeframes for Coverage Determinations Involving an Exception*.

        i. If the prescriber's supporting statement is not received by the end of the 14 calendar days, then notification must occur not later than 24 (expedited) or 72 (standard) hours from the end of the 14 calendar days from receipt of the exception request.

3. Non-formulary exception requests and requests for Exceptions to Prior Authorization criteria require the submission of supporting documentation which indicates that the requested medication should be approved because:

    a. All covered Part D drugs on any tier of a plan's formulary would not be as effective for the enrollee as the non-formulary drug, and/or would have adverse effects;

    b. The number of doses available under a dose restriction for the prescription drug:

i. Has been ineffective in the treatment of the enrollee's disease or medical condition or;

ii. Based on both sound clinical evidence and medical and scientific evidence, the known relevant physical or mental characteristics of the enrollee, and known characteristics of the drug regimen, is likely to be ineffective or adversely affect the drug's effectiveness or patient compliance; or

c. The prescription drug alternative(s) listed on the formulary or required to be used in accordance with step therapy requirements:

i. Has been ineffective in the treatment of the enrollee's disease or medical condition or, based on both sound clinical evidence and medical and scientific evidence, the known relevant physical or mental characteristics of the enrollee, and known characteristics of the drug regimen, is likely to be ineffective or adversely affect the drug's effectiveness or patient compliance; or

ii. Has caused or based on sound clinical evidence and medical and scientific evidence, is likely to cause an adverse reaction or other harm to the enrollee.

4. Tiering exceptions are limited to applicable cost-sharing tiers containing the same type of alternative drug(s) to treat the enrollee's condition.

a. For the Alliance/PBM, non-preferred brand name medications on tier 3 would be eligible for a cost tiering exception to tier 2, the preferred brand tier. Refer to 40.5.1-Tiering Exceptions. (Depends on specific formulary tiers and medications.)

b. Plans are not required to offer tiering exceptions for brand name drugs or biological products at a cost sharing level of alternative drugs, where the alternatives include only generic or authorized generic drugs. (This would be tier 1 – generic tier.)

c. Tiering Exception requests require the submission of supporting documentation which indicates that the drug in the lower cost-sharing tier for the treatment of the enrollee's condition.

i. Would not be as effective as the requested drug in the higher cost-sharing tier; and/or

ii. Would have adverse effects.

5. Exception Approvals- If an exception request is approved; members or members' representatives are notified verbally within 24 hours for an expedited coverage determination and within 72 hours for a standard coverage determination.

a. Tiering Exception approval

i. When the Alliance/PBM approves a tiering exception, the Alliance/PBM will provide coverage for the drug in the higher cost-sharing tier at the cost-sharing level that applies to the drug in the applicable lower cost-sharing tier.

1. Tier 3 non-preferred brand paid at Tier 2 – preferred brand cost sharing

ii. Tiering exceptions cost sharing is based on Part D sponsor bid submissions: the Alliance is not required to approve a tiering exception for a drug in a higher cost-sharing tier at the generic tier cost-sharing level if the Alliance/PBM maintains a separate tier that only includes generic drugs (only medications with an FDA ANDA designation). The Alliance/PBM maintains a formulary tier which includes very high cost and unique medications designated on the specialty tier. The medications placed in the specialty tier are not eligible for a tiering exception.

b. Non-formulary Exception approval

i. Approved formulary exceptions are granted through at least the remainder of the plan year (or 12 months) without requiring additional justification for refills or new prescriptions.

ii. The Alliance/PBM applies the non-preferred formulary tier X as the level of cost-sharing for non-formulary brand drugs approved under the exception process.

iii. The Alliance/PBM applies a second less expensive level of cost sharing for approved formulary exceptions for generic drugs. (Depending on formulary tiering configuration)

c. The written notification of an exception request approval will be written in a manner that is understandable to the enrollee and provides the conditions of approval which would include the following:

i. The duration of an approval;

ii. Limitations associated with an approval; and/or

iii. Any coverage rules applicable to subsequent refills.

6. Exception Denials- The Alliance/PBM will use the standard CMS denial notice when issuing denials for coverage determination requests. The denial rationale provided in the notice will be specific to each individual case and the reason for the denial using language the enrollee can understand. The denial notice will include the following:

a. The specific reason for the denial that considers the enrollee's presenting medical condition, disabilities, and special language requirements, if any;

b. A description of the specific formulary criteria that must be satisfied for approval. The denial notice must explicitly state the need for a prescriber's supporting statement and clearly state the type of information that needs to be submitted when seeking a formulary or tiering exception.

    i. For example, if the drug is subject to step therapy, the denial notice must clearly explain the step criteria and indicate that if the enrollee can't take the step drug(s), the enrollee's prescriber must submit a supporting statement explaining why the enrollee can't tolerate the step drug(s).

c. A list of relevant formulary alternatives that the member's prescriber should consider for the member (formulary alternatives should only include medications that have the FDA labeled indication to treat the member's condition and are in the same drug class, same dosage form and/or have the same mechanism of action).

d. Information regarding the right to appoint a representative to file an appeal (redetermination) on the enrollee's behalf;

e. For coverage denials, a description of both the standard and expedited redetermination processes and time frames, including conditions for obtaining an expedited reconsideration, and the rest of the appeals process; and

f. The denial rationale must be specific to each individual case and written in language that an enrollee can understand.

7. Medical Necessity

    a. If the Alliance/PBM expects to issue a partially or fully adverse medical necessity decision based on the initial review of the request, the coverage determination must be reviewed by a physician or other appropriate health care professional with sufficient medical and other expertise, including knowledge of Medicare coverage criteria, before the Part D plan sponsor issues the coverage determination decision.

    b. The physician or other health care professional must have a current and unrestricted license to practice within the scope of his or her profession in a State, Territory, Commonwealth of the United States (that is, Puerto Rico), or the District of Columbia. A pharmacist would generally be considered an appropriate health care professional for purposes of meeting this requirement.

    c. A decision to deny based on a determination that the clinical documentation supporting the coverage request is unavailable or insufficient (i.e., there is unmet criteria) is generally considered a denial based on the lack of medical necessity.

a. The Alliance employs a medical director(s) who is responsible for ensuring the clinical accuracy of all coverage determinations and redeterminations involving Medical Necessity.

4.4 PROCEDURES FOR REIMBURSEMENT REQUESTS

Member reimbursement requests for Part D drugs purchased out of pocket must be resolved within fourteen (14) days. There is no tolling for reimbursement requests.

1. Members of the Alliance may request reimbursement for Part D drugs purchased out of pocket under the following circumstances:
2. Drugs or vaccine medications purchased at a retail pharmacy;
3. Drugs received while in an observation stay at a hospital or other out-patient facility (referred to as Self-Administered Drugs, or "SADs");

Members will need to present their request with a list of drugs purchased and a receipt of payment. The Alliance/PBM will then consider each drug for reimbursement under the coverage determination process. Out of Network claims are limited to a thirty (30) day supply and will be reimbursed at the Alliance/PBM's standard pharmacy reimbursement rate. The member may not be reimbursed for the full amount they paid at the pharmacy and reimbursement will be minus any required cost share or copay.

For Self Administered Drug reimbursement requests, if the claim for drugs went first to the Alliance Claims Department, they will send a denial letter to the member that states they need to request from the facility an itemized statement of the SADs.

4.4.1. Requests for Reimbursement for Drugs or Vaccine Medications Purchased at a Retail Pharmacy:

A member may mail or call in a request for reimbursement for drugs they paid out of pocket for at a retail pharmacy.

a. Before the Alliance/PBM considers reimbursement under the coverage determination process, a printout from the pharmacy with the member's name, drug and what they paid for the drug is required.
b. If the reimbursement request is called or mailed in and the receipt and/or list of drugs is still needed, a maximum of 3 phone call attempts will be made to the member to attain this information, These attempts are call-tracked.
c. Once the Alliance/PBM has the list of drug(s) and proof of payment, the clock starts and a reimbursement coverage determination may be started.
    i. If the member insists that a coverage determination be started even before they have the proof of payment and itemized list to present to the Alliance/PBM, then a case will be started and reviewed based on the request alone.
    ii. If the 14 day time limit comes before the member has provided the necessary information, the case will be decided at that time and the necessary notifications will be made. If denied, the member would need to appeal to have the case reviewed again.

d. The Alliance/PBM representative will process a claim in the PBM online system for the drug.
e. If the drug is approved for reimbursement, the amount owed to the member (minus any deductible and/or copay/coinsurance) will be mailed to the member via check from PBM per the below payment cycle:

Insert PBM check paying cycle

g. Member is notified via phone call from the Alliance/PBM that the reimbursement request has been approved and the amount of the check they will be receiving.
h. A decision letter is also mailed to the member.
i. The reimbursement case is closed in the internal case documentation system.

4.4.2 Requests for Reimbursement for Self-Administered Drugs (SADs):

There are times when a member has a stay in the hospital (or other out-patient facility) that is considered an observation stay. During this time, the hospital (or other outpatient facility) provides the member his/her medications some of which may not be covered under the Part C benefit. The member may turn in the bill to the Alliance Pharmacy Operations department for consideration of reimbursement.

a. Member may mail or call in a request for reimbursement for drugs they were provided at the hospital during an observation stay (not inpatient), or other outpatient facility.

b. Before the Alliance/PBM considers reimbursement under the coverage determination process, the member must show proof of payment from the hospital or other outpatient facility via a receipt or printout. Along with the proof of payment the member must present an itemized list of drugs that they paid for with the date(s) of service.

    i. It is possible that the member may state the amount of money they owe for their drugs is beyond what they can pay on their own. Hardship cases will be reviewed on a case by case basis, taking into consideration the member's circumstances at that time.

c. If the receipt and/or list of drugs is still needed, the request will be treated as an inquiry and a maximum of 3 phone call attempts will be made to the member to attain this information. These attempts are call-tracked. d. Once the Alliance/PBM has this information the clock starts and a redetermination coverage determination may be started.
    i. If the member insists that a coverage determination be started even before they have the proof of payment and itemized list to present to the Alliance, then a case will be started and reviewed based on the request alone.

ii. If the fourteen (14) day time limit comes before the member has provided the necessary information, the case will be decided at that time and the necessary notifications will be made. If denied, the member would need to appeal to have the case reviewed again.

d. The Alliance/PBM representative will process a claim in the PBM online system for the drug(s).
e. If the drug is approved for reimbursement, the amount owed to the member (minus any deductible and/or copay/coinsurance) will be mailed to the member via check from PBM per the below payment cycle:

f. Insert PBM payment cycle
g. Member is notified via phone call from the Alliance/PBM that the reimbursement request has been approved and the amount of the check they will be receiving. If the request has been denied, the member receives a phone call with an explanation as to why they will not be receiving any reimbursement.
h. A decision letter is also mailed to the member.
i. The reimbursement case is closed in the internal case documentation system.

4.4.3 Requests for Reimbursement with a Formulary Edit:

There will be times when a Reimbursement Request or Self Administered Drug is presented for reimbursement and the medication is either non-formulary (NF) or has a formulary edit (Prior Authorization (PA), Step Therapy (ST), or Quantity Limit (QL) exception).

a. A case is opened in the Alliance/PBM coverage determination tracking system.
b. The receipt of the NDCs and other pertinent information specific to the case will be the requested as well as receipt date and time of the exception request. A supporting statement from the prescriber must be obtained per the exception process.
c. Once all information received is entered, the drug is sent for review by the Alliance/PBM clinical pharmacist.
d. This decision must be made in exactly 72 hours as it will be processed under the standard coverage determination timeframe.
e. If approved, the duration of the override follows the same process as a regular coverage determination.
f. The request for reimbursement for this drug must then be processed and paid within the original 14 day timeframe from when the request was received.

4.4.4. Processing a Direct Member Reimbursement (DMR) Request for a Days' Supply of an Opioid Longer than 7 days:

A request for payment for any drug the enrollee believes may be covered by the plan must be processed as a coverage determination, including opioids.

a. If the enrollee making the request was not opioid naïve, the plan should not apply the 7 day supply limit and process the request based on any other applicable plan rules and the facts and circumstances of the case.
b. If the enrollee was opioid naïve, the Alliance/PBM will process the member reimbursement as an exception request, and request a supporting statement from the prescriber (verbal or written) attesting that the longer days' supply was medically necessary.
c. If there are no other plan limitations on coverage, even if the longer days' supply is denied, the Alliance/PBM will cover up to a 7 days' supply, consistent with state and federal law.

4.5 PROCEDURES FOR WITHDRAWALS, DISMISSALS

Please refer to Medicare Parts C & D Enrollee Grievances, Organization /Coverage Determinations, and Appeals Guidance in its entirety for specific guidance if a request for a reopening is received from the member or if the plan sponsor decides to reopen a case.

4.5.1 Withdrawals

The party that submits the request for an initial determination may voluntarily withdraw the request verbally at any time before the decision is issued. The Alliance/PBM will clearly document the date and the reason for the withdrawal and issue the written notice.

b. A dismissal notification is required indicating the reason as "withdrawal" to the entity requesting the withdrawal. [See "(e)(iv) under Dismissals below]

4.5.2 Dismissals

CMS 4190-F2, effective January 1, 2022, updated dismissal requirements.

A dismissal of a request is when a plan decides to stop consideration of a request before issuing a decision.

c. A plan may dismiss a request when any of the following apply:

    i. The entity making the request is not permitted to make a coverage determination request;
    ii. The entity making the request failed to make a valid request for a coverage determination;
    iii. The enrollee dies while the request is pending;

iv. The entity making the request submits a timely written request for a withdrawal of their coverage determination;

d. Written notice of dismissal must be provided to the entity who made the request. The notice must include information as appropriate, including applicable appeal rights.

e. A dismissal of a coverage determination is binding unless it is modified or reversed by the plan or vacated.
    i. A dismissal may be vacated by the entity that issued the dismissal (plan or IRE), if good cause for doing so is established within six (6) months of the date of the dismissal.

4.6 FAILURE TO MEET THE COVERAGE DETERMINATION TIMEFRAME

a. If the Alliance/PBM does not provide notice of its standard or expedited coverage determination within the required time frame, the complete case file will be forwarded by the Alliance/PBM to the IRE within 24 hours of the expiration of the adjudication time frame.

    i. If the Alliance/PBM makes a completely favorable decision soon after the adjudication timeframe expires (i.e., within 24 hours) and notifies the member of the decision, the Alliance/PBM does not forward the case file to the IRE. This process should only happen rarely. Effectuation should also be completed to avoid delay for the member to access the drug. Written notification of approval should also be sent to the member.

    ii. For cases forwarded to the IRE, the plan must make reasonable and diligent efforts to gather and forward all pertinent information for the IRE.

b. The Alliance/PBM will notify the enrollee that it has forwarded his or her request to the IRE for review.

    i. The Alliance/PBM will send the CMS Notice of Case Status within 24 hours of the expiration of the adjudication time frame.

    ii. The notice will advise the enrollee of his/her right to submit additional evidence that may be pertinent to the enrollee's case, if the enrollee chooses, and direct the enrollee to submit such evidence to the IRE, and include information on how to contact the IRE.

c. Upon receipt of the decision from the IRE, the Alliance/PBM effectuates the decision within 24 hours of the IRE decision unless the case is dismissed which may be the case when a coverage determination is completely favorable shortly after expiration of the adjudication timeframe.

d. Effectuation pursuant to an IRE decision except for dismissal includes the Alliance/PBM providing oral and written notification to the member of the IRE decision. All outcomes of the IRE decision are logged into the PBM Coverage Determination tracking system.

e. The Alliance/PBM notifies the IRE of effectuation within 14 days of receipt of the IRE decision in the manner dictated in the IRE notification. Notice of effectuation copy is entered into the case file.

5.0 Oversight and Monitoring of Coverage Determinations

Audits are done on a regular basis (monthly) to ensure accuracy of cases that have been completed. All denials are audited and up to 100% of all approvals are audited. When temporary help is needed, "real-time" audits are conducted to assure that errors are caught in a timely manner.

Monitoring for Timeliness

The PBM Coverage Determination system will monitor the coverage determination and exception cases for timeliness; however, the Alliance Pharmacy Operations will have to monitor the PBM system.

Effectuation Timeliness

Upon approval of a coverage determination, the coverage determination specialist enters the appropriate override for the medication in the claims adjudication system. The date stamp of when the override was entered is tracked in the system to show effectuation of the approval*. If this is a request for a new drug, the override is entered with an effective date of when the request was made and to term the end of the calendar year unless in the last quarter as stated in the policy and procedure. If the request is due to the denial of a claim at the pharmacy, the override is entered to allow for coverage of the last denied claim and to term the end of the calendar year unless in the last quarter as stated in the policy and procedure. Please refer to "Length of Approvals" above for additional timeframes.

*Please note: The time stamped on effectuation shown may be different than the time zone of the PBM. The Alliance will ensure that time change differences are accounted for in the processing of coverage determinations. The actual effectuation time in the case will reflect the time zone where the decision was rendered and entered into the PBM system.

CROSS-REFERENCED P&PS

Insert numbers/names of associated P&Ps.

DEFINITIONS / ACRONYMS

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

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

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

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

Effectuation - refers to payment of a claim, authorization or provision of a benefit The Alliance has approved. For the purpose of this policy, effectuate is intended to include oral and written notification to the member, written notification to the prescriber and override entry in PBM claims payment system so that a claim is paid.

Exceptions - refer to requests for a non-formulary Part D covered drug, changing the tier copay ("tiering exception") or waiver of Prior Authorization requirements.

Formulary - refers to the list of Part D drugs covered by The Alliance for members enrolled in its plans/ The Formulary is a continually updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis and/or treatment of disease and promotion of health.

Independent Review Entity (IRE) - An independent entity contracted by CMS to review adverse level 1 (redetermination) appeal decisions made by the plan. The current contractor is C2C Innovative Solutions Inc. (C2C).

Low Income Cost-share Subsidy (LICS) - refers to the Medicare subsidy specific to Part D for qualified beneficiaries in the form of reduced co-payments.

Pharmacy Benefits Manager (PBM) - Perform Rx is The Alliance's PBM and provides the POS claims processing system for pharmacy claims.

Part D drug - A drug that may be dispensed only upon a prescription, is being used for medically-accepted indication as defined by section 1927(k)(6) of the Social Security Act, and is one of the following:

- A drug that is described in sections 1927(k)(2)(A)(i) through (iii) of the Act;

- A biological product described in sections 1927(k)(2)(B)(i) through (iii) of the Act;
- Insulin described in section 1927(k)(2)(C) of the Act;
- Medical supplies associated with the delivery of insulin;
- A vaccine licensed under section 351 of the Public Health Service Act and its administration.

Prior Authorization (PA) - An evaluation of the drug's prescribed use against a predetermined set of CMS approved criteria in order to determine whether the drug/drug class will be covered by the beneficiary's insurance plan.

Provider Supporting Statement - refers to the reasons provided by the prescriber when a drug being requested is not on the Formulary or the prescriber requests a waiver of the UM requirements. The statement has to indicate reasons why the member cannot use a Formulary drug, a Formulary drug with no UM edits or a lower-cost sharing drug.
Quantity Limits (QL) - refers to a dose restriction, including the number and/or dosage form, that causes a particular Part D drug not to be covered for the number of doses and/or dosage form prescribed

Step Therapy (ST) - refers to a particular Part D drug not to be covered until the requirements of the plan's coverage policy are met, which requirements are approved by CMS

Redetermination - Level 1 Part D appeal which reviews an adverse coverage determination, including the findings upon which the decision was based and any other submitted evidence.

Reopening - A remedial action taken to change a binding determination or decision even though the determination or decision may have been correct at the time it was made.

Tolling - The start of the timeframe for a standard or expedited exception request if the sponsor is waiting to receive the prescriber's supporting statement. A plan may toll a request for up to 14 (fourteen) days. Reimbursement requests are not eligible for tolling.

Utilization Management (UM) edits - refer to the requirements for the approval of a drug which can be one of the following: prior authorization (PA), step therapy (ST), or a quantity limit (QL).

Withdrawal - A verbal or written request to rescind or cancel an initial determination.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

42 CFR §423.560

Part C&D Enrollee Grievances, Organization/Coverage Determinations, and Appeals Guidance (01.01.2020), Section 50 – Reconsiderations and Redeterminations (Level 1 Appeals), Section 60 – Reconsiderations by the Independent Review Entity (Level 2 Appeal), Sections 70, 80 and 90, and Appendix 2 – Medicare Prescription Drug (Part D) Appeals Process Overview.

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POLICY AND PROCEDURE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Drug Utilization Management
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCARE
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

The Alameda Alliance for Health's (the "Alliance") Pharmacy Services unit has established Drug Utilization Review (DUR) procedures. The objective of DUR is to improve the quality of pharmaceutical care by ensuring that prescriptions are appropriate, medically necessary, and unlikely to result in adverse medical outcomes. The Alliance's DUR procedures comply with CMS Medicare requirements [CFR 423.2430(b)(7)] as well as the Alliance's contract with the California Department of Health Care Services (DHCS). The Alliance will provide drug utilization encounter data to DHCS monthly or as required.

PROCEDURE

A. Drug Utilization Review (DUR) Overview:

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

B. Concurrent DUR:

1. The Alliance's PBM ensures the safety of dispensed medications by notifying

dispensing pharmacies of potential adverse events at the point-of-sale. The online messaging process classifies events at different levels of severity.

3. The PBM provides on-line, concurrent DUR messaging to pharmacies and takes appropriate action. Concurrent DUR includes but is not limited to the following edits:

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

C. Retrospective DUR:

1. The Alliance's PBM will provide a list of on-demand retrospective DUR reports of various topics to monitor fraud, waste, or abuse. These reports are reviewed and may be used by the Alliance to support quality improvement programs (QIPs) and Disease Management programs.
2. The Alliance pharmacy staff or third-party vendor will run these reports as appropriate.
3. For Medicare line of business, the Alliance will provide active and ongoing outreach to educate providers on common drug therapy problems (e.g., asthma medication ratio monitoring, opioid and naloxone co-prescribing, new prescribing guidelines, and advisories) with the goals of improving prescribing and dispensing practices, increasing medication compliance, and improvement of over-all beneficiary health.
4. For Medicare line of business, the Alliance will be required to submit an annual DUR report [42 CFR §423.514(a) requires each Part D sponsor to have a procedure to develop, compile, evaluate, and report to CMS, to its enrollees, and to the general public, at the times and in the manner that CMS requires, statistics indicating the following: 1) The cost of its operations. 2) The patterns of utilization of its services. 3) The availability, accessibility, and acceptability of its services. 4) Information demonstrating that the Part D sponsor has a fiscally sound operation. 5) Pharmacy performance measures. 6) Other matters that CMS may require] to include any descriptions of any retro DUR activities and any innovative practices implemented by the plan in the prior federal fiscal year.
5. For Medicare line of business, the Alliance SIU (Special Investigations Unit) monitors and has a process for identifying and addressing fraud and abuse of controlled substances by the Alliance members and the health care Providers who are prescribing these drugs and pharmacies dispensing these drugs to the Alliance members. The Alliance SIU actively investigates any allegations of fraud, waste or abuse regarding controlled substances.

D. Drug Utilization Data Submission

1. On a regular basis, no less than once monthly, the Alliance's PBM sends the encounter data in the mutually agreed-upon format to the Alliance.
2. The Alliance's IT team will prepare the data for monthly submission. (See Policy

IT Monthly Encounter Data)

E. Monitoring of DUR Process

1. Concurrent DUR reports and Retrospective DUR reports are reviewed by the Alliance pharmacy staff or third-party vendor and Senior Director, Pharmacy Services or designee and reported to the UM Committee and Quality Improvement Health Equity Committee (QIHEC).
2. For Medicaid, pursuant to 42 CFR 438.3(s)(4) and (5), the Alliance is to operate a drug utilization review (DUR) program that complies with the requirements described in Section 1927 (g)of the Social Security Act (the Act) and submit an annual report on the operation of its DUR program activities to DHCS.

F. Preventing Opioid Overutilization

1. Refer to Overutilization Monitoring System (OMS) -Opioids, APAP (DUR Level 1), QLs (DUR Level 2) Policy.

DEFINITIONS / ACRONYMS

PBM : Pharmacy Benefit Manager (Currently, PerformRx)

IT: Information Technology Department

MME: Morphine Milligram Equivalent

PA: Prior Authorization

AFFECTED DEPARTMENTS/PARTIES

PBM
IT

RELATED POLICIES AND PROCEDURES

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

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

Need to get for Medicare

MONITORING

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

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

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POLICY AND PROCEDURE TEMPLATE

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

POLICY STATEMENT

Review of the daily rejected pharmacy claims to ensure compliance with the Centers for Medicare and Medicaid Services (CMS) guidance for Medicare Part D sponsors. Alameda Alliance for Health (Alliance) will perform oversight of its Pharmacy Benefit Manager (PBM) to ensure the beneficiaries' pharmacy benefit is being administered accurately. Identified issues will be resolved expeditiously and appropriate outreach performed to ensure beneficiary medication access.

PROCEDURE

1 Access Daily Reject Report from PBM

1.1 Link to location of PBM Daily rejected claims report and instructions on how to retrieve

1.2 Directions where to store original report
1.3 Directions on where to store edited/reviewed copy.

2 Rejected claims research is to validate that each rejected claim is compliant with CMS rules and regulations.

2.1 Determine that rejection is appropriate. Research is required – common research:

- What is the source of the reject (e.g., Medicare D exclusions, BvsD, Prior Authorization (PA), Step Therapy (ST) etc.)?
- Is PBM coding functioning as intended (e.g., step therapy, grandfathering etc.)?
- Does the member have a history of paid claims for the drug in question?
- Is the messaging appropriate for the reject code?
- Product Not on Formulary (Reject MR;569)
- B vs D (Reject 75;569;)
- This Product May Be Covered Under Hospice – Medicare Part A (Reject A3;569)
- This Product May Be Covered Under Medicare Part B Bundled Payment to an End-Stage Renal Disease (ESRD) Dialysis Facility (Reject A4;569)
- PROTECTED CLASS (YES)
  - Immunosuppressant (for prophylaxis of organ transplant rejection)
  - Antidepressant
  - Antipsychotic
  - Anticonvulsant
  - Antiretroviral
  - Antineoplastic classes
- TRANSITION ELIGIBLE (TRANSD3)
- Coordination of Benefits (COB) (Reject 41)
- Refill Too Soon (RTS) (79) – sample review
- Plan Limitation Exceeded (Maximum Daily Dose) (Reject 76)
- Step Therapy (Reject 608;569;)
- Quantity Dispensed Exceeds Maximum Allowed (Reject 9G;569;)
- Prior Authorization (Reject 75;569;)
- DUR Reject Error (Reject 88;569;) – sample review
- Initial Fill Days' Supply Exceeds Limits (Reject 925;569;88;) – sample review
- Product/Service Not Covered Plan/Benefit Exclusion - Compound Drug (Reject 70;) – sample review
- Days' Supply Exceeds Plan Limitation (Reject 7X;569) – sample review
- Not Covered Under Part D Law (Column H – Reject A5) – sample review

Point of Sale (POS) or administrative rejects (e.g. Reject 04 M/I PCN, 09 M/I DOB) can be filtered out of the manual review process but should be monitored for trends overall and per NCPCP.

2.2 Validating Rejected Claims

2.2.1 Retrieve most current CMS approved formulary for plan located at: <location link >

2.2.2 Identification of potentially inappropriate rejections which may require verification against the current CMS approved formulary/utilization management criteria and requirements by using data filter on rejection codes.

2.2.3 Priority review is needed for B vs D rejections; CMS expectations are that B vs D rejections should be able to be resolved at point of sale, otherwise, the claim should be resolved and the medication dispensed to the beneficiary within 24 hours.

2.2.4 Filter for reject 79 and complete refill threshold calculations on a sample which includes retail (75%) and ophthalmic (70%) claims.

3. Transition Fill (TF)

CMS requires that all Part D sponsors have an appropriate transition process in place for new and renewing beneficiaries to assure continuity of care and avoid interruptions in drug therapy until a switch to a therapeutically equivalent medication or approved coverage determination has occurred.

Rejected claims should be reviewed to determine if the claim should have paid as a TF. The following factors must be considered.

- Is member within transition window (e.g., first 90 days of enrollment)
  - Is member considered a new or renewing member?
  - What is the current transition policy for renewing members (e.g., is ANOC applicable or do current members follow new member logic etc.)?
- If outside of transition window, is member transition eligible due to level of care change or in need of emergency supply?
- Is drug transition eligible?
  - Negative formulary changes across plan years (if applicable per transition policy/logic)
- Location (LTC vs. retail)
- Minimum day supply (retail = 30 days, LTC = 98 days except limited day supply = 14 days and package size exceptions)
- Package size exceptions may allow for greater than 30 or 98-day supply if drug is supplied in an unbreakable package (e.g., inhaler, ophthalmic solutions, syringe, vial etc.).

The following are scenarios and drug types which are excluded from the automated TF logic at point of sale.

- B versus D drugs- TF does not apply to Part B drugs. Determinations must be completed, and assessment of TF eligibility of any determination made as Part D.
- Part B Drugs
- Drugs on a specific transition exclusions list that require indication validation (e.g., Transmucosal Fentanyl etc.)
- Non-Med D/excluded drugs (e.g., drugs used for cosmetic purposes etc.)
- Over The Counter (OTC) drugs (except insulins); OTCs are covered outside the Part D claims system through XXX
- ESRD drugs- TF does not apply to drugs determined to be bundled under the ESRD benefit. Determinations must be completed, and assessment of TF eligibility of any determination made as 'D'
- Safety edits (FDA approved maximum dose) - If a claim is rejected for safety purposes evaluation is required to ensure plan provides refills for transition prescriptions dispensed for less than the written amount due to quantity limits for safety purposes or drug utilization edits that are based on approved product labeling. The reference source of truth for maximum daily dose is the FDA labeling for the medication. (Labeling verbiage states Maximum Daily Dose = xxxx).

Claims that are identified as a transition eligible must have transition eligibility confirmed by verifying member eligibility and/or other parameters which determine member to be TF eligible (e.g., Level of Care , Emergency Supply). Claims determined to be TF eligible with reject codes of 70, 75, 9G, 7x, 608 and MR will be targeted for manual review.

4. Transition Fill (TF) Eligibility

A member is defined as new when 1 or more of the following criteria is met:

- A new enrollee following the annual election period
- Transition of newly eligible Medicare member from other coverage
- Transition from one plan to another after the start of the contract year
- Current enrollees affected by a negative formulary change across contract years
- Enrolled residing in LTC facilities

Renewing members within the same plan at the start of the contract are allowed a transition if there is history of a paid claim within **180 day look back**. Year over year evaluation of transition fill logic is required to determine how renewing members' transition fill eligibility will be handled. If renewing members are only allowed transition supplies for drugs on the ANOC, this must be considered in assessing a beneficiary's transition eligibility.

DEFINITIONS / ACRONYMS

ANOC- Annual Notice of Change
CMS- Centers for Medicare and Medicaid Services

COB- Coordination of Benefits
DUR-Drug Utilization Review
ESRD- End-Stage Renal Disease
FDA- Federal Drug Administration
LTC- Long Term Care
OTC- Over the Counter (medication not requiring a prescription)
PA- Prior Authorization
PBM- Pharmacy Benefit Manager
POS- Point of Sale
RTS- Refill too Soon
ST- Step Therapy
TF- Transitional Fill

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

42 CFR §423.120(b)(3) Part D Transition requirements

Prescription Drug Benefit Manual, Ch. 6: Part D Drugs and Formulary Requirements, Rev. 18, 01-05-16

HPMS Memo - Part D Transition Monitoring Analysis (TMPA), January 17, 2018

HPMS Memo – Job Aids Replace the Common Conditions, Best Practice Audit Memos, April 20, 2016

HPMS Memo – Common Conditions, Improvement Strategies, and Best Practices based on 2013 Program Audit Reviews, August 27, 2014

HPMS Memo – Best Practices and Common Findings Memo #2 from 2012 Program Audits, July 30, 2013

HPMS Memo – Best Practices and Common Findings from 2012 Program Audits, September 10, 2012

HPMS Memo – 2011 Program Audit Findings and Best Practices, January 20, 2012

MONITORING

The If/Then Tables below are designed to provide an overview of each reject code, potential research required, and the action based on the outcome of the research. Research required may vary based on unique claim scenarios and are not comprehensive.

Reject Code	Messaging	Research Points	If	Then
MR	Non-Formulary	✓Is the member transition eligible	If member is transition eligible	Refer to Transition Table
		✓Verify if drug filed on CMS approved formulary for specific plan	If drug is not on approved formulary	Valid
			If drug is on approved formulary	Send for research and provide override if deemed appropriate
		✓ If member has an active MPA on file for the drug	If member has a formulary exception	Send for research and provide override if deemed appropriate
			If member does not have an active formulary exception	Valid
75	Prior Authorization Required	✓Is the member transition eligible?	If member is transition eligible	Refer to Transition Table
		✓Verify drug filed on CMS approved formulary as PA Required (PA=1 or 2)	If drug is not listed with PA required on CMS approved formulary	Send for research and provide override if deemed appropriate
		✓If drug is PA=2, verify if member has prior use within defined lookback period	If no prior use	Valid
			If history of paid claim within lookback period	Send for research and provide override if deemed appropriate

		✓Verify if there is an active PA on file for the drug	If active PA on for drug is on file	Send for research and provide override if deemed appropriate
			If drug does require PA and no active PA on file	Valid
		✓Verify if the drug has previously paid	If drug has previously paid	Validate how claim paid (e.g., Negative formulary change, expired PA)
75	Prior Authorization Required- BvsD	✓Verify drug filed on CMS approved formulary as PA Required-BvsD (PA=3)	If drug is on CMS approved formulary as BvsD	Valid- Send for BvsD review
			If drug is not BvsD	Send for research and provide override if deemed appropriate
		✓Verify if drug utilizes autologic based on location code (LTC or retail claim) to determine payment	If autologic applies drug should pay D without determination	Send for research and provide override if deemed appropriate
608	Step Therapy	✓Is the member transition eligible	If member is transition eligible	Refer to Transition Table
		✓Verify drug filed on CMS approved formulary as Step Therapy (Step=1 or 2)	If drug is not filed with Step on CMS approved formulary	Send for research and provide override if deemed appropriate
		✓Verify if there is an active MPA on file for the drug	If active MPA on for drug is on file	Send for research and provide override if deemed appropriate
		✓If step=2, verify if member has prior use within defined 365 lookback period	If member has history of drug within lookback period	Send for research and provide override if deemed appropriate
			Drug has ST requirements, no active PA or drug history which satisfies Step	Valid

AC	Product Not Covered Non-Participating Manufacturer	✓Verify if manufacturer is on current CMS Labeler Code File http://cms.gov/Medicare/Prescription-DrugCoverage/PrescriptionDrugCovGenIn/Pharma.html	For brand drugs if manufacturer is not listed	Valid
			For brand drugs if manufacturer is listed on CMS Labeler File	Send for research and provide override if deemed appropriate
A3	This Product May be Covered Under Hospice - Part A	✓ Verify member is active hospice status in <PBM> claims system and MARx	If member is not in active hospice	Send for research and provide override if deemed appropriate
			If member has active hospice status and drug is on hospice list	Valid
		✓Verify if there is an active PA on file for the drug to document drug is not for terminal illness	If active PA on for drug is on file	Send for research and provide override if deemed appropriate
A4	This Product May be Covered Under the Medicare Part B Bundled Payment to an ESRD Dialysis Facility	✓ Verify member has active ESRD status in <PBM> claims system and/or Marx	If member is not on active dialysis status	Send for research and provide override if deemed appropriate
		✓Verify if there is an active PA on file for the drug to document drug is not related to treatment of ESRD	If active PA on for drug is on file	Send for research and provide override if deemed appropriate
A5	Not Covered Under Part D Law	✓ Verify drug is Med D excluded (e.g., agents used for cosmetic, weight loss, purposes, bulk powders, drugs	If drug is Med D excluded	Valid
			If drug is not Med D excluded	Send for research and provide override

		used for sexual dysfunction etc.)		if deemed appropriate
		✓ Verify if drug is eligible for coverage as part of administrative cost (e.g., OTC) for specific plan benefit	If drug is eligible for payment as part of benefit	Send for research and provide override if deemed appropriate
A6	This Product/Service May Be Covered Under Medicare Part B	✓ Verify claim processed on Part B if applicable to plan benefit	If drug is Med B and processed on Part B benefit	Valid
		✓ Verify drug/supply is Med B covered (e.g., diabetic testing supplies)	If drug/supply is not Med B	Send for Further Research--Evaluate if override is needed
9G	Plan Limits Exceeded	✓Verify drug filed on CMS approved formulary as having a quantity limit	If drug does have days' supply limits and claims exceeds approved limit	Valid
			If drug was not filed with a quantity limit	Send for further research and evaluate if override is needed
		✓Verify drug the quantity rejection matches what is on file with CMS	If quantity limit reject differs from CMS approved limit	Send for further research and evaluate if override is needed
		✓Verify quantity submitted exceeds CMS approved limit ✓Verify quantity is coded appropriately as a daily dose or quantity versus time to assess if limit was exceeded	If claim exceeds approved amount without an MPA	Valid
		✓Verify if there is an active MPA on file for the drug	If active MPA on for drug is on file which overrides QL	Send for further research and evaluate if override is needed

			If no active PA on file	Valid
79	Refill Too Soon	✓ Determine if pharmacy is mail or retail/LTC ✓ Verify projected refill date based on the following thresholds Retail/LTC-75%. Ophthalmic 70%	If refillable date is outside of expected threshold	Send for further research and evaluate if override is needed
			If refillable date threshold is exceeded	Valid
7x	Days' Supply Exceeds Plan Limitation	✓ Verify if drug has special limits based on overarching plan limits (e.g., Extended days' supply network, High Cost or Specialty Tier)	If drug is on tier 3 (non-preferred brand or tier 4 (specialty) which limits days' supply	Valid
			If drug is on not on tier which limits days' supply	Send for Further Research--Evaluate if override is needed
		✓ Verify if drug is dispensed in an unbreakable package (e.g., Copaxone)	If drug is dispensed in unbreakable package and is dispensed in smallest package size	Send for Further Research--Evaluate if override is needed
70	Compounds Does Alliance pays for non-covered ingredients in a compound. Preferred Pharmacy limit = $150 Non Preferred Pharmacy = $50 Reject can be overridden by PA	✓ Verify if compound contains any Part B or BvsD payable drug	If Part B drug is in compound-whole compound should pay Part B; verify if claim paid on Part B based on benefit	Valid
		✓ Verify if compound contains at least 1 Med D payable drug	If drug has Part D payable ingredient and SCC 08 assumed	Send for Further Research--Evaluate if override is needed
			If SCC not assumed; verify SCC 08 not submitted	Valid
88/925	DUR Reject			
	Drug Safety Alert (e.g., drug interaction)	Evaluate rejection message and validate DUR reason	If rejection cannot be validated (e.g., no interacting drug present in history)	Send for Further Research--Evaluate if override is needed

			DUR rejection reason validated	Valid
76	Max Dose	✓ Verify FDA labelled max dose is exceeded	If claim exceeds FDA labelled maximum dose	Valid
			If drug does not have FDA labelled maximum dose or max dose is not exceeded	Send for further research and evaluate if override is needed
42-45	Prescriber ID rejections	✓Prescriber validation rejection resolved within 24 hours	Rejection resolved and claim paid within 24 hours	Valid
			Rejection not resolved within 24 hours	Send for Further Research--Evaluate if override is needed
Yes	Protected Class			
	Refill Too Soon – select a few samples	✓ Determine if pharmacy is mail or retail/LTC ✓ Verify projected refill date based on the following thresholds Retail/LTC-75%;	If refillable date is outside of expected threshold or if quantity and day supply has changed	Contact the pharmacy and confirm if the member is needing an override due to a change in dose. Enter a Dose Increase override to allow the claim to pay.
			If refillable date threshold is exceeded	Valid

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POLICY AND PROCEDURE TEMPLATE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Medicare Part D End Stage Renal Disease (ESRD)
Department Name	[e.g., "Compliance"]
Department Officer	[e.g., "Compliance Officer"]
Policy Owner	[Title of Owner]
Line(s) of Business	Medicare Advantage
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the name of the committee here, otherwise put N/A
Subcommittee Approval Date	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

It is the policy of Alameda Alliance for Health (Alliance) to ensure proper payment of End Stage Renal Disease (ESRD) medications under pharmacy Part D benefit. Drugs and biologics, except "oral only" drugs, included in the Part B bundled payment to an ESRD dialysis facility are not covered under Part D. Immunosuppressive therapy for a beneficiary who has received a Medicare covered kidney or non-renal transplant are not payable under Part D.

