PHARMACY & THERAPEUTICS COMMITTEE

Tuesday, September 26th, 2023
5:00pm – 7:00pm

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

Location: Microsoft Teams
Meeting ID: 246 114 925 350
Password: JxyXDh

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

STATE OR LOCAL OFFICIALS CONTINUE TO IMPOSE OR RECOMMEND MEASURES TO PROMOTE SOCIAL DISTANCING. AS A RESULT OF THE COVID-19 VIRUS, AND RESULTING ORDERS AND DIRECTION FROM THE PRESIDENT OF THE UNITED STATES, THE GOVERNOR OF THE STATE OF CALIFORNIA, AND THE ALAMEDA COUNTY HEALTH OFFICER, THE PUBLIC WILL NOT BE PERMITTED TO PHYSICALLY ATTEND THE ALAMEDA ALLIANCE FOR HEALTH MEETING TO WHICH THIS AGENDA APPLIES.

YOU MAY SUBMIT COMMENTS ON ANY AGENDA ITEM OR ON ANY ITEM NOT ON THE AGENDA, IN WRITING VIA MAIL TO "ATTN: ALLIANCE PHARMACEUTICAL AND THERAPEUTICS COMMITTEE" 1240 SOUTH LOOP ROAD, ALAMEDA, CA 94502; OR THROUGH E-COMMENT AT 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. 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** *Steve O'Brien, MD, Chief Medical Officer – Alameda Alliance* • Agenda Overview	2 min	-
II)	**Informational Updates** *Steve O'Brien, MD, Chief Medical Officer – Alameda Alliance* *Helen Lee, PharmD, MBA, Senior Pharmacy Director – Alameda Alliance* • Anthem • ICF-DD • DMHC Audit • Medi-Cal Rx MCDAC Drugs (See Next Page)	15 min	-
III)	**Pharmacy Utilization Reports (Quarter 2, 2023)** *Helen Lee, PharmD MBA, Senior Pharmacy Director – Alameda Alliance* • Top 50 Drugs by Cost • Top 50 PA Reviewed Drugs	2 min	-

MCDAC Drug	Indication	CDL Status	Recommendation Based on - Safety, Efficacy, Essential Need, Misuse Potential, etc.
Accrufer (ferric maltol) 30mg capsules	Adult iron deficiency	F-PA	Keep F-PA
Konvomep (omeprazole and sodium bicarbonate) oral suspension	Short-term treatment (4 to 8 weeks) of active benign gastic ulcer; Reduction of risk of upper gastrointestinal (GI) bleeding in critically ill adult patients	F-PA	Keep F-PA
Triptodur (triptorelin) 22.5mg single-use kit	Pediatric (2 years and older) central precocious puberty	F-PA	Keep F-PA
Lyvispah (baclofen) oral granules 5mg, 10mg and 20mg	Spasticity from multiple sclerosis	F-PA	Keep F-PA
Tremfya (guselkumab) 100mg/mL prefilled syringe and 100mg/mL one-press patient-controlled injector	Plaque Psoriasis; Adult Psoriatic arthritis	F-PA	Keep F-PA
Veozah (fezolinetant) 45mg tablets	Vasomotor symptoms due to menopause	F-PA	Keep F-PA
Vowst (fecal microbiota spores, live-brpk) capsules	Recurrent Clostridium Difficile infection (CDI) following bacterial treatment of recurrent CDI	F-PA	Keep F-PA
Zonisade (zonisade) 100mg/5mL oral suspension	Adjuntive therapy for partial-onset seizures	F-PA	Keep F-PA

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

Discussion will Concern: *Review and Recommendations to changes to the AAH Formulary and utilization management for selected drug classes*
Estimated Date of Public Disclosure: 9/26/2023 *(formulary changes only; no trade secrets will be disclosed)*

IV) E-Voting Material/Consent Agenda

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

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

Monographs/Class Reviews	Changes
Macrolides	• No change
Bowel Prep	• No change
Medication Request Guidelines	**Changes**
Moxifloxacin Oral Tablet	• Minor wording update
Physician Administered Medication (PAD)/ Medical Benefit Guidelines	• Minor clarification update
Off-label uses	• Minor clarification update
Non-Formulary and PA Required Medications without Drug-Specific	• Minor clarification update

10 min EV

Erythropoiesis-Stimulating Agents	• Retacrit availability is no longer an issue, update preferred agents. • Minor zidovudine clarification
Vancomycin	• Minor wording clarifications
Scabicides and Pediculicides	• Minor wording clarifications
Dronabinol	• Minor spelling update
Constipation agents	• No change
Multaq (dronedarone)	• No change
Safety Edit Exception	• No change
Quantity Limit Exception	• No change
Atovaquone-proguanil (Malarone)	• No change
Santyl Ointment	• No change
Spravato (esketamine) Intranasal	• No change
Topical Acne Agents	• No change
Memantine ER (Namenda XR)	• No change
Tranexamic acid (Lysteda)	• No change
Biologic Agents for Nasal Polyposis	• No change
Rapid-Acting Insulin	• No change
Antiemetics	• No change
Rifabutin (Mycobutin)	• No change
Topical Antibiotics	• No change
Fertility Agents	• No change
Erectile Dysfunction Medications	• No change
Physician Administered Drug (PAD) Guidelines	**Changes**
Exondys 51	• Minor wording update
Erythropoiesis-Stimulating Agents	• Remove duplicate Procrit Minor zidovudine clarification
Adakveo	• No change
Interim Formulary Updates	
• See p. 105 in packet	
Pharmacy Policy & Procedure Updates	
• RX-002 – PA Review Process	• DMHC Contraceptive language addition
• RX-003 – Exception Review Process	• DMHC Step Therapy language addition
ED Oversight	
• None	

90 Day Maintenance List updates
• 365-day contraceptive coverage language
P&T Meeting Minutes
• P&T Meeting Minutes Q2 June 20, 2023

V) New Business

Natalee Felten, PharmD, Pharmacist – PerformRx

New MRGs

- Specialty Biologic Agents
- Transthyretin-mediated amyloidosis agents
- Vowst
- Vyjuvek (beremagene geperpavec-svdt)

New PADs

- Omisirge (omidubicel-onlv)
- Qalsody (tofersen)
- Lamzede (velmanase alfa)
- Enzyme Replacement Therapies for Fabry Disease
- Vyjuvek (beremagene geperpavec-svdt)
- Elevidys (delandistrogene moxeparvovec-rokl)
- Specialty Biologic Agents for FDA approved indications
- Leqembi (lecanemab-irmb)
- Gene Therapy for Regular Red Blood Cell (RBC) Transfusion Dependent Beta-Thalassemia
- Roctavian (valoctocogene roxaparvovec)
- Enzyme replacement therapy for acid sphingomyelinase deficiency (ASMD)
- Generalized Pustular Psoriasis (GPP) Agents

VI) Class Reviews, Monographs, and Recommendations

Natalee Felten, PharmD, Pharmacist – PerformRx

45 min V

1. Humira Biosimilar Comparative Review and Strategy
2. Abrysvo Monograph
3. Arexvy Monograph
4. Ophthalmic Antibiotics & Ophthalmic Antibiotics -Steroid Combinations Class Review
5. Ulcerative Colitis Class Review
6. Chelating agents Class Review
7. Respiratory Aids and Devices Class Review

VII) Medication Request Guidelines

Rahel Negash, PharmD, Pharmacist – Alameda Alliance

1. Nuedexta (dextromethorphan/quinidine)
2. Cartilaginous Repair Agents
3. Ophthalmic Anti-inflammatory Immunomodulators
4. Desvenlafaxine succinate (Pristiq) - RETIRE
5. White Blood Cell Stimulators
6. Drugs for Gender Dysphoria For Less Than 21 Years Old