PROCEDURE

To ensure Alliance does not pay for drugs and or biologics under the Part D prescription benefit, that are in included in the Medicare Part B prospective payment system (PPS), to an ESRD dialysis facility or for immunosuppressive therapy for a beneficiary who has received a Medicare covered kidney transplant or non-renal transplant. Alliance will establish a process regarding notification, analysis and record keeping by Alliance staff for enrollees utilizing Medicare Part B End Stage Renal Disease PPS to ensure payment accuracy as early in the process as possible.

Background: The Center for Medicare and Medicaid Services (CMS) requires that Part D sponsors ensure that Part D does not pay for drugs or biologics that may be covered under Medicare Part B per diem payment to ESRD facilities, or for immunosuppressants covered under Part B.

The Medicare Improvements for Patients and Providers Act of 2008 (MIPPA) amended section 1881(b) of the Social Security Act to require the implementation of an ESRD bundled payment system effective January 1, 2011. Under MIPPA, the ESRD PPS replaced the previous basic case-mix adjusted composite payment system and the methodologies for the reimbursement of separately billable outpatient ESRD-related items and services. The ESRD PPS provides a case-mix adjusted single payment to ESRD facilities for renal dialysis services provided in an ESRD facility or in a beneficiary's home

1. The Pharmacy Benefit Manager (PBM), on behalf of Alliance has established procedures (attached) for:

   a. Rejections coded for ESRD members
      i. Identify PBM process to avoid duplicate payment under Part D side of the plan.

      ii. Upon receiving an ESRD Transaction Reply Code (TRC) for the beneficiary via the Daily Transaction Reply Report (DTRR), plan sponsors may then utilize segment 08 within the Type 24 file to indicate that the member has one of the following ESRD attributes. Kidney transplants for beneficiaries are conveyed through CMS' MARx system. In similar fashion, the ABII portal can be used to convey Medicare-covered non-renal transplants for beneficiaries.

   b. Beneficiary level Prior Authorization POS requirements for CMS classified 'always' ESRD medications and 'maybe' ESRD medications.

      i. ESRD 'always' medications include those used for:
         1) Access Management
         2) Anemia management
         3) Bone and Mineral metabolism
         4) Cellular Management.

ii. ESRD 'maybe' medications include:
    1) Antiemetics
    2) Anti-infectives
    3) Antipruritics
    4) Anxiolytics,
    5) Excess fluid management
    6) Fluid and Electrolyte Management including volume expanders
    7) Pain Management.

iii. Retrospectively reviewing ESRD claims identified based on the Transaction Reply Codes (TRCs) provided by CMS on the daily Transaction Reply Reports (TRR) and providing a report monthly to Alliance.

2. With the FDA approval of injectable Parsabiv (etelcalcetide) under the bone and mineral metabolism category it was included in the ESRD PPS as of January 1, 2018. Therefore Sensipar (cincacalcet) is also included in the ESRD PPS and is not payable under Part D.

3. The inclusion in the ESRD PPS of oral-only ESRD drugs and biologicals- " *Under 42 C.F.R. § 413.174(f)(6), effective January 1, 2025, payment to an ESRD facility for renal dialysis service drugs and biologicals with only an oral form furnished to ESRD patients is incorporated within the prospective payment system rates established by CMS in § 413.230 and separate payment will no longer be provided*".

PROCESS

1. Alliance will perform a retrospective review of Part D claims paid after the ESRD/Dialysis start date period for CMS classified drugs as 'always' and/or 'maybe related to ESRD treatment for the purpose of determining if the drugs were related to the beneficiary's ESRD treatment:

    a. Determining if the drugs were unrelated to the ESRD beneficiary's dialysis treatment. As needed, Alliance will conduct outreach to the ESRD facility or prescriber to determine payment responsibility of the drug.

    b. In the 2019 Final Call letter CMS announced the launch of a web portal called Additional Beneficiary Information Initiatives (ABII, pronounced 'Abby"). The portal will be part of the group of Acumen web portals to which all Part D contracts already have access. As part of this initiative CMS will begin populating ABII with Medicare -covered transplant data derived from Medicare fee-for-service claims.

    c. Alliance will notify the PBM if a paid claim during the election period is determined to be either an ESRD facility liability or a beneficiary liability (such as when a member requests a non-formulary drug and agrees to assume financial liability). The PBM establishes and maintains a process to reverse the claim, negate the PDE and adjust the beneficiaries TrOOP and total drug spend.

d. Alliance will have processes in place to handle payment resolution directly with the ESRD facility. In the case of beneficiary liability, Alliance will send a recovery notice directly to the beneficiary. In both scenarios, payment resolution will be accomplished without requiring the retail pharmacy to reverse and rebill the original claim.

2.The Alliance will perform a retrospective review of claims for ESRD members to determine proper coverage.

a. Daily reject reviews
b. Monthly retrospective reviews.

i. PBM generates the ESRD Report on a monthly basis so that Part D plan sponsors may regularly review claims approved under the Part D benefit that are associated with their beneficiaries receiving dialysis treatment. Plan sponsors may use the report to:

ii. Identify claims for prescriptions that should have been covered under Part B instead of Part D and then work with the dialysis facility to recover any inappropriate payments; and or any claims that paid inappropriately under Part D, work with PBM to exclude the PDE record.

iii. PBM's ESRD Report includes both the "ESRD Always" drugs in addition to the "ESRD Maybe" drugs. Consistent with the CMS memo dated November 14, 2014, titled "Part D Payment for Drugs for Beneficiaries Receiving Renal Dialysis Services," drugs in the "ESRD Always" seven categories may be used for the treatment of ESRD. Alliance may use the report to:

a. Identify claims for prescriptions that should have been covered under Part B instead of Part D, and then work with the dialysis facility to recover any inappropriate payments; and
b. For any claims that paid inappropriately under Part D, work with PBM to exclude the PDE record.

3. Drugs in the "ESRD Maybe" category of seven (7) drugs may be used for the treatment of ESRD.

i. For drugs in the "Maybe" category, if the drug was used for the treatment of ESRD, it should be covered under the bundled payment to the facility and plan sponsors should work the facility to recover the Part D payment.

ii. PBM utilizes two different PPDLs to support ESRD and Transplant processes.

- CMS ESRD Always for the four (4) categories always covered by ESRD.
- CMS Kidney Transplant (KTRANS) lists the immunosuppressants used for transplants.

iii. If the NDC submitted on the claim is not found on either list OR if the drug is a compound, normal processing rules apply. Each compound represents a unique drug entity and PBM is unable to determine at the point of sale the medical condition for which the compound was prescribed.

4. Payment Recovery

Alliance will work with the dialysis facility to recover the Part D payment. Beneficiaries should also be directed to the dialysis facility to recover any cost sharing incurred on the claim.

DEFINITIONS / ACRONYMS

ABII- Additional Beneficiary Information Initiatives (ABII portal)

Coverage Determination- A decision made by or on behalf of a Part D plan sponsor

Daily Transaction Reply Reporting (DTRR)- The file will be transmitted daily in reply to any action that initiates or impacts a beneficiary's status or its enrollment. It also will communicate changes affecting a beneficiary throughout all enrollment periods and accordingly, all affected Plans will receive a notification on a TRR. This is especially valuable regarding retroactive enrollments.

End State Renal Disease r(ESRD)-resulting in permanent kidney failure that requires a regular course of dialysis or a kidney transplant .

HPMS – Health Plan Management System

PBM- Pharmacy Benefit Manager

Point of Sale (POS)- A capability of retail pharmacies to electronically access plan design and eligibility information to process and transmit drug claims data at the time of purchase.

Prescription Drug Event (PDE)- is a summary record submitted to CMS. The PDE data is not the same as individual drug claim transactions but are summary extracts using CMS defined standard fields.

Prior Authorization (PA) – A process whereby certain designated preferred drugs must meet established before the prescription can be covered.

Prospective Payment System (PPS)- is a method of reimbursement in which Medicare payment is made based on a predetermined, fixed amount.

Transaction Reply Code (TRC)- Codes used to explain what action MARx took in response to new information from CMS systems or in response to input from Plans, CMS or other users.

Transaction Reply Report (TRR)- A report that CMS provides to Part D sponsors containing details of the rejected and accepted enrollment transactions that CMS has processed for a Part D sponsor's contract(s) over a specified period of time.

PPS – Prospective Payment System

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

HPMS Memo – Sensipar (cinacalcet) Furnished for the Treatment of ESRD Moving from Part D to ESRD PPS, Effective January 1, 2018 – published August 18, 2017.

HPMS Memo - Part D Payment for Drugs for Beneficiaries Receiving Renal Dialysis Services, November 14, 2014.

HPMS Memo – Two Updates Pertaining to End-Stage Renal Disease (ESRD) Related Drugs, May 12, 2015.

The calendar year 2011 ESRD PPS final rule (CMS-1418-F), which appeared in the Federal Register on August 12, 2010, requires the inclusion in the ESRD PPS payment bundle of all drugs and biologicals used in the treatment of ESRD, effective January 1, 2011.

MONITORING

Alliance Pharmacy Department Staff will include results of ongoing monitoring in monthly Delegated Function Oversight/Monitoring statistics.

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POLICY AND PROCEDURE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Part D Appeals (Redeterminations)
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	MCARE
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	Pharmacy and Therapeutics Committee
Subcommittee Approval Date	
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

To ensure that Alameda Alliance for Health (the "Alliance) handles all verbal and written member redeterminations per established CMS regulations and guidelines. The Alliances Appeals and Grievances (A&G) Department and Member Services are trained to distinguish between coverage requests, appeals, and grievances, and to conduct redeterminations (Part D appeals) accurately and timely.

PROCEDURE

The Alliance has established and maintains procedures for accepting oral and written redetermination requests for expedited, standard coverage and standard payment requests when submitted within 60 calendar days from the date of the notice of the initial coverage determination. Upon receipt of request a case is built using the A&G database.

1. The Alliance accepts standard coverage and standard payment redeterminations beyond the 60-day required timeframe when good cause has been established.

2. The Alliance will accept a redetermination request from a member, a member's designated representative or prescribing physician when filed on behalf of a member, and physician's office staff when acting on the physician's behalf.

    a. A member's designated representative must be given permission in writing. The CMS Form 1696 Appointment of Representative (AOR) is the most complete way for a member to give permission for family or friend to represent them.
    b. This form is available on the plan website or mail upon request.
        i. Health Plan Member Services: _____
        ii. Health Plan website: _____

3. Processing timeframes for standard and expedited redeterminations (Part D appeals):

    a. For *standard pre-service redetermination requests* the processing timeframe begins when the plan, any unit in the plan, or a delegated entity receives a request. If an appeal is received in the incorrect department, Plan has a policy for prompt transfer of the call or document(s) to the A&G department.
        i. The plan has seven (7) days to process the standard pre-service request and redetermination requests may not be tolled for receipt of a physician's statement
    b. For *expedited pre-service redetermination requests*, the processing timeframe begins when the appropriate department receives the request.
        i. The plan has seventy-two (72) hours to process the expedited request and it may not be tolled for a physician's statement.
    c. For *standard Part D redetermination payment* requests the processing timeframe begins when the plan receives a request. If the request is received in the incorrect department, Plan has a policy for prompt transfer to the A&G department.
        i. The plan has fourteen (14) days to process the payment request.
    d. Extensions of the adjudication timeframes are not permitted in Part D. The Alliance will not extend the adjudication timeframe by dispensing a temporary supply of the requested medication.

4. The Alliance provides the member, their designated representative, or the prescribing physician, an opportunity to present evidence in person, or in writing, to support the redetermination request. All evidence is added to the case file and documented in the A&G database.

5. The Alliance acknowledges standard, expedited or claim payment redeterminations in writing to the member, the member's representative and the prescribing physician as appropriate and documents in the case file.

6. The Alliance requests any additional medical information necessary for a standard or standard payment redetermination within the required appeal timeframes; and within 24 hours of receiving an initial request for an expedited redetermination. This can be done verbally for the best interest of the member.

7. The Alliance issues a decision for an expedited redetermination request as expeditiously as the member's health condition requires, but not more than 72 hours from receipt. Notification to the member (or their designated representative) is provided orally and in writing.

    a. If the expedited request is made or supported by a physician and indicates that the member's life, health, or ability to regain maximum function may be jeopardized by applying the standard timeframe, Plan accepts the request as expedited.
        i. The Alliance may choose to expedite a redetermination request from a member without requiring the member's prescribing physician to submit a new statement indicating that applying the standard timeframe could seriously jeopardize the life or health of the member or the member's ability to regain maximum function.
        ii. The Alliance should ensure the member has not obtained the medication in dispute.
    b. If the Alliance determines that an expedited redetermination request will not be accepted as an expedited request, the Alliance notifies the member (or their designated representative), both orally and in writing, of the decision to process the request under the standard 7 calendar day timeframe, within 72 hours. The Alliance also informs the member (or their designated representative) of their right to file an expedited grievance and that the member can resubmit the expedited request along with a prescribing physician's support.The Alliance will determine if all requests for expedited review will be accepted as such or further review and decision as to expedited or not is needed.

8. The Alliance ensures that the person or persons conducting the redetermination were not involved in the coverage determination.

        i. When the issue is a denial of a coverage based on a lack of medical necessity, the redetermination must be made by a physician with expertise in the field of medicine that is appropriate for the services at issue. The physician does not have to be the same specialty or subspecialty as the treating physician.

9. Notification timelines for standard and expedited redeterminations:

        i. For a *standard pre-service redetermination request*, the member (or their designated representative) is notified in writing as expeditiously as the member's health condition requires, but no later than 7 calendar days from receipt of the request. Decision letters are documented in the case file and recorded in the A &G database.

        ii. For an *expedited pre-service redetermination request*, the member (or their designated representative) is notified orally and in writing as expeditiously as the member's health condition requires, but no later than 72 hours after receipt of the request. Decision letters are documented in the case file and recorded in the A&G database.

1. If The Alliance initially provides verbal notification of its decision, it must deliver written confirmation of its decision within three (3) calendar days of the verbal notification.

iii. For a *standard payment redetermination request*, the Alliance will authorize payment for the benefit within fourteen (14) calendar days from the date is receives the request and make payment (i.e., mail the payment) no later than thirty (30) calendar days after the date the request was received.

10. Notification requirements for Part D:
    a. Favorable decisions
        i. Notify the member in a readable and understandable form, in accordance with the regulatory requirements at 42 CFR §423.590(h). If the representative filed the appeal, the representative must be notified in lieu of the enrollee. Plans may send written notice to the member and representative, but it is not required.
        ii. If the member's prescriber filed the request, Plan will provide notice (verbal or written) to the prescriber and written notice to the member.
        iii. Written notices must explain the conditions of the approval and must include (but are not limited to):
            1. The duration of the approval;
            2. Any limitations associated with the approval;
            3. Any coverage rules applicable to the subsequent refills.
    b. Adverse decisions
        i. Notify the member in writing. If the representative filed the appeal, the representative must be notified in lieu of the member. Written notice may be sent to both the member and representative but is not required.
        ii. If the member's prescriber filed the request, Plan will provide notice (verbal or written) to the prescriber and written notice to the member.
        iii. Notify the member in a readable and understandable form, in accordance with the regulatory requirements at 42 CFR §423.590(g).
            1. Include the specific reason for the denial that takes into account the member's presenting medical condition, disabilities, and any special language requirements, if any;
            2. Contain member's HICN or MBI, the Alliance's name, the Alliance's identification number, contract identification number, and formulary identification number.
            3. Provide a description of the applicable coverage rule or any other applicable plan policy upon which the denial was based, including any specific formulary criteria that must be satisfied for approval.
                a. If the drug could be approved under exception rules, the notice must explicitly state the need for a physician's supporting statement (PSS) and clearly identify the type of information that should be submitted when seeking a formulary or tiering exception; and

4. Inform the member of his or her right to a reconsideration (level 2 appeal)

11. If the Alliance overturns the redetermination (expedited or standard) the A&G department will contact Plan Pharmacy Operations (Pharmacy Ops) to enter the appropriate authorization(s) to allow the pharmacy claim(s) to process.
12. Pharmacy Ops will create an authorization in adjudication system and document the appeal and adjudication.

    a. If necessary to complete this task:

        i. Pharmacy Ops will reach out to the member or member representative to obtain prescription information and have it taken to pharmacy or facsimile sent to the dispensing pharmacy.

        ii. Pharmacy Ops will also contact the processing pharmacy to confirm that medication is adjudicating correctly and being dispensed for the member.

        iii. Adjudication confirmation will be documented in A&G database and added to the case file.

13. If the Alliance fails to provide the member with a redetermination decision within the allowed time frames for an expedited, standard coverage or standard payment determination, the case is forwarded to the IRE for review within 24 hours of the expiration of the adjudication time frame by overnight mail. Written notification to the member is done concurrently with the case referral to the IRE. Auto forward to IRE is documented in the A&G database.

    a. If the plan makes a fully favorable determination on a level one (1) appeal less than twenty-four (24) hours after the end of the adjudication timeframe, Planwill effectuate and notify the member of the favorable appeal decision in lieu of forwarding the appeal to the IRE.

        i. This should only occur on a limited basis. If CMS determines that the plan has a pattern of not processing level 1 appeals within the required timeframes, the plan may be considered out of compliance with its Medicare contract and/ or subject to intermediate sanctions in accordance with 42 CFR Part 423, subpart O.

14. When a member files a reconsideration (level 2 appeal) request with the IRE, the Alliance forwards a copy of the case file to the IRE within 24 hours (for an expedited request) or within 48 hours (for a standard request) from the time notice is received from the IRE, via overnight mail (or via facsimile). Notification to the member is done concurrently with the case referral to the IRE.

15. The Alliance complies with determinations that are fully or partially reversed by the IRE. The IRE's decision is binding on the Alliance, although the member may appeal further should the IRE fail to rule in the member's favor. All decisions by IRE are documented in the A&G database and copies of decisions attached to case file.

    a. *Standard Coverage*: If the IRE or other higher level of appeal entity reverses Plan standard determination in part or in whole regarding a request for standard coverage benefits, Planauthorizes or provides the benefit under dispute within 72 hours from the date it receives notice reversing the determination.

    b. *Expedited Coverage*: If the IRE or other higher level of appeal entity reverses Plan standard determination in part or in whole regarding a request for expedited benefits, Plan authorizes or provides the benefit under dispute as expeditiously as the member's health condition requires but no later than 24 hours from the date it receives notice reversing the determination.

    c. *Payment***:** If the IRE or other higher level of appeal entity reverses Plandetermination in part or in whole regarding a request for payment, Planmust authorize payment for the benefit within 72 hours but make payment no later than thirty 30 calendar days from the date it receives notice reversing the coverage determination.

16. CMS requires its Part D IRE to monitor Plan compliance with determinations or decisions that fully or partially reverse an original Plan denial, when the decision comes from the IRE. All documentation is noted in A&G's database and entered into the case file.
    a. The IRE issues a copy of the decision to the Alliance, accompanied by a notice of requirement to comply. In response to this notice, Planis required to mail a statement to the IRE attesting to its compliance with the entity's determination.
    b. To comply with the above, notification to the IRE is done concurrently with the effectuation of the re-determined decision.
17. Notification to the IRE that Plan will pay for or provide a service in the future is not sufficient proof of compliance.

    a. Proof of compliance to show that the effectuation has already occurred. Include the following:
        i. A copy of a check sent for payment;
        ii. An authorization number (including its effective dates, name of the issuing authority, and the date that the authorization was entered into the Alliance's system); or
        iii. Any other evidence that compliance has already occurred.
18. If the IRE does not obtain the compliance notice from the Alliance, it will mail a reminder notice to Plan stating that it must receive Plan compliance report within 30 days of the reminder notice.
        i. Failure by the Alliance to submit its compliance report to the IRE will result in the IRE reporting the Alliance non-compliance to CMS. The Alliance will not be copied on the non-compliance notice to CMS.

19. Anytime a higher level of appeal entity reverses Plan determination, in part or in whole, the Alliance will pay for, authorize, or provide the services under dispute as expeditiously as the member's health condition requires, but no later than 72 hours for a standard request or 24 hours for an expedited request, from the date it receives notice reversing the determination made by the Alliance.

    a. If a higher level of appeal entity reverses a standard payment request, the Alliance must authorize the payment within 72 hours and then make payment within 30 calendar days from the date that the notification of reversal is received.
    b. Notification to the IRE is done concurrently with the effectuation of the reversal determinations.

20. Anytime the Alliance reverses its standard coverage determination for a request for benefits, the Alliance authorizes or provides the benefit under dispute as expeditiously as the member's health condition requires, but no later than 7 calendar days from the date it receives the request for redetermination.

21. If the Alliance reverses an adverse expedited coverage determination regarding a request for benefits, the Alliance authorizes or provides the benefit under dispute as expeditiously as the member's health condition requires, but no later than 72 hours after the date the Alliance receives the request for redetermination.

22. If the Alliance reverses an adverse coverage determination regarding a request for payment, the Alliance authorizes payment for the benefit within 7 calendar days from the date it receives the request for reconsideration and makes payment no later than 30 calendar days after the date the Alliance receives the request for redeterminations.

DEFINITIONS / ACRONYMS

Appeal - The procedures that deal with the review of adverse initial determinations made by the plan on health care services or benefits under Part C or D. A redetermination is a Part D appeal.

Dismissal – A decision not to review a request for a grievance, initial determination, or appeal because it is considered invalid or does not otherwise meet Part D requirements.

Effectuation – Authorization or provision of a benefit that a plan has approved, payment of a claim or compliance with a complete or partial reversal of a plan's original adverse determination.

Enrollee (Member) – An eligible individual who is enrolled in the Medicare health plan.

Grievance – An expression of dissatisfaction with any aspect of the operations, activities or behavior of a plan or its delegated entity in the provision of health care items, services, or

prescription drugs, regardless of whether remedial action is requested or can be taken. A grievance does not include, and is distinct from, a dispute of the appeal of a coverage determination.

Independent Review Entity (IRE) – An independent entity contracted by CMS to review Medicare Part D adverse level two appeal decisions made by the plan. The current Part D Qualified Independent Contractor (QIC) is C2C Innovative Solutions Inc. (C2C).

Redetermination – A Medicare Part D *level one appeal* of an adverse coverage determination, including the findings upon which the decision was based and any other evidence submitted or obtained.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

42 CFR §423.560

Part C&D Enrollee Grievances, Organization/Coverage Determinations, and Appeals Guidance (01.01.2020), Section 50 – Reconsiderations and Redeterminations (Level 1 Appeals), Section 60 – Reconsiderations by the Independent Review Entity (Level 2 Appeal), Sections 70, 80 and 90, and Appendix 2 – Medicare Prescription Drug (Part D) Appeals Process Overview.

MONITORING

Internal audits are done on a regular basis (monthly) to ensure accuracy of cases that have been completed. All denials are audited and up to 100% of all approvals are audited. When temporary help is needed, "real-time" audits are conducted to assure that errors are caught in a timely manner. If internal auditing is. satisfactory for the first quarter, auditing sampling of approved and denied cases may occur each month for the rest of the plan year.

Monitoring for Timeliness

The x system will monitor the redeterminations; however, Pharmacy Operations will have to monitor the x system.

Effectuation Timeliness

Upon approval of a redetermination, the redetermination specialist enters the appropriate override for the medication in the claims adjudication system. The date stamp of when the override was entered is tracked in the system to show effectuation of the approval*.

If this is a request for a new drug, the override is entered with an effective date of when the request was made and to term the end of the calendar year unless in the last quarter as stated in the policy and procedure. If the request is due to the denial of a claim at the pharmacy, the override is entered to allow for coverage of the last denied claim and to term the end of the calendar year unless in the last quarter as stated in the policy and procedure. Please refer to "Length of Approvals" above for additional timeframes.

*Please note: The time stamped on effectuation shown is three (3) hours behind due to the time zone of the PBM. The actual effectuation time in the case will reflect Eastern time.

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POLICY AND PROCEDURE TEMPLATE

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

POLICY STATEMENT

Alameda Alliance for Health (Alliance) must develop and maintain an appropriate formulary in accordance with federal regulations which includes only Part D covered drugs and excludes drugs or classes of drugs or their medical uses that may be excluded or restricted from coverage under the Medicare program or are available under Part A or Part B of Medicare. This policy and procedure establishes guidance for the development and management of the Alliance formulary(s) by the contracted PBM. Oversight and monitoring of these processes is the responsibility of the Alliance Department of Pharmacy.

PROCEDURE

I. General Formulary Requirements

A. Minimum Content: Alliance's formulary adheres to the following requirements:

1. Includes at least two-Part D drugs within each therapeutic category and class of Part D drugs that are not therapeutically equivalent and bioequivalent, with different strengths and dosage forms available for each of those drugs. If the category or class includes only one Part D drug, then only one Part D drug must be included in a particular category or class of covered Part D drugs.

2. Include at least one Part D drug within a particular category or class of Part D drugs if Alliance demonstrates, and CMS approves, the following: A) that only two drugs are available in that category or class of Part D drugs; and B) that one drug is clinically superior to the other drug in that category or class of Part D drugs.

3. Include adequate coverage of the types of drugs most commonly needed by Part D enrollees, as recognized in national treatment guidelines.

4. Approved by CMS.

B. Protected Classes

Alliance's formulary includes all or substantially all drugs in the following six classes: immunosuppressant (for prophylaxis of organ transplant rejection), antidepressant, antipsychotic, anticonvulsant, antiretroviral and antineoplastic.

1. Limitation of Utilization Management: Alliance will not implement prior authorization or step therapy requirements that are intended to steer enrollees to preferred alternatives for enrollees currently taking a drug within these classes. See Continuity of Care policy.

2. If Alliance cannot determine at the point of sale that an enrollee is not currently taking a drug (e.g. new enrollee filling a prescription for the first time), Alliance will treat such enrollees as currently taking the drug within these classes.

3. New drugs or newly approved uses for drugs within the six classes that come onto the market will be subject to an expedited P&T Committee review. The P&T Committee shall make a decision within 90 days, rather than the usual 180-day requirement. These drugs will be added to the Alliance formulary by the end of the 90-day period.

4. For HIV/AIDS drugs, UM tools such as prior authorization and step therapy are generally not employed in widely used, best practice formulary models.

C. Specialty Tiers

Alliance develops its specialty tier within the formulary in accordance with the following requirements:

1. Only two tiers can be designated as specialty tiers that are exempt from cost-sharing exceptions.

2. Cost-sharing associated with the specialty tiers is limited to 25% (or except as otherwise permitted by CMS pursuant to bid review) in the initial coverage stage (or actuarially equivalent for plans with decreased or no deductible basic alternative benefit designs).

3. Only Part D drugs with negotiated prices that exceed the dollar-per-month amount of $XXX established by CMS in the annual Call Letter may be placed in the specialty tiers.

4. If not all drugs (including all strengths) within a category or class meet the criteria for inclusion in the specialty tiers, Alliance must ensure that placement of the remaining drugs among the other tiers of the formulary does not substantially discourage enrollment.

5. If a Part D drug is available in multiple strengths, package sizes and formulations, CMS will only allow inclusion on the specialty tiers of those strengths, package sizes and formulations that would reasonably exceed the dollar-per month threshold.

D. Other Formulary Processes

Lack of access to FDA labeled indications: Sponsors must generally cover formulary drugs for all FDA approved indications not otherwise excluded from Part D. All Alliance UM criteria include all FDA approved indications not otherwise excluded from Part D

E. Use of "off-label" indications: Part D sponsors will not be permitted to require an enrollee to try and fail drugs supported only by an off-label indication before providing access to a drug supported by an FDA approved indication (on-label indication) unless the off-label indication is supported by widely used treatment guidelines or clinical literature that CMS considers representing best practices.

F. When creating Step/Contingent Therapy criteria, Alliance reviews all FDA approved indications, off-label indications, and treatment guidelines to ensure that the enrollee will not be required to try/fail a Step 1 drug supported only by an off-label indication before providing access to a Step 2 drug supported by an FDA approved indication, unless the Step 1 drug is supported by widely used treatment guidelines or CMS approved best practice drug information compendia. If the member is unable to obtain the Step 2 medication at the point of sale, the coverage determination process is used to request that Step 2 medication.

G. Non-specific or vague criteria: Part D sponsors must provide a level of detail in their UM criteria that allows a prescriber to readily understand what criteria must be satisfied to permit access to the identified formulary drug. Non- specific or vague criteria will not be accepted. All UM is reviewed on an annual basis, or as needed based on updated medical literature, to ensure that new indications or new safety concerns are addressed within the UM criteria.

H. Overly burdensome criteria: Part D sponsors must not submit overly burdensome UM criteria. The Alliance process ensures that the criteria are not overly burdensome and will not require a trial and failure of more than two (2) formulary entities as Prior Authorization criteria.

I. Submission Errors: Part D sponsors must follow the technical instructions regarding HPMS submission of the formulary and UM criteria and ensure quality control of their work prior to submission. Alliance and its PBM go through a thorough quality assurance process to ensure that the criteria files submitted to CMS are accurate and meet all submission requirements as set forth in the CMS guidelines.

J. Over the counter (OTC) Drugs and Supplemental Drugs: Part D sponsors have the option to provide OTCs and Supplemental Formulary Drugs as part of their administrative cost structure. These OTC products and Supplemental Formulary Drugs do not count toward a member's TrOOP (true-out-of-pocket cost) or gross drug spend.

K. Alliance makes no changes to the therapeutic categories or classes other than at the beginning of each plan year (unless permitted by CMS in order to address new therapeutic uses and newly FDA-approved Part D drugs).

L. After the final September or October formulary submission for the upcoming contract year, no additional maintenance or non-maintenance changes will be made to the formulary file. In addition, in accordance with CMS formulary rules, non-maintenance negative changes will not be made between the beginning of the annual election period and 60 days after the beginning of the contract year associated with the annual election period (i.e. March 1).

M. Uniformity and Anti-discrimination

In developing its formulary, Alliance covers the most widely used medications, or therapeutically similar medications, for the most common conditions. Alliance's formulary (including its tiered structure) does not substantially discourage certain Part D eligible individuals from enrollment. Alliance's formulary is developed and applied uniformly, without regard to a certain subset of enrollees, and without discrimination against certain populations or disease groups.

N. Non-Matched NDC List

CMS will reject prescription drug event (PDE) submissions with national drug codes (NDCs) for which the FDA is unable to provide regulatory status determination of a Part D drug through their regular processes. Alliance's PBM will reject claims for NDCs that are not listed with the FDA, based on the NDC Directory. A reject message will be sent to the pharmacy explaining that the NDC is not listed with FDA, and so is not a Part D covered drug. To determine if a NDC is properly listed with FDA, CMS has published a list of NDCs which do not match the FDA NDC Directory (the Non-matched list). CMS has directed Part D plans and Alliance's PBM has developed processes to check the FDA NDC Directory periodically to determine if any NDCs on the non-matched list have subsequently been listed with FDA and thus should be covered.

II. **Formulary Development by P&T Committee**

Alliance's formulary is developed and reviewed by the P&T Committee of its contracted PBM. See Policy # XXXXXX Pharmacy and Therapeutics Committee. The committee adheres to the following requirements:

A. Membership

1. Comprised of members from various clinical specialties that adequately represent the needs of plan beneficiaries.

2. Comprise of a majority of members who are practicing physicians and practicing pharmacists.

3. Comprised of at least one practicing physician and at least one practicing pharmacist who are and free of conflict relative to: Alliance, Alliance's PBM, pharmaceutical manufacturers.

4. Comprised of at least one practicing physician and one practicing pharmacist who are experts in the care of elderly or disabled persons. Alliance defines "expert" as board certified in geriatrics, pharmacy certified in geriatrics or equivalent patient practice or site of practice.

5. Alliance and its PBM require that P&T Committee members sign a conflict-of-interest statement disclosing economic or other relationships with entities affected by drug coverage decisions that may influence committee decisions.

III. **Formulary Management Principles by P&T Committee**

1. Review medications for clinical appropriateness, and the policies of formulary management activities, including exceptions, prior authorization, step therapies, quantity limits, generic substitutions and other drug utilization activities that affect drug access.

2. Base clinical decisions and formulary decisions on the strength of scientific evidence and standards of practice, including assessing peer-reviewed medical literature, pharmacoeconomic studies, outcomes research data, and other such information as it determines appropriate.

3. Establish and document procedures to ensure appropriate drug review and inclusion. This includes documentation of decisions regarding formulary development and revision and utilization management. P&T recommendations regarding which Part D drugs are placed on the Alliance formulary are binding on the plan. P&T recommendations regarding tier placement and utilization management edits are advisory to the plan.

4. Consider whether the inclusion of a particular Part D drug in a formulary or formulary tier has any therapeutic advantages in terms of safety and efficacy.

5. Evaluate and analyze, at least annually, treatment protocols and procedures related to the plan's formulary, and inclusion or exclusion of the therapeutic classes, consistent with written policy guidelines and other CMS instructions.

6. Meet on a regular basis, at least quarterly.

7. Document in writing all decisions regarding formulary development and revision, and utilization management activities.

8. Make a reasonable effort to review a new chemical entity, as well as products with new FDA-approved indications, within 90 days of market release and make a decision within 180 days. (Protected class drugs will be reviewed and added to the formulary within 90 days).

DEFINITIONS / ACRONYMS

CMS Compendia: Section 1860D-2(e)(1)(B) of the Act limits "medically-accepted indication," by reference to section 1927(k)(6) of the Act, to any use of a covered Part D drug which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included or approved for inclusion in any of the compendia described in section 1927(g)(1)(B)(i) of the Act. The compendia are:

- American Hospital Formulary Service Drug Information (AHFS-DI)
- National Comprehensive Cancer Network (NCCN) Drug and Biologics Compendia
- Micromedex Drug Dex
- Clinical Pharmacology
- Lexi-Drugs

Part D sponsors are responsible for ensuring that covered Part D drugs are prescribed for "medically accepted indications." Part D sponsors may rely on utilization management policies and procedures to make such determinations, but pharmacists are not required to contact each prescriber to verify whether a prescription is being used for other than a medically accepted indication.

Designee: Another company or vendor that Alliance retains to perform certain PBM-related functions on behalf of Alliance (currently Vendor Name is its external vendor for P&T activities related to Alliance formularies and utilization management.)

Excluded Part D Drug Categories: Part D drugs do not include drugs or classes of drugs, or their medical uses, which may be excluded from coverage or otherwise restricted under Section 1927(d)(2) of the Act, except for smoking cessation agents.
Excluded:
- Agents when used for anorexia, weight loss, or weight gain (even if used for a non-cosmetic purpose (i.e., morbid obesity)).
- Agents when used to promote fertility.
- Agents when used for cosmetic purposes or hair growth.
- Agents when used for the symptomatic relief of cough and colds.
- Prescription vitamins and mineral products, except prenatal vitamins and fluoride preparations.
- Nonprescription drugs.
- Covered outpatient drugs which the manufacturer seeks to require as a condition of sale that associated tests or monitoring services be purchased exclusively from the manufacturer or its designee.
- Agents when used for the treatment of sexual or erectile dysfunction (ED). ED drugs will meet the definition of a Part D drug when prescribed for medically accepted indications approved by the FDA other than sexual or erectile dysfunction (such as pulmonary hypertension). However, ED drugs will not meet the definition of a Part D drug when used off-label, even when the off-label use is listed in one of the compendia found in section 1927(g)(1)(B)(i) of the Act: American Hospital Formulary Service Drug Information, United States Pharmacopeia-Drug Information (or its successor publications), and DRUGDEX Information System.

Food and Drug Administration (FDA): The federal agency that reviews drug products for safety and efficacy. A drug may not be marketed in the United States unless it has received approval from the FDA.

Part D Drug: A Part D drug means a drug that may be dispensed only upon a prescription, is being used for a medically accepted indication as defined by section 1927(k)(6) of the Act, and is one of the following:
- A drug that is described in sections 1927(k)(2)(A)(i) through (iii) of the Act.
- A biological product described in sections 1927(k)(2)(B)(i) through (iii) of the Act.
- Insulin described in section 1927(k)(2)(C) of the Act.
- Medical supplies associated with the delivery of insulin.
- A vaccine licensed under section 351 of the Public Health Service Act and its administration.

A covered Part D drug is a Part D drug that is included in a Part D sponsor's formulary, or treated as being included in a Part D plan's formulary as a result of a coverage determination or appeal under 42 CFR 423.566, 423.580, and 423.600, 423.610, 423.620 and 423.630, and obtained at a network pharmacy or an out-of-network pharmacy in accordance with 42 CFR 423.124.

Pharmacy & Therapeutics (P&T) Committee: An external advisory committee comprised of healthcare professionals (physicians, pharmacists, nurses, etc.) that is responsible for managing and administering the drug formulary system, including utilization management strategies.

Prior Authorization (PA): A utilization management strategy used for drugs that have:
- A high potential for misuse or inappropriate use.
- Severe adverse effects associated with use.
- Special monitoring required; and/or
- High cost, especially if other agents are available.
- Ensures coverage of drugs for FDA-approved uses, or for unapproved, or off-label, uses that are supported by adequate medical evidence.

Protected Classes: Part D sponsor formularies must include all or substantially all drugs in the immunosuppressant (for prophylaxis of organ transplant rejection), antidepressant, antipsychotic, anticonvulsant, antiretroviral, and antineoplastic classes.
Formularies must include substantially all drugs in these six categories that are FDA approved by the last CMS specified Health Plan Management System (HPMS) formulary upload date for the upcoming contract year. New drugs or newly approved uses for drugs within the six classes that come onto the market after the CMS specified formulary upload date will be subject to an expedited P&T committee review.

The expedited review process requires P&T committees to decide within 90 days, rather than the normal 180-day requirement. At the end of the 90-day period, these drugs must be added to Part D plan formularies. Part D sponsors may not implement prior authorization or step therapy requirements that are intended to steer beneficiaries to preferred alternatives within these classes for enrollees who are currently taking a drug.

Non-Formulary Drug: Means both Part D drugs that are not on the Sponsor's formulary and that are on the Sponsor's formulary but require prior authorization or step therapy under a plan's utilization management rules.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

42 CFR § 423.120(b)(4); § 423.120(b)(6), 42 CFR § 423.120(b)(5) (i-iii); § 423.578(d),
42 CFR § 423.120(b)(7), Chapter 6 – Part D Drug and Formulary Requirements
Medicare Marketing Guidelines for MAs, MA-PDs, PDPs, and 1876 Cost Plans

MONITORING

1. After monthly generation of the formulary file by Alliance's PBM, the Department of Pharmacy staff at Alliance will be responsible for the monthly review and quality assurance check of the formulary file prior to HPMS uploading.

2. The formulary file and UM edits will be uploaded to HPMS by XXXXXX

3. The CMS approved formulary file will be compared to the formulary file displayed on the website to ensure 100% accuracy. This monthly review and documentation will be conducted by Alliance Department of Pharmacy staff and the website updated to reflect the most recent review date.

4. Medicare Plan Finder monthly pricing files will be reviewed by the Alliance Pharmacy Department staff and any notices of non-compliance will be provided to the Alliance Compliance Officer.

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POLICY AND PROCEDURE TEMPLATE

Policy Number	[Assigned by compliance with format ABC-###]
Policy Name	Pharmacy and Therapeutics (P&T) Committee Delegation Oversight and Monitoring
Department Name	Pharmacy
Department Officer	Pharmacy Director
Policy Owner	Pharmacy Manager
Line(s) of Business	Medicare Advantage
Effective Date	[Original date policy was approved by committee - MM/DD/YYYY – TBD for new policies]
Subcommittee Name	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the name of the committee here, otherwise put N/A
Subcommittee Approval Date	If your department reviews policies at a subcommittee (Quality Improvement Health Equity Committee, Pharmacy and Therapeutics Committee, Peer Review and Credentialing Committee) put the date it was last approved at that subcommittee here, otherwise put N/A
Administrative Oversight Committee Approval Date	[Date policy was last approved at Compliance Department's Administrative Oversight Committee - MM/DD/YYYY – TBD when awaiting approval at Administrative Oversight Committee]

POLICY STATEMENT

This document outlines the functions and scope of responsibilities for Alameda Alliance for Health (Alliance) oversight and monitoring of the contracted Pharmacy Benefit Manager (PBM)'s Pharmacy and Therapeutics (P&T) Committee and the Alliance P&T Committee (if applicable). The P&T Committee is a standing committee of PerformRx and is responsible for review, guidance and clinical recommendations for the therapeutic use of drugs as contained within PerformRx and specified client formularies.

PROCEDURE

Alliance's formulary must be developed and reviewed by a P&T committee that meets specific requirements with respect to:

1. Membership

- P&T committee members must come from various clinical specialties that adequately represent the needs of sponsors' enrollees.
- A majority of the P&T committee members must be practicing physicians, practicing pharmacists, or both. CMS defines a practicing physician or pharmacist to be an individual who has an active professional license to practice in the United States or one of its Territories and is currently practicing in the U.S. or one of its Territories.
- At least one P&T committee practicing pharmacist and one practicing physician must be an expert in the care of elderly or disabled persons.
- At least one P&T committee practicing pharmacist and one practicing physician must be independent and free of conflict with respect to the Part D sponsor and pharmaceutical manufacturers. Such P&T committee members may have certain non-employee relationships with pharmaceutical manufacturers (for example consulting, advisory, or research relationships) and still be considered independent and free of conflict provided those relationships do not constitute significant sources of income and they do not otherwise have a conflict of interest that would compromise their independence. In addition, panel providers in a staff model HMO may be considered independent and free of conflict to the extent that any remuneration received from a Part D sponsor is limited to his or her clinical responsibilities for the care of plan enrollees.

2. Conflict of interest

- P&T committee members should sign a conflict-of-interest statement revealing economic or other relationships with entities affected by drug coverage decisions that could influence committee decisions.

3. P&T member disclosure to CMS

In the event the Part D sponsor has entered into a confidential agreement such that the Pharmacy Benefits Manager (PBM) will not disclose its P&T committee membership to the Part D sponsor, then it is the Part D sponsor's responsibility to notify CMS that this information will be submitted by the sponsor's PBM. Moreover, the Part D sponsor must ensure that the PBM notifies CMS of the P&T committee membership. The Part D sponsor maintains ultimate responsibility for adhering to and otherwise fully complying with all terms and conditions of its contract and the sponsor must ensure that the PBM notifies the sponsor that this information has been successfully submitted to CMS.

4. Meeting administration

- The P&T committee should meet on a regular basis, but no less than quarterly. P&T committee decisions regarding formulary development or revision must be documented in writing.

5. Formulary management

- The P&T committee must review for clinical appropriateness the practices and policies for formulary management activities, such as prior authorizations, step therapies, quantity limitations, generic substitutions, and other drug utilization activities that affect access. P&T committee recommendations regarding these activities are advisory only and not binding on the Part D sponsor.

- Formulary management decisions must be based on scientific evidence and may also be based on pharmacoeconomic considerations that achieve appropriate, safe, and cost-effective drug therapy.

- The P&T committees will be required to establish and document procedures to ensure appropriate drug review and inclusion. This includes documentation of decisions regarding formulary development and revision and utilization management activities (42 CFR §423.120(b)(1)(viii)). P&T committee recommendations regarding which Part D drugs are placed on a sponsor's formulary are binding on the Part D sponsor.

- Clinical decisions by the P&T committee should be based on scientific evidence and standards of practice, including peer reviewed medical literature, well-established clinical practice guidelines, and pharmacoeconomic studies, as well as other sources of appropriate information.

- Drugs' therapeutic advantages in terms of safety and efficacy must be considered when selecting formulary drugs and placing them on formulary tiers.

- The P&T committee will make a reasonable effort to review a new FDA approved drug product (or new FDA approved indication) within 90 days of its release onto the market and will make a decision on each new FDA approved drug product (or new FDA approved indication) within 180 days of its release onto the market, or a clinical justification will be provided if this timeframe is not met.

- The P&T committee will evaluate and analyze treatment protocols and procedures related to the sponsor's formulary at least annually.

- The P&T committee will approve inclusion or exclusion of the therapeutic classes in the formulary on an annual basis.

- Part D sponsors that change pharmacy benefit managers (PBMs) mid-year are required to continue the existing formulary. Decisions regarding formulary inclusion made by the previous PBM's P&T committee are binding on the assuming PBM. CMS will not approve negative formulary change requests for the purpose of aligning an existing formulary with that of a new PBM.

6. Formulary exceptions

- P&T committees must review clinical appropriateness protocols and procedures for the timely use of and access to both formulary and non-formulary drug products.

7. P&T committee role in transition

- At a minimum, a sponsor's transition process will address procedures for medical review of non-formulary drug requests and, when appropriate, a process for switching new Part D sponsor enrollees to therapeutically appropriate formulary alternatives failing an affirmative medical necessity determination. CMS will look to transition process submissions for assurances that a sponsor's P&T committee will review and provide recommendations regarding the procedures for medical review of non-formulary drug requests. P&T committee involvement will help ensure that transition decisions appropriately address situations involving enrollees stabilized on drugs that are not on the sponsor's formulary (or that are on the formulary but require prior authorization or step therapy under a sponsor's utilization management requirements) and which are known to have risks associated with any changes in the prescribed regimen. See Continuity of Care policy.

DEFINITIONS / ACRONYMS

CMS Centers for Medicare and Medicaid Services
Excluded Drug A drug that is not considered by CMS to be a Part D drug
Part D Formulary A list of drugs covered by Medicare Part D
HPMS Health Plan Management System
PA Prior Authorization
Part D Drug A drug that may be dispensed only upon a prescription, that is being used for a medically accepted indication, and is approved by the FDA
P&T Pharmacy and Therapeutics. Committee dedicated to evaluating the efficacy, safety, and cost effectiveness of medications.
QL Quantity Limit
UM Utilization Management. Describes formulary management tools such as Prior Authorization (PA), Step Therapy (ST), and Quantity Limit (QL) used to ensure safe, efficacious, and cost-effective use of medication.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

Medicare Prescription Drug Benefit Manual Chapter 6 – Part D Drugs and Formulary Requirements Section 30.1 42
CFR 423.120(b) and 42 CFR 423.120 (f),

MONITORING

A. Annual attestation – Alliance will require an annual attestation from the PBM's senior leadership of the delegated P&T Committee compliance with CMS requirements. Alliance's oversight and monitoring of the PBM's P&T Committee activity will include the following in addition to the annual attestation:

- Copies of executed conflict of interest forms by P&T Committee members at each scheduled meeting
- Copies of P&T Committee agenda one month in advance of the P&T Committee meeting
- Copy of P&T Committee minutes 30 days after date of the P&T Committee meeting
- Copy of minutes of any other standing committee (pricing, rebate, advisory committee) meetings held in conjunction with business items pertaining to the P&T Committee meeting agenda.
-

4.0 MONITORING

All P&T Committee oversight and monitoring documentation will be provided to the Alliance's Compliance Officer on an annual (attestation) or quarterly (P&T Committee meetings) basis.

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POLICY AND PROCEDURE TEMPLATE

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

POLICY STATEMENT

This policy is to establish guidelines for the review and monitoring of the Prescription Drug Event (PDE) development process. PDEs are a CMS requirement as the source of truth for member prescription drug dispensing events. PDEs are also used to reconcile the plans overall costs (and comparison to prospective monthly payments), Low Income Cost-sharing subsidies, coverage gap discounts, and for risk corridor purposes. It is important for plans to validate that their PDEs are complete, correct and submitted in total.

This policy and procedure applies to the Pharmacy Operations department to ensure PDEs are submitted timely and in a complete and accurate format per CMS requirements.

PROCEDURE

1.1 PDE development and submission to CMS is delegated to the PBM

1.2 PDE files are to be generated and submitted to CMS within 30 days of the date of the service or the date the claim was processed.

1.2.1 The PBM is delegated to generate the claims and perform initial audits to verify the previous PDE cycle has been closed, verify the cycle sequence and validate the batches against Alliance contract ID(s).

1.2.2 Prior to PDE upload, the PBM will validate file headers and trailers, batch headers and trailers and verify proper formatting and sequencing and then upload to CMS.

1.3 CMS posts the DDPS Transaction Validation File and the DDPS Transaction Error Summary Report on the PDFS portal.

1.3.1 The PBM is delegated to retrieve the outbound (or response) files from the PDFS portal and load the files into the PBM's database.

1.3.2 The PBM uses the data in the DDPS Transaction Validation file to generate Alliance's rejection reports:

1.3.2.1 Contract ID_cycle#_pde_error_summary_yymmddhhmmss.csv

1.3.2.2 Contract ID_cycle#_pde_error_detail_yymmddhhmmss.csv

1.3.2.3 Contract ID_cycle#_pde_error_summary_yymmddhhmmss.csv

1.3.2.4 Contract ID_cycle#_pde_informational_detail_yymmddhhmmss.csv

1.4 The reports are posted to Alliance's FTP site or designated location.

1.4.1 The PBM notifies Alliance via email of the posting and additionally provides a narrative summary of the results of the PDE submission.

1.4.2 The PBM may also attach the PDE Edit Resolution Guidelines and any other reports or information that might be helpful for the resolution of any rejected errors.

1.4.3 Alliance has an Analyst assigned to them by the PBM. The analyst works with the PBM's internal team and Alliance to correct rejected PDEs.

1.4.3.1 It is imperative that Alliance keep all eligibility files up to date

1.4.4 Rejected records whether corrected or not are submitted to CMS as new or adjusted PDEs on the next PDE upload cycle.

1.5 The PBM audits the PDE files and documents results in the PDE Documentation Audit Log. The audits occur throughout the PDE cycle and include:

1.5.1 File Audit – validation of file submissions; verifying the header and trailer data, batch header and trailer data, and claim detail sequence.

1.5.2 PDE Record Audit – validation of randomly selected PDE records (to include New, Adjustment, and Deletion records) for correct population from source data fields.

1.5.3 PDE Member Audit – validation of member claim activity throughout the Plan year for a randomly selected member; verifying each month that claims are processing in the appropriate benefit phase based on the member's TrOOP and Gross Covered Drug Cost, and that the financial fields on the PDE are correctly calculated.

1.6 Please refer to TrOOP/True-Up P & P for TrOOP PDE calculations considerations.

1.7 Please refer to Retro Low-Income Subsidy P & P for Retro-LICS calculations considerations.

1.8 The PBM will manage any post-production outliers (to include explanations) that are issued to the Acumen PDE Analysis website. These outliers are referenced as "Tickets".

1.8.1 Alliance will designate the PBM's PDE Team as a user of Acumen's PDE Analysis Website.

1.8.1.1 Users will be notified when Tickets are posted

1.8.1.2 The PBM PDE Team will download the ticket and analyze the issue

1.8.2 The PBM PDE Team will develop and provide Alliance with a written response to the Ticket. The response will be provided five business days before the response is due to Acumen.

1.8.2.1 Alliance will review the response and make edits as

necessary.

1.8.2.2 Alliance will upload responses to the Acumen PDE Analysis Website

DEFINITIONS / ACRONYMS

PBM – Pharmacy Benefit Manager
CMS – Centers for Medicare and Medicaid Services
DDPS – Drug Data Processing System
FTP – File transfer protocol
LICS – Low Income Subsidy
PBM – Pharmacy Benefit Manager
PDE – Prescription Drug Event
PDFS – Prescription Drug Front-End System

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

TrOOP True-Up
Low Income Subsidy

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

CMS Prescription Drug Event Participant Guide – 2011 Regional IT Technical Assistance
CSSC Operations Prescription Drug Program (Part D) (www.csscoperations.com)

MONITORING

To reduce the number of rejected PDEs, Alliance will:

- review TRRs and MMRs in a timely manner and make all necessary eligibility changes and provide the most current Eligibility File to the PBM
- review at least weekly, all PDE Reject reports, narrative result summaries of the PDE submissions. and PDE Edit Resolution Guidelines, and any other reports or information that might be helpful for the resolution of any rejected errors
- review PDE Reject reports daily during the first three months of the year (transition

period) and work with the PBM to correct any errors or issues

- track, trend and monitor resolutions through to closure during the first three months of the year
- monitor TrOOP and Retro-LICS PDE calculations per the TrOOP/True-Up Policy & Procedure and the Retro-LICS Policy & Procedure
- review the PBM PDE Documentation Audit Log at least weekly and work with the PBM to correct any errors or issues
- review all Acumen tickets and PBM written responses in a timely manner, make edits, and upload responses to the Acumen PDE Analysis Website

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POLICY AND PROCEDURE TEMPLATE

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

POLICY STATEMENT

1.1 Overview

Alameda Alliance for Health (Alliance) administers a transition process that is compliant with the established CMS transition requirements.

This policy is necessary with respect to:

(1) New enrollees following the annual coordinated election period.

(2) Newly eligible Medicare beneficiaries from other coverage.

(3) Enrollees who switch from one plan to another after the start of a contract year.

(4) Current enrollees affected by negative formulary changes across contract years; and

(5) Enrollees residing in long-term care (LTC) facilities.

Alliance will ensure that its transition policy will apply to non-formulary drugs, meaning both (1) Part D drugs that are not on a plan's formulary and, (2) Part D drugs that are on a plan's formulary but require prior authorization or step therapy, or that have an approved QL lower than the beneficiary's current dose, under the plan's utilization management rules. Alliance ensures that its policy addresses procedures for medical review of non-formulary drug requests, and when appropriate, a process for switching new Part D plan enrollees to therapeutically appropriate formulary alternatives failing an affirmative medical necessity determination.

Also, in accordance with CMS requirements, Alliance ensures that drugs excluded from Part D coverage due to Medicare statute are not eligible to be filled through the transition process.

However, to the extent that a Plan covers certain excluded drugs under an Enhanced benefit, those drugs should be treated the same as Part D drugs for the purposes of the transition process.

1.2 Transition Population

Alliance will maintain an appropriate transition process consistent with 42 CFR §423.120(b)(3) that includes a written description of how, for enrollees whose current drug therapies may not be included in their new Part D plan's formulary, it will effectuate a meaningful transition for: (1) new enrollees into prescription drug plans at the start of a contract year, (2) newly eligible Medicare beneficiaries from other coverage, (3) enrollees who switch from one plan to another after the start of a contract year, (4) current enrollees affected by negative formulary changes across contract years, (5) enrollees residing in long-term care (LTC) facilities

1.3 Transition Period

Alliance meets the CMS requirement of a minimum of 90-day transition period from the start date of a beneficiary's enrollment. Alliance will ensure that it will apply all transition processes to a brand-new prescription for a non-formulary drug if it cannot make the distinction between a brand-new prescription for a non-formulary drug and an ongoing prescription for a non-formulary drug at the point-of-sale.

1.4 Implementation Statement

a) **Claims Adjudication System:** Alliance's PBM has systems capabilities that allow the PBM to provide a temporary supply of non-formulary Part D drugs in order to accommodate the immediate needs of an enrollee, as well as to allow the Plan and/or the enrollee sufficient time to work with the prescriber to make an appropriate switch to a therapeutically equivalent medication or the completion of an exception request to maintain coverage of an existing drug based on medical necessity

reasons.

b) **Pharmacy Notification at Point-Of-Sale:** Alliance's PBM utilizes the current NCPDP Telecommunication Standard to provide POS messaging. Alliance's PBM reviews NCPDP reject, and approval codes developed during the External Codes List (ECL) process. Pharmacy messages are modified based on industry standards.

c) **Edits During Transition:** Alliance's PBM will only apply the following utilization management edits during transition at point-of-sale: edits to determine Part A or B versus Part D coverage, edits to prevent coverage of non-Part D drugs, edits to help determine Part D coverage (i.e., member level PAs) and edits to promote safe utilization of a Part D drug. Step therapy and prior authorization edits must be resolved at point-of-sale.

   Alliance's PBM will ensure that the transition policy provides refills for transition prescriptions dispensed for less than the written amount due to quantity limit safety edits, drug utilization edits that are based on approved product labeling and unit of use packaging size.

   As outlined in 42 CFR §423.153(b), the PBM has implemented Point-of-Sale (POS) PA edits to determine whether a drug is covered under Medicare Parts A or B as prescribed and administered, is being used for a Part D medically accepted indication or is a drug or drug classor its medical use that is excluded from coverage or otherwise restricted under Part D (Transmucosal Immediate Release Fentanyl (TIRF)) and Cialis drugs as an example).

d) **Pharmacy Overrides at Point-Of-Sale:** During the member's transition period, all edits (with the exception of those outlined in section 1.4(c)) associated with non-formulary drugs are automatically overridden at the point-of-sale. Pharmacies can also contact the PBM's Pharmacy Help Desk directly for immediate assistance with point-of-sale overrides. The PBM can also accommodate overrides at point-of-sale for emergency fills as described in section 1.7.

   Please see section 1.10 for specific information for the processing of non-formulary drugs in the Six Classes of Clinical Concern.

1.5 Transition Fills for New Members in the Outpatient (Retail) Setting

Alliance will ensure that in the retail setting, the transition policy provides for at least a one-time temporary fill of at least a month's supply of medication (unless the enrollee presents with a prescription written for less than a month's supply in which case the Part D Sponsor must allow multiple fills to provide up to a total of a month's supply of medication.) anytime during the first 90 days of a beneficiary's enrollment in a plan, beginning on the enrollee's effective date of coverage. If a brand medication is being filled under transition, the previous claim

must also be brand (based on Comprehensive NDC SPL Data Elements File [NSDE] marketing status). If a generic medication is being filled under transition, the previous claim can be either brand or generic (based on NSDE marketing status).

1.6 Transition Fills for New Members in the LTC Setting

Alliance will ensure that in the long-term care setting: (1) the transition policy provides for a one time temporary fill of at least a month's supply (unless the enrollee presents with a prescription written for less), which should be dispensed incrementally as applicable under 42 CFR §423.154 and with multiple fills provided if needed during the first 90 days of a beneficiary's enrollment in a plan, beginning on the enrollee's effective date of coverage (2) after the transition period has expired, the transition policy provides for a 31-day emergency supply of non-formulary Part D drugs (unless the enrollee presents with a prescription written for less than 31 days) while an exception or prior authorization is requested and (3) for enrollees being admitted to or discharged from a LTC facility, early refill edits are not used to limit appropriate and necessary access to their Part D benefit, and such enrollees are allowed to access a refill upon admission or discharge.

1.7 Emergency Supplies and Level of Care Changes for Current Members

An Emergency Supply is defined by CMS as a one-time fill of a non-formulary drug that is necessary with respect to current members in the LTC setting. Current members that need a one-time Emergency Fill or that are prescribed a non-formulary drug due to a level of care change can be placed in transition via an NCPDP pharmacy submission clarification code.
Alliance's PBM can also accommodate a one-time fill in these scenarios via a manual override at point-of-sale.

Upon receiving an LTC claim transaction where the pharmacy submitted a Submission Clarification Code (SCC) value of "18", which indicates that the claim transaction is for a new dispensing of medication due to the patient's admission or readmission into an LTC facility, the PBM's claims adjudication system will recognize the current member as being eligible to receive transition supplies and will only apply the point-of-sale edits described in section 1.4(c) of this policy. In this instance, the Plan does not need to enter a point-of-sale override.

For current enrollees whose drugs will be affected by negative formulary changes in the upcoming year, the Sponsor will effectuate a meaningful transition by either: (1) providing a transition process at the start of the new contract year or (2) effectuating a transition prior to the start of the new contract year.

If a brand medication is being filled under transition, the previous claim must also be brand (based on NSDE marketing status). If a generic medication is being filled under transition, the previous claim can be either brand or generic (based on NSDE marketing status)

Negative changes are changes to a formulary that result in a potential reduction in benefit to members. These changes can be associated with removing the covered Part D drug from the formulary, changing its preferred or tiered cost-sharing status, or adding utilization management. The transition across contract year process is applicable to all drugs associated to mid-year and across plan-year negative changes.

1.8 Transition Extension

Alliance will decide to continue to provide necessary Part D drugs to enrollees via an extension of the transition period, on a case-by-case basis, to the extent that their exception requests or appeals have not been processed by the end of the minimum transition period and until such time as a transition has been made (either through a switch to an appropriate formulary drug or a decision on an exception request). On a case-by-case basis, point-of-sale overrides can also be entered by Alliance or the plan's PBM (if authorized by the Plan to do so) to provide continued coverage of the transition drug(s).

1.9 Cost-Sharing for Transition Supplies

Alliance will ensure that cost-sharing for a temporary supply of drugs provided under its transition process will never exceed the statutory maximum co-payment amounts for low-income subsidy (LIS) eligible enrollees. For non-LIS enrollees, a sponsor must charge the same cost sharing for non-formulary Part D drugs provided during the transition that would apply for non- formulary drugs approved through a formulary exception in accordance with 42 CFR §423.578(b) and the same cost sharing for formulary drugs subject to utilization management edits provided during the transition that would apply if the utilization management criteria were met.

1.10 Six Classes of Clinical Concern

Per CMS guidance, members transitioning to a plan while taking a drug within the six classes of clinical concern must be granted continued coverage of therapy for the duration of treatment, up to the full duration of active enrollment in the plan. Utilization management restrictions (PA and/or StepTherapy), which may apply to new members naïve to therapy, are not applied to those members transitioning to the Medicare Part D plan on agents within these key categories.

The six classes include:

1) Antidepressant.
2) Antipsychotic.
3) Anticonvulsant.
4) Antineoplastic.
5) Antiretroviral; and
6) Immunosuppressant (for prophylaxis of organ transplant rejection).

For new members, protected class drug logic will always override transition logic to process the claim. Additionally, for new members, a 120-day transition period from their member start date isprovided.

1.11 Member Notification

Alliance's PBM provides the plan (via FTP) with two daily files called the Transition Notification "All" File and the Transition Notification "Print" file. The Transition Notification "All" File, which contains claims data and other member information, provides Plans with all of the information needed to contact members and providers regarding transition fills. The Transition Notification "Print" File includes necessary member and claims data needed to produce member notices. This file was created to allow the ability to produce one transition notice per member within a 100-day period where the drug, transition type and applicable drug restrictions are the same. [Refer to specific PerformRx file names. PerformRx can send out transition notices or the Alliance can send notices out from PerformRx file]

Alliance will send written notice via U.S. first class mail to enrollee within three business days of adjudication of the temporary transition fill. If the enrollee completes his or her transition supply in several fills, the sponsor is required to send notice with the first transition fill only. The notice must include (1) an explanation of the temporary nature of the transition supply an enrollee has received; (2) instructions for working with the plan sponsor and the enrollee's prescriber to satisfy utilization management requirements or to identify appropriate therapeutic alternatives that are on the plan's formulary; (3) an explanation of the enrollee's right to request a formulary exception; and (4) a description of the procedures for requesting a formulary exception. For long-term care residents dispensed multiple supplies of a Part D drug in increments of 14-days-or-less, consistent with the requirements under 42 CFR 423.154(a)(1)(i), the written notice must be provided within 3 business days after adjudication of the first temporary fill. Alliance will use the CMS model Transition Notice via the file-and-use process or submit a non-model Transition Notice to CMS for marketing review subject to a 45-day review. Alliance will ensure that reasonable efforts are made to notify prescribersof affected enrollees who receive a transition notice.

Alliance will utilize a print vendor to facilitate the fulfillment process of member notification.

Alliance's print vendor adheres to all guidelines as set forth in the Medicare Communication and Marketing Guidelines (MCMG).

Alliance will make their transition policy available to enrollees via link from Medicare Prescription Drug Plan Finder to the Alliance website and include in pre- and post-enrollment marketing materials as directed by CMS.

Alliance's PBM provides plans with a file to assist in producing a Prescriber Transition Notification letter to be mailed to the prescriber at the same time the transition letter is mailed to themember. This information is obtained from the

existing Transition Notification Files that are sent to plans daily, as described above. The file/letter includes the following:

- Prescriber information
- Member information
- Transition claim details

1.12 PDE Reporting

Since this is a CMS required process, any drugs dispensed that qualify under the transition period are reported as covered Part D drugs with appropriate fields populated on the Prescription Drug Event (PDE) including Plan and member cost sharing amounts

1.13 CMS Submission

Alliance will submit a copy of its transition process policy to CMS.

1.14 Pharmacy and Therapeutics Committee Role

Alliance uses the PBM's Pharmacy and Therapeutics Committee (P&T) which maintains a role in the transition process in the following areas:

1) The PBM's P&T committee reviews and recommends all formulary step therapy and prior authorization guidelines for clinical considerations; and
2) The PBM's P&T committee reviews and recommends procedures for medical review of non-formulary drug requests, including the exception process.

PROCEDURE

For all new members to the plan who require transitional fills for non-formulary medication(s), or medications requiring a step therapy, prior authorization or quantity limits, the transitional fill will process automatically per the specifications of the Plan Sponsor's transition policy.

For all members that require additional transitional fills outside of the first 90 days of eligibility with the plan for non-formulary medications, or medications requiring prior authorization, step therapy or quantity limits, these additional fills will require manual intervention for the transitional claim to process. The member, the member's appointed representative, or physician must call Customer Service to have a transition override placed into the pharmacy claims adjudication system.

Existing members who require a transition across plan years will receive an automated transitional fill for up to a one month's supply using a feature that performs a minimum 180-day look-back in claims history based on drugs identified by the Plan Sponsor as being eligible for transition across plan years. The pharmacy claims adjudication system will be

configured to review the member's history for the identified drugs per the Plan Sponsor's direction.

Alliance's transition process addresses situations in which an individual first presents at a network pharmacy with a prescription for a drug that is non-formulary and should be presumed to be unaware of what is covered by the plan or of the sponsor's exceptions process for providing access to Part D drugs that are not covered.

A beneficiary's transition period begins with the date of each enrollment. CMS receives frequent questions about who constitutes a "new" enrollee, and who constitutes a current enrollee affected by negative formulary changes, who are entitled to a transition fill. CMS believes these questions should first be considered in the context of the purpose of the transition policy. The purpose of the transition policy is to address situations when an enrollee's ongoing drug therapy (whether the Part D sponsor is able to actually ascertain ongoing therapy or not) could be potentially interrupted by a drug being non-formulary. Thus, an enrollee who stays with the same contract number but changes PBPs is potentially entitled to a transition fill because the enrollee could experience a negative formulary change. However, just because a member's drug therapy could potentially be interrupted does not mean that the member will necessarily receive a transition fill. In this example, for instance, the formulary may not have changed (which means there have also been no addition of utilization management edits). Also, in some cases, the sponsor may have the claims history for the member from the just prior PBP, and thus, the sponsor may be able to determine that the member is not taking a non-formulary medication. In other words, the sponsor may be able to determine at the POS that there will be no interruption in medication therapy for the member, and therefore the member is not eligible for a transition fill.

DEFINITIONS / ACRONYMS

CMS - the Centers for Medicare & Medicaid Services, the Federal agency within the Department of Health and Human Services (DHHS) that administers the Medicare program and oversees all Medicare Advantage Plan (MAPD) and Prescription Drug Plan (PDP) organizations.

Emergency Supply - An Emergency Supply is defined by CMS as a one-time transition fill that is necessary withrespect to members that are outside of their initial 90-day transition period and that are in the LTC setting.

FTP - File Transfer Protocol – One of the methods used by the Alliance and their PBM to transfer electronic files via the Internet. The first two bits of the file indicate the type offile.

ILI-Ingredient List Identifier (Formerly Hierarchical Ingredient Code List Sequence Number) or HICL, identifies a combination of active ingredients irrespective of manufacturer.

Level of Care Changes - Level of care changes include the following changes from one treatment setting toanother:

- Enter LTC facility from hospitals or other settings.

- Leave LTC facility and return to the community.
- Discharge from a hospital to a home.
- End a skilled nursing facility stay covered under Medicare Part A (including pharmacycharges), and revert to coverage under Part D.
- Revert from hospice status to standard Medicare Part A and B benefits; and
- Discharge from a psychiatric hospital with medication regimens that are highly individualized.

LTC – Long Term Care

NSDE - The FDA's Comprehensive NDC Structured Product Labeling Data Elements file. This fileis used to provide structured product labeling of Brand and Generic drugs.

PA - Prior Authorization - The process undertaken to make a benefit determination that is madeprior to the intended delivery of the healthcare service, treatment, or supply under review (e.g., a Pre-Service Claim). Prior Authorization includes requests for coverage determination for medications that are designated on the client part D formulary as "Prior Authorization Required", "Step Therapy", "Quantity Restrictions" or for requests for exception for non-formulary medications or co-insurance amount.

PBM – Pharmacy Benefit Manager

PDE – Prescription Drug Event – File that reports all claim transactions to CMS for inclusion in the annual financial reconciliation between CMS and health plans.

POS - The acronym given to the point-of-sale prescription transaction processing computer system. Also indicates that the actual retail transaction occurs when the claim is submitted electronically by the pharmacy.

P & T Committee - Pharmacy & Therapeutics Committee – An independent group of external & internal healthcare practitioners that are responsible for evaluating the efficacy, safety, and cost effectiveness of medications to determine potential additions, subtractions, and other changes to a formulary.

UM - Utilization Management – A set of guidelines that can be applied independently or jointly that otherwise restrict access to the dispensing or consumption of prescription drugs. Thefour basic restrictions are prior authorization (PA), quantity limits (QL), step therapy (ST) and tier placement. UM is a tool used by health plans to ensure safe, efficacious, and cost-effective.

AFFECTED DEPARTMENTS/PARTIES

[List the departments impacted by this policy, or required to comply with this policy]

RELATED POLICIES AND PROCEDURES

[List related Policies]

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

[List related documents]

REVISION HISTORY

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

REFERENCES

Federal Register, Vol. 76, No. 73, Part II, 42 CFR, §423.120(b)(3), §423.153(b), §423.154

Medicare Prescription Drug Benefit Manual, Chapter 6, Part D Drugs and Formulary Requirements, January 15, 2016, Section 30.4

MONITORING

In addition to daily rejected claims review, Alliance staff will perform XXXXX transition sample reviews to ensure compliance with CMS regulations and Alliance policies and procedures. The results of these internal audits will be provided to Alliance Compliance Department.