7. Drugs for Gender Dysphoria For At Least 21 Years Old
8. Intranasal Steroids
9. Opioid Use Disorder (OUD) Agents
10. Alosetron (Lotronex)
11. Viberzi (eluxadoline)
12. Rifamycin Antibiotics
13. Injectable/Infusible Bone-Modifying Agents for Oncology Indications
14. Medications for the treatment of Multi-Drug Resistant Tuberculosis
15. Adenosine Triphosphate-Citrate Lyase (ACL) inhibitors
16. Vaginal Progesterone
17. Injectable/Infusible Agents for Osteoporosis and Paget's Disease
18. Synagis - RETIRE
19. Specialty Biological Agents Preferred Products - RETIRE
20. Specialty biologics for Chron's - RETIRE
21. Specialty Biological Agents for Ulcerative Colitis - RETIRE
22. Specialty Biological Agents for Rheumatoid Arthritis - RETIRE
23. Specialty Biological Agents for Adult Psoriatic Arthritis (PsA) - RETIRE
24. Specialty Biological Agents for Psoriasis - RETIRE
25. Specialty Biological Agents for Juvenile Idiopathic Arthritis - RETIRE
26. Specialty Biological Agents for Ankylosing Spondylitis - RETIRE
27. Specialty Biological Agents for Nonradiographic Axial Spondyloarthritis (nr-axSpA) - RETIRE
28. Specialty Biological Agents for Hidradenitis Suppurativa - RETIRE
29. Specialty Biological Agents for Giant Cell Arteritis - RETIRE
30. Specialty Biological Agents for Uveitis- RETIRE

VIII) Physician Administered Drug (PAD) Policies

Natalee Felten, PharmD, Pharmacist – PerformRx

1. Aduhelm
2. Rebyota
3. Injectable/Infusible Agents for Osteoporosis and Paget's Disease
4. White Blood Cell Stimulators
5. Iron-containing Products
6. Tepezza
7. Specialty biologics for Chron's - RETIRE
8. Specialty Biological Agents for Ulcerative Colitis - RETIRE
9. Specialty Biological Agents for Rheumatoid Arthritis - RETIRE
10. Specialty Biological Agents for Adult Psoriatic Arthritis (PsA) - RETIRE
11. Specialty Biological Agents for Psoriasis - RETIRE
12. Specialty Biological Agents for Ankylosing Spondylitis - RETIRE
13. Specialty Biological Agents for Nonradiographic Axial Spondyloarthritis (nr-axSpA) - RETIRE
14. Specialty Biological Agents for Juvenile Idiopathic Arthritis - RETIRE
15. Specialty Biological Agents for Hidradenitis Suppurativa - RETIRE
16. Specialty Biological Agents for Giant Cell Arteritis - RETIRE
17. Specialty Biological Agents for Uveitis - RETIRE

10 min V

IX) Informational Updates on New Developments in Pharmacy

Natalee Felten, PharmD, Pharmacist – PerformRx

- New Product Review

2 min -

X) Old Business

Natalee Felten, PharmD, Pharmacist – PerformRx 2 min -

- None

RECONVENE IN OPEN SESSION

XI) Public Comment

XII) Adjournment

-

ACTION / FOLLOW-UP ITEMS

ITEM	DUE DATE	RESPONSIBLE

FUTURE P&T MEETINGS

NEXT MEETING	2024 P&T MEETINGS
December 19, 2023	March 19, 2024
	June 11, 2024
	September 24, 2024
	December 17, 2024

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

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

This meeting is wheelchair accessible. Please contact Helen Lee at 510-747- 6241 or hlee@alamedaalliance.org at least 72 hours before the meeting to request agenda materials in an alternative format, or any other reasonable disability-related accommodations or services that may be necessary for you to participate in and enjoy the benefits of the meeting.