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

PHARMACY & THERAPEUTICS COMMITTEE

Record of Committee Meeting Minutes

Tuesday, September 24, 2024 | 5:00pm – 7:00pm

Status	Voting Committee Members	Organization	Initials	Officer / Notes
P	Donna Carey, MD	Chief Medical Officer-Alliance	DC	Chairman
P	Rahel Negash, Pharm D	Pharmacy Services Supervisor – Alliance	RN	Co-Chair
P	Nora Tomassian, Pharm D	Intermittent Director of Pharmacy Services	NT	
P	Aaron Basrai, PharmD	Haller's Pharmacy	AB	BOG
P	Paul Bayard, MD	La Clinica de la Raza (CHCN)	PB	
P	Ivan Lee, MD	Private Practice	IL	
P	Bao Dao, MD	Epic Care	BD	
P	Betsy Yuan, PharmD	Alameda County Behavioral Health Dept.	BY	

P=Present; PH=Call-in; A=Absent; CMO = Chief Medical Officer; DOPS=Director of Pharmacy Services; BOG = Board of Governors Representative

Status	Regular Guests	Organization	Initials	Role / Department
P	Iryna Makukh	PerformRx	IM	Pharmacy Formulary Management.
P	Liza Rosendale	PerformRx	LR	Clinical Program Manager
P	Pat DeHoratius	PerformRx	PD	Manager Formulary/DUR
P	Barrie Cheung	PerformRx	BC	Regional Pharmacy Director
A	Ramon Tran Tang, PharmD	Alameda Alliance	RT	Clinical Pharmacist
P	Jefferey Bencini, Pharm D	Alameda Alliance	JB	Clinical Pharmacist
P	Timothy Tong, Pharm D	Alameda Alliance	TT	Clinical Pharmacist
A	Beverly Juan, MD	Alameda Alliance	BJ	Medical Director
A	Sanjay Bhatt, MD	Alameda Alliance	SB	Medical Director
A	Darryl Crowder	Alameda Alliance	DC	Provider Relations
P	Bibek Sandhu, PharmD, MBA	PillarRX	SB	Consulting Pharmacist

Other Guests	

Follow-up Items:

Clerk of the Committee: Benita Ochoa

Agenda Item	Discussion Leader	Discussion Summary	Action	Notes
I) Call to Order	D. Carey	• Agenda Overview	Called to order at: 6:05PM	
II) Informational Updates	D. Carey R. Negash	Informational Update • DHCS Audit - We are still waiting for our official findings. They were slated to come by the end of September. We still have a few more days left. As soon as we have those results of the audit of course we will share those results here as they pertain to pharmacy. • Search for Permanent/Interim Director - In terms of our search for our permanent/interim director I am happy to report we have an interim director of pharmacy. Nora Tomassian introduction. Nora started today and is our interim pharmacy director. We will be continuing our search for a permanent director of pharmacy hopefully that position will open next week or the week after. We are happy to have Dr. Tomassian with us, she is very experienced and has a wealth of knowledge about Medicaid and DSNP. As we are moving into that line of business. She has been a previous director of pharmacy. Nora introduced herself. • DSNP Readiness **<u>Questions:</u>**		

III) Pharmacy Utilization Reports (Quarter 2, 2024)	R. Negash	(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) o The top 50 drugs accounted for 1,095 claims for 588 members and cost $1,442,371, which is an increase of $85,169 in spend from the previous quarter. o Biktarvy remains at number one, claims have gone up by 1, and there are two additional members since the previous quarter. o Zejula remains at number 2 with 3 claims for 1 member. This medication is managed via the Oral and Injectable Oncology Medications MRG. o Ozempic is at numbers 3, 5 and 7, with 209 total claims for 103 members. There was an increase of 28 claims and of 14 members from the previous quarter. o Vemlidy is down to number 4 with 51 claims for 21 members. This medication is managed via the Hepatitis B MRG, which requires trial and failure of, intolerance to, or reason not to use, entecavir. o Verzenio is up at number 6 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. - Top 50 Drugs by Cost (Medi-Cal) o The top 50 drugs accounted for 37,622 claims for 32,013 members and cost $53,049,668.03, which is an increase of $4,633,273.16 in spend from the previous quarter. o Biktarvy remains at the number 1 spot with 884 claims for 656 members. An increase of 34 claims from last quarter. o Ozempic also remains at the number 2 spot, with 2,115 claims for 1,704 members. This is an increase of 238 claims from last quarter. o Skyrizi has risen from the number 6 from the number 4 spot with 99 claims for 87 members. This is an increase of 10 claims since last quarter. o Jardiance 25mg has risen from the number 5 to the number 3 spot with 1,677 claims for 1,570 claims, while Jardiance 10mg has fallen from the number 4 to the number 5 spot with 1,755 claims for 1,577 members. Both Jardiance 25mg and Jardiance 10mg had an increase of 141 and 108 claims, respectively, since last quarter. **Questions:** DC: The jump in Ozempic do we know outside of advertising, do you think that accounts for why we are seeing this jump? 238 claims have increased? RN: We do tend to get a lot of requests for IHSS line of business. Sometimes those requests are inappropriately received for anti-obesity when it should be in the diabetic population so that is a potential reason an increase in utilization. With skyrizi moving from number six to number four it did have increase of about 10 claims in the last quarter. There are potentially more members being identified with some type of rheumatologic issues. It's hard to say why there is that jump. Perform Rx is something that you also see in your other plans?		

		PD: From another plan perspective we are skyrizi trend up in a lot of other plans we do attribute that to the aggressive marketing that the other manufacturers are doing. We are seeing this with other plans, and we think that is part of the cause. PB: Can I ask about the Ozempic versus the rybelsus I see that rybelsus in the list as well. Is there a cost difference? Is a month's supply of rybelsus less than a month's supply of Ozempic? I'm not sure if anyone has done a head-to-head but rybelsus does the same agent as Ozempic. PD: I can answer that one essentially the injectable Ozempic has better weight loss numbers than the rybelsus even though it's the same product. So, we think that is why that is driving up the injectable use. PB: Are we addressing this some way? Are the better are the weight loss numbers? PD: I don't have the exact number, but I think it was like four plus pounds not tremendous, but it was higher numbers. PB: what is the cost of a month's worth of say rybelsus versus Ozempic? PD: We can pull that together and get back to you. Hopefully before this meeting is over. PB: if it is cheaper that would be really helpful so that we would divert people to that and Steglatro is our preferred agent in this class and some people are getting Jardiance, not sure why they can't make do with Steglatro. Are there other reasons why they are getting approved. RN: This particular utilization is for Medi-Cal we technically do not have control. PB: That is right. AB: My cost for Rybelsus and Ozempic is the same. IM: To be exact Rybelsus is $1,100 and Ozempic is around $1,200. NT: Could it be the member request since there is a lot more information about the injectables vs. Rybelsus in the public. RN: That is very possible. I would imagine that Rybelsus is less convenient since they have to take it every day and the other injectable are weekly. That might be another driver to the injectable option. DC: In the appeals that I've been seeing its member driven. Members are requesting for these medications because they heard about it, friends. RN: Yes, definitely it's something we are seeing at different pharmacies conventions everyone is discussing the GLP-1's because there is such a high volume of requests and popularity around this. - Top 50 PA Reviewed Drugs by Volume (IHSS) Top 50 PA requests = 175. There were 256 total PA requests for quarter 2. o 73 requests (42%) were approved. This approval rate is higher, by 7%, than what was observed last quarter. o 102 requests (58%) were denied or partially approved. Wegovy is up at numbers 1 and 6 with 36 total requests and 5 approvals (13%). o Wegovy to reduce excess body weight requires a diagnosis of obesity or BMI ≥27 and at least one weight-related comorbidity (diabetes, hypertension, hyperlipidemia) or history of heart attack, despite diet and exercise, and trial and failure or inability to use Qsymia and Contrave. o Wegovy to reduce the risk of major adverse cardiovascular events requires a documentation that the patient is obese or has BMI ≥27, has an established cardiovascular disease (prior myocardial infarction, stroke or symptomatic peripheral		

arterial disease), patient is on standard of care treatment for CVD and does not have diabetes.

Jardiance is at numbers 2 & 8 with 19 total requests and 12 approvals (63%).

- Jardiance requires trial and failure of one of the following: metformin, branded/generic drug containing metformin, branded angiotensin receptor/neprilysin inhibitor (ARNi), generic angiotensin-converting enzyme inhibitor (ACEi), generic angiotensin receptor blocker (ARB), generic mineralocorticoid receptor antagonist (MRA), or generic beta blocker.

Ozempic and Vemlidy are at numbers 3 and 4 with 10 requests for each drug. There were 6 approvals (60%) for Ozempic and 7 approvals (70%) for Vemlidy.

- Ozempic requires a trial and failure of metformin.
- Vemlidy requires a diagnosis of Hepatitis B, and trial and failure of, intolerance to, or inability to use entecavir tablets.

Zepbound is at numbers 5 and 19 with 12 total requests and 4 approvals (33%).

- Zepbound 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.

- Top 50 PA Reviewed Drugs by Volume (Medi-Cal)
  - The top 50 drugs accounted for 214,548 claims for 192,167 members and cost $4,709,064.19. This is an increase of 6,017 claims from last quarter.
  - Albuterol remains at the number 1 spot with 13,338 claims for 10,992 members. Note: there was a decrease of 892 claims from last quarter.
  - Fluticasone has risen from the number 4 to the number 2 spot with 10,933 claims for 10,232 members. There was an increase of 2,297 claims from last quarter.
  - Ibuprofen has fallen to the number 3 spot with 9,391 claims for 8,464 members. This is a decrease of 115 claims from last quarter.
  - Aspirin has fallen from the number 3 to the number 4 spot with 9189 claims for 8,436 members. This is a decrease of only 45 claims from last quarter.
  - Loratadine remains at the number 5 with 8,189 claims for 7,374 members.

IV) E-Voting Material/Consent Agenda

R. Negash
B. Ochoa

E-Voting Material/Consent Agenda

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

Rahel Negash, PharmD, Pharmacy Supervisor – Alameda Alliance
Benita Ochoa, CPhT, Lead Pharmacy Technician – Alameda Alliance
(All matters listed on the Consent Calendar are to be approved with one motion unless a member of the P&T Committee removes an item for separate action. Any consent calendar item for which separate action is requested shall be heard as the next Agenda item in closed session.)

Monographs/Class Reviews	Changes
Chelating Agents Class Review	• No changes
Continuous Glucose Monitors (CGMs) Class Review	• No changes
Pancreatic Enzymes Class Review	• No changes
Medication Request Guidelines	**Changes**
Physician Administered Medication (PAD)/ Medical Benefit Guidelines	• No changes
Off-label uses	• No changes
Safety Edit Exception	• No changes
Quantity Limit Exception	• No changes
Antibiotic Eye Medications	• No changes
Antiemetics	• Remove Zuplenz as it has been discontinued
Nuedexta (dextromethorphan/quinidine)	• No changes
Cartilaginous Repair Agents	• No changes
Memantine ER (Namenda XR)	• No changes
Ophthalmic Anti-inflammatory Immunomodulators	• No changes
Penicillamine (Depen, Cuprimine), Trientine HCl (Syprine) for Wilson's disease	• No changes

Approved via e-voting:
Yes: 6
No: 0
Abstained: 1

		Iron-chelating Agents	• No changes			
		Vancomycin	• No changes			
		Dronabinol	• No changes			
		Multaq (dronedarone)	• No changes			
		Erythropoiesis-Stimulating Agents	• No changes			
		Drugs for Gender Dysphoria For Less Than 21 Years Old	• No changes			
		Drugs for Gender Dysphoria For At Least 21 Years Old	• No changes, add 10mg available dosage form for medroxyprogesterone			
		Mesalamine	• Remove Mesalamine DR (Asacol HD) tablet as it has been discontinued			
		Corticosteroids for Ulcerative Colitis and Crohn's disease	• Add Ortikos to coverage duration section			
		Atovaquone-proguanil (Malarone)	• No changes			
		Intranasal Steroids	• Remove Rhinocort Allergy brand product as it was discontinued			
		Scabicides and Pediculicides	• Remove Lindane product as it was discontinued			
		Rifamycin Antibiotics	• No changes			
		Topical Acne Agents	• No changes			
		Injectable/Infusible Bone-Modifying Agents for Oncology Indications	• Remove Aredia and Zometa brands as they were discontinued			
		Alosetron (Lotronex)	• No changes			
		Viberzi (eluxadoline)	• No changes			
		Rifabutin (Mycobutin)	• No changes			
		Medications for the treatment of Multi-Drug Resistant Tuberculosis	• No changes			
		Tranexamic acid (Lysteda)	• No changes			
		Moxifloxacin Oral Tablet	• No changes			
		Spravato (esketamine) Intranasal	• No changes			

		Santyl Ointment	• No changes			
		Topical Antibiotics	• No changes			
		Fertility Agents	• No changes			
		Erectile Dysfunction Medications	• Remove IFE PG20 as it has been discontinued			
		Vowst	• No changes			
		Physician Administered Drug (PAD) Guidelines	**Changes**			
		Adakveo	• No changes			
		Exondys 51	• No changes, minor grammatical correction			
		Erythropoiesis-Stimulating Agents	• No changes			
		Iron-containing Products	• No changes			
		Tepezza	• No clinical changes, minor formatting change			
		Fecal microbiota	• No changes			
		Omisirge	• No changes, addition of medical necessity review statement			
		Qalsody (tofersen)	• No changes, addition of medical necessity review statement			
		Lamzede	• No changes, addition of medical necessity review statement			
		Enzyme Replacement Therapies for Fabry Disease	• No changes, addition of medical necessity review statement			
		Roctavian	• No changes, addition of medical necessity review statement			
		Enzyme replacement therapy for acid sphingomyelinase deficiency (ASMD)	• No changes, addition of medical necessity review statement			
		Interim Formulary Updates				
		• See p. 150 in packet				
		Interim Physician Administered Drug (PAD) Updates				
		• See p. 151 in packet				
		Pharmacy Policy & Procedure Updates				
		• RX-002 Pharmacy Benefit Prior Authorization Review Process	• Add G&A submission for appeal language			

		• RX-005 P&T Committee Roles and Scope • Language to include DMHC psychiatric specialist requirement **ED Oversight** • None **90 Day Maintenance List updates** • Formatting change with dates **P&T Meeting Minutes** • P&T Meeting Minutes Q2 June 11, 2024			

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
Fasenra Subcutaneous Solution Prefilled Syringe 10 MG/0.5ML	NF to F-PA
Acthar Gel Subcutaneous Auto-injector 80 UNIT/ML	NF to F-PA
Acthar Gel Subcutaneous Auto-injector 40 UNIT/0.5ML	NF to F-PA
Entresto Oral Capsule Sprinkle 6-6 MG	NF to F-QL (240/30 days)
Entresto Oral Capsule Sprinkle 15-16 MG	NF to F-QL (240/30 days)
Afluria Intramuscular Suspension	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Afluria Preservative Free Intramuscular Suspension Prefilled Syringe 0.5 ML	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Fluad Intramuscular Suspension Prefilled Syringe 0.5 ML	NF to F-AL-QL (65 years and up) (1 fill per 270 days)
Fluarix Intramuscular Suspension Prefilled Syringe 0.5 ML	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Flublok Intramuscular Solution Prefilled Syringe 0.5 ML	NF to F-AL-QL (18 years and up) (1 fill per 270 days)
Flucelvax Intramuscular Suspension	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Flucelvax Intramuscular Suspension Prefilled Syringe 0.5 ML	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Flulaval Intramuscular Suspension Prefilled Syringe 0.5 ML	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Fluzone High-Dose Intramuscular Suspension Prefilled Syringe 0.5 ML	NF to F-AL-QL (65 years and up) (1 fill per 270 days)
Fluzone Intramuscular Suspension	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Fluzone Intramuscular Suspension Prefilled Syringe 0.5 ML	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
FluMist Nasal Liquid	NF to F-AL-QL (12-49 years) (1 fill per 270 days)

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	HCPCS Description	Action
J7682	TOBRAMYCIN NON-COMP UNIT	Remove from PA
J9057	COPANLISIB	Remove from PA
J9070	CYCLOPHOSPHAMIDE	Remove from PA

V) New Business	Iryna Makukh	**New MRG** IM-Good evening, everyone. So, for the new business we'll start on page 204 with the new MRG criteria for Xolremdi. **Xolremdi** - Xolremdi was recently approved for patients 12 years of age and older with WHIM syndrome to increase the number of circulating mature neutrophils and lymphocytes. Just to go into disease state, WHIM stands for warts, hypogammaglobulinemia, infections and myelokathexis. It is an ultra-rare, combined immunodeficiency. It is caused by genetic variations in the CXCR4 receptor which helps to regulate movement of neutrophils and lymphocytes. Hypogammaglobulinemia refers to a deficiency with infection fighting antibodies and myelokathexis is a type of severe congenital neutropenia. - Patients suffering with WHIM syndrome are more vulnerable to bacterial and HPD infections causing severe skin and genital warts. Typically, symptoms of bacterial infections can present in early childhood but resolve with oral antibiotics. However, more severe infections can lead to chronic ear infections, hearing loss, pneumonia, respiratory and heart failure. - The total population of those affected by WHIM syndrome is unknown due to varying clinical presentations but it is estimated that about 0.2 per 1 million are affected and approximately 100 cases have been reported in medical literature. So, it's a very rare syndrome. - Xolremdi is the first FDA approved treatment indicated for patients with WHIM syndrome. It is an orally viable CXCR4 antagonist that blocks the binding of the ____which plays a role in trafficking leukocytes to and from the bone marrow. - Treatment for Xolremdi results in increased mobilization of neutrophils and lymphocytes from the bone marrow into the peripheral circulation. Xolremdi is dosed once daily based on weight and is available as a 100mg oral capsule that is priced at $40,800 for patients weighing more than 50kg and $30,600 for patients weighing 50kg or less. And that's the price per month. - As for the criteria, patients must be 12 years or older and that's per indication. Prescriber must be an immunologist or a hematologist and for the initial authorization, we are asking for diagnosis of WHIM syndrome confirmed by genotype variant chemokine receptor 4 and absolute neutrophil count (ANC) of ≤ 400 cells/μL. This is from exclusion criteria from the trial and higher ANC wouldn't be considered for treatment. Also, we require documentation of baseline neutrophil counts and absolute lymphocyte counts	Move to approve: 1st: DB 2nd:PB	

since these were primary endpoint of the trial. And documentation of member weight, medication is prescribed at a FDA approved dose.

- And for reauthorization, we ask for documentation or provider attestation of positive clinical response such as improvements of baseline ANC and ALC and documentation of member weight and medication is prescribed at a FDA approved dose.
- For coverage duration, the initial request will be approved for 6 months and that's in line with efficacy and safety of pivotal trial. The re-authorization request will be approved for 12 months since this is a chronic condition.
- This is it for the criteria. Any questions about the criteria?

New PAD

We go to the next page, page 205 and here we have a new physician administered drug policy for Rytelo.
Rytelo

- Rytelo was recently approved for the treatment of adults with low or intermediate risk of myelodysplastic syndromes with transfusion-dependent anemia requiring 4 or more red blood cell units over 8 weeks who have not responded to or have lost response to or ineligible for erythropoiesis-stimulating agents
- Rytelo is an oligonucleotide telomerase inhibitor, and it blocks the interaction between telomerase and telomeres leading to the increased destruction of malignant cells with high telomerase activity.
- This can improve hematolysis in the bone marrow.
- In terms of the state of the disease, myelodysplastic syndromes are a group of disorders characterized by abnormal block forming cells in the bone marrow resulting in the reduction of peripheral blood cells and elevated risk of acute myeloid leukemia, bone marrow failure, and reduced survival.
- Severe fatigue is the problematic symptoms reported by patients. Other symptoms include bleeding, night sweat, bone pain, and recurrent infections.
- There are currently between 60,000 and 125,000 people living with MDS in the US which is about 3.4 cases per 100,000 people in general population and prevalence is higher in older population over the age of 65.
- Approximately 40 percent of lower risk MDS patients become dependent on blood transfusions to treat their anemia. ESAs are usually the first line therapy for patients; however, some patients do not respond to ESA's, some stop responding, and some are ineligible for therapy.
- Rytelo is an IV infusion that is $27,800 per 28 days. The recommended dosage is 7.1mg/kg administered as an IV over 2 hours every 4 weeks.
- As for the criteria, it is based largely on trial data and labeling
- The first thing to point out is the coverage duration. Per label, treatment should be discontinued if the patient doesn't experience a decrease in RBC transfusion burden after 24 weeks of treatment and that's six consecutive doses.
- So, the initial request would be approved for 6 months based on that. For the initial authorization, patients must have diagnosis of MDS with transfusion dependent anemia. That's the only indication for PI, then a characterization for IPSS-R scoring system that was recently updated and widely accepted for managing the risk of progression of the disease

		- This indication is only for low or intermediate-1 risk of progression; therefore, we included a requirement that a patient has, or low or intermediate-1 risk of progression for this standard. - Next transfusion burden 4 or more red blood cell (RBC) units within an 8-week period over the last 4 months and this is very specific for key trial inclusion data per label. - Also, prescriber attestation that complete blood cell count (CBC) will be obtained prior to initiation weekly for first two cycles and prior to each cycle thereafter. This is specifically from labeling as far as dosing and there is a pretty high risk of thrombocytopenia and neutropenia associated with this medication and before we need to assure the prescriber is on board with the CBC counts at dose times. - Also, member weight should be provided because of the weight-based dosing and medication is prescribed at an FDA approved dose. - For the re-authorization, we're looking for clinical benefit or reduction of RBC transfusion burden as compared with baseline and additionally, it is important by attestation the member is tolerate of medication and does not have any serious adverse reactions like thrombocytopenia and neutropenia. Per the label, Rytelo should be discontinued if unacceptable toxicity occurs at any time. Also, we are looking for members weight and FDA approved dose for this criteria. - Any Questions on this criteria?		
VI) Class Reviews, Monographs, and Recommendations-	Iryna Makukh	**Duvyzat Monograph** **New MRG: Duvyzat** - Duvyzat monograph on page 206. - Duvyzat is a new medication recently approved treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older, it is a histone deacetylase inhibitor. DMD is a rare fatal genetic disease caused by mutation in the DMD gene that leads defects or absence of dystrophy in protein. This results in progressive muscle degeneration leading to loss of ambulation and eventually respiratory orthopedic and cardiac complications. - Clinically DMD presents as a progressive and irreversible muscle deterioration - DMD primarily affects boys but can affect girls in rare cases - That incident is estimated to be approximately 1 in 3500 to 5000 newborn boys and prevalence estimates between 10,000 and 15,000 males - Most DMD patients are diagnosed at 3 to 5 years of age - Patients commonly require wheelchairs by age 12, breathing support by age 20, and may get to respiratory and cardiac failure. - Currently, there is curative treatment for DMD. There are 2 primary treatment strategies. o The first strategy therapy is improving muscle function that is caused by the lack of muscle dystrophy. This would include anti-inflammatory agents such as steroids like prednisone o The send category of therapy would focus on restoring dystrophene function. This would be gene therapy LBD's - Currently, pharmacological treatment with steroids such as prednisone are the mainstays of DMD treatment. They provide beneficial effects when improving motor function and pulmonary		

		function, reducing the risk of scoliosis, delaying the loss of ambulation, and possibly delaying progression of cardiomyopathy, and improving survival. - What's unique about Duvyzat is that it's the first non-steroidal drug approved for treatment of all patients with all genetic variance of DMD - Duvyzat is a histone deacetylase inhibitor. This may activate and repair mechanisms that prevent muscle degeneration - This approval is based on results from stage 3 efficacy trial. They were looking at boys six to seventeen years old that were treated with either Duvyzat twice a day or placebo and all were on steroids concurrently. - They were followed for eighteen months and results show that patients with Duvyzat showed slower decline on the primary endpoint of the assessment compared to patients who received placebo. - There is a study underway to investigate Duvyzat in non-ambulatory patients with DMD and ongoing extension study evaluating the long-term safety and efficacy - Duvyzat comes in oral suspension and dosing is based on weight - The cost is $55,500 per month and this based on a 30kg weight child - We have the new criteria on page 213 - We are asking that prescriber is a neurologist or provider or specializes in the treatment of Duchenne Muscular Dystrophy - For additional authorization, we ask that medication be prescribed at an FDA approved dose according to body weight - We ask for a diagnosis of DMD, and copies of testing should be included with request - Patient has been stable on corticosteroids for at least 6 months, since steroids are standard of care and there is lack of data that Duvyzat can be used as monotherapy - Patient is in trials with background steroid treatment as well - Patient must be ambulatory because patients included in the trial were ambulatory - For re-authorization, pretty much the same as the initial requirements o Documentation or provider attestation of positive clinical response such as improved muscle function, muscle strength, or disease stabilization o Patient is on concurrent steroid treatment o Patient is ambulatory still o Medication is prescribed at an FDA approved dose according to body weight - Coverage duration is for 12 months for both initial and re-authorization request since primary was measured at 18 months - We recommend approving the new Duvyzat criteria without changes to formulary status. Any Questions? DC**:**Is this treatment meant to be lifelong or after one or two 12-month trials for therapy to be discontinued? IM: This treatment can be used more than once. It hasn't shown great efficacy in the trials so as long as they have positive clinical response, they probably can use it again but yes, it's a chronic condition so likely it has to be ongoing NT: I have a question too. Since clinical trials for patients 6 to 12 years of age, is this indicated for adults as well? And would you approve it for adults?		

		IM: It is indicated for ages 6 and older, so it can be approved for anybody above the age of 6. Usually, this disease is diagnosed in childhood between the ages of 3 to 5 years of age but yes, it can be approved for the ages of 20 and 30 NT**:** Right, so if there is a 22-year-old with the diagnosis, you would approve if they met the criteria even though the clinical trials were not done on adults IM**:** yes NT**:** OK, thank you**.**		
		Glaucoma Agents Class Review **a. New MRG: Rho Kinase Inhibitors** - **IM**-Next we will look at Glaucoma agents class review and we have a new MRG Rho Kinase Inhibitors and that's on page 216 - We had 196 claims for 100 members, for a total cost of $4,792.42 and an average cost per claim of $24.45. The most highly utilized medication was Latanoprost 0.005% ophthalmic drops, with 120 claims, followed by Brimonidine 0.2% ophthalmic drops with 30 claims. There were 2 prior authorizations with 1 approval (50%). - Let's look at the utilization table on page 231 - So, pharmacotherapy agents include Prostaglandins, Beta Blockers, Alpha-2 Adrenergic agonists, Carbonic Anhydrase Inhibitors, Cholinergic Agonists, Rho Kinase inhibitors, Acetylcholinesterase Inhibitors, and Combination agents from these categories - When we look at utilization in that class is overall well managed and most utilization is with cost effective products from beta blockers all utilization was with Timolol ophthalmic drops which is the most cost-effective product. So, we recommend no changes in this category - With Alpha-2 Adrenergic agonists all utilization is with Brimonidine, and it is a lower cost agent on formulary as well - We have recognized moving Apraclonidine 0.5% which is on formulary with PA to non-formulary status since there is no utilization and more cost-effective alternatives is on formulary which is Brimonidine - Also, Apraclonidine 0.5% is only used for short term adjunctive therapy and additionally there is no specific PA criteria, and you would just use the general criteria for non-formulary PA requirement medications without drug or class specific prior authorization criteria. So, for these reasons, we recommended to move it to non-formulary - Next are the Carbonic Anhydrase Inhibitors on page 232 - Here we the utilization includes mostly Dorzolamide which is a lower cost agent, and no changes are recommended in this drug category - Per the American Academy of Ophthalmology, Prostaglandin Analogues are the initial choice in most situation due to their efficacy, tolerability, safety and convenient once daily dosing. - Here we have almost all utilization is Latanoprost which is the most cost-effective agent		

		- There were several claims for Travoprost which is found to be equal or superior to Latanoprost in lower pressure based on several studies and there was no significant difference in adverse effects between them. - It is also on formulary with step therapy Latanoprost, so we do not recommend any changes in this category as well - Administration in the form of ocular implants are the most recent advancements in care - Here we have Durysta and iDose which provide options for patients with poor adherence to topical therapy. They are delivering drugs for an extended period of time - Durysta is expected to provide efficacy for 6 to 12 months and iDose may last up to 3 years. - Currently neither product is FDA approved for repeat administration and we do not recommend any changes in the drug category - From the combination product on page 233, we have Dorzolamide-Timolol on formulary with most of the utilization. It is the most cost-effective agent here, so no changes are needed. - There was 1 claim for Rocklatan which is the combination of netarsudil which is a Rho Kinase inhibitor and latanoprost. - Rho Kinase inhibitors increase outflow. They have convenient once daily dosing and maybe another option for patients with otherwise maximum tolerated medical therapy - Rhopressa and Rockatan are non-formulary, and we recommend implementing the new MRG criteria for their management without changes to formulary status - On page 234, you have the new criteria and here the members must be 18 years or older since patient efficacy has not established younger than 18 years. - For the initial authorization, patient/member must have diagnosis of ocular hypertension or open angle glaucoma - We ask for a documented trial and failure of a prostaglandin inhibitor or beta-adrenergic since these are the 2 most common class of medication use and also, they're efficacious and safe - We also ask that member does not have previous glaucoma intraocular surgery or glaucoma laser procedure in the affected eye or ocular surgery or laser treatment within three months prior to initiation - Or Member does not currently have any of the following: • Ocular infection • Inflammation • Blepharitis • Conjunctivitis • Ocular disease - And these are all based on exclusion criteria in trials - For re-authorization, member must continue to meet above criteria and member has demonstrated efficacy-reduction in intraocular pressure		

		- Criteria is pretty straight forward Questions:		
		Hepatitis B Class Review **NP-**Now we can go the next page, page 236 where we will look at Hepatitis B class review - There were 101 claims for 49 members, for a total cost of $86,350.36 and an average cost per claim of $854.95. The most highly utilized medication was Vemlidy 25 mg tablet, with 51 claims, followed by Entecavir 0.5 and 1 mg tablet with 35 claims. There were 15 prior authorizations with 11 approvals. - Let's look at the utilization table on page 251 - Overall, Alameda has adequate coverage with oral and injectable medications indicated and approved in the treatment of Hepatitis B - American Society for Liver Diseases recommends entecavir or tenofovir disoproxil fumarate also known as TDF or brand Viread, or tenofovir alafenamide or Vemlidy, as preferred initial therapy with immune active chronic hepatitis B which decreases the risk of liver related complications - The World Health Organization offers similar recommendations but excludes peginterferon which has fallen out of favor in clinical practice due to its extensive adverse effect - We have tenofovir disoproxil fumarate generic 300mg tablet on formulary - Tenofovir can be used as first line therapy in treatment with patients and those who had prior exposure or have developed drug resistance to other nucleoside such as - Viread lower strength tablets are available only as branded products. They are on formulary with PA that require documentation of weight as a rationale supporting why the generic disoproxil fumarate cannot be used. - For the disoproxil fumarate oral powder medical justification for use such as difficulty swallowing needs to be provided - Vemlidy was added to the list of agents in the most recent update of all guidelines		

		- This drug was noted for lower incidents of bone and renal toxicity compared to viread but it is not preferred over viread over guidelines, so we recommend no changes to the formulary status. Keep it as is - Lamivudine and Adefovir are also available generically but are not preferred. - Lamivudine is not a preferred agent due to high rates of resistance and Adefovir is not typically used because of its weaker antiviral activity - So, we recommend moving Lamivudine and Adefovir to F-PA formulary with prior authorization status based on no utilization and other cost effective and guidelines recommended alternatives on formulary and to reflect the MRG criteria status - Entecavir is the next agent on formulary and its main advantages are its potent antiviral activity and low rate of drug resistance - It should not be used in patients with lamivudine resistant HBV since resistance has been observed in up to 50 percent of lamivudine refractory patients after 5 years of treatment - For patients that have been treated with lamivudine in the past, tenofovir is preferred - And lastly, Pegasys subaqueous solution is on formulary, and we don't recommend changes here as well. It's on formulary with PA. It is not preferred agent in practice due to severe side effects and black box warning - Overall, the class is well managed and the only changes that we recommend are for Adefovir and Lamivudine to have a formulary with PA status. Questions:		
VII) Medication Request Guidelines	R. Negash	The committee has reviewed and discussed the following updates and additions to the Medication Review Guidelines (MRG) Guideline (Changes): **1. Specialty Biologic Agents** - Pg. 256 So here we have our specialty biologic agents. - And so, the first changes we see here are in the medication section. We do have biosimilars for Humira and Actemra, so these are the changes you see here on the first page. - We're adding Yuflyma and Simlani to Step 1 preferred status. - There's also availability of the 80-milligram formulation and we'll address that later in the criteria as preferred. - In Step 2, you can see that we are adding Tyenne and Tofidence, so biosimilars for Actemra, and then Actemra is being moved to the non-preferred section. - Pg. 257 If we scroll down to the top of page 257, we're also adding three non-preferred agents to the non-preferred PA required Step 3 portion of the medication section.	Move to approve: 1st: BD 2nd: PB	

		- Pg. 258 The next change on this policy is on page 258. So here we're striking the previous language that allows for Humira 80 milligram exception formulation. - Well, to try the 40 milligrams when wanting to achieve the 80-milligram dose strength. - So, we'll prefer the new biosimilar that 80 milligram per .8 ML over other formulations like Humira or any other non-preferred biosimilars due to cost. - And then there's no other changes to this policy. - Are there any questions on this? And feel free to stop me as well as we move down if I don't pause long enough. **Comments:** Guideline (Changes): **2. White Blood Cell Stimulators** - Pg. 259 So, we'll go to page 259 for White Blood Cell simulators. - OK. So here the changes start in the medication section. - The first one is a simple brand to generic switch since for Mozobil there is now a generic available. - And then we're going to have preferred Fulphila products based on cost efficacy and then we're adding Aphexda to the non-formulary section as it's an available product for this class. - Pg. 260 And then we can move down to page 260. - So here in the PA review section, we do have those updates that relate to the Fulphila that is now preferred. So that's what you see in the first bullet points there. - Also, we are changing preference for Neulasta since we now have other products to treat acute hematopoietic radiation injury syndrome. - So that bullet point with all the red is simply preferring the cost-effective options for that condition like the Ziextenzo, Udenyca, or Stimufend. - And at the bottom of the PA review criteria section, if you scroll down a little bit, we see the section for the generic Mozobil and Aphexda. - So here we are preferring the generic Mozobil over Aphexda and that's in short what this criterion is getting updated for. Everything else stays the same. - Are there any questions with this MRG? **Comments:** Guideline (Changes): **3. Constipation agents** - Pg. 262 We can go to page 262. - This is our Constipation Agents MRG. - And here we have changes, the first one is in the age restriction section.		

- So Linzess has a new indication, so we're including functional constipation for pediatric patients aged 6 to 17.
- Pg. 263 So if we scroll down on this section on this policy to page 263 towards the bottom, we're also adding that language to include criteria for review when we get these requests for Linzess for these patients.
- And so, we'll be looking for appropriate diagnosis of functional constipation, appropriate dose and then that they have tried two laxatives that we have available and scrolling down a little more in the reauthorization criteria, it will be the same as the other conditions.
- So, we would just want to see clinical benefit and appropriate dosing when they're renewing requests and there's no other changes with this policy.
- We can move to the next one if there's no questions, on page 265.

Comments:

Guideline (Changes): **4. Vaginal Progesterone**

- Pg. 265 So this is for our vaginal progesterone.
- So here we're making a simple change based on ACOG recommendation.
- So, in short, we would allow for approval if we get an appropriate request with current singleton pregnancy, for a patient with current singleton pregnancy and short cervix, previous preterm births are no longer required.
- There are no other changes with this policy.
- Did you have any questions? Page 267 is our next policy.

Comments:

Guideline (Changes): **5. Injectable/Infusible Agents for Osteoporosis and Paget's Disease**

- Pg. 267 is our next policy. So, this is for Injectable and Infusible agents for Osteoporosis and Paget's Disease.
- So, looking at the medication section, we see our changes here.
- We're going to have Co-preferred status for the generic Forteo and Tymlos and this is based on cost efficacy.
- Pg. 268 And if we move down to page 268, scrolling to the next section and we're updating the preferred status of the generic Forteo in the above section above the glucocorticoid-induced osteoporosis.
- And then we also are including based on guidelines, we're including review for glucocorticoid-induced osteoporosis.
- So, requests that come in for those who are 60 years and older, we should be looking for them to be on long-term glucocorticoid therapy for at least three months.
- We would also be looking for appropriate dosage of prednisone and that they have moderate to very high risk of fracture based on at least one of the following parameters which include osteoporotic fracture, BMD less than one and then the appropriate FRAX 10-year probability of the hip one.

- If there are requests that are received for an adult of any age and we see that they are utilizing a high dose of glucocorticoid therapy, then we would still look for moderate to very high risk of fracture as defined as one of the following:
    - History of fracture, or glucocorticoid dose over 30 mg/day or cumulative dose of over 5g per year of prednisone or equivalent.
- Pg. 269 And then another parameter would be continuing over or equal to 7.5 milligrams a day of prednisone or its equivalent for greater than six months and BMD Z score of less than -3 or significant BMD loss.
- And there's no additional changes for this policy. Any questions on this?

Comments:

Guideline (Changes): **6. Fabhalta**

- Pg 270 So, the first change here for our Fabhalta policy is to update the name.
- We're adding Voydeya tablets. And so, the new name will include just the class Complement Inhibitors for the Treatment of Paroxysmal Nocturnal Hemoglobinuria.
- And so, in the coverage duration section, you can see updates there to differentiate between the two products.
- So initial requests for Voydeya will be approved for up to three months and then up to six months on reauthorization.
- We're also inserting specific language for requests that come in for that Voydeya.
- And so, we want to see that they've been receiving Soliris or Ultomiris for at least six months.
- Also, that they have clinically evident extravascular hemolysis and despite using Soliris or Ultomiris and then want to see that they're going to be using this Voydeya in addition to Soliris or Ultomiris.
- It's an add on therapy.
- And then there's no update other than that on this policy.
- If there's no questions on that, I'll go to Page 272.

Comments:

Guideline (Changes): **7. Vasodilators for Pulmonary Arterial Hypertension (PAH)**

- Pg. 272 So here we have our Vasodilators for Pulmonary Arterial Hypertension policy.
- And so, we're changing the name here to be inclusive for all these products.
- So, some will be used to treat PAH. That's the parent indication, so we're updating there.
- In the medication section, we're going to add two new non-formulary products in their respective areas.
- So, see there the Opsynvi, that's the combination product.
- And then we also have the Winrevair, which is a new MOA.
- Pg. 273 Also, if we scroll down, we can see in the coverage duration section, we're adding the initial criteria link for the combination product Opsynvi and then just rewording some language here throughout the policy like reauthorization.
- And then in the PA review criteria section, we're simplifying the requirement with diagnosis, especially considering specialists are utilizing and requesting here.

		- So, we'll no longer require vasoreactivity testing, just appropriate disease. - And then as we move down to the next, there's just a rewording change there to reflect the package insert labeling for clarity. - Pg. 274 And then we go down to the next, page 274: Here we have criteria for those two products that were mentioned earlier in the medication section. - So, for the combination product, the Opsynvi, we would be looking for stability on the combination therapy with the PDE-5 inhibitor and an ERA and then the reason why they can't use these agents. - And then for requests for Winrevair, we would look for treatment failure of combination therapy including a PDE-5 inhibitor and one ERA or the combination product of Opsynvi. - And then we also want to see that their platelet count is above 50,000 since it's recommended to have at least that much when initiating therapy since there's more platelet drop and in the reauthorization criteria, we're going to just strike that that bullet point for medical necessity confirmation and rationale when the dosage is increasing. - There are no other changes on this policy. - OK, if there's no questions on that? Guideline (Changes): **8. Palforzia** - Pg 275 The next policy is the last one for our MRGS for pharmacy and pharmacy benefit and it's for Palforzia oral powder capsules. - And so here we're just making a simple change based on expanding age and indication. - So instead of 4 to 17, this will be available for 1 to 17 years, not making any other changes. - And that concludes the pharmacy benefit MRGs. PAD is next. **Comments:** **Comments:** No changes recommended at this time. No further discussion.		

VIII) Physician Administered Drug (PAD) Policies	Iryna Makukh	Guideline (Changes): **1. Injectable/Infusible Agents for Osteoporosis and Paget's Disease** - Pg. 276 We recommend changing naming convention to reflect generic availability of Forteo and Teriparatide. - Pg. 277 We revised preferred agents for post-menopausal or main osteoporosis with Tymlos and Teriparatide as preferred since Teriparatide is available as generic and is more cost effective. - We also need to revise treatment accommodation based on new Glucocorticoid-Induced Osteoporosis guidelines. Now, due to new guidelines, they also recommend treatment for patients with moderate risk, on long term glucocorticoid therapy for patients 40 years and older, and for all adult patients on high dose glucocorticoid therapy regardless of age. So, here similarly to the MRG policy, we separated this indication into 2 sections for patients on long term glucocorticoid therapy, 40 years and older. Also, for patients receiving high dose glucocorticoid therapy. Both for patients with moderate to very high risk of fracture. Patients with moderate risk would include BMD of less than -1 now at the hip or spine, versus the BMD of -2.5 for high risk. Also, FRAX 10-year probability of hip or combined major osteoporotic fracture percentages, they must be lowered as well to encompass for the patients with moderate risks. - In the next section we have members receiving a high dose of glucocorticoid therapy, also moderate to very high risk of fracture. That would constitute one of the following, here we have a history of prior fracture which would constitute a very high risk, and glucocorticoid dose of more or equal to 30 mg per day or cumulative 5 grams per year of prednisone or its equivalent. - On the next page just continuing glucocorticoid treatment of at least 7.5mg per day of prednisone or its equivalent for at least 6 months and BMD Z score of less than -3 or significant BMD loss and that would constitute moderate risk. - These are all changes for this BMD policy, very similar to our MRG policy. **Comments:** PB: You were saying earlier that Forteo is now more generically available? IM: Forteo is generically available, yes. PB: But you still want them to try/fail a class of Prolia? IM: Yes, in both cases they go higher on the guidelines, so you would try the injectable bisphosphonates first. PB: Are the oral agents not indicated for some of these? Because what's relatively new is starting people on a therapy when they're on high dose steroids, but you have lowered the T score cut off. Did I miss the oral agent part? IM: So here for oral requests, we have them try the oral bisphosphonates first. So, we start with oral bisphosphonates unless someone is very high risk, then they don't need to try all of that. So, they would try oral, then injectable, and go to the PA agents. Guideline (Changes): **2.White Blood Cell Stimulators**		

		- Pg. 279 Here we recommend changing the naming convention to reflect generic availability of Mozobil (plerixafor), similar to our MRG policy. We added the new product Aphexda, which share similar indication to plerixafor. Which is indicated for Hematopoietic stem cell mobilization. Just as Mozobil, in combination with filgrastim in patients with multiple myeloma. - Pg. 280 Here we added Aphexda to Plerixafor criteria, since they share similar indication. We added the requirement to prefer Plerixafor since it is generically available and significantly less expensive than Aphexda. - We removed criteria for pegfilgratim formulations for acute hematopoietic radiation injury syndrome, to approve Neulasta without prior use of biosimilar. Since 3 of the pefilgrastim biosimilars now they have this indication and can be tried first. These include Ziextenzo, Udenyca, and Stimufend. - No other changes to this policy. **Comments:** N/A Guideline (Changes): **3. Gene Therapy for Hemophilia** - Pg. 281 We recommend adding Begvez, which is a new one-time gene therapy indicated for the treatment of adults with moderate to severe Hemophilia B. - Begvez is an adeno-associated virus-based gene therapy, it's designed to introduce a functional copy of the IX gene factor. It works very similar to Hemgenix, which is also a viral factor carrying gene for clotting factor IX. - It was approved in 11/2022, the price of Begvez is $3.5M per one time treatment and it matches the cost of Hemgenix. There is little needed to be updated on this criteria. - We updated the name of this policy as both Hemgenix and Begvez treat Hemophilia type B. - We updated exclusion and coverage duration since repeat use of these agents, we're using one agent after another have not been started. - We've updated age restrictions since both agents are approved only in adults. - Most of the criteria stay the same as 2 therapies work similarly and the condition for the initial authorization matches both labels and clinical trial requirements. - The only addition here is a specific test requirement for Begvez, to indicate that the patient does not have neutralizing antibodies to adena-associated virus seroytype Rh74var capsid as detected by an FDA-approved test. This is the requirement from the label for Begvez. - Also, we added medical necessity review statement in the end. As standard on all our policies. - These are all the changes to this policy. **Comments:** N/A Guideline (Changes): **4.Elevidys**		

		- Pg. 282 Was previously approved under accelerated approval for ambulatory individuals 4-5 years of age with DMD (Duchenne Muscular Dystrophy) with a confirmed mutation in the DMD gene. - We have an updated approval where Elevidys received traditional approval in ambulatory individuals 4 years of age and older with DMD. With a confirmed mutation in the DMD gene and received accelerated approval in non-ambulatory individuals 4 years of age and older. Elevidys is a one-time treatment, so coverage duration stays the same. - In the initial authorization we revised DMD diagnosis requirement just for more clarity and to be more thorough. - We removed ambulatory requirements since Elevidys is now approved for DMD patients regardless of angulation status. - We added antibody titer testing per recommendation in the prescribing information. According to PI only patients with an anti-AAVrh74 total binding antibody titer of less than 1:400 should be selected for treatment. - We removed baseline micro dystrophy protein level requirement because it is not commonly measured in practice. - We also recommend adding additional monitoring parameters that prescribers must assess liver function, platelet count, and troponin-I as per dosage and administration recommendations in the package insert. Also, there are warnings of serious liver damage, thrombocytopenia, myocarditis, that's why we included monitoring of these parameters. - Lastly, we added medical necessity review statements as it is standard on all the policies. - These are all changes for this Elevidys criteria. **Comments:** N/A Guideline (Changes): **5. B-Cell Maturation Antigen (BCMA) Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy** - Pg. 283 Here Abecma and Carvykti received early line indication approvals. They were previously approved and shared the same indication, relapsed or refractory multiple myeloma for patients who have received at least 4 prior lines of therapy. - Now both agents have received new indications that allow them to be used as earlier lines of treatment for relapsed or refractory multiple myeloma. - Exclusion criteria, coverage duration, prescriber restriction, and age restrictions are all staying the same. Both agents intended to be one-time treatments once specialist prescribers both only indicated in adults. - We only updated the indication section for Abecma, it can now be used after only 2 prior lines of therapy. Including an immunomodulatory agent, a proteasome inhibitor, and an anti CD38 monoclonal antibody. - For Carvykti it is now indicated for patients that are refractory to lenalidomide and have received at least 1 prior line of therapy.		

		- The only other change here was the addition to patients who does not have an active infection or inflammatory disorder. We added inflammatory disorder as both our boxed warnings on the label for each agent. - No reauthorization since these are intended for one-time treatment. There's no evidence to support multiple or repeat use. - These are all the changes for this policy. **Comments:** N/A		
IX) Informational Updates on New Developments in Pharmacy	Iryna Makukh	New Product Review • New Products were discussed. - Page 284: So, we will go over some new products that we have recommendations for. - The first recommendation we have is for Tofidence. And Tofidence we recommend adding to formulary with a PA, we updated MRG policy for specialty biologic agents. - It's an IV Actemra biosimilar and it's indicated for rheumatoid arthritis, polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis. - Next product is Rextovi, and we recommend adding to formulary as another cost-effective alternative to naloxone nasal spray. It's also prescription only naloxone nasal spray. - It's a little bit more cost effective. The price is $45 per package which is slightly less costly than naloxone spray. - Next, Xolremdi remains non-formulary and new MRG criteria was presented. - Pg. 285 And on the next page 285 we have Omvoh which remains non-formulary. We added it to MRG criteria for specialty biologic agents as non-preferred. - It's just a new dosage form for the treatment of moderate to severe ulcerative colitis in adults. - We have Beqvez which remains non-formulary, and we updated PAD policy for gene therapy for hemophilia B. Fasenra is on formulary with PA, and we already added via CRF. That's just a new strength. - Pg. 286 Next page 286, all these remain non-formulary. - We have Myhibbin which remains non-formulary. - We have a generic mycophenolate which is on formulary with better pricing. - And Austedo XR remains non-formulary, just a new strength as well. - Pg. 287 And on next page 287, we have Rinvoq liquid also remains non-formulary. It's just a new form of formulation as an oral liquid. - Duvyzat remains non-formulary. We presented new MRG criteria for it.		

		- Pg. 288 And on the next page, page 288, we have Capvaxive. - Capvaxive is a new pneumococcal vaccine. It was approved by the FDA two months ago as the latest vaccine for prevention of pneumonia and invasive disease caused by pneumonia. - It is approved in adults and covers 21 serotypes responsible for around 84% of invasive pneumococcal disease in adults 50 years and older. Eight of these serotypes are not covered by currently approved pneumococcal vaccines. - It is administered as a single dose and cost is in line with other pneumococcal vaccines $288. - We recommend adding it to formulary with a quantity limit and age limit, 0.5 milliliters per one dose and one fill per lifetime and age limit of 18 years and older as per indication. - And next we have Tyenne. Tyenne also adding to formulary with PA, It's another biosimilar for Actemra, around 35% less costly than Actemra. And we updated MRG criteria for specialty biologic agents. - Pg. 289 Next on page 289, we have mResvia, which is a new RSV vaccination. - The FDA recently approved Moderna's mResvia and it is the first mRNA vaccine for prevention of RSV. It is approved for those 60 years and older. - The price is $290.00 and it's in line with other RSV vaccines on formulary. - We recommend adding to formulary with quantity limit and age limit, 1 vial for one dose and one dose per lifetime and age limit 60 years and older as per indication. - We also have Tyenne, another formulation. It's a prefilled syringe. We already saw subcutaneous auto injector. - We also recommend to add to formulary with PA. It's a biosimilar for Actemra. We also updated MRG criteria for specialty biologic agents. - And on this page, we also have Entresto. It's on formulary with quantity limit. We already added it via CRF. It's just a new dosage strength and form. - Pg. 290 And on the next page 290 we have everything remains non-formulary. - We have ondansetron new strength which is a lot more expensive than what we have on formulary. - Pg. 291 Let's go to page 291 and here the one product we have recommendations on is Acthar Gel and it's a new dosage form auto-injector. - We have them on formulary with PA and we already added via CRF and all other agents on this page remain non-formulary and that's all I have for new product reviews. - Any questions? - DC: I have a question regarding the naloxone product. Did you say that was over the counter as well or is that prescription? - IM: I'm sorry, which product? - DC: I don't remember the name. It's the one that's similar to naloxone. - IM: Oh yeah, yeah, it's prescription only. Yeah, it's not available OTC. Prescription only, but more cost effective. That's why we decided to add it.		

BRAND NAME	GENERIC NAME/DOSAGE FORM	RECOMMENDATION
Cyltezo	adalimumab-adbm 40 mg/0.4 ml subcutaneous syringe; 40 mg/0.4 ml subcutaneous auto-injector	Non-formulary
Adalimumab-adbm	adalimumab-adbm 40 mg/0.4 ml subcutaneous syringe; 40 mg/0.4 ml subcutaneous auto-injector	Non-formulary
Tofidence	tocilizumab-bavi 80 mg/4 ml, 200 mg/10 ml, 400 mg/20 ml intravenous vials	Add to formulary with PA; (see updated MRG policy)
Ingrezza	valbenazine 40 mg, 60 mg, 80 mg sprinkle capsules	Non-formulary
Rextovy	naloxone 4 mg nasal spray	Add to formulary
Xolremdi	mavorixafor 100 mg oral capsules	Non-formulary (see new MRG policy)
Omvoh	mirikizumab-mrkz 100 mg/ml subcutaneous syringe	Non-formulary (see updated MRG policy)
Beqvez	fidanacogene elaparvovec-dzkt 1 × 10^{13} vector genomes/ml	Non-formulary (see updated PAD policy)
Fasenra	benralizumab 10 mg/0.5 ml subcutaneous syringe	F; PA (Already added via CRF)

			Imdelltra	tarlatamab-dlle 1 mg, 10 mg intravenous vials	Non-formulary			
			Kionex	sodium polystyrene sulfonate 15 g/60 ml oral or rectal suspension	Non-formulary			
			Hepzato	melphalan w/50mm catheter intra-arterial solution reconstituted 50 mg melphalan w/62mm catheter intra-arterial solution reconstituted 50 mg	Non-formulary			
			Myhibbin	mycophenolate mofetil oral suspension 200 mg/ml	Non-formulary			
			Focinvez	fosaprepitant intravenous solution 150 mg/50ml	Non-formulary			
			Austedo XR	deutetrabenazine oral tablet extended release 24 hour 30, 36, 42, 48 mg	Non-formulary			
			Rinvoq LQ	upadacitinib oral solution 1 mg/mL	Non-formulary			
			Vijoice	alpelisib oral packet 50 mg	Non-formulary			
			Duvyzat	givinostat oral suspension 8.86mg/mL	Non-formulary (see new MRG policy)			

			Iqirvo	elafibranor oral tablet 80 mg	Non-formulary			
			Capvaxive	pneumococcal 21-valent conjugate vaccine	Add to formulary with QL and AL (0.5 ml per 1 dose,1 fill per lifetime; age limit 18 years and older)			
			Tyenne	tocilizumab-aazg 162 mg/0.9 ml subcutaneous auto-injector	Add to formulary with PA; (see updated MRG policy)			
			Sitagliptin/Metformin	sitagliptin/metformin 50 mg-500 mg, 50 mg-1000 mg oral tablets	Non-formulary			
			mResvia	respiratory syncytial virus vaccine	Add to formulary with QL and AL (0.5 ml per 1 lifetime; age limit 60 years and older)			
			Scemblix	asciminib 100mg oral tablet	Non-formulary			
			Tyenne	tocilizumab-aazg 162 mg/0.9 ml subcutaneous prefilled syringe	Add to formulary with PA; (see updated MRG policy)			
			Adbry	Tralokinumab-ldrm 300mg/2ml auto-injector	Non-formulary			
			Entresto	Sacubitril-valsartan oral capsule sprinkle 6-6mg, 15-16mg	F; QL (Already added via CRF)			
			Rystiggo	Rozanolixizumab-noli 420mg/3ml, 560mg/4ml, 840mg/6ml	Non-formulary			

				subcutaneous solution			
			Ondansetron	Ondansetron 16mg oral disintegrating tablet	Non-formulary		
			Ohtuvayre	Ensifentrine 3mg/2.5ml inhalation suspension	Non-formulary		
			Sofdra	Sofpironium bromide external gel 12.45 %	Non-formulary		
			Kisunla	donanemab-azbt intravenous solution 350 mg/20ml	Non-formulary		
			Elfabrio	pegunigalsidase alfa-iwxj intravenous solution 5 mg/2.5ml	Non-formulary		
			Acthar Gel	Corticotropin subcutaneous auto-injector 80 unit/ml, 40 unit/0.5ml	F; PA (Already added via CRF)		
			Austedo XR	Deutetrabenazine oral tablet extended release 24 hour 18mg	Non-formulary		
			Austedo XR	Deutetrabenazine titration oral tablet therapy pack 12 & 18 & 24 & 30 mg	Non-formulary		
			Zoryve	Roflumilast external cream 0.15%	Non-formulary		
X) Old Business		• **Tadalafil (Cialis) for BPH MRG** - Here we have removed prescriber restriction since sometimes PCP can manage this condition as well.					

		- We also removed requirements for phosphodiesterase inhibitor trial since it takes longer to work. • **Febuxostat (Uloric) MRG** - We added the inclusion of intolerance to allopurinol to the policy, for cases such as development of a rash to allopurinol. - This is everything we have for the old business. **Comments:** RN: We have a question in the chat from Nora asking about pharmacists being able to prescribe Naloxone. We've done that for our NRT products, have we coded that or allowed that option for Naloxone as well? I don't believe we have but we can't, right? LR: I don't believe we have either, I can look into it and see if it is something we are allowed to do, like similarly to the birth control, having the pharmacy NPI as the prescriber? RN: Right, and there was difficulty getting that, I believe it was a billing issue previously because we tried to lift that for NRT, and we did it for the COVID vaccine. Are we able to extend that for Naloxone? LR: I will look into that, to see if that's something we can do.		
XI) Public Comment	D. Carey	• No comment		
Adjournment	D. Carey	• P&T Committee Member Forms **Meeting adjourned at 6:36PM**	None	

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Rahel Negash, PharmD
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10/29/2024 | 3:55 PM PDT
Date

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

10/31/2024 | 10:21 AM PDT
Date

ALAMEDA Alliance FOR HEALTH

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POLICY AND PROCEDURE

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

POLICY STATEMENT

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

PROCEDURE

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

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

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

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

DEFINITIONS / ACRONYMS

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

AFFECTED DEPARTMENTS/PARTIES

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

RELATED POLICIES AND PROCEDURES

P&T Charter
RX-007-Pharmaceutical Patient Safety

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

None.

REVISION HISTORY

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

New

Ohtuvayre	
Therapeutic Classes (AHFS)	Dual Phosphodiesterase Inhibitor
Medications	Ohtuvayre (ensifentrine)
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	• Primary diagnosis of asthma • Concomitant use of oral PDE4 inhibitors
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	According to package insert Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 12 months. If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review
PA Review Criteria	**Initial Authorization:** • Diagnosis of chronic obstructive pulmonary disease (COPD) • Documentation of a pre- and post-albuterol FEV1/FVC ratio of <0.70 • Documentation of a score of ≥ 2 on the Modified Medical Research Council (mMRC) Dyspnea Scale or a score of ≥ 10 on the COPD Assessment Test (CAT) • Documented trial and failure of maintenance triple therapy consisting of a long-acting muscarinic antagonist (LAMA), long-acting beta2 agonist (LABA), and inhaled corticosteroid (ICS) (or a documented medical reason must be provided why the member is unable to use these therapies) • The drug is being prescribed at an FDA approved dose **Re-Authorization:** • The member has clinically benefitted from the medication (e.g. improvement in symptoms and exacerbations, improvement in mMRC or CAT, improvement in FEV1/FVC ratio, etc.) • The drug is being prescribed at an FDA approved dose
Criteria Statement	Ohtuvayre is reserved for members who have a diagnosis of COPD, mMRC Dyspnea Scale score ≥ 2 or a score of ≥ 10 on the COPD Assessment Test (CAT) and tried and failed or were unable to use maintenance triple therapy.
Last P&T Review Date	12/2024

Nemluvio	
Therapeutic Classes (AHFS)	Immunomodulatory Agent
Medications	Nemluvio (nemolizumab-ilto)
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 and older Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be allergist, immunologist, or a dermatologist
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 12 months. If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review

PA Review Criteria	**Initial Authorization:**
	• Diagnosis of severe prurigo nodularis (PN) with ≥ 6 weeks of pruritus
	• Member has ≥ 20 PN lesions
	• Documentation of member weight
	• Member has a ≥ 2-week trial of one of the following:
	  ○ Moderate potency or higher topical corticosteroid (TCS)
	  ○ Topical calcineurin inhibitor (TCI)
	• Medication is prescribed at an FDA approved dose
	
	Re-Authorization:
	• Documentation or provider attestation of positive clinical response (reduced nodular lesion count, decreased pruritis, etc.)
	• Documentation of member weight
	• Medication is prescribed at an FDA approved dose

Criteria Statement	Nemluvio is reserved for members who have a diagnosis of severe PN with pruritus for at least 6 weeks, ≥ 20 PN lesions, and trial of moderate potency or higher topical corticosteroid or topical calcineurin inhibitor for at least 2 weeks.
Last P&T Review Date	12/2024

Yorvipath	
Therapeutic Classes (AHFS)	Parathyroid Agents
Medications	Yorvipath (palopegteriparatide)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Members with acute postsurgical hypoparathyroidism (HP) or those who are at increased risk for osteosarcoma
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	18 years of age and older Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be an endocrinologist or in consultation with an endocrinologist
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 12 months. If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review

PA Review Criteria	**Initial Authorization:**
	• Confirmed diagnosis of chronic hypoparathyroidism (HP) of postsurgical, autoimmune, genetic, or idiopathic origins, for at least 6 months
	• Provider attestation that patient is currently receiving conventional therapy, including active vitamin D (calcitriol) and elemental calcium, and that patient's disease cannot be adequately controlled on conventional therapy alone
	• Current labs (within 60 days of request) have been submitted for the following:
	  ○ Albumin-corrected serum calcium (must be ≥ 7.8mg/dL to start therapy)
	  ○ Serum vitamin D level (must be ≥ 20 ng/mL to start therapy)
	• Medication is prescribed at an FDA approved dose
	
	Re-Authorization:
	• Documentation of a recent albumin-corrected serum calcium in the lower-half of the normal reference range or just below the normal reference range (~8–9 mg/dL)
	• ONE of the following:
	  ○ Patient no longer requires active vitamin D or therapeutic doses of calcium, OR
	  ○ Patient has had a significant reduction in required dosages of active vitamin D or therapeutic doses of calcium and is still actively titrating doses of Yorvipath
	• Medication is prescribed at an FDA approved dose

Criteria Statement	Yorvipath is reserved for members who have a confirmed diagnosis of HP of postsurgical, autoimmune, genetic, or idiopathic origins for at least 6 months, and are not adequately controlled on conventional therapy, and have albumin-corrected serum calcium ≥ 7.8mg/dL and serum vitamin D ≥ 20 ng/mL to start therapy.
Last P&T Review Date	12/2024

Ileal bile acid transporter inhibitors (IBATs)	
Therapeutic Classes (AHFS)	Cholelitholytic Agents
Medications	Bylvay (odevixibat), Livmarli (maralixibat)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	According to package insert
Prescriber Restrictions	Prescribed by or in consultation with a gastroenterologist or hepatologist
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 12 months. If the conditions are not met, the request will be sent to a clinical reviewer for medical necessity review

PA Review Criteria	**Initial Authorization:**
	Progressive Familial Intrahepatic Cholestasis
	• Diagnosis of progressive familial intrahepatic cholestasis (PFIC).
	  ○ For Bylvay: PFIC type 1 or 2 with confirmed biallelic mutations via genetic testing.
	  ○ For Livmarli: PFIC type 1, 2, 3, 4 or 6, with confirmed biallelic mutations via genetic testing
	• Documentation that patient does not have an *ABCB11* variant that results in non-functional or complete absence of bile salt export pump protein
	• Documented history of moderate to very severe pruritus
	• Documentation of patient's weight
	• Prescriber attests to monitor liver function tests and fat soluble vitamin (FSV) levels during treatment
	• Baseline serum bile acid level is provided
	• Documentation of trial and failure OR contraindication to at least ONE of the following:
	  ○ Ursodiol
	  ○ Cholestyramine or colesevelam
	• The prescribed dose is within FDA approved dosing guidelines
	
	Alagille Syndrome
	• Diagnosis of Alagille syndrome (ALGS)
	• Documented history of moderate to very severe pruritus
	• Documentation of trial and failure OR medical reason why the member is unable to use all of the following:
	  ○ Ursodiol
	  ○ Cholestyramine or colesevelam
	  ○ Rifampin
	• Prescriber attests that the member has cholestasis
	• Baseline serum bile acid level is provided
	• Documentation of patient's weight
	• Prescriber attests to monitor liver function tests and fat soluble vitamin (FSV) levels during treatment
	• The prescribed dose is within FDA approved dosing guidelines
	
	Re-Authorization:
	• Documentation of clinical benefit indicating each of the following:

	○ An improvement in pruritus (e.g. improved observed scratching, decreased sleep disturbances/nighttime awakenings due to scratching, etc.) ○ Reduction in serum bile acid level from baseline • Documentation of patient's weight • Prescriber attests to monitor liver function tests and FSV levels during treatment • Prescriber attests that patient has had no evidence of hepatic decompensation (e.g. variceal hemorrhage, ascites, hepatic encephalopathy, portal hypertension, etc.) • The prescribed dose is within FDA approved dosing guidelines
Criteria Statement	Bylvay and Livmarli are reserved for members who have a diagnosis of PFIC with confirmed biallelic mutations and history of moderate to very severe pruritis, do not have ABCB11 variant, and had trial and failure or contraindication to either ursodiol, cholestyramine or colesevelam. Additionally, Bylvay and Livmarli are reserved for members who have a diagnosis of ALGS with history of moderate to very severe pruritus, and had trial and failure or contraindication to ursodiol, cholestyramine or colesevelam, and rifampin.
Last P&T Review Date	12/2024

New

Kisunla (donanemab-azbt)	
Medications	Kisunla (donanemab-azbt)
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 a condition other than AD
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Age 60-85 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 dementia 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
	  ○ Mini-Mental State Examination (MMSE) score ≥ 20 and ≤ 28
	  ○ Montreal Cognitive Assessment (MoCA) score of ≥16
	• 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., integrated Alzheimer's Disease Rating Scale [iADRS], Alzheimer's Disease Assessment Scale-Cognitive Subscale [ADAS-Cog], Alzheimer's Disease Cooperative Study-instrumental Activities of Daily Living [ADCS-iADL], 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 MCI caused by AD or mild AD dementia 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
	  ○ MMSE score of 20-28
	  ○ MoCA score of ≥16
	• 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 (i.e., stabilization or decreased rate of decline in symptoms from baseline on CDR-SB, iADRS, ADAS-Cog, or ADCS-iADL scales) • No recent (past 1 year) history of stroke, seizures or TIA 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	12/2024

New

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) Agents	
Medications	Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “Other Criteria” below
Age Restrictions	Per FDA-approved labeling Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a neurologist or neuromuscular specialist
Coverage Duration	Initial requests will be approved for 3 months. Reauthorization requests will be approved for 12 months.
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Diagnosis of CIDP confirmed by electrodiagnostic test results (e.g. electromyography or nerve conduction studies) • Patient has progressive or relapsing/remitting disease course for ≥2 months • Patient has an inadequate response, significant intolerance, or contraindication to intravenous immunoglobulin (IVIG) or subcutaneous immunoglobulin (SCIG) • Medication is prescribed at an FDA approved dose **Re-Authorization:** • Documentation or provider attestation of significant clinical improvement in neurologic symptoms or stabilization of disease • Medication is prescribed at an FDA approved dose If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	12/2024

Topical Agents for Actinic Keratosis

Executive Summary

CLASS OVERVIEW

Actinic keratosis (AK) is a chronic skin condition in which keratinocyte neoplasms, or actinic keratoses (AKs), occur on the skin due to long term exposure to ultraviolet radiation. AKs most often present as erythematous, scaly macules, papules, or plaques and are generally diagnosed based on appearance alone. AK primarily appears in areas of the body with high sun exposure, such as the scalp, face, ears, lateral neck, and distal extremities. Prevalence in the United States is estimated to be 14% of the population, which is lower than the prevalence in other geographical locations with more sun exposure. Male sex, old age, fair-skin, baldness, and a high tendency for sunburn are also associated with an increased risk of developing AK. Despite being a chronic skin condition, AK is routinely treated due to the risk for progression to keratinocyte carcinomas, including squamous cell carcinoma.

Treatment options for AK include topical medications and destructive therapies, such as photodynamic therapy, cryosurgery, and laser ablation. Choice of treatment depends primarily on the amount of lesions. According to interdisciplinary guidelines published in the Journal of the European Academy of Dermatology and Venerology (JEADV) as well as the most updated guidelines from the Academy of Dermatology (AAD), for patients with few or isolated AKs, lesion-directed treatment with cryosurgery is recommended. For patients with multiple AKs, field-directed treatment with topical medications or photodynamic therapy is recommended to limit the spread or recurrence of AK. The scope of this class review will focus only on topical medications used for AK. Topical medications approved for AK include: the antineoplastics fluorouracil and tirbanibulin, the immunomodulator imiquimod, and the non-steroidal anti-inflammatory drug (NSAID) diclofenac. Current guidelines support the use of fluorouracil, imiquimod, or tirbanibulin for first line topical therapy in field-directed treatment, with diclofenac recommended as a second line option based on lower quality of evidence.

UTILIZATION FINDINGS

There were 7 claims for 6 members, for a total cost of $249.42 and an average cost per claim of $35.63. The most highly utilized medication was Imiquimod 5% topical cream packet, with 6 claims, followed by Diclofenac 3% topical gel with 1 claim. There were no prior authorization requests.

RECOMMENDATIONS

- Change from F to F-PA based on cost and to reflect MRG criteria status
  - Diclofenac (Solaraze®) 3 % topical gel

CLINICAL SUMMARY

Actinic keratosis (AK), also known as solar keratosis, is a chronic skin condition in which keratinocyte neoplasms, or actinic keratoses (AKs), occur on the skin due to long term exposure to ultraviolet (UV) radiation. AKs most often present as erythematous, scaly macules, papules, or plaques and are generally diagnosed based on appearance alone. If uncertain, biopsy can be used to rule out cancer or another type of skin condition. AKs can also be classified as mild to severe based on their thickness, and subsequently receive a grade from I to III. AK primarily appears in areas of the body with high sun exposure, such as the scalp, face, ears, lateral neck, and distal extremities. As a result, UV protection with sunscreen is recommended to decrease the incidence of AK. Prevalence in the United States is estimated to be approximately 14% of the population, which is lower than the prevalence in other geographical locations with more sun exposure. Male sex, old age, fair-skin, baldness, and a high tendency for sunburn are associated with an increased risk of developing AK. Despite being a chronic skin condition, AK is routinely treated due to the risk for progression to keratinocyte carcinomas, including squamous cell carcinoma (SCC).

Treatment options for AK include topical medications and destructive therapies, such as photodynamic therapy (PDT), cryosurgery, and laser ablation. Topical medications approved for AK include: the antineoplastics fluorouracil and tirbanibulin, the immunomodulator imiquimod, and the non-steroidal anti-inflammatory drug (NSAID) diclofenac. Imiquimod and tirbanibulin are indicated specifically for AK of the face and scalp and are limited to treating areas $\leq$25 cm^2. Fluorouracil and imiquimod have additional indications for treatment in basal cell carcinoma. Diclofenac is associated with most of the same safety concerns as oral NSAIDs, including a black box warning for risk of cardiovascular events. Imiquimod has concerns over its use in immunocompromised patients, based on limited data in this population and the potential to cause onset or an exacerbation of an auto-immune disease. Comparative trials have shown strong evidence of fluorouracil being the most efficacious at treating AK.

Choice of treatment for AK depends primarily on the amount of lesions, along with other factors including the patient's preference and tolerability for side effects and the availability and cost of the treatment. According to interdisciplinary guidelines published in the Journal of the European Academy of Dermatology and Venerology (JEADV) as well as the most updated guidelines from the Academy of Dermatology (AAD), for patients with few or isolated AKs, lesion-directed treatment with cryosurgery is recommended. For patients with multiple AKs, field-directed treatment with topical medications or photodynamic therapy is recommended to limit the spread or recurrence of AK. Current guidelines support the use of fluorouracil, imiquimod, or tirbanibulin for first line topical therapy in field-directed treatment. Diclofenac is recommended as a second line option based on lower quality of evidence. Actikerall® (fluorouracil and salicylic acid) is a popular combination product used in Europe that is currently not available in the U.S.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Fluorouracil (Carac®) 0.5 % topical cream Fluoroplex® (fluorouracil) 1 % topical cream Fluorouracil (Efudex®) 5 % topical cream Fluorouracil 2 %, 5% topical solution Tolak® (fluorouracil) 4 % topical cream	Management of multiple actinic or solar keratoses Treatment of superficial basal cell carcinoma when conventional methods are impractical (5% cream and solution only)	<u>Actinic Keratosis:</u> 0.5% cream: Apply thin film to lesions once daily for up to 4 weeks as tolerated 1% cream: Apply to lesions twice daily for 2 to 6 weeks 4% cream: Apply to lesions once daily for 4 weeks as tolerated 5% cream, 2% and 5% solution: Apply to lesions twice daily for 2 to 4 weeks until inflammatory response reaches erosion stage, then stop <u>Basal Cell Carcinoma:</u> Apply to affected lesions twice daily for 3 to 6 weeks; may continue for up to 10 to 12 weeks
Klisyri® (tirbanibulin) 1 % topical ointment in packet	Treatment of actinic keratosis of the face or scalp	Apply once daily to evenly cover up to a 25 cm^2 area (using no more than 1 single-dose packet per application) for 5 consecutive days
Diclofenac sodium 3 % topical gel	Treatment of actinic keratosis in conjunction with sun avoidance	Apply to lesion area twice daily for 60 to 90 days; normally, 0.5 g is used on each 5 cm × 5 cm lesion
Imiquimod (Zyclara®) 3.75 % topical cream packet, cream in a pump Zyclara® (imiquimod) 2.5 % topical cream in a pump Imiquimod (Aldara®) 5 % topical cream packet	Treatment of clinically typical, nonhyperkeratotic, nonhypertrophic, visible or palpable actinic keratoses on the full face or scalp in immunocompetent adults Topical treatment of biopsy-confirmed, primary superficial basal cell carcinoma in immunocompetent adults with a maximum tumor diameter of 2 cm located on the trunk (excluding anogenital skin), neck, or extremities (excluding hands and feet), only when surgical methods are medically less appropriate and patient follow-up can be reasonably assured (Aldara® only) Treatment of external genital and perianal warts in patients 12 years and older (3.75% and 5% cream only)	<u>Actinic Keratosis:</u> 2.5% and 3.75% cream: Apply thin film (using up to 2 packets or 2 full pump actuations) once daily before bedtime for 2 weeks to the skin of the affected area; leave on for ~8 hours, then remove with mild soap and water; after a 2-week period of no treatment, repeat with a second 2-week treatment 5% cream: Apply 2 times per week (using up to 1 packet per application), prior to normal sleeping hours, to a defined treatment area(s) on the face or scalp; leave on for ~8 hours, then remove with mild soap and water; treatment should continue for 16 weeks <u>Basal Cell Carcinoma:</u> Apply once daily 5 days per week, prior to normal sleeping hours, for 6 weeks; leave on skin for ~8 hours, then remove with mild soap and water

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Fluorouracil (Carac®, Efudex®, Tolak®)	None	Hypersensitivity to fluorouracil or any component of the formulation; dihydropyrimidine dehydrogenase (DPD) enzyme deficiency; patients who are or may become pregnant
Klisyri® (tirbanibulin)	None	None
Diclofenac sodium	Cardiovascular events: NSAIDs cause an increased risk of serious (and potentially fatal) adverse cardiovascular thrombotic events, including MI and stroke. Risk may occur early during treatment and may increase with duration of use. Diclofenac is contraindicated in the setting of coronary artery bypass graft surgery.	Hypersensitivity to diclofenac; history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs; use in the setting of coronary artery bypass graft surgery; use on nonintact or damaged skin, including exudative dermatitis, eczema, infected lesions, burns, or wounds
Imiquimod (Zyclara®, Aldara®)	None	None

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Fluorouracil (Carac®, Efudex®, Tolak®)	Concerns related to adverse effects: • Hypersensitivity: Delayed-type hypersensitivity reactions have been reported. Patch testing may not be useful in the evaluation of these reactions. Treatment should be discontinued immediately for signs of hypersensitivity. • Local skin reactions: When applied to a lesion, erythema followed by vesiculation, desquamation, erosion and reepithelialization occurs. Increased absorption through ulcerated or inflamed skin is possible. • Ocular adverse reactions: Corneal and conjunctival disorders have occurred; application to the periocular area should be avoided. • Photosensitivity: Prolonged exposure to sunlight or UV irradiation during treatment should be avoided; reaction intensity may be increased. Disease-related concerns: • Dihydropyrimidine dehydrogenase (DPD) enzyme deficiency: DPD enzyme deficiency may result in increased cytotoxic activity and severe toxicity. Treatment should be discontinued if signs of DPD deficiency develop. Dosage form specific issues: • Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates. • Peanut oil: Some dosage forms contain peanut oil. • Polysorbate 80: Some dosage forms may contain polysorbate 80. Hypersensitivity reactions, usually a delayed reaction, have been reported. Thrombocytopenia, ascites, pulmonary deterioration, and renal and hepatic failure have been reported in premature neonates. • Propylene glycol: Some dosage forms may contain propylene glycol; large amounts are potentially toxic and have been associated with hyperosmolality, lactic acidosis, seizures and respiratory depression. Other warnings/precautions: • Appropriate use: Application to mucous membranes should be avoided due to potential for local inflammation and ulceration. Occlusive dressings may increase the severity of inflammation in nearby skin areas. • Household pet safety: Small amounts ingested by cats or dogs may result in toxic hyperammonemia and high rates of mortality.
Klisyri® (tirbanibulin)	Concerns related to adverse effects: • Dermatologic reactions: Local reactions, including severe erythema, flaking, scaling, crusting, swelling, vesiculation/pustulation, and erosion/ulceration, may occur. Skin should be healed from any prior drug, procedure, or surgery at the application site before using. • Ocular effects: May cause eye irritation; contact with eyes or periocular area during and after application should be avoided.
Diclofenac sodium	Concerns related to adverse effects: • Anaphylactoid reactions: Even in patients without prior exposure, anaphylactoid reactions may occur; patients with "aspirin triad" may be at increased risk. • Drug reaction with eosinophilia and systemic symptoms (DRESS): Potentially serious, sometimes fatal, DRESS has been reported with NSAIDs. Signs and symptoms (e.g., fever, rash, lymphadenopathy, eosinophilia) in association with other organ system involvement should be monitored. Treatment should be discontinued and further evaluated if DRESS is suspected. • Hematologic effects: Platelet adhesion and aggregation may be decreased; may prolong bleeding time; patients with coagulation disorders or who are receiving anticoagulants should be monitored closely. Anemia may occur.

Medication	Warnings/Precautions
	• Hyperkalemia: NSAID use may increase the risk of hyperkalemia, particularly in the elderly, diabetics, renal disease, and with concomitant use of other agents capable of inducing hyperkalemia. Potassium should be monitored closely. • Renal effects: NSAID use may compromise existing renal function; Patients with impaired renal function, dehydration, hypovolemia, heart failure, hepatic impairment, those taking diuretics and ACE inhibitors, and the elderly are at greater risk of renal toxicity. Long-term NSAID use may result in renal papillary necrosis and other renal injury/toxicity. • Skin reactions: May cause potentially fatal serious skin adverse events, including exfoliative dermatitis, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN); treatment should be discontinued at first sign of skin rash (or any other hypersensitivity). Disease-related concerns: • Asthma: Severe and potentially fatal bronchospasm may occur. • Hepatic impairment: Treatment should be used with caution in patients with hepatic impairment. • Renal impairment: Treatment should be avoided in advanced renal disease. Special populations: • Elderly: Elderly patients are at greater risk for serious GI, cardiovascular and/or renal adverse events; treatment should be used with caution. Dosage form specific issues: • Benzoyl alcohol and derivatives: Some dosage forms may contain benzoyl alcohol; large amounts of benzoyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates. • Occlusive dressings and/or heat application to treated area should be avoided. • Combination use with oral NSAIDs is not recommended due to increased risk of adverse reactions unless benefit outweighs risks, and patient will be monitored with periodic laboratory evaluations.
Imiquimod (Zyclara®, Aldara®)	Concerns related to adverse effects: • Local inflammatory reactions: Intense local inflammatory reactions may occur after a few applications; may require treatment interruption and may be accompanied by systemic symptoms; reactions may extend beyond the application site. Imiquimod has the potential to exacerbate inflammatory conditions of the skin. • Photosensitivity: Due to the potential for increased sensitivity to sunlight, avoid or minimize sunlight exposure during treatment. Patients should be advised not to wear protective clothing during treatment. Patients with sunburn should not use imiquimod until full recovery form sunburn. Patients with a potential for considerable sun exposure or inherent sensitivity to sunlight should use caution during treatment. • Systemic reactions: Flu-like symptoms may accompany or precede local inflammatory reactions; may require treatment interruption. • Vulvar swelling: Severe local inflammation of female external genitalia following topical application may lead to severe vulvar swelling and urinary retention; treatment should be interrupted or discontinued for severe symptoms. Disease related concerns: • Actinic keratosis: Safety and efficacy have not been established in the treatment of actinic keratosis with repeat use (more than 1 treatment course) in the same area. Safety of imiquimod 5% applied to areas of skin larger than 25 cm^2 has not been established. Lymphadenopathy has occurred in patients being treated for actinic keratosis; lymphadenopathy resolved within 4 weeks after completion of treatment.

Medication	Warnings/Precautions
	• Autoimmune disorders: Safety and efficacy in immunosuppressed patients have not been established. Treatment should be used with caution in patients with preexisting autoimmune disorders (onset or exacerbation of disease has been reported). • Basal cell carcinoma: Use should be limited to superficial carcinomas with a maximum diameter of 2 cm. Safety and efficacy in treatment of other types of basal cell carcinoma (BCC) lesions of the face, head, and anogenital area, or other subtypes of BCC (including nodular and morpheaform), have not been established. Patients with superficial BCC treated with imiquimod should have regular follow up of the treatment site. • Human papilloma viral disease: Imiquimod has not been evaluated for the treatment of urethral, intravaginal, cervical, rectal, or intra-anal human papilloma viral disease and is not recommended for these conditions. Dosage forms specific issues: • Benzyl alcohol and derivatives: Some dosage forms may contain benzyl alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates Other warnings/precautions: • Appropriate use: Not intended for oral, nasal, intravaginal, or ophthalmic use. Administration is not recommended until tissue is healed from any previous drug or surgical treatment. Treatment should not be prolonged beyond recommended period due to missed doses or rest periods. Safety and efficacy have not been established for basal cell nevus syndrome, in immunocompromised patients, or for xeroderma pigmentosum. Safety and efficacy of the 2.5% cream in the treatment of external genital warts have not been established.

PRACTICE GUIDELINES

Kandolf L, Peris K, Malvehy J, et al; European Association of Dermato-Oncology, European Dermatology Forum, European Academy of Dermatology and Venereology and Union of Medical Specialists (Union Européenne des Médecins Spécialistes). European consensus-based interdisciplinary guideline for diagnosis, treatment and prevention of actinic keratoses, epithelial UV-induced dysplasia and field cancerization on behalf of European Association of Dermato-Oncology, European Dermatology Forum, European Academy of Dermatology and Venereology and Union of Medical Specialists (Union Européenne des Médecins Spécialistes). J Eur Acad Dermatol Venereol. 2024 Jun;38(6):1024-1047.

- **Prevention of AKs**
  - Individuals at high-risk of AKs, including those occupationally exposed to UV irradiation and immunocompromised and all patients with AK should be advised to apply the appropriate protective measures against UV irradiation (B, 2)
- **Topical Agents**
  - Topical 5-fluorouracil shall be offered for the treatment of single or multiple AK and field cancerization. Available are the following 5-FU formulations: 5% 5-FU cream, 4% fluorouracil in aqueous cream, 0.5% fluorouracil in salicylic acid 10% solution, 5% fluorouracil plus calcipotriol 0.005% cream (A, 1)
  - 5% or 3.75% imiquimod should be offered for the treatment of single or multiple AKs and field cancerization treatment. (B, 1-2)
  - 3% diclofenac in 2.5% sodium hyaluronate is less effective than other treatments of single or multiple AKs and field cancerization treatment (A, 1)
  - Tirbanibulin 1% ointment should be offered for the treatment of single or multiple AKs and field cancerization treatment of the face and scalp (B, 1)
- **Cryosurgery**
  - Cryosurgery shall be offered as a first-line standard treatment for solitary AK (A, 1)
  - Cryosurgery in combination with curettage and topical treatments shall be offered in multiple AKs and field cancerization. (A, 1)
- **Photodynamic Therapy (PDT)**
  - Conventional or daylight photodynamic therapy with 5-aminolevulinic acid and/or methyl aminolaevulinate should be offered for the treatment of single or multiple AK and field cancerization. (A, 1-2)

Recommendation Definitions

Strength of Recommendation	Definition
A	Strong recommendation. Syntax: 'shall'
B	Recommendation. Syntax: 'should'
C	Weak recommendation. Syntax: 'may/can'.
X	Should not be recommended.
0	Recommendation pending. Currently not available or not sufficient evidence to make a recommendation in favour or against.
Level of Evidence	**Definition**
1	Systematic review and meta-analysis, prospective multicentre study, randomized placebo-controlled trials, trials with active comparator arm
2	Single-centre randomized controlled trials

Eisen DB, Dellavalle RP, Frazer-Green L, Schlesinger TE, Shive M, Wu PA. Focused update: Guidelines of care for the management of actinic keratosis. J Am Acad Dermatol. 2022 Aug;87(2):373-374.e5.

- **Topical Agents**
  - For patients with AKs, we recommend field treatment with topical tirbanibulin (Strong recommendation, High quality of evidence).

Recommendation Definitions

Strength of Recommendation	Definition
Strong, *for*	Benefits clearly outweigh risks and burden, or risks and burden clearly outweigh the benefits; applies to most patients in most circumstances.
Conditional, *for*	Benefits finely balanced with risks and burden; applies to most patients, but appropriate action may differ, depending on the patient or other stakeholder values.
Strong, *against*	Risk and burden clearly outweigh benefits; applies to most patients in most circumstances.
Conditional, *against*	Risks and burden closely balance with benefits; applies to most patients, but appropriate action may differ, depending on the patient or other stakeholder values.
Good Practice Statement	Strong recommendations, as the certainty surrounding the impact of the recommended intervention is high. Implementation of these strong recommendations is considered to clearly result in beneficial outcomes.
Certainty of Evidence	**Definition**
High	Very confident that the true effect lies close to that of the estimate of the effect.
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.
Low	Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low	Very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Eisen DB, Asgari MM, Bennett DD, et al. Guidelines of care for the management of actinic keratosis. J Am Acad Dermatol. 2021;S0190-9622(21)00502-8.

- **UV Protection**
  - For patients with AK, we recommend the use of UV protection (Strong recommendation, Good Practice Statement).
- **Topical Agents**
  - For patients with AKs, we recommend field treatment with 5-fluorouracil (Strong recommendation, Moderate quality of evidence).
  - For patients with AKs, we recommend field treatment with imiquimod (Strong recommendation, Moderate quality of evidence).
  - For patients with AKs we conditionally recommend the use of diclofenac (Conditional recommendation, Low quality of evidence).
- **Cryosurgery**
  - For patients with AKs, we recommend the use of cryosurgery (Strong recommendation, Good Practice Statement).
  - For patients with AKs, we conditionally recommend treatment with cryosurgery over CO_2 laser ablation (Conditional recommendation, Moderate quality of evidence).
- **Photodynamic Therapy (PDT)**
  - For patients with AKs, we conditionally recommend aminolevulinic acid (ALA)-red light PDT (Conditional recommendation, Low quality of evidence).
  - For patients with AKs, we conditionally recommend 1 to 4-hour 5-ALA incubation time to enhance complete clearance with red light PDT (Conditional recommendation, Low quality of evidence).
  - For patients with AKs, we conditionally recommend ALA-daylight PDT as less painful than but equally effective as ALA-red light PDT (Conditional recommendation, Moderate quality of evidence).
  - For patients with AKs, we conditionally recommend treatment with ALA-red light PDT over trichloroacetic acid peel (Conditional recommendation, Moderate quality of evidence).
  - For patients with AKs, we conditionally recommend ALA-blue light PDT (Conditional recommendation, Moderate quality of evidence).
  - For patients with AKs, we conditionally recommend against pretreatment with alpha hydroxy acid solution prior to ALA-blue light PDT (Conditional recommendation, Very Low quality of evidence).

- For patients with AKs, we conditionally recommend treatment with ALA-red light PDT over cryosurgery alone (Conditional recommendation, Low quality of evidence).

- **Combination Therapy**
  - For patients with AKs, we conditionally recommend the combined use of 5-fluorouracil and cryosurgery over cryosurgery alone (Conditional recommendation, Moderate quality of evidence).
  - For patients with AKs, we conditionally recommend the combined use of imiquimod and cryosurgery over cryosurgery alone (Conditional recommendation, Low quality of evidence).
  - For patients with AKs, we conditionally recommend against the use of diclofenac in addition to cryosurgery compared to cryosurgery alone (Conditional recommendation, Low quality of evidence).
  - For patients with AKs, we conditionally recommend against the use of topical adapalene in addition to cryosurgery compared to cryosurgery alone (Conditional recommendation, Low quality of evidence).
  - For patients with AKs, we conditionally recommend against the addition of imiquimod following ALA-blue light PDT (Conditional recommendation, Moderate quality of evidence).

Recommendation Definitions

Strength of Recommendation	Definition
Strong, *for*	Benefits clearly outweigh risks and burden, or risks and burden clearly outweigh the benefits; applies to most patients in most circumstances.
Conditional, *for*	Benefits finely balanced with risks and burden; applies to most patients, but appropriate action may differ, depending on the patient or other stakeholder values.
Strong, *against*	Risk and burden clearly outweigh benefits; applies to most patients in most circumstances.
Conditional, *against*	Risks and burden closely balance with benefits; applies to most patients, but appropriate action may differ, depending on the patient or other stakeholder values.
Good Practice Statement	Strong recommendations, as the certainty surrounding the impact of the recommended intervention is high. Implementation of these strong recommendations is considered to clearly result in beneficial outcomes.
Certainty of Evidence	**Definition**
High	Very confident that the true effect lies close to that of the estimate of the effect.
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.
Low	Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low	Very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Ezzedine K, Painchault C, Brignone M. Systematic Literature Review and Network Meta-analysis of the Efficacy and Acceptability of Interventions in Actinic Keratoses. Acta Derm Venereol. 2021;101(1):adv00358.	This systematic review/network meta-analysis (NMA) was conducted to assess the comparative efficacy and acceptability of field-directed treatments in immunocompetent adult patients with head region lesions of AK. Treatments assessed were 5-fluorouracil (5-FU), diclofenac (DIC), imiquimod (IMQ), ingenol mebutate (Ing Meb), and 5-aminolevulinic acid (ALA) or methyl aminolevulinate (MAL) plus photodynamic therapy (PDT). Therapies were assessed using surface under the cumulative ranking (SUCRA) probabilities. A total of 31 randomized controlled trials covering 13 interventions were included in the comparative NMA.	• Efficacy outcomes: Complete (100%) and partial (≥75%) clearance of AK lesions • Acceptability outcome: Withdrawal due to adverse events (AEs)
Results: Compared with placebo, significantly higher complete clearance rates were achieved with 5-FU 4%, 5-FU 5%, 5-FU 0.5% (cream), 5-FU 0.5% + 10% salicylic acid (solution), ALA-PDT, IMQ 5%, Ing Meb 0.015%, and MAL-PDT. Significantly higher partial clearance rates were achieved with 5-FU 5%, 5-FU 4%, IMQ 5% and Ing Meb 0.015% compared to placebo. For complete and partial clearance, the SUCRA values ranked 5-FU 5% and 5-FU 4%, respectively, as having the probability of being the best treatment. No agents showed significance for a lower risk of withdrawals due to AEs. **Conclusion**: 5-FU interventions had the best efficacy, with a satisfactory acceptability profile.		

Citation	Design	Endpoints
Jansen MHE, Kessels JPHM, Nelemans PJ, et al. Randomized Trial of Four Treatment Approaches for Actinic Keratosis. N Engl J Med. 2019;380(10):935-946.	This multicenter, single-blind, randomized trial involved 624 adult patients with 5 or more AK lesions in 1 continuous area of skin measuring 25 to 100 cm^2 in the head and neck area. Patients were excluded if they received prior treatment for AK in the target area, used systemic retinoid or immunosuppressants in the last 3 months, or were suspected for cancer or pregnancy. Patients were randomized 1:1:1:1 to receive 5% fluorouracil cream, 5% imiquimod cream, methyl aminolevulinate photodynamic therapy (MAL-PDT), or 0.015% ingenol mebutate. A modified-intention-to-treat analysis, based on 602 randomly assigned patients who started treatment and for whom data regarding the primary outcome were available, was used.	• Primary efficacy endpoint: Proportion of patients who remained free from treatment failure (reduction of < 75% in number of AK lesions from baseline) during 12 months of follow-up after the last treatment
Results: The cumulative probability of treatment success for fluorouracil was 74.7% (95% confidence interval [CI], 66.8 to 81.0). For imiquimod, MAL-PDT, and ingenol mebutate, these percentages were 53.9% (95% CI, 45.4 to 61.6), 37.7% (95% CI, 30.0 to 45.3), and 28.9% (95% CI, 21.8 to 36.3), respectively. As compared with fluorouracil, the hazard ratio for treatment failure was 2.03 (95% CI, 1.36 to 3.04) with imiquimod, 2.73 (95% CI, 1.87 to 3.99) with MAL-PDT, and 3.33 (95% CI, 2.29 to 4.85) with ingenol mebutate (P≤0.001 for all comparisons). **Conclusion**: 5% fluorouracil cream was the most effective of four field-directed treatments.		

Citation	Design	Endpoints
Jansen MHE, Kessels JPHM, Merks I, et al. A trial-based cost-effectiveness analysis of topical 5-fluorouracil vs. imiquimod vs.	This trial-based cost effectiveness analysis was an economic evaluation from a healthcare perspective. Data was collected alongside the trial from the previous publication (Randomized Trial of Four Treatment Approaches for Actinic Keratosis).	• Primary efficacy endpoint: Incremental cost-effectiveness ratio (ICER; incremental costs per additional patient

ingenol mebutate vs. methyl aminolaevulinate conventional photodynamic therapy for the treatment of actinic keratosis in the head and neck area performed in the Netherlands. Br J Dermatol. 2020;183(4):738-744.		with ≥ 75% lesion reduction compared with baseline)
Results: Based on the ICER, fluorouracil (€433) was a dominant cost-effective treatment (more effective and less expensive) compared with imiquimod (€728), ingenol mebutate (€775), and methyl aminolevulinate photodynamic therapy (€1621), 12 months post-treatment. **Conclusion:** Fluorouracil 5% cream is considered as the first-choice treatment option for multiple AKs in the head and neck area.		

Citation	Design	Endpoints
Gollnick H, Dirschka T, Ostendorf R, Kerl H, Kunstfeld R. Long-term clinical outcomes of imiquimod 5% cream vs. diclofenac 3% gel for actinic keratosis on the face or scalp: a pooled analysis of two randomized controlled trials. J Eur Acad Dermatol Venereol. 2020;34(1):82-89.	These two almost identically designed randomized, active-controlled, open-label, multicenter, multinational, phase IV studies involved 479 immunocompetent adult patients with 5-10 visible AK lesions in 1 contiguous area of up to 50 cm^2 on the face/scalp and grade I/II AK. Patients were excluded if they received prior treatment for AK in the target area or systemically. Patients were randomized 1:1 to receive treatment with imiquimod 5% cream or diclofenac 3% gel.	• Primary efficacy endpoint: Inhibition of histological change to grade III AK or invasive SCC, observed until month 36
Results: Histological change to grade III AK or invasive SCC was observed up to month 36 in 13(5.4%) patients in the imiquimod group and 26 (11.0%) patients in the diclofenac group (absolute risk difference: –5.6%; 95% CI –10.7 to –0.7). The treatment difference observed for histological change at month 36 was also apparent at month 12 and significantly apparent at month 24 (absolute risk difference: –4.7%; 95% CI –9.2 to –0.5). Time to histological change was greater in the imiquimod group than in the diclofenac group (P=0.0266). **Conclusion**: Over the long-term, imiquimod is more effective than diclofenac at treating AK lesions, with superior lesion clearance, fewer recurrences and less histological change to grade III AK or invasive SCC.		

Citation	Design	Endpoints
Blauvelt A, Kempers S, Lain E, et al. Phase 3 Trials of Tirbanibulin Ointment for Actinic Keratosis. N Engl J Med. 2021;384(6):512-520.	These two identically designed phase 3, multicenter, double-blind, parallel-group, vehicle-controlled trials involved 702 adult patients with 4 to 8 clinically typical, visible, and discrete AK lesions on the face or scalp measuring 25 cm^2.Patients were excluded for atypical AKs, suspected cancer, previous tirbanibulin treatment, and prior treatment to the area within the last 2 weeks. Patients were randomized 1:1 to receive tirbanibulin 1% ointment or vehicle ointment, applied for 5 consecutive days.	• Primary efficacy endpoint: Percentage of patients with complete (100%) clearance of all lesions within the application area at day 57 • Secondary efficacy endpoint: Percentage of patients with a partial (≥75%) reduction in the number of lesions within the application area at day 57
Results: Complete clearance in trial 1 occurred in 44% of the patients in the tirbanibulin group and in 5% of those in the vehicle group (difference, 40%; 95% CI, 32 to 47; P<0.001). In trial 2, the percentages were 54% and 13%, respectively (difference, 42%; 95% CI, 33 to 51; P<0.001). Partial clearance in trial 1 occurred in 68% of the patients in		

the tirbanibulin group and in 16% of those in the vehicle group (difference, 52%; 95% CI, 43 to 60; P<0.001). In trial 2, the percentages were 76% and 20% respectively (difference, 57%; 95% CI, 48 to 65; P<0.001).
Conclusion: Tirbanibulin 1% ointment applied once daily for 5 days was superior to vehicle for the treatment of AK at 2 months.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (07-01-2024 to 09-30-2024)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Topical Antineoplastic Premalignant Lesion Agents								
Fluorouracil (Carac®) 0.05 % topical cream	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fluoroplex® (fluorouracil) 1 % topical cream	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Fluorouracil (Efudex®) 5 % topical cream	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Fluorouracil 2 %, 5% topical solution	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Tolak® (fluorouracil) 4 % topical cream	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Klisyri® (tirbanibulin) 1 % topical ointment in packet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Diclofenac (Solaraze®) 3 % topical gel	1	1	$65.04	$65.04	0	0 (0%)	F	→F-PA
Immunomodulators								
Imiquimod (Zyclara®) 3.75 % topical cream packet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Imiquimod (Zyclara®) 3.75 % topical cream in a pump	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Zyclara® (imiquimod) 2.5 % topical cream in a pump	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
imiquimod (Aldara®) 5 % topical cream packet	6	5	$184.38	$30.73	0	0 (0%)	F	No change
TOTAL	**7**	**6**	**$249.42**	**$35.63**	**0**			

^Brand drug pricing is based on wholesale acquisition cost (WAC) and generic drug pricing is based on maximum allowable cost (MAC) for 1 month supply unless otherwise noted.
*Preferred pricing listed

PRIOR AUTHORIZATION CRITERIA

No changes

Diclofenac sodium (Solaraze) 3% gel	
Therapeutic Classes (AHFS)	Antineoplastic Agents
Medications	Formulary, PA required Diclofenac sodium (Solaraze) 3% gel
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 dermatologist
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to 3 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	Criteria for approval • Diagnosis of actinic keratosis (AK) • Documented trial and failure of one formulary alternative [i.e. fluorouracil (Efudex) cream or imiquimod (Aldara) cream]
Criteria Statement	Diclofenac sodium 3% gel is reserved for members who have actinic keratosis and have used (or cannot/should not use) one formulary alternative such as fluorouracil (Efudex) or Imiquimod (Aldara) creams.
Last P&T Review Date	~~12/2023~~12/2024

REFERENCES

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2. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on August 2, 2024.
3. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: https://clinicaltrials.gov/. Accessed on August 2, 2024.
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Drug Name: Cobenfy (xanomeline and trospium chloride)

Manufacturer: Bristol-Myers Squibb

Approval Date: 9/26/2024

Marketing Date: 10/2/2024

Recommendation

Implement the newly developed Cobenfy (xanomeline and trospium chloride) MRG Criteria with no changes to formulary status.

Prescribing Information

Indication

Cobenfy™ is indicated for the treatment of schizophrenia in adults.

Mechanism of Action

The mechanism of action of xanomeline in the treatment of schizophrenia is unclear; however, its efficacy is thought to be due to its agonist activity at M1 and M4 muscarinic acetylcholine receptors in the central nervous system.

Trospium chloride is a muscarinic antagonist. Trospium chloride antagonizes the muscarinic receptors primarily in the peripheral tissues.

Dosage and Administration

- The recommended starting dosage is one 50 mg/20 mg capsule (contains 50 mg of xanomeline and 20 mg of trospium chloride) orally twice daily for at least two days.
- Increase the dosage to one 100 mg/20 mg capsule (contains 100 mg of xanomeline and 20 mg of trospium chloride) orally twice daily for at least five days.
- The dosage may be increased to one 125 mg/30 mg capsule (contains 125 mg of xanomeline and 30 mg of trospium chloride) orally twice daily based on patient tolerability and response.
- Maximum recommended dosage is 125 mg/30 mg orally twice daily.

Black Box Warning

None

Adverse Reactions

Most common: nausea, dyspepsia, constipation, vomiting, hypertension, abdominal pain, diarrhea, tachycardia, dizziness, and gastrointestinal reflux disease.

Serious: risk of urinary retention, risk in patients with biliary disease, decreased gastrointestinal motility, risk of angioedema, risk of use in patients with narrow-angle glaucoma, increases in heart rate, reactions in patients with renal impairment, CNS effects

Use in Specific Populations, Pregnancy

There are no available data on Cobenfy™ use in pregnant women to evaluate for a drug associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes.

Drug Interactions

The table below displays clinically significant drug interactions with Cobenfy™.

Strong Inhibitors of CYP2D6	
Clinical Implication:	CYP2D6 contributes significantly to the metabolism of xanomeline, a component of COBENFY. Concomitant use of COBENFY with strong CYP2D6 inhibitors may increase plasma concentrations of xanomeline, which may increase the frequency and/or severity of adverse reactions from COBENFY *[see Clinical Pharmacology (12.3)]*.
Prevention or Management:	Monitor patients for increased frequency and/or severity of adverse reactions related to COBENFY in patients taking COBENFY with strong inhibitors of CYP2D6.
Drugs Eliminated by Active Tubular Secretion	
Clinical Implication:	Concomitant use of COBENFY with drugs that are eliminated by active tubular secretion may increase plasma concentrations of trospium a component of COBENFY, and/or the concomitantly used drug due to competition for this elimination pathway, which may increase the frequency and/or severity of adverse reactions from COBENFY or the drug eliminated by active tubular secretion *[see Clinical Pharmacology (12.3)]*.
Prevention or Management:	Monitor patients for increased frequency and/or severity of adverse reactions related to COBENFY and adverse reactions related to drugs eliminated by active tubular secretion in patients concomitantly receiving such drugs.
Oral Drugs That Are Sensitive Substrates of CYP3A4	
Clinical Implication:	Xanomeline, a component of COBENFY, transiently inhibits CYP3A4 locally in the gut but not systemically. Concomitant use of COBENFY with oral drugs that are sensitive substrates of CYP3A4 may result in increased plasma concentrations of the oral drugs that are sensitive substrates of CYP3A4. This may increase the frequency and/or severity of adverse reactions from such substrates *[see Clinical Pharmacology (12.3)]*.
Prevention or Management:	Monitor patients for increased frequency and/or severity of adverse reactions related to oral drugs that are sensitive substrates of CYP3A4 in patients taking COBENFY with such substrates.
Oral Drugs That Are Substrates of P-glycoprotein	
Clinical Implication:	Xanomeline, a component of COBENFY, transiently inhibits P-glycoprotein locally in the gut but not systemically. Concomitant use of COBENFY with oral drugs that are substrates of P-glycoprotein may result in increased plasma concentrations of the oral drugs that are substrates of P-glycoprotein, which may increase the frequency and/or severity of adverse reactions from such substrates *[see Clinical Pharmacology (12.3)]*.
Prevention or Management:	Monitor patients for increased frequency and/or severity of adverse reactions related to oral drugs that are narrow therapeutic index substrates of P-glycoprotein in patients taking COBENFY with such substrates.

- Concomitant use of Cobenfy™ with other antimuscarinic drugs that produce anticholinergic adverse reactions may increase the frequency and/or severity of such effects. Monitor patients for increased frequency and/or severity of anticholinergic adverse reactions when Cobenfy™ is used concomitantly with other antimuscarinic drugs.
- Cobenfy™ may potentially alter the absorption of some concomitantly administered drugs due to anticholinergic effects on gastrointestinal motility. Dosage adjustment of concomitant medications may be necessary based on clinical response and tolerability.

How Supplied

50 mg/20 mg, 100 mg/20 mg, 125 mg/30 mg oral capsules

Price

$1,850

(Per month, based on WAC.)

Clinical Studies

Completed

Title	Efficacy and safety of the muscarinic receptor agonist KarXT (xanomeline-trospium) in schizophrenia (EMERGENT-2) in the USA: results from a randomised, double-blind, placebo-controlled, flexible-dose phase 3 trial Efficacy and Safety of Xanomeline-Trospium Chloride in Schizophrenia: A Randomized Clinical Trial (EMERGENT-3) NCT: 04659161 (study 1) and 04738123 (study 2) PMID: 38104575 and 38691387
Design	Phase 3, randomized, double-blind, placebo-controlled, multi-center studies in adult patients with a diagnosis of schizophrenia according to the DSM-5 criteria
Population	N = 470 Median age was 46 years (range 19 to 65 years). Twenty-five percent of patients were female, 31% were White, 68% were Black or African American, and 1% were Other (or not reported).
Arms	Experimental Arm: Cobenfy™ • Cobenfy™ 50 mg/20 mg twice a day for the first 2 days followed by Cobenfy™ 100 mg/20 mg twice a day on days 3 to 7. On day 8, dosing was to be titrated upwards to Cobenfy™ 125 mg/30 mg twice a day unless the subject was continuing to experience adverse events from the previous dose of Cobenfy™ 100 mg/20 mg twice a day. Placebo Arm: Placebo • Placebo capsule administered twice a day
Endpoint(s)	Primary: • Change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at Week 5 Secondary: • Change from baseline in PANSS positive score at Week 5
Inclusion Criteria	• Aged 18 to 65 years old at screening • Primary diagnosis of schizophrenia established by a comprehensive psychiatric evaluation based on the DSM-5 criteria and confirmed by the Mini International Neuropsychiatric Interview for schizophrenia and Psychotic Disorder Studies (MINI) version 7.0.2 • Subject is experiencing an acute exacerbation or relapse of psychotic symptoms, with onset less than 2 months before screening • PANSS total score between 80 and 120 • Subject has a CGI-S score of ≥4 at screening and baseline visits

<table>
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- Subject taking a long-acting injectable antipsychotic could not have received a dose of medication for at least 12 weeks (24 weeks for Invega Trinza) before baseline visit.

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<tr><td>Exclusion Criteria</td><td>

- Any primary DSM-5 disorder other than schizophrenia within 12 months before screening
- Subjects who are newly diagnosed or are experiencing their first treated episode of schizophrenia
- Subjects with HIV, cirrhosis, biliary duct abnormalities, hepatobiliary carcinoma, and/or active hepatic viral infections based on either medical history or liver function test results
- Risk of suicidal behavior during the study as determined by the investigator's clinical assessment and Columbia-Suicide Severity Rating Scale (C-SSRS)
- Pregnant, lactating, or less than 3 months postpartum

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<tr><td>Results</td><td>

Table 4: Primary Efficacy Results for Change from Baseline in PANSS Total Score at Week 5 in Adults with Schizophrenia (Studies 1 and 2)

			Primary Efficacy Endpoint: PANSS Total Score		
Study Number	Treatment Group	N	Mean Baseline Score (SD)	LS Mean Change from Baseline (SE)	Placebo-subtracted Difference (95% CI)[a]
1	COBENFY	117	98.2 (8.9)	-21.2 (1.7)	-9.6 (-13.9, -5.2)*
	Placebo	119	97.7 (9.4)	-11.6 (1.6)	
2	COBENFY	114	96.9 (8.8)	-20.6 (1.6)	-8.4 (-12.4, -4.3)*
	Placebo	120	96.5 (8.8)	-12.2 (1.6)	

The PANSS Total Score may range from 30 to 210; higher scores reflect greater symptom severity.
SD: standard deviation; SE: standard error; LS Mean: least-squares mean; CI: confidence interval.
[a] Difference (drug minus placebo) in LS mean change from baseline.
* Statistically significantly superior to placebo.

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<tr><td>Conclusion</td><td>

In the EMERGENT-2 trial, xanomeline-trospium was effective in reducing positive and negative symptoms and was generally well tolerated. These results support the potential for xanomeline-trospium to represent a new class of effective and well tolerated antipsychotic medicines based on activating muscarinic receptors, not the D_2 dopamine receptor-blocking mechanism of all current antipsychotic medications.

In the EMERGENT-3 trial, xanomeline-trospium was efficacious and well tolerated in people with schizophrenia experiencing acute psychosis. These findings, together with the previously reported and consistent results from the EMERGENT-1 and EMERGENT-2 trials, support the potential of xanomeline-trospium to be the first in a putative new class of antipsychotic medications without D2 dopamine receptor blocking activity.

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<tr><td>Interpretation</td><td>

EMERGENT-2 and EMERGENT-3, Cobenfy™ achieved its primary endpoint, with a 9.6-point and an 8.4-point reduction in the PANSS score compared to placebo at week five, respectively. While Cobenfy™ demonstrated favorable efficacy and a generally well tolerated safety profile, it is important to note that the duration of this trial was only 5 weeks and did not assess long-term efficacy and safety. Additionally, this new antipsychotic drug was compared to placebo, rather than being compared to the current standard of care treatment options. Results from additional trials, including the 52-week,

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	open-label EMERGENT-4 and EMERGENT-5 trials, will provide additional information on the efficacy and safety of xanomeline-trospium in people with schizophrenia.

Ongoing

Title	An Open-label Extension Study to Assess the Long-term Safety, Tolerability, and Efficacy of KarXT in Subjects With DSM-5 Schizophrenia (EMERGENT-4) NCT: 04659174
Design	Phase 3, multicenter, 53-week, outpatient, open-label extension study
Completion Date	10/3/2023; Results have not yet been published

Title	An Open-label Study to Assess the Long-term Safety, Tolerability, and Efficacy of KarXT in De Novo Subjects With DSM-5 Schizophrenia (EMERGENT-5) NCT: 04820309
Design	Phase 3, multicenter, 56-week, outpatient, open-label study
Completion Date	5/24/2024; Results have not yet been published

Title	A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of Adjunctive KarXT in Subjects With Inadequately Controlled Symptoms of Schizophrenia (ARISE) NCT: 05145413
Design	Phase 3, 6-week, randomized, double-blind, placebo-controlled, multicenter, outpatient study
Completion Date	2/28/2025

Guidelines

**Note guidelines have not been updated since the approval of Cobenfy™.*

American Psychiatric Association. The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia. American Psychiatric Association. 2020;3. doi:https://doi.org/10.1176/appi.books.9780890424841

Pharmacotherapy

- APA recommends (1A) that patients with schizophrenia be treated with an antipsychotic medication and monitored for effectiveness and side effects.*
- APA recommends (1A) that patients with schizophrenia whose symptoms have improved with an antipsychotic medication continue to be treated with an antipsychotic medication.*
- APA suggests (2B) that patients with schizophrenia whose symptoms have improved with an antipsychotic medication continue to be treated with the same antipsychotic medication.*
- APA recommends (1B) that patients with treatment-resistant schizophrenia be treated with clozapine. *
- APA recommends (1B) that patients with schizophrenia be treated with clozapine if the risk for suicide attempts or suicide remains substantial despite other treatments.*
- APA suggests (2C) that patients with schizophrenia be treated with clozapine if the risk for aggressive behavior remains substantial despite other treatments.*
- APA suggests (2B) that patients receive treatment with a long-acting injectable antipsychotic medication if they prefer such treatment or if they have a history of poor or uncertain adherence.*
- APA recommends (1C) that patients who have acute dystonia associated with antipsychotic therapy be treated with an anticholinergic medication.
- APA suggests (2C) the following options for patients who have parkinsonism associated with antipsychotic therapy: lowering the dosage of the antipsychotic medication, switching to another antipsychotic medication, or treating with an anticholinergic medication.
- APA suggests (2C) the following options for patients who have akathisia associated with antipsychotic therapy: lowering the dosage of the antipsychotic medication, switching to another antipsychotic medication, adding a benzodiazepine medication, or adding a beta-adrenergic blocking agent.
- APA recommends (1B) that patients who have moderate to severe or disabling tardive dyskinesia associated with antipsychotic therapy be treated with a reversible inhibitor of the vesicular monoamine transporter2 (VMAT2).

**This guideline statement should be implemented in the context of a person-centered treatment plan that includes evidence-based nonpharmacological and pharmacological treatments for schizophrenia.*

Hasan A, Falkai P, Wobrock T, et al. World Federation of Societies of Biological Psychiatry (WFSBP) Guidelines for Biological Treatment of Schizophrenia, part 1: update 2012 on the acute treatment of schizophrenia and the management of treatment resistance. World J Biol Psychiatry. 2012;13(5):318-378. doi:10.3109/15622975.2012.696143

Recommendations for first-episode schizophrenia

- FGAs and SGAs are both effective in the treatment of first-episode schizophrenia (A, 1)
- Patients suffering from their first-episode should be treated with lower antipsychotic dosages than chronically ill patients (A, 1)
- Due to the reduced risk of inducing neurological side effects, the first-line use of SGAs in first-episode schizophrenia patients is recommended with limited evidence (C3, 4)
- Limited evidence is available to support superiority of SGAs with regard to treatment discontinuation in first-episode patients (B/C3, 3/4)
- Haloperidol is the best approved FGA for first-episode schizophrenia (A, 2)
- Risperidone, olanzapine and quetiapine are the best approved SGAs for first-episode schizophrenia (A, 1)
- Clozapine is not recommended for the first-line treatment in first-episode schizophrenia (A, 2)

Recommendations for treatment of multi-episode patients (acute relapse)

- FGAs and SGAs are both effective in the treatment of acute relapse. All established FGAs and SGAs can be used in the treatment of acute schizophrenia (A, 1)

- Some evidence is available to support superiority of SGAs with regard to treatment discontinuation and relapse prevention in chronically ill patients (B/C3, 3/4)
- The increased risk of neurological side effects following treatment with FGAs could favor certain SGAs (C3. 4)
- For FGAs and SGAs, the dose may be titrated as quickly as tolerated but as slowly as possible with special consideration of regard to uncomfortable and potentially dangerous side effects. In general, the lowest effective dose should be used to treat an acute schizophrenia episode (C, 4)
- Before switching to another antipsychotic drug, a treatment trial with the optimal dose for each patient should last for at least 2 weeks, but not longer than 8 weeks, unless there is unacceptable tolerance or contraindication for the continuation of the present drug (C, 4)

Recommendations for treatment of negative symptoms in schizophrenia

- A general superiority of SGAs compared to FGAs for secondary negative symptoms cannot be concluded, but SGAs are superior in the treatment of primary negative symptoms (B, 3)
- Amisulpride/olanzapine display good evidence (A, 1) and quetiapine/ziprasidone some evidence (B, 3) for the efficacy of treatment of schizophrenia patients suffering from predominantly negative symptoms
- The combination of antipsychotics administered with antidepressants might be promising (D, 5) and mirtazapine should be favored (B, 3)

Recommendations for augmentation therapy

- There is only little evidence that the augmentation with antidepressants is effective, whereas mirtazapine seems to be an exception (B-F)
- There is only little evidence supporting the add-on treatment with benzodiazepines in schizophrenia, in catatonic schizophrenia and in antipsychotic-induced acute akathisia (C1-C3, 4). However, benzodiazepines have a prominent effect of agitation (B, 3)
- There is only inconsistent data for memantine, other glutamatergic drugs and other neuroactive agents in the treatment of schizophrenia (D, 5)

Clinical Opinions

Schizophrenia is a chronic psychiatric disorder with variable outcome characterized by persistent psychotic symptoms of delusions, hallucinations, and disorganized speech. Schizophrenia is thought to be the result of interactions between genetic and environmental risk factors that influence early brain development and dysregulate cognition used for interpretation/adaptation to life experiences. Schizophrenia is the most common psychotic illness or disease with the estimated prevalence ranging from 0.6%-1.9% in the US and 0.3%-0.7% globally. Current treatment options include nonpharmacologic therapies such as family intervention and cognitive behavioral therapy (CBT) alone or in addition to antipsychotic medication. Antipsychotic medications are available in two main classes: first generation, also known as “typical” antipsychotics,” and second generation, also known as “atypical” antipsychotics. While current treatments can be effective in managing symptoms for some patients, approximately 30% of people do not respond to therapy, with an additional 50% experiencing only a partial improvement in symptoms or unacceptable side effects.

Cobenfy™ represents the first new mechanism of action to treat schizophrenia in more than 30 years. Cobeny™ is a combination of xanomeline, a muscarinic agonist, and trospium chloride, a muscarinic antagonist. Notably, Cobenfy™ did not cause weight gain or extrapyramidal symptoms in the clinical trial program and does not carry the same black box warning as traditional atypical antipsychotics. The approval of Cobenfy™ was based on evidence from two pivotal trials (EMERGENT-2 and EMERGENT-3), which included 470 patients aged 18 to 65 with diagnosed schizophrenia. Both trials assessed the change from baseline in positive and negative syndrome scale (PANSS) total score at week 5. Of the

patients who participated in EMERGENT-2 and EMERGENT-3, participants in the Cobenfy™ group experienced a 9.6-point and 8.4-point greater reduction, respectively, in PANSS total score at week 5 compared to placebo.

In January of 2024, the Institute for Clinical and Economic Review (ICER) released its revised evidence report assessing the value and comparative clinical efficacy Cobenfy™. ICER noted that reviewed data indicate that Cobenfy™ was associated with significantly lower weight gain, which may translate into fewer cases of metabolic syndrome, diabetes, and cardiovascular complications over the longer term. However, available Cobenfy™ data on the efficacy and side effect profile of the agent are for five weeks of in-hospital treatment of patients having an acute exacerbation of schizophrenia. Given the lack of long-term data, ICER rated the net health benefit of Cobenfy™ as promising, but inconclusive. ICER has calculated a health-benefit price benchmark (HBPB) for Cobenfy™ to be between $16,000 to $20,000 per year.

The approval of Cobenfy™ adds to the already existing landscape of antipsychotic medications available for the treatment of schizophrenia in adults. Although Cobenfy™ is priced at parity with other branded antipsychotics, it stands out due to its lack of undesirable side effects, such as weight gain. Results from additional trials will provide additional information on the efficacy and safety of xanomeline-trospium in individuals with schizophrenia.

Alternatives

Drug Name^	Formulary Status	Dosage Form	Price*
Aripiprazole (Abilify®)	F	2mg, 5mg, 10mg, 15mg, 20mg, 30mg oral tablets 10mg, 15mg orally disintegrating tablets	$7
Lurasidone (Latuda®)	NF	20 mg, 40 mg, 60 mg, 80 mg, 120 mg oral tablets	$16
Caplyta® (lumateperone)	NF	10.5mg, 21mg, 42mg oral capsules	$1,662
Rexulti® (brexpiprazole)	NF	0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg oral tablets	$1,472
Vraylar® (cariprazine)	NF	1.5 mg, 3 mg, 4.5 mg, 6 mg oral capsules	$1,446

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

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

Medication Request Guideline

New:

Cobenfy	
Therapeutic Classes (AHFS)	Antipsychotics, Miscellaneous
Medications	Cobenfy (xanomeline and trospium chloride)
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 and older Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by a psychiatrist or in consultation with a psychiatrist
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 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 schizophrenia, consistent with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria
	• Documented trial and failure with two alternative formulary/preferred antipsychotic agents, or a medical reason is provided for not using any typical or atypical antipsychotic agents
	• Medication is prescribed at an FDA approved dose
	• Provider attestation is provided patient does not have any of the following:
	  ○ Moderate (Child-Pugh Class B) or severe (Child-Pugh Class C) hepatic impairment
	  ○ Untreated Narrow-Angle Glaucoma
	  ○ Urinary Retention
	  ○ Gastric Retention
	
	Re-Authorization:
	• Documentation or provider attestation of positive clinical response (i.e. improvement in positive and/or negative symptoms of schizophrenia)
	• Medication is prescribed at an FDA approved dose

Criteria Statement	Cobenfy is reserved for members who have a diagnosis of schizophrenia, who tried and failed or were unable to use two alternative formulary/preferred antipsychotic agents, and who do not have hepatic impairment, untreated narrow-angle glaucoma, urinary and gastric retention.
Last P&T Review Date	12/2024

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Drug Name: Tecelra (afamitresgene autoleucel)

Manufacturer: Adaptimmune, LLC.

Approval Date: 8/1/2024

Marketing Date: 8/5/2024

Recommendation

Implement the newly developed Tecelra (afamitresgene autoleucel) PAD Criteria with no changes to formulary status.

Prescribing Information

Indication

Tecelra® is indicated for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and whose tumor expresses the melanoma-associated antigen A4 (MAGE-A4) antigen as determined by FDA-approved or cleared companion diagnostic devices.

This indication is approved under accelerated approval based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Mechanism of Action

Tecelra® is a genetically modified autologous T cell immunotherapy consisting of CD4 and CD8 positive T cells transduced with a self-inactivating LV to express an affinity enhanced T cell receptor (TCR) specific for human MAGE-A4 on the cell surface.

The TCR recognizes an HLA-A*02 restricted MAGE-A4 peptide. MAGE-A4 is an intracellular cancer-testis antigen that has restricted expression in normal tissues and is expressed in synovial sarcoma. Antigen-specific activation of Tecelra® via TCR- peptide HLA-A*02 complex results in T cell proliferation, cytokine secretion, and killing of MAGEA4/HLA-A*02 expressing synovial sarcoma cells.

Dosage and Administration

Prior to infusion:

- Verify patient's identity prior to infusion
- Administer a lymphodepleting regimen of cyclophosphamide and fludarabine
- Premedicate with acetaminophen and an H1-antihistamine

Tecelra® Dose and Administration:

- The recommended dose is between 2.68 x 10 to 10 x 10 MAGE-A4 TCR positive T cells
- Administer each infusion bag within one hour of thawing
- DO NOT USE a leukodepleting filter
- DO NOT USE prophylactic systemic corticosteroids

Black Box Warning

Cytokine Release Syndrome (CRS): CRS, which may be severe or life threatening, occurred in patients receiving Tecelra®. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care. Ensure that healthcare providers administering Tecelra® have immediate access to medications and resuscitative equipment to manage CRS

Adverse Reactions

Most common: cytokine release syndrome, nausea, vomiting, fatigue, infections, pyrexia, constipation, dyspnea, abdominal pain, non-cardiac chest pain, decreased appetite, tachycardia, back pain, hypotension, diarrhea, and edema. Grade 3 or 4 laboratory abnormalities were lymphocyte count decreased, neutrophil count decreased, white cell blood count decreased, red blood cell decreased, and platelet count decreased

Serious: CRS, pleural effusion, immune effector cell associated neurotoxicity syndrome (ICANS), prolonged cytopenia, infections, secondary malignancies

Use in Specific Populations, Pregnancy

There are no available data with Tecelra® use in pregnant women. No animal reproductive and developmental toxicity studies have been conducted with Tecelra® to assess whether it can cause fetal harm when administered to a pregnant woman. It is not known if Tecelra® has the potential to be transferred to the fetus and cause fetal toxicity. Therefore, Tecelra®is not recommended for women who are pregnant, and pregnancy after Tecelra® administration should be discussed with the treating physician.

Drug Interactions

None

How Supplied

Infusion bag(s) containing 2.68 x 10 to 10 x 10 MAGE-A4 TCR positive T cells

Price

$727,000 one-time treatment

Clinical Studies

Completed

Title	A Phase 2 Single Arm Open-Label Clinical Trial of ADP-A2M4 SPEAR™ T Cells in Subjects With Advanced Synovial Sarcoma or Myxoid/Round Cell Liposarcoma (SPEARHEAD-1, Cohort-1) NCT: 04044768 PMID: 38554725

Design	Phase II, multicenter, single-arm, open-label trial
Population	N = 44 Median age was 41 years (range: 19 to 73 years), 50% were female, and 89% were White, and 96% were HLA-A*02:01P. The median number of prior lines of systemic therapies was three (range: 1 to 12 lines). Prior therapies included ifosfamide (100%), doxorubicin (95%), pazopanib (48%), trabectedin (25%), dacarbazine (11%), and gemcitabine (11%). Between leukapheresis and initiation of lymphodepletion, 16 (36%) of the 44 patients received bridging therapy. The most used bridging therapy was pazopanib (69%).
Arms	• Single infusion of autologous genetically modified afamitresgene autoleucel ○ Dose: 1.0 x109 to 10x109 transduced by a single intravenous infusion
Endpoint(s)	Primary: • Overall response rate (ORR) according to RECISTv1.1 evaluated by independent review committee (IRC) Secondary: • Duration of response (DOR)
Inclusion Criteria	• HLA-A*02:01P, HLA-A*02:02P, HLA- A*02:03P, and HLA-A*02:06P allele positive patients with inoperable or metastatic synovial sarcoma • Prior systemic therapy with either doxorubicin and/or ifosfamide • Measurable disease according to RECIST v1.1 prior to lymphodepletion • Tumor shows MAGE-A4 expression confirmed by central laboratory • Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1. • Glomerular filtration rate (GFR) ≥ 60 mL/min
Exclusion Criteria	• HLA-A*02:05 in either allele • Patients on systemic corticosteroids for at least 14 days prior to leukapheresis and lymphodepletion • Recipients of allogeneic hematopoietic stem cell transplants
Results	Primary: **Table 4. Efficacy Results* for SPEARHEAD-1 (Cohort 1)** **Endpoint** / **TECELRA Treated population N=44** Overall Response Rate / 43.2% (95% CI)† / (28.4, 59.0) Complete response rate, n (%) / 2 (4.5%)

	<table><tr><td>Partial response rate, n (%)</td><td>17 (38.6%)</td></tr><tr><td>Median Duration of Response‡ in months (95% CI)§ Min, Max Patients with DoR ≥ 6 months, %§ Patients with DoR ≥ 12 months, %§</td><td>6.0 (4.6, NR) 1.9, 36.1+ 45.6% 39.0%</td></tr></table> CI= confidence interval; NR= not reached. * Efficacy assessment was by independent review committee according to Response Evaluation Criteria In Solid Tumors (RECIST) v1.1. † Two-sided 95% confidence interval based on exact Clopper-Pearson (exact Binomial) method. ‡ Duration of response only applies to patients with a complete or partial response. § Two-sided 95% confidence interval and % of patients with response duration ≥6 and ≥12 months based on Kaplan-Meier method. Secondary: • The median time to response from Tecelra® treatment was 4.9 weeks (95% CI: 4.4 weeks, 8 weeks) by Kaplan Meier estimation.
Conclusion	afamitresgene autoleucel treatment resulted in durable responses in heavily pre-treated patients with HLA-A*02 and MAGE-A4-expressing synovial sarcoma. This study shows that T-cell receptor therapy can be used to effectively target solid tumors and provides rationale to expand this approach to other solid malignancies.
Interpretation	Tecelra® had an ORR of 43%, with 4.5% of patients experiencing a complete response. The median duration of response was six months, and 39% of patients who responded had a response that lasted at least 12 months. Teclera® represents the first treatment option for synovial sarcoma in more than a decade. Although Teclera® is approved in HLA-A*02:01P,-A*02:02P,-A*02:03P, or -A*02:06P positive disease, 96% of patients in trial were HLA-A*02:01P positive, making the results not entirely generalizable. Additional data is needed from the confirmatory trials to verify clinical benefit.

Ongoing

Title	A Phase 2 Single Arm Open-Label Clinical Trial of ADP-A2M4 SPEAR™ T Cells in Subjects With Advanced Synovial Sarcoma or Myxoid/Round Cell Liposarcoma (SPREARHEAD) NCT: 04044768
Design	Phase II, multicenter, single-arm, open-label trial studying the Replication -competent Retrovirus and overall survival of MAGE-A4 positive subjects with metastatic or inoperable (advanced) Synovial Sarcoma (Cohort 1, 2 and 3) or Myxoid/Round Cell Liposarcoma (Cohort 1) .

Completion Date	April 2038

Guidelines

*Note guidelines have not been updated since the approval of Tecelra.

National Comprehensive Cancer Network (NCCN) Guidelines. Soft Tissue Sarcoma. Version 2.2024.

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2024
Soft Tissue Sarcoma

NCCN Guidelines Index
Table of Contents
Discussion

SYSTEMIC THERAPY AGENTS AND REGIMENS WITH ACTIVITY IN SOFT TISSUE SARCOMA SUBTYPES[a,b,c,d] AND AGGRESSIVE SOFT TISSUE NEOPLASMS

Regimens Appropriate for General Soft Tissue Sarcoma[e,f]; see other sections for histology-specific recommendations[g]

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Neoadjuvant/ Adjuvant Therapy	• AIM (doxorubicin, ifosfamide, mesna)[1-4] • Ifosfamide, epirubicin, mesna[5]	• AD[1,2,10,11] for LMS, or if ifosfamide is not considered appropriate • Doxorubicin[1,2,6,7]	• Ifosfamide[5,7,21-25] • Trabectedin (for myxoid liposarcoma)[30] • Gemcitabine and docetaxel[21,22] (category 2B)
First-Line Therapy Advanced/Metastatic	• Anthracycline-based regimens: ▸ Doxorubicin[1,2,6,7] ▸ Epirubicin[8] ▸ Liposomal doxorubicin[9] ▸ AD (doxorubicin, dacarbazine)[1,2,10,11,12] ▸ AIM[1-4,6] ▸ Ifosfamide, epirubicin, mesna[5] • *NTRK* gene fusion-positive sarcomas only (regardless of soft tissue sarcoma subtype) ▸ Larotrectinib[h,13] ▸ Entrectinib[i,14] ▸ Repotrectinib[15]	• Gemcitabine • Gemcitabine and docetaxel[21,22] (category 2B)	• Pazopanib[k,15] (patients ineligible for IV systemic therapy or patients who are not candidates for anthracycline-based regimens) • MAID (mesna, doxorubicin, ifosfamide, dacarbazine)[1,2,31,32] • Trabectedin and doxorubicin (for LMS)[33,34] • Selpercatinib (for *RET* gene fusion-positive tumors[35]) (regardless of soft tissue sarcoma subtype) • Gemcitabine and dacarbazine[23] (category 2B)
Subsequent Lines of Therapy for Advanced/Metastatic Disease	• Pazopanib[j,k,16] • Eribulin[j,17] (category 1) recommendation for liposarcoma, category 2A for other subtypes • Trabectedin[j,18-20] (category 1 recommendation for liposarcoma and LMS, category 2A for other subtypes) • Gemcitabine and docetaxel[21,22] • *NTRK* gene fusion-positive sarcomas only (regardless of soft tissue sarcoma subtype) ▸ Repotrectinib[15] (if not previously given)	• Dacarbazine[23] • Ifosfamide[5,7,22,24,25,26] • Temozolomide[j,27] • Vinorelbine[j,28] • Regorafenib[k,29] • Gemcitabine • Gemcitabine and dacarbazine[23]	• Gemcitabine and vinorelbine[24] (category 2B) • Gemcitabine and pazopanib[36] (category 2B) • Pembrolizumab[37,38] or nivolumab ± ipilimumab[39-42] ▸ For myxofibrosarcoma, UPS,[f] dedifferentiated liposarcoma, cutaneous angiosarcoma, and undifferentiated sarcomas OR ▸ For TMB-H (≥10 mutations/megabase [mut/Mb])[l] regardless of soft tissue sarcoma subtype • Pembrolizumab[43] ▸ For MSI-H or dMMR tumors[m] (regardless of soft tissue sarcoma subtype) • Cabozantinib[44] (category 2B)

Footnotes and References (SARC-G, 8 of 13)

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Opinions

Sarcoma is the broad term for a group of cancers that begin in the bones and soft tissue. There are many different types of sarcomas and treatment varies based on the location and type of sarcoma. Soft tissue sarcoma forms in the tissues that connect and surround other body structures. Approximately 13,000 patients are diagnosed with soft tissue sarcoma in the United States each year. Of these 13,000 patients, 5-10% of these individuals have synovial sarcoma. Synovial sarcomas are a type of rare solid tumor cancer that typically form in areas around joints. This can include bones and soft

tissues such as fat, nerves, muscle, and blood vessels. The five-year survival rate of synovial sarcoma is about 20%, with most patients undergoing multiple lines of chemotherapy treatment.

Treatment options for soft tissue sarcoma include surgery as the main treatment to remove the tumor with a margin of healthy tissue, radiation therapy either preoperatively to shrink the tumor or postoperatively to kill remaining cancer cells, chemotherapy for certain types or advanced cases, targeted therapy using drugs that target specific molecules involved in tumor growth and survival, and immunotherapy to stimulate the immune system to attack cancer cells.

Tecelra®, a T-cell immunotherapy, is indicated for the treatment of unresectable or metastatic synovial sarcoma. Tecelra® makes use of a patient's own immune cells and modifies them to target cancer cells. Tecelra® recognizes and attacks MAGE-A4 proteins, which is commonly overexpressed in synovial sarcoma. Tecelra® is designed to treat synovial sarcoma by targeting the MAGE-A4 antigen in cancer cells in tumors containing HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P alleles. This approval represents several important milestones, including being the first engineered cell therapy for solid tumors, the first TCR therapy to reach the market, and the first new treatment for synovial sarcoma in more than a decade.

Tecelra® was granted accelerated approval based on the Phase 2 SPREADHEAD-1 trial results. Tecelra® demonstrated a 43.2% overall response rate, a 4.5% complete response rate, and a median response duration of six months. A confirmatory trial is currently ongoing to verify Tecelra's clinical benefits. It's estimated that 400 patients per year in the United States will qualify for Teclera® treatment. Due to the specific cancer type and high cost, management tools such as prior authorization are warranted to ensure appropriate utilization of Tecelra®.

Alternatives

None

PAD Criteria

New

Tecelra (afamitresgene autoleucel)	
Medications	Tecelra (afamitresgene 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	Homozygous or heterozygous for HLA-A*02:05P
Required Clinical Information	See “Other Criteria” below
Age Restrictions	According to package insert Check AAH active CCS cases for members < 21 years of age
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
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Diagnosis of unresectable or metastatic synovial sarcoma • Documentation that patient is HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive • Documentation that the tumor expresses the MAGE-A4 antigen • Documentation of treatment with prior chemotherapy • Member must have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 • Medication is being prescribed at an FDA approved dose **The safety and effectiveness of repeat administration of Tecelra has not been evaluated and will not be approved.** 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	12/2024

References

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7. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: http://www.fda.gov/. Accessed on August 15, 2024.
8. D'Angelo SP, Araujo DM, Abdul Razak AR, et al. Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1): an international, open-label, phase 2 trial. Lancet. 2024 Apr 13;403(10435):1460-1471. doi: 10.1016/S0140-6736(24)00319-2. Epub 2024 Mar 27. PMID: 38554725.

Alameda MRGs for review Q4 2024 P&T

Recommendation: Remove all references to RediTrex as it has been discontinued

Injectable Methotrexate	
Therapeutic Classes (AHFS)	Antineoplastic agents
Medications	~~RediTrex (methotrexate)~~ Rasuvo (methotrexate) Otrexup (methotrexate) Any other newly approved injectable methotrexate 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	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 is a dermatologist or rheumatologist.
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 of Rasuvo~~RediTrex~~:
	• For diagnosis of severe, active polyarticular juvenile idiopathic arthritis, approve if:
	  ○ Documented trial and failure, intolerance, contraindication, or inability to use methotrexate tablet AND generic methotrexate injection solution
	• For diagnosis of severe, recalcitrant psoriasis, approve if:
	  ○ Documented trial and failure, intolerance, contraindication, or inability to use one of the following alternatives: topical corticosteroids AND topical vitamin D analogue (e.g., calcipotriene)
	  ○ Documented trial and failure, intolerance, contraindication, or inability to use methotrexate tablet AND generic methotrexate injection solution
	• For diagnosis of severe, active rheumatoid arthritis, approve if:
	  ○ Documented trial and failure, intolerance, contraindication, or inability to use methotrexate tablet AND generic methotrexate injection solution
	~~Criteria for approval of Rasuvo:~~
	~~• Criteria above for RediTrex must be met, per diagnosis AND~~
	~~• Documented trial and failure, intolerance, contraindication, or inability to use RediTrex~~
	
	Criteria for approval of Otrexup:
	• Criteria above for ~~RediTrex~~ Rasuvo must be met, per diagnosis AND
	• Documented trial and failure, intolerance, contraindication, or inability to use ~~RediTrex AND~~ Rasuvo

Criteria Statement	For members with juvenile idiopathic arthritis or severe rheumatoid arthritis, ~~RediTrex~~ Rasuvo is reserved for members who have used (or cannot/should not use) generic

	methotrexate tablet and injection. ~~Additionally, Rasuvo is reserved for members who have used (or cannot/should not use) RediTrex and~~ Otrexup is reserved for members who have used (or cannot/should not use) ~~RediTrex AND~~ Rasuvo. For members with severe psoriasis, ~~RediTrex~~ Rasuvo is reserved for members who have used (or cannot/should not use) topical corticosteroids AND topical vitamin D analogue (e.g., calcipotriene) AND methotrexate tablet AND methotrexate injection. ~~Additionally, Rasuvo is reserved for members who have used (or cannot/should not use) RediTrex and~~ Otrexup is reserved for members who have used (or cannot/should not use) ~~RediTrex AND~~ Rasuvo.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: Add 2 new vaccines Capvaxive and MResvia; add Ixchiq vaccine to PA Review criteria and criteria statement sections as it was missing.

Immunizations	
Therapeutic Classes (AHFS)	Toxoids;vaccines
Medications	Formulary, 1st line (fill limits indicated if applicable) Influenza vaccine (only most recent strain is on formulary) – 1 fill per 270 days ActHib (Haemophilus influenzae type b) – 3 fills per lifetime Hiberix (Haemophilus influenzae type b) – 3 fills per lifetime Havrix, Vaqta (Hepatitis A) – 2 fills per lifetime Twinrix (Hepatitis A and B) – 4 fills per lifetime; age minimum 18 years Engerix-B (Hepatitis B) – 4 fills per lifetime Recombivax HB (Hepatitis B) – 3 fills per lifetime Heplisav-B (Hepatitis B) – 2 fills per lifetime; age minimum 18 years PreHevbrio (Hepatitis B trivalent) - 3 fills per lifetime; age minimum 18 years Gardasil-9 (HPV) – 3 fills per lifetime; age maxiumum 45 years IPOL (Polio) – 5 fills per lifetime M-M-R II (Measles, Mumps, Rubella) – 2 fills per lifetime Proquad (Measles, Mumps, Rubella) – 2 fills per lifetime Priorix (Measles, Mumps, Rubella) – 2 fills per lifetime Menactra, Menveo A-C-Y-W (Meningococcal) – 2 fills per lifetime; age maximum 55 years MenQuadfi (Meningococcal) – 2 fills per lifetime Penbraya (Meningococcal) – 2 fills per lifetime; age maximum 25 years Bexsero (Meningococcal) – 2 fills per lifetime; age maximum 25 years Trumenba (Meningococcal) – 3 fills per lifetime; age maximum 25 years Prevnar-13 (Pneumococcal) – 1 fill per lifetime Prevnar 20 (Pneumococcal) – 1 fill per lifetime Pneumovax 23 (Pneumococcal) – 2 fills per lifetime Vaxneuvance (Pneumococcal) – 1 fill per lifetime Capvaxive (Pneumococcal) – 1 fill per lifetime, age minimum 18 years Imovax Rabies and Rabavert (Rabies) Tenivac, TDVax (Tetanus/diphtheria) Boostrix and Adacel (Tetanus, diphtheria, pertussis) Pentacel (Tetanus, diphtheria, pertussis, polio, Haemophilus influenzae type b) – 4 fills per lifetime Vaxelis (Tetanus, diphtheria, pertussis, polio, Haemophilus influenzae type b) – 3 fills per lifetime Varivax (Chicken pox) – 2 fills per lifetime Shingrix (Shingles) – 2 fills per lifetime; age minimum 18 years Vivotif oral capsules (Typhoid) – 4 capsules per 1 fill; age 6 years and older Abrysvo (RSV) – 1 fill per lifetime Arexvy (RSV) – 1 fill per lifetime MResvia (RSV) – 1 fill per lifetime, age 60 years and older Non-Formulary, with PA required Biothrax (Anthrax) Ixiaro (Japanese encephalitis) Typhim Vi (Typhoid) YF-Vax (Yellow Fever) Dengvaxia (dengue) Ticovac (tick-borne encephalitis) Ixchiq (chikungunya)

Immunizations	
	Any other newly marketed vaccine
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	See "Medication/Fill limits" above
Coverage Duration	**Initial Approval** As defined based on guidelines for covered uses **Later Approvals** As defined based on guidelines for covered uses If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For Biothrax, Ixiaro, Typhim Vi, Dengvaxia, Ticovac, Ixchiq, and YF-Vax, approve if: • Documentation showing destination of travel where vaccines are recommended per ACIP and CDC: ACIP Vaccine Recommendations and CDC Travel Vaccine Recommendations • Documentation showing departure and return dates of travel. • Dosage and frequency are appropriate according to the FDA and manufacturer package inserts For formulary vaccines above the fill limit, approve if: Dosage and frequency are appropriate according to the FDA and manufacturer package inserts For all other non-formulary vaccines, approve if: • Documentation of trial and failure, inability to use, contraindication, or intolerance to formulary alternatives. • Dosage and frequency are appropriate according to the FDA and manufacturer package inserts.
Criteria Statement	Biothrax, Ixiaro, Typhim Vi, Dengvaxia, Ixchiq,Ticovac, and YF-Vax are reserved for members who are traveling to destinations that require vaccines recommended by the CDC and/or ACIP.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation: Add candesartan as an option for trial and failure for the diagnosis of chronic migraines, since per newest guidelines from the AHS candesartan is considered as one of the first-line therapies for migraine prevention.

Botulinum Toxins A&B	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS
Medications	PA required Xeomin (incobotulinumtoxinA) - Preferred Non-Formulary Botox (onabotulinumtoxinA) Myobloc (RimabotulinumtoxinB) Dysport (ibobotulinumtoxinA) Daxxify (daxibotulinumtoxinA) 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	Cosmetic use
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all of the conditions are met, the request will be approved for 12 month duration. If the conditions are not met, the request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	***The use of these medications for cosmetic purposes is NOT a covered benefit*** **Xeomin is the preferred product for all FDA approved indications** The following criteria must be met for initial requests: • Dose is appropriate per label or supported by compendia/standard of care guidelines • Documentation was submitted, that the member had an adequate trial (consistent with pharmacy claims) standard first line therapy for their condition and/or has a documented medical reason (intolerance, hypersensitivity, contraindication, etc) for not taking first line therapy to treat their medical condition. • If the diagnosis is **chronic migraine** (≥15 days per month with headache lasting 4 hours a day or longer), the member has a documented adequate trial, for at least 4 weeks EACH, at minimum effective doses (consistent with pharmacy claims data) of two of the following classes of drugs: o Beta blockers (e.g. propranolol, timolol, etc.) or candesartan o Amitriptyline or venlafaxine o Divalproex ER or DR, valproic acid or topiramate o Or a medical reason was submitted (intolerance, hypersensitivity, contraindication, etc) why the member is not able to utilize these therapies. • If the diagnosis is **overactive bladder**, the member has a documented adequate trial (consistent with pharmacy claims data) of at least 2 formulary medications (e.g. oxybutynin)

	• If the diagnosis is **Hyperhidrosis,** the member has tried and failed a prescription strength antiperspirant (e.g. 20% aluminum chloride hexahydrate)
	• If the diagnosis is **Chronic Sialorrhea**,
	  ○ Documentation is provided that the member has had sialorrhea lasting at least 3 months
	  ○ The member has tried and failed at least two anticholinergic medications (e.g. glycopyrrolate, hyoscyamine, benztropine)
	• For all FDA-approved indications, if the medication request is for a botulinum toxin other than Xeomin, the member has a documented medical reason (intolerance, hypersensitivity, contraindication, treatment failure etc) for not using to treat their medical condition.
	
	The following criteria must be met for re-authorization requests:
	• Dose and indication continue 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	Xeomin is reserved for members with medical conditions which these medications are approved for use in. The member should have used (or cannot/should not use) other preferred treatments for the condition prior to the approval of Xeomin. Non-formulary botulinum toxin medications are reserved for members with medical conditions which these medications are approved for use in and who have used (or cannot/should not use) other preferred treatments for the condition and who have used (or cannot/should not use) Xeomin.
Last P&T Review Date	~~12/2023~~12/2024

Recommendation:

- Rename criteria to encompass newly approved Vafseo
- Add Vafseo that was recently approved and shares the same mechanism of action and indication as Jesduvroq, except for time adults must have been receiving dialysis (at least 3 months for Vafseo vs. 4 months for Jesduvroq)
- Update hemoglobin level between 8.0 and 11.0 g/dL per inclusion criteria in pivot trials for both agents, and per BBW that states that targeting a hemoglobin level greater than 11 g/dL is expected to further increase the risk of death and arterial and venous thrombotic events
- Add "For Jesduvroq" to criteria on documentation of the current ESA product and dose, since only Jesduvroq requires dosing based on the dose regimen of the ESA at the time of substitution. This does not apply to Vafseo—standard dosing is used regardless of prior ESA use
- Remove exclusion criteria of concomitant use of strong CYP2C8 inhibitors as it was a specific interaction with Jesduvroq that does not apply to Vafseo. With these medications being prescribed by a specialist, it is reasonable to expect labeled dosing, warnings, and interactions will be followed.

~~Jesduvroq~~HIF-PH Inhibitors (Hypoxia-inducible Factor Prolyl Hydroxylase Inhibitors) for CKD Anemia	
Therapeutic Classes (AHFS)	Hematopoietic Agents
Medications	Jesduvroq (daprodustat), Vafseo (vadadustat)
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	Diagnosis of uncontrolled hypertension ~~Concomitant use of strong CYP2C8 inhibitors (e.g., gemfibrozil~~
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Member must be at least 18 years of age
Prescriber Restrictions	Prescriber must be a hematologist or nephrologist
Coverage Duration	If all conditions are met, the request will be approved with a 6 month duration. If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**Initial Authorization:**
	• Member has a diagnosis of chronic kidney disease (CKD) and has been undergoing dialysis for minimum time required by FDA-approved labeling ~~at least four months~~
	• Member has a documented hemoglobin between 8.0 and 11.0~~5~~ g/dL
	• Member has documentation of trial and failure, intolerance, contraindication, or inability to use erythropoietin stimulating agents (ESA)
	• For Jesduvroq: ~~D~~documentation of the current ESA product (e.g., Procrit, Aranesp, etc.) and dose.
	• The following lab results must be submitted and demonstrate normal values, otherwise, the member MUST be receiving, or is beginning therapy, to correct the deficiency:
	  ○ Serum ferritin level (> 100ng/mL)
	  ○ Transferrin saturation (TSAT) (> 20%)

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	• Provider attests that member has no history of myocardial infarction, cerebrovascular event, or acute coronary syndrome in the past 3 months
	• Member will not be receiving concurrent treatment with an ESA
	• Request is for an FDA-approved dose
	• All submitted lab results have been drawn within 30 days of the request
	
	Reauthorization:
	• All submitted lab results have been drawn within 30 days of the reauthorization request.
	• Member has a documented increase in hemoglobin from baseline
	• The following lab results must be submitted and demonstrate normal values, otherwise, the member MUST be receiving, or is beginning therapy, to correct the deficiency:
	  ○ Serum ferritin level (> 100ng/mL)
	  ○ Transferrin saturation (TSAT) (> 20%)
	• Member will not be receiving concurrent treatment with an ESA
	• Request is for an FDA-approved dose

Criteria Statement	Jesduvroq and Vafseo areis reserved for members with a diagnosis of chronic kidney disease (CKD) who have been undergoing dialysis for minimum time required by FDA-approved labeling at least four months, with a documented hemoglobin between 8.0 and 11.05 g/dL, with normal serum ferritin and transferrin saturation lab values (or the member MUST be receiving, or is beginning therapy, to correct the deficiency), with no history of myocardial infarction, cerebrovascular event, or acute coronary syndrome in the past 3 months who have used (or cannot should not use) erythropoietin stimulating agents (ESA).
Last P&T Review Date	12/202312/2024

Recommendation:

- Add two new products indicated for primary biliary cholangitis: Iqirvo and Livdelzi
- Change the name of the criteria to encompass all drugs covered in the policy
- Remove specific dosing for Ocaliva in the coverage duration section. All products showed efficacy after 3 months of treatment in clinical trials analyses
- Like Ocaliva, both Iqirvo and Livdelzi are indicated in the second-line setting after UDCA, therefore, changed language appropriately to include all products
- Separate prescriber attestation for Ocaliva that the patient does not have compensated cirrhosis with evidence of portal hypertension, since it only applies to Ocaliva
- Separate prescriber attestation requirement for Ocaliva in the reauthorization section
- Add dose titration for Ocaliva to reauthorization section, because per label if the patient is not showing efficacy with 5mg daily dose but is tolerating the medication, dose should be increased to 10mg daily

~~Ocaliva~~Agents for Primary Biliary Cholangitis	
Therapeutic Classes (AHFS)	GI Drugs, Miscellaneous
Medications	Ocaliva (obeticholic acid), Iqirvo (elafibranor), Livdelzi (seladelpar)
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 Member must be 18 years of age or older
Prescriber Restrictions	Prescriber must be a hepatologist or gastroenterologist
Coverage Duration	If the criteria are met, the request will be approved for ~~5 mg once daily for~~ a 3 month duration for initial authorization and up to ~~10 mg once daily for up to~~ a 12 month duration for reauthorization
PA Review Criteria	**Initial Authorization**: • Diagnosis of primary biliary cholangitis (PBC) with confirmation of diagnosis by the following tests: a) Positive antimitochondrial antibody test b) Elevated serum alkaline phosphatase (ALP) level • ~~Ocaliva~~Drug is being requested in addition to ursodeoxycholic acid (UDCA) due to patient having an inadequate response to UDCA monotherapy for at least 1 year, OR member has a documented medical reason (e.g. contraindication, intolerance, hypersensitivity) why UDCA cannot be used and is taking ~~Ocaliva~~ the requested drug as monotherapy • Prescriber attests the patient does not have complete biliary obstruction, decompensated cirrhosis (e.g., Child-Pugh Class B or C)~~,~~ • For Ocaliva, prescriber must also attest the patient does not have ~~or~~ compensated cirrhosis (Child-Pugh Class A) with evidence of portal hypertension • Submission of the following test results within 30 days of request: a) Serum ALP b) Total bilirubin **Re-authorization**: • Provider attests that the patient has not developed complete biliary obstruction, decompensated cirrhosis (e.g., Child-Pugh Class B or C)~~,~~

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	• For Ocaliva, provider must also attest that the patient has not developed ~~or~~ compensated cirrhosis (Child-Pugh Class A) with evidence of portal hypertension • Submission of lab tests confirming each of the following: o A decrease in ALP of ≥ 15% from baseline o ALP is less than 1.67 times the upper limit normal (ULN); defined as 118 U/L for females and 124 U/L for males o Total bilirubin ≤ ULN defined as 1.1 mg/dL for females and 1.5 mg/dL for males o First reauthorization request for Ocaliva following 3 months at the 5 mg once daily dose can be authorized for the 10 mg once daily dose for 3 months without submission of lab tests confirming clinical benefit
Criteria Statement	Ocaliva, Iqirvo, and Livdelzi ~~is~~are reserved for members with a diagnosis of primary biliary cholangitis (PBC) with confirmation of the diagnosis by the following tests: positive antimitochondrial antibody test and an elevated serum alkaline phosphatase (ALP) level, who have used (or cannot/should not use) ~~to~~ ursodeoxycholic acid (UDCA)~~,~~. Members should not have ~~a diagnosis of~~ complete biliary obstruction, or decompensated cirrhosis (e.g., Child-Pugh Class B or C)~~,~~ members should also not have ~~or~~ compensated cirrhosis (Child-Pugh Class A) with evidence of portal hypertension for Ocaliva. Recent (within 30 days of the request) serum ALP and total bilirubin lab test results must be submitted.
Last P&T Review Date	~~12/2023~~12/2024

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Recommendation: Add new formulation of vigabatrin: Vigafyde oral solution

vigabatrin (Sabril)	
Therapeutic Classes (AHFS)	Anticonvulsants, Miscellaneous
Medications	Formulary, PA required • Vigabatrin (Sabril) powder packet and vigabatrin (Sabril) tablet ~~1.~~• Vigafyde (vigabatrin) oral 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), 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 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 or oral solution) • Member is age 1 month to 2 years • Vigabatrin (Sabril or Vigafyde) 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 and Vigabatrin oral solution:** Vigabatrin (Sabril) powder for oral suspension and vigabatrin (Vigafyde) oral solution are ~~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 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	~~6/2024~~9/2024

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Recommendation: Retire policy, take Oxbryta off formulary

On September 25th, 2024, Pfizer announced its voluntary withdrawal of Oxbryta from the market, ceasing distribution and discontinuing all active clinical trials and expanded access programs. The decision was based on recent data indicating the benefit of Oxbryta did not outweigh the risks for the sickle cell patient population. In post marketing clinical trials of Oxbryta, Pfizer reported an imbalance in vaso-occlusive crisis and fatal events which require further assessment.

Oxbryta (voxelotor)	
Therapeutic Classes (AHFS)	BLOOD FORM.,COAG,THROMBOSIS AGENTS MISC.
Medications	Formulary, PA required Preferred: Oxbryta (voxelotor) 300mg tablets NDC 72786-0102-03 Oxbryta (voxelotor) 500mg tablets NDC 72786-0101-01 Oxbryta (voxelotor) 300mg tablets for suspension NDC 72786-0111-03 Non-Preferred: Oxbryta (voxelotor) 300mg tablets NDC 72786-0102-02 Oxbryta (voxelotor) 300mg tablets for suspension NDC 72786-0111-02
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a hematologist
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 conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**Initial Authorization:**
	• Member has a confirmed diagnosis of sickle cell disease
	• Baseline labs have been submitted for the following:
	  ○ Hemoglobin (Hb)
	  ○ Indirect bilirubin
	  ○ Reticulocytes
	• Documentation was provided that the member has had 1 or more vaso-occlusive pain crises in the last 12 months
	• Member has a baseline Hb level less than or equal to 10.5 g/dL
	• Documentation was provided that the member has been taking hydroxyurea at the maximum tolerated dose and was compliant within the last 6 months as evidenced by paid claims (or a medical reason was provided why the patient is unable to use hydroxyurea)
	• If the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used
	• Request is for an FDA-approved dose
	
	Reauthorization:

	• Documentation submitted indicates clinical benefit at 6 months from initiation, and continued clinical benefit at subsequent 12-month intervals defined as the following:
	• Documentation of one of the following:
	  ○ Hb increase from baseline (at 6 months from initiation) or maintenance of such Hb increase (at 12-month intervals thereafter)
	  ○ A reduced (from baseline) number of vaso-occlusive/pain crises since Oxbryta was started
	• Documentation of one of the following:
	  ○ Decrease in indirect bilirubin from baseline
	  ○ Or decrease in percentage of reticulocytes from baseline
	• Documentation of consistent fills since the previous authorization

Criteria Statement	Oxbryta is reserved for members with sickle cell disease with baseline hemoglobin levels less than or equal to 10.5g/dL, with one or more pain crises during a 12 month period, and who have used (or cannot/should not use) hydroxyurea.
Last P&T Review Date	3/2024

Alameda Q4 2024 PADs for Review Changes

Recommendation:

- Add PiaSky (crovalimab-akkz)—new complement C5 inhibitor indicated for the treatment of adult and pediatric patients 13 years and older with PNH and body weight of at least 40kg
- Add coverage duration for PiaSky—6 months for initial requests since efficacy was assessed at 24 weeks in trial
- Add "body weight" language to ensure appropriate dosing since PiaSky is only indicated for patients with weight of at least 40 kg
- Add PiaSky to the initial authorization section and update language on documentation of vaccination against meningococcal disease to better align with prescribing information
- Rewrite diagnosis requirement for PNH to apply to all agents and specify that hemoglobin requirement applies only to Empaveli per treatment population in the trial
- Correct formatting in reauthorization section

Complement Inhibitors	
Medications	Soliris (eculizumab), Ultomiris (ravulizumab), Empaveli (pegcetacoplan), Syfovre (pegcetacoplan injection), Izervay (avacincaptad pegol injection), PiaSky (crovalimab-akkz)
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	Prescriber must be a hematologist, nephrologist, neurologist, oncologist, ophthalmologist, or other appropriate specialist.
Coverage Duration	If the criteria are met, the initial request will be approved as follows: For Soliris (eculizumab), Ultomiris (ravulizumab), and Empaveli (pegcetacoplan): initial request will be approved for up to a 3 month duration; reauthorization requests will be approved for up to 6 months. For PiaSky (crovalimab-akkz): initial request will be approved for up to 6 months, reauthorization requests will be approved for up to 12 months. For Syfovre (pegcetacoplan injection): initial and reauthorization requests will be approved for up to 12 months. For Izervay (avacincaptad pegol injection): initial request will be approved for up to 12 month duration with no reauthorization.
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • The request is age appropriate according to FDA approved package labeling or nationally recognized compendia; AND • The request is for a dose that is FDA approved or in nationally recognized compendia in accordance with the patient's diagnosis, age, body weight, and concomitant medical conditions; AND • For Soliris (eculizumab), Ultomiris (ravulizumab), and Empaveli (pegcetacoplan), and PiaSky (crovalimab-akkz)

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- Documentation patient complies with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against encapsulated bacteria.~~Documentation of vaccination against meningococcal disease or a documented medical reason why the patient cannot receive vaccination or vaccination needs to be delayed AND~~
- ~~Antimicrobial prophylaxis with oral antibiotics (penicillin, or macrolides if penicillin-allergic) for two weeks will be administered if the meningococcal vaccine is administered less than 2 weeks before starting therapy or a documented medical reason why the patient cannot receive oral antibiotic prophylaxis.~~

For Generalized Myasthenia Gravis (gMG):
- Refer to the "Myasthenia Gravis Agents" policy

For Neuromyelitis Optica Spectrum Disorders (NMOSD):
- Refer to the: **"Neuromyelitis Optica Spectrum Disorder (NMOSD) Agents"** policy

For paroxysmal nocturnal hemoglobinuria (PNH):
- Documentation of diagnosis~~Type III PNH red blood cell (RBC) clone~~ by high sensitivity flow cytometry ~~greater than 10%~~
- For Empaveli (pegcetacoplan): Hemoglobin (Hgb) < 10.5 g/dL
- If the request is for Empaveli (pegcetacoplan), documented trial and failure of, contraindication to, or medical reason for not using Soliris (eculizumab) or Ultomiris (ravulizumab)

Atypical Hemolytic Uremic Syndrome (aHUS)/Complement-Mediated HUS)
- Documentation of confirmed diagnosis as evidenced by complement genotyping and complement antibodies; **OR**
- Provider attestation treatment is being used empirically and delay in therapy will lead to unacceptable risk to the patient

Geographic Atrophy (GA):
- If the request is for Syfovre (pegcetacoplan injection), member must be ≥ 60 years of age
- If the request is for Izervay (avacincaptad pegol injection), member must be ≥ 50 years of age
- Diagnosis of GA secondary to age-related macular degeneration (AMD)
- Absence of choroidal neovascularization (CNV) in treated eye
- Best-corrected visual acuity (BCVA) 24 letters (approximately 20/320) or better using Early Treatment Diabetic Retinopathy Study (ETDRS)
- GA lesion size ≥2.5 and ≤17.5 mm2 with at least 1 lesion ≥1.25 mm2

Re-Authorization:
- Re-authorization may be considered for all agents included in these criteria with the exception of Izervay (avacincaptad pegol injection), which is only indicated for a 12 month duration
- Provider has submitted documentation of clinical response to therapy (e.g., reduction in disease severity, improvement in quality of life scores, increased Hgb, reduced need for blood transfusions, slowing of growth rate of GA lesions, etc.); **AND**
- The request is for a dose that is FDA approved or in nationally recognized compendia in accordance with the patient's diagnosis, age, and concomitant medical condition

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	• **If the request is for atypical hemolytic uremic syndrome (aHUS)/ complement-mediated HUS:**
	  ○ Documentation of confirmed diagnosis as evidenced by:
	  ▪ Complement genotyping
	  ▪ Complement antibodies
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.

Last Review Date	~~12/2023~~12/2024

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Recommendation: Add Ultomiris as it was approved for the treatment of adult patients with NMOSD who are anti-aquaporin-4 antibody positive

Neuromyelitis Optica Spectrum Disorder (NMOSD) Agents	
Medications	Rituximab (Rituxan, Truxima - biosimilar , Ruxience - biosimilar, Riabni - biosimilar) Enspryng (satralizumab-mwge) Uplizna (inebilizumab-cdon) Soliris (eculizumab) Ultomiris (ravulizumab-cwvz)
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	For Enspryng, Uplizna, Soliris, Ultomiris: Anti-aquaporin-4 (AQP4) antibody **negative** neuromyelitis optica spectrum disorder (NMOSD)
Required Clinical Information	See "other criteria"
Age Restrictions	N/A
Prescriber Restrictions	Prescribed by an immunologist, neurologist or hematologist
Coverage Duration	If all of the conditions are met, requests will be approved for 12 months.
Maximum Billable Units	Variable

Other Criteria	**** When the biosimilar is indicated, the member must have documented dates of trial and failure, intolerance, inability to use, or contraindication to the biosimilar medication prior to the brand medication approval OR the currently available biosimilar product does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested, in addition to meeting all applicable criteria below.**
	
	Initial Authorization:
	For rituximab:
	• Member has a diagnosis of NMOSD
	• Documentation indicating that the member has been screened for HBV (hepatitis B virus) prior to initiation of treatment
	• Dosing is supported by compendia or standard of care guidelines
	
	For Enspryng:
	• Member has a diagnosis of anti-aquaporin-4 (AQP4) antibody **positive** NMOSD
	• Provider attests to completion of the following assessments prior to the first dose of Enspryng as outlined in the prescribing information:
	  ○ Hepatitis B virus screening
	  ○ Tuberculosis screening
	  ○ Liver transaminase screening
	  ○ Member has not received live or attenuated-live virus vaccines within 4 weeks before the start of Enspryng therapy
	• Documented medical contraindication to rituximab, azathioprine, or mycophenolate mofetil
	• Dosing is consistent with FDA-approved labeling or is supported by compendia or standard of care guidelines
	
	For Uplizna:

	• Member has a diagnosis of anti-aquaporin-4 (AQP4) antibody **positive** NMOSD
	• Provider attests to completion of appropriate assessments prior to the first dose of Uplizna as outlined in the prescribing information:
	  ○ Hepatitis B virus screening
	  ○ Quantitative serum immunoglobulins
	  ○ Tuberculosis screening
	  ○ Member has not received live or attenuated-live virus vaccines within 4 weeks before the start of Uplizna therapy
	• Documented medical contraindication to rituximab, azathioprine, or mycophenolate mofetil
	• Dosing is consistent with FDA-approved labeling or is supported by compendia or standard of care guidelines
	
	For Soliris/Ultomiris:
	• Member has a diagnosis of anti-aquaporin-4 (AQP4) antibody **positive** NMOSD
	• Documented medical contraindication to rituximab, azathioprine, or mycophenolate mofetil
	• Documentation of vaccination against meningococcal disease or a documented medical reason why the member cannot receive vaccination or vaccination needs to be delayed
	• Antimicrobial prophylaxis with oral antibiotics (penicillin, or macrolides if penicillin-allergic) for two weeks if the meningococcal vaccine is administered < 2 weeks before starting therapy or a documented medical reason why the member cannot receive oral antibiotic prophylaxis.
	• Dosing is consistent with FDA-approved labeling or is supported by compendia or standard of care guidelines
	
	Reauthorization:
	• Documentation that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit)
	• Request is for an FDA approved/medically accepted 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	~~12/2023~~12/2024

Recommendation: Add candesartan as an option for trial and failure for the diagnosis of chronic migraines as per newest guidelines from the AHS candesartan is considered as one of the first-line therapies for migraine prevention.

Botulinum Toxins A&B	
Medications	Xeomin (incobotulinumtoxinA) Botox (onabotulinumtoxinA) Myobloc (rimabotulinumtoxinB) Dysport (ibobotulinumtoxinA) Daxxify (daxibotulinumtoxinA) Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	Cosmetic use
Required Clinical Information	See "other criteria"
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	If all of the criteria are met, the initial request will be approved for up to a 12 month duration; reauthorization requests will be approved for up to 12 months.
Maximum Billable Units	Variable
Other Criteria	***The use of these medications for cosmetic purposes is NOT a covered benefit*** The following criteria must be met for initial requests: • Dose is appropriate per label or supported by compendia/standard of care guidelines • Documentation was submitted, that the member had an adequate trial (consistent with pharmacy claims) standard first line therapy for their disease state and/or has a documented medical reason (intolerance, hypersensitivity, contraindication, etc.) for not taking first line therapy to treat their medical condition. • If the diagnosis is **chronic migraine** (≥15 days per month with headache lasting 4 hours a day or longer), the member has a documented adequate trial, for at least 4 weeks EACH, at minimum effective doses (consistent with pharmacy claims data) of two of the following classes of drugs: o Beta blockers (e.g. propranolol, timolol, etc.) or candesartan o Amitriptyline or venlafaxine o Divalproex ER or DR, valproic acid or topiramate o Or a medical reason was submitted (intolerance, hypersensitivity, contraindication, etc.) why member is not able to utilize these therapies. • If the diagnosis is **overactive bladder**, the member has a documented adequate trial (consistent with pharmacy claims data) of at least 2 formulary medications (e.g. oxybutynin) • If the diagnosis is **Hyperhidrosis,** the member has tried and failed a prescription strength antiperspirant (e.g. 20% aluminum chloride hexahydrate) • If the diagnosis is **Chronic Sialorrhea**, o Documentation is provided that the member has had sialorrhea lasting at least 3 months o The member has tried and failed at least two anticholinergic medications (e.g. glycopyrrolate, hyoscyamine, benztropine)

	The following criteria must be met for re-authorization requests: • Dose and indication continue 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 If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~12/2023~~12/2024

Recommendation: Update language on documentation of vaccination against meningococcal disease for Soliris/Ultomiris to better align with prescribing information

Myasthenia Gravis Agents	
Medications	Vyvgart (efgartigimod) Vyvgart Hytrulo (efgartigimod alfa and hyaluronidase) Rystiggo (rozanolixizumab) Soliris (eculizumab) Ultomiris (ravulizumab)
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 ≥ 18 years
Prescriber Restrictions	Prescribed by a neurologist or rheumatologist
Coverage Duration	If all of the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 12 months.

Other Criteria	**Initial Authorization:**
	• Diagnosis of generalized myasthenia gravis (gMG)
	• Patient has a positive serological test for one of the following:
	  ○ Anti-AChR antibodies
	  ○ Anti-muscle-specific tyrosine kinase (MuSK) antibodies (Rystiggo only)
	• 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
	• Patient is not using agents covered by this policy concurrently (i.e. no concurrent use of Vyvgart, Vyvgart Hytrulo, Rystiggo, Soliris, or Ultomiris)
	
	• Requests for Soliris (eculizumab) and Ultomiris (ravulizumab) will also require ~~all of~~ the following:
	  ○ Documentation that patient complies with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal infections in patients receiving a complement inhibitor ~~Documentation of vaccination against meningococcal disease or a documented medical reason why the patient cannot receive vaccination or vaccination needs to be delayed~~
	  ○ ~~Antimicrobial prophylaxis with oral antibiotics (penicillin, or macrolides if penicillin-allergic) for two weeks will be administered if the meningococcal vaccine is administered less than two weeks before starting therapy or a documented medical reason why the patient cannot receive oral antibiotic prophylaxis~~
	
	Re-Authorization:

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	• 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. 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	~~12/2023~~12/2024

Recommendation: Update trial and failure in the policy as a result of Oxbryta being removed from the market.

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

Other Criteria	**Initial Authorization:**
	• Medication is prescribed at an FDA approved dose
	• Member has a diagnosis of sickle cell disease
	• Member has experienced at least 2 severe vaso-occlusive crises/events (VOE) per year in the past 2 years defined as either:
	  ○ VOE requiring a hospitalization or multiple visits to an emergency department/urgent care over 72 hours and receiving intravenous medications at each visit
	  ○ priapism lasting > 2 hours and requiring a visit to a medical facility
	  ○ acute chest syndrome
	  ○ splenic sequestration
	  ○ hepatic sequestration
	• Documentation was provided that the member has been taking hydroxyurea at the maximum tolerated dose and has been compliant within the last 6 months (or a medical reason was provided why the patient is unable to use hydroxyurea)
	• Documentation was provided that the member had a trial and failure of, or a medical reason was provided why the patient is unable to trial ~~two~~one of the following agents
	  ○ Endari
	  ○ Adakveo
	  ~~○ Oxbryta~~
	• Prescriber attests pregnancy has been ruled out prior to initiation of treatment (if applicable)
	• Patient has not had a prior HSCT or gene therapy treatment
	
	The safety and effectiveness of repeat administration of Casgevy or Lyfgenia have not been evaluated and will not be approved.
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review

Last Review Date	~~3/2024~~12/2024

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Piasky	Crovalimab-akkz injection solution 340 mg/2ml	Genentech	• For the treatment of adult and pediatric patients 13 years and older with paroxysmal nocturnal hemoglobinuria (PNH) and body weight of at least 40 kg.	$35,380 (maintenance dosing for ≥ 40 kg to < 100 kg patient)	Soliris, Ultomiris, Empaveli	Non-formulary (see updated PAD policy)
Vafseo	Vadadustat oral tablet 150mg, 300mg	Akebia Therapeutics, Inc.	• For the treatment of anemia due to chronic kidney disease (CKD) in adults who have been receiving dialysis for at least three months. Limitations of Use: Not been shown to improve quality of life, fatigue, or patient well-being. Not indicated for use: • As a substitute for transfusion in patients requiring immediate correction of anemia. • In patients with anemia due to CKD not on dialysis.	$639 - $2,556	Jesduvroq	Non-formulary (see updated MRG policy)
Adalimumab-ryvk	Adalimumab-ryvk (2 Syringe) Subcutaneous Prefilled Syringe Kit 40 MG/0.4ML	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
Taltz	Ixekizumab 20mg/0.25ml, 40mg/0.5ml prefilled syringe	Eli Lilly	• Treatment of patients aged 6 years or older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy • Treatment of adults with active psoriatic arthritis • Treatment of adults with active ankylosing spondylitis • Treatment of adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation.	$6,915 per syringe	Cosentyx, Bimzelx	Non-formulary

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Otezla	Apremilast 20 mg oral tablet Apremilast oral tablet Therapy Pack 4 x 10 & 51 x20 MG	Amgen Inc.	• Treatment of adult patients with active psoriatic arthritis • Treatment of adult patients with plaque psoriasis who are candidates for phototherapy or systemic therapy • Treatment of pediatric patients 6 years of age and older and weighing at least 20 kg with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy • Treatment of adult patients with oral ulcers associated with Behçet's Disease	$4,980	Zoryve, Humira, Skyrizi, Stelara, Enbrel, etc.	F-PA (already added via CRF)
Livmarli	Maralixibat 19mg/ml oral solution	Mirum Pharmaceuticals	• Teatment of cholestatic pruritus in patients 3 months of age and older with Alagille syndrome (ALGS) • Treatment of cholestatic pruritus in patients 12 months of age and older with progressive familial intrahepatic cholestasis (PFIC) ○ Limitations of Use: Livmarli is not recommended in a subgroup of PFIC type 2 patients with specific ABCB11 variants resulting in nonfunctional or complete absence of bile salt export pump (BSEP) protein	$226,380 (per month for max dose of 38mg/day)	Bylvay	Non-formulary (see new MRG policy)
Pantoprazole Sodium-NaCl	Pantoprazole Sodium-NaCl Intravenous Solution 40-0.9 MG/100ML-%, 80-0.9 MG/100ML-%	Baxter	• For the short-term treatment (7 to 10 days) of gastroesophageal reflux disease (GERD) associated with a history of erosive esophagitis (EE) • For the treatment of pathological hypersecretory conditions including Zollinger-Ellison Syndrome in adults.	$8-12 per 100ml solution	Esomeprazole, lanzoprazole	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Vancomycin	Vancomycin HCl intravenous solution reconstituted 1.75 gm, 2 gm	Mylan	• Indicated in adult and pediatric patients (neonates and older) for the treatment of: septicemia, infective endocarditis, skin and skin structure infections, bone infections, lower respiratory tract infections To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vancomycin Hydrochloride for Injection and other antibacterial drugs, Vancomycin Hydrochloride for Injection should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.	$35-42 per vial	Linezolid, daptomycin, ceftriaxone, daptomycin, tigecycline, etc.	Non-formulary
Cyclophosphamide	cyclophosphamide intravenous solution 1 gm/2ml, 2 gm/4ml	Avyxa	• For treatment of adult and pediatric patients with: Malignant Diseases: ○ malignant lymphomas: Hodgkin's disease, lymphocytic lymphoma, mixed-cell type lymphoma, histiocytic lymphoma, Burkitt's lymphoma; multiple myeloma, leukemias, mycosis fungoides, neuroblastoma, adenocarcinoma of ovary, retinoblastoma, breast carcinoma.	$1,730 per gram	Carmustine, bleomycin, mitomycin	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Zepbound	Tirzepatide subcutaneous solution 2.5mg/0.5ml, 5mg/0.5ml	Eli Lilly	• Indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of: ○ 30 kg/m or greater (obesity) or ○ 27 kg/m orgreater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea or cardiovascular disease) Limitations of Use: • Coadministration with other tirzepatide-containing products or any GLP-1 receptor agonist is not recommended. • The safety and efficacy of coadministration with other products for weight management have not been established. • Zepbound has not been studied in patients with a history of pancreatitis.	$1,316	Wegovy, Saxenda, Contrave, Qsymia, Xenical	F-PA (already added via CRF)

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Retevmo	Selpercatinib 40mg, 80mg, 120mg, 160mg oral tablet	Eli Lilly	• Treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a rearranged during transfection (RET) gene fusion, as detected by an FDA-approved test • Treatment of adult and pediatric patients 2 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a RET mutation, as detected by an FDA-approved test, who require systemic therapy. • Treatment of adult and pediatric patients 2 years of age and older with advanced or metastatic thyroid cancer with a RET gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).[1] • Treatment of adult and pediatric patients 2 years of age and older with locally advanced or metastatic solid tumors with a RET gene fusion, as detected by an FDA-approved test, that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options.[1] [1]This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).	$22,560	Gavreto	Non-formulary

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Vigafyde	Vigabatrin 100mg/ml oral solution	Pyros	• Monotherapy for the treatment of infantile spasms in pediatric patients 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss.	$9,700 per month for 10kg patient	Sabril, Vigadrone, Vigpoder	Add to F-PA (see updated MRG policy)
MydCombi	Tropicamide-phenylephrine ophthalmic solution cartridge 1-2.5%	Eyenovia	• Indicated to induce mydriasis for diagnostic procedures and in conditions where short term pupil dilation is desired.	$143 per cartridge	None	Non-formulary
Tecelra	Afamitresgene Autoleucel intravaneous suspension 10000000000 cells	Adaptimmune	• For the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and whose tumor expresses the MAGE-A4 antigen as determined by FDA-approved or cleared companion diagnostic devices. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.	$727,000 (one time treatment)	None	Non-formulary (see new PAD policy)
Nemluvio	nemolizumab Subcutaneous Auto-injector 30 MG	Galderma	• For the treatment of adults with prurigo nodularis.	$4,240 (for adults weighing <90kg)	Dupixent	Non-formulary (see new MRG policy)
Crexont	Carbidopa and levodopa 35-140mg, 52.5-210mg, 70-280mg, 87.5-350mg oral capsule extended release	Amneal	• For the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication in adults.	$520 (depending on dose and titration schedule)	Rytary, Sinemet, Dhivy	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Voranigo	Vorasidenib 10mg, 40mg, oral tablet	Servier Pharmaceuticals	• for the treatment of adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation following surgery including biopsy, sub-total resection, or gross total resection.	$39,870	None	Non-formulary
Neffy	Epinephrine nasal solution 2mg/0.1ml	ARS Pharmaceuticals	• For emergency treatment of type I allergic reactions, including anaphylaxis, in adult and pediatric patients who weigh 30 kg or greater.	$710 for two doses	EpiPen	Non-formulary
Livdelzi	Seladelpar oral capsule 10mg	Gilead Sciences	• For the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. This indication is approved under accelerated approval based on a reduction of alkaline phosphatase (ALP). Improvement in survival or prevention of liver decompensation events have not been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).	$12,600	Iqirvo	Non-formulary (see updated MRG policy)
Lazcluze	Lazertinib mesylate 80mg, 240mg oral tablet	Janssen Biotech Inc.	• First-line treatment (in combination with amivantamab) of locally advanced or metastatic non–small cell lung cancer with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations (as detected by an approved test).	$18,198	Tagrisso	Non-formulary

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Tevimbra	Tislelizumab-jsgr intravenous solution 100mg/10mL	Beigene	• Treatment of adult patients with unresectable or metastatic esophageal squamous cell carcinoma (ESCC) after prior systemic chemotherapy that did not include a programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1) inhibitor.	$10,408 per 3 weeks	Keytruda, Opdivo	Non-formulary
Vabysmo	Faricimab-svoa intravitreal solution prefilled syringe 6 mg/0.05mL	Genentech, Inc.	• Treatment of neovascular (wet) age-related macular degeneration. • Treatment of diabetic macular edema. • Treatment of macular edema following retinal vein occlusion.	$2,860 per dose (dosing every 4-16 weeks depending on symptoms)	Avastin, Eylea, Lucentis, Beovu	Non-formulary
Onyda XR	clonidine hydrochloride Oral Suspension Extended Release 0.1 MG/ML	Tris Pharma, Inc.	• For the treatment of Attention Deficit Hyperactivity Disorder (ADHD) as monotherapy or as adjunctive therapy to central nervous system (CNS) stimulant medications in pediatric patients 6 years of age and older.	$480 per bottle	Adderall, Focalin, Vyvanse, Strattera, Intuniv	Non-formulary
Yorvipath	Palopegteriparatide subcutaneous solution pen-injector 168 mcg/0.56ml, 294 mcg/0.98ml, 420 mcg/1.4ml	Ascendis Pharma A/S	• For the treatment of hypoparathyroidism in adults. <u>Limitations of Use:</u> • Not studied for acute post-surgical hypoparathyroidism. • Titration scheme only evaluated in adults who first achieved an albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D treatment.	$21,924	Natpara	Non-formulary (see new MRG policy)

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Tryvio	Aprocitentan oral tablet 12.5mg	Idorsia Pharmaceuticals US Inc.	• For the treatment of hypertension in combination with other antihypertensive drugs, to lower blood pressure in adult patients who are not adequately controlled on other drugs. Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions	$775	Spironolactone, hydralazine, minoxidil,	Non-formulary
Rytelo	Imetelstat 47 mg, 188 mg intravenous vial	Geron	• Treatment of adult patients with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring 4 or more red blood cell (RBC) units over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis stimulating agents (ESA).	$27,181 (for 70kg adult)	Reblozyl	Non-formulary (new PAD policy was added in Q3 2024)
Veltassa	Patiromer 1 gram packet	Vifor Pharma	• For the treatment of hyperkalemia in adults and pediatric patients 12 years and older.	$512 per box (60 per box. 1 gram packets used for dose adjustments)	Lokelma, SPS	Add to F-ST-QL (ST—requires trial and failure of Lokelma; QL—60/30 days)
Freestyle Libre	Freestyle Libre 3 Plus Sensor	Abbott	• A real time continuous glucose monitoring (CGM) device with alarms capability indicated for the management of diabetes	$144 per 30 days (plus $70 reader)	FreeStyle Libre 2 Reader Device, FreeStyle Libre Reader Device, Freestyle Libre 3 Device, Dexcom G6 Receiver Device, Dexcom G7 Receiver Device	Non-formulary

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Ebglyss	lebrikizumab subcutaneous solution auto-injector 250 mg/2ml	Eli Lilly	• For the treatment of adults and pediatric patients 12 years of age and older who weigh at least 40 kg with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. EBGLYSS can be used with or without topical corticosteroids.	$3,500	Dupixent, Adbry	Non-formulary
Femlyv	norethindrone acetate and ethinyl estradiol orally disintegrating tablets 1-0.02 mg	Millicent	• Indicated for use by females of reproductive potential to prevent pregnancy	$196	Oral contraceptives: Junel, Larin, Loestrin, Taytulla, etc.	Add to formulary
Tremfya	guselkumab 200 mg/2ml subcutaneous prefilled syringe, 200mg/2ml subcutaneous pen-injector, 200 mg/2ml via	Janssen Biotech, Inc.	• Treatment of moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy • Treatment of active psoriatic arthritis • Treatment of moderately to severely active ulcerative colitis	$13,872	Stelara, Skyrizi, Humira	Non-formulary
Tecentriq Hybreza	atezolizumab and hyaluronidase-tqjs subcutaneous solution 1875-30000 mg-ut/15ml	Genentech	• Treatment of Non-Small Cell Lung Cancer (NSCLC) • Treatment of Small Cell Lung Cancer (SCLC) • Treatment of Hepatocellular Carcinoma (HCC) • Treatment of Melanoma • Treatment of Alveolar Soft Part Sarcoma (ASPS) *Note: See full prescribing information for details of each indication.*	$10,920 per vial	Keytruda, Imfinzi, Opdivo	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Ocrevus Zunovo	ocrelizumab & hyaluronidase-ocsq subcutaneous solution 920-23000 mg-ut/23ml	Genentech	• Treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults • Treatment of primary progressive MS, in adults	$39,422 per vial	Tysabri, Kesimpta, Lemtrada	Non-formulary
Miplyffa	Arimoclomol oral capsule 47mg, 62mg, 93mg, 124mg	Zevra Therapeutics, Inc	• For use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older	$40,000 - $106,000	Aqneursa, miglustat	Non-formulary
Dolobid	Diflunisal oral tablet 250mg	Ina Pharmaceuticals	• Acute or long-term use for symptomatic treatment of the following: ○ Mild to moderate pain ○ Osteoarthritis ○ Rheumatoid arthritis	$7,515 (max dose of 1.5g per day)	NSAIDs	Non-formulary
Cobenfy	xanomeline and trospium chloride 50-20mg, 100-20mg, 125-30mg oral capsule xanomeline and trospium chloride oral capsule therapy pack 50-20 & 100-20 mg	Bristol-Myers Squibb	• For the treatment of schizophrenia in adults.	$1,850	Abilify, Saphris, Clozaril, Rexulti, Latuda, etc.	Non-formulary (see new MRG policy)

New Product Review

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Truqap	Capivasertib oral tablet therapy pack 160mg, 200mg	AstraZeneca	• In combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.	$23,000	Piqray	Non-formulary
Lumryz	Sodium oxybate starter pack oral therapy pack 4.5 & 6 & 7.5 gm	Avadel CNS Pharmaceuticals, LLC	• For the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.	$11,400 per pack	Xyrem, Xywav	Non-formulary
Aqneursa	Levacetylleucine 1 g oral packet	IntraBio Inc.	• For the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adults and pediatric patients weighing ≥15 kg.	$28,800 - $57,600	Miplyffa, miglustat	Non-formulary
Zituvimet XR	sitagliptin and metformin hydrochloride extended release 24 hour oral tablet 50-500mg, 50-1000mg, 100-1000mg	Zydus Pharmaceuticals	• As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Limitations of use: • Zituvimet is not recommended in patients with type 1 diabetes mellitus. • Zituvimet has not been studied in patients with a history of pancreatitis.	$544	Janumet, Jentadueto	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
FreeStyle Libre 2 Plus sensor	FreeStyle Libre 2 Plus sensor	Abbott	• A real time continuous glucose monitoring (CGM) device with alarms capability indicated for the management of diabetes	$144 per 28 days (plus $70 reader)	FreeStyle Libre 2 Reader Device, FreeStyle Libre Reader Device, Freestyle Libre 3 Device, Freestyle Libre 3 Plus Sensor, Dexcom G6 Receiver Device, Dexcom G7 Receiver Device	Non-formulary

*	Pricing reflects Wholesale Acquisition Cost (WAC) per month unless otherwise noted.
^	The recommendation may be affected by state specific requirements including carve out lists and individual state mandates.
†	Pricing based on standard twice-monthly dosing for most indications.
‡	Pricing is per each kit on items listed as a kit.

Alameda December Q4 2024 P&T Old Business

Pharmacists to prescribe Naloxone at POS

- Title 16 California Code of Regulations section 1746.3 allows a pharmacist to furnish naloxone without a prescription in the following forms:
    - IM injection
    - Intranasal Spray
    - Autoinjector
    - Any FDA approved product form
- Furnishing pharmacist MUST
    - Complete required CE/training
    - Screen recipient appropriately
    - Provide recipient with training, counseling, naloxone fact sheet
    - Notify PCP if recipient gives consent
    - Maintain documentation for at least 3 years
- IPS, our third party conducting audits will monitor Naloxone claims during audit and will validate the pharmacy is following requirements
- Only formulary products will be covered by the plan with or without a prescription
- Pharmacist can submit their own NPI if available
- Pharmacist can submit the pharmacy NPI along with SCC code 42

Recommendation pending P&T Committee Approval:

- Allow pharmacists to prescribe at dispensing pharmacies?
- Recoup payment from pharmacies that do not follow state requirements (as listed in FAQ and above) while dispensing naloxone via pharmacist prescribing?

FAQ for Naloxone Protocol

Q: Where are the provisions that authorize a pharmacist to furnish naloxone without a prescription?
A: Title 16 California Code of Regulations section 1746.3 establishes the protocol.

Q: What training or continuing education (CE) is required prior to furnishing naloxone?
A: Pharmacists using the protocol have two options to meet the required training/CE prior to administering naloxone:

1. The pharmacist must have successfully completed a minimum of a one hour approved CE program specific to all routes of naloxone administration as identified in 16 CCR 1746.3 (c)(4); or,
2. The pharmacist must have successfully completed an equivalent curriculum-based training program completed in a board recognized school of pharmacy.

Q: Is the pharmacist required to screen the recipient prior to furnishing naloxone in accordance with the protocol?
A: Yes. The pharmacist must screen the recipient using the following questions:

1. Whether the potential recipient currently uses or has a history of using illicit or prescription opioids. (If the recipient answers yes, the pharmacist may skip screening question 2.);
2. Whether the potential recipient is in contact with anyone who uses or has a history of using illicit or prescription opioids. (If the recipient answers yes, the pharmacist may continue);
3. Whether the person to whom the naloxone would be administered has a known hypersensitivity to naloxone. (If the recipient answers yes, the pharmacist may not provide naloxone. If the recipient responds no, the pharmacist may continue.)

Q: Who is the recipient?
A: A recipient is the person to whom the naloxone is furnished.

Q: Who is the patient?
A: The patient is the person to whom the naloxone would be administered. (Note: The recipient may or may not also be the patient.)

Q: Are these screening questions available in different languages? Where can I get the translated versions?
A: Yes, the screening questions are available in Spanish, Traditional Chinese, Korean, Russian, Tagalog, and Vietnamese. The translated screening questions may be downloaded from the board's website: http://www.pharmacy.ca.gov/licensees/naloxone_info.shtml

Q: Is the pharmacist required to provide the recipient with training? If so, what type of training is required?
A: Yes, the pharmacist is required to provide the recipient with training. Training must include the following topics: opioid overdose prevention, recognition, response and administration of the antidote naloxone.

Q: What is required to be provided to the recipient when naloxone is furnished?
A: When a pharmacist provides naloxone to a recipient, the following must be provided to the recipient:

1. Appropriate counseling and information on the furnished naloxone including dosing, effectiveness, adverse effects, storage conditions, shelf-life, and safety. The recipient is not permitted to waive the required consultation.
2. Any informational resources on hand and/or referrals to appropriate resources if the recipient indicates interest in addiction treatment, recovery services, or medication disposal resources at the time of furnishing naloxone.
3. Responses to any questions the recipient may have about naloxone.

Q: When the pharmacist initiates patient consultation to the recipient of the naloxone, is the recipient allowed to waive the patient consultation?
A: No, the recipient is not allowed to waive the patient consultation for naloxone.

Q: What forms of naloxone may the pharmacist provide to the recipient?
A: The pharmacist may supply naloxone in the following forms:

1. Intramuscular injection;
2. Intranasal spray;
3. Auto-injector; or
4. FDA-approved product form.

Q. Does the board have sample naloxone labels available?
A. Yes. The board's sample naloxone labels can be found at:
http://www.pharmacy.ca.gov/licensees/naloxone_labels.shtml

Q: Is the pharmacist required to provide the naloxone fact sheet upon furnishing naloxone?
A: Yes, the pharmacist shall provide a copy of the board-approved naloxone fact sheet. It can be found at: http://www.pharmacy.ca.gov/publications/naloxone_fact_sheet.pdf. The fact sheet is also available in other languages including Spanish, Traditional Chinese, Korean, Russian, Tagalog, and Vietnamese. The translated fact sheets can be found at:
http://www.pharmacy.ca.gov/licensees/naloxone_info.shtml

Q: Is the pharmacist authorized to notify a physician about the dispensing of naloxone?
A: If consent is given by the patient, the consent can be either verbal or written. The pharmacist is required to notify a patient's primary care provider (PCP) of any drug(s) and/or device(s) furnished or enter information in a patient record system shared with the PCP.

Q: If the patient does not have a PCP or chooses not to give notification consent, what must the pharmacist do?
A: The pharmacist is required to provide a written record of the drug(s) and/or device(s) furnished and advise the patient to consult a health care provider of the patient's choice.

Q: How long must records of furnishing naloxone be kept?
A: Documentation shall be maintained for at least three years from date of furnishing.

Q: Do privacy laws apply to furnishing naloxone?
A: The same laws apply to naloxone as to other dangerous drugs.