636 IHSS Top 50 Drugs by Cost for 2nd Quarter 2023

- The top 50 drugs accounted for **964 claims** for **488 members** and cost **$1,227,621,** which is an increase of $76,992 in spend from the previous quarter.
- Cabometyx has risen from number 5 to number 1, with 4 claims for one member. Requests for this medications are reviewed via the oncology MRG.
- Biktarvy is now at number 2, with an increase of 2 claims since the previous quarter.
- Skyrizi is at number 3 with 4 claims for 2 members. This medication is currently preferred in the biologic DMARD PA policies.
- Vemlidy is down to number 4 with 49 claims for 21 members. This is an increase of one claim since last quarter. This medication is managed via the Hepatitis B MRG, which was loosened during Q4 2022 P&T to require trial and failure of, or reason not to use, entecavir (previously generic Viread and entecavir).
- Revlimid is at 5 and Jakafi at number 6, both with 3 claims for one member. These are managed via the oncology MRG and the non-oncology indication of Revlimid is reviewed via the Agents for graft versus host disease MRG.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	41146	CABOMETYX 20 MG TABLET	4	1	$97,636.44
2	44426	BIKTARVY 50-200-25 MG TABLET	21	7	$78,389.38
3	49591	SKYRIZI 150 MG/ML PEN	4	2	$77,675.40
4	42624	VEMLIDY 25 MG TABLET	49	21	$76,826.37
5	26314	REVLIMID 5 MG CAPSULE	3	1	$51,341.01
6	30892	JAKAFI 5 MG TABLET	3	1	$49,561.47
7	53536	OZEMPIC 0.25-0.5 MG/DOSE PEN	43	26	$39,623.47
8	37169	TRULICITY 0.75 MG/0.5 ML PEN	39	15	$35,783.88
9	48208	OZEMPIC 1 MG/DOSE (4 MG/3 ML)	37	17	$34,071.95
10	40133	TAGRISSO 80 MG TABLET	2	1	$31,949.32
11	27257	SPRYCEL 20 MG TABLET	2	1	$27,506.04
12	97400	JANUVIA 100 MG TABLET	49	21	$26,124.95

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
13	43699	MAVYRET 100-40 MG TABLET	2	1	$25,407.36
14	48277	DUPIXENT 300 MG/2 ML PEN	7	2	$25,014.99
15	37171	TRULICITY 1.5 MG/0.5 ML PEN	27	10	$24,739.86
16	33935	ELIQUIS 5 MG TABLET	44	19	$24,255.31
17	44248	STEGLATRO 5 MG TABLET	61	30	$23,857.02
18	40092	GENVOYA TABLET	6	2	$22,482.48
19	46966	RYBELSUS 14 MG TABLET	23	9	$21,302.83
20	44259	STEGLATRO 15 MG TABLET	63	26	$21,216.05
21	37789	COSENTYX SNRDY 300MG DOSE-2PEN	3	1	$20,440.41
22	43904	HUMIRA(CF) PEDI CROHN 80MG/0.8	1	1	$20,186.44
23	43506	HUMIRA(CF) PEN 40 MG/0.4 ML	3	1	$20,186.34
24	97005	HUMIRA PEN 40 MG/0.8 ML	3	1	$20,186.34
25	43334	TYMLOS 80 MCG DOSE PEN INJECTR	8	2	$19,875.60
26	49099	CABENUVA ER 600 MG-900 MG SUSP	3	2	$18,778.61
27	43989	SHINGRIX VIAL KIT	91	84	$17,853.42
28	41444	OCALIVA 5 MG TABLET	2	1	$16,870.60
29	46965	RYBELSUS 7 MG TABLET	17	9	$15,676.29
30	41729	SOFOSBUVIR-VELPATASVIR 400-100	2	1	$15,456.00
31	43916	VERZENIO 150 MG TABLET	2	1	$14,303.12
32	45082	ACTEMRA ACTPEN 162 MG/0.9 ML	3	1	$13,960.83

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
33	37633	ODEFSEY TABLET	4	1	$13,683.08
34	43505	HUMIRA(CF) 40 MG/0.4 ML SYRING	1	1	$13,457.57
35	40848	TALTZ 80 MG/ML AUTOINJECTOR	1	1	$13,278.18
36	46024	TREMFYA 100 MG/ML INJECTOR	1	1	$12,921.52
37	30819	XARELTO 20 MG TABLET	21	8	$12,260.43
38	36723	JARDIANCE 25 MG TABLET	21	10	$12,225.63
39	52125	OZEMPIC 2 MG/DOSE (8 MG/3 ML)	13	8	$11,946.46
40	49993	INSULIN GLARGINE-YFGN U100 PEN	82	44	$11,652.77
41	34394	FARXIGA 10 MG TABLET	20	7	$11,189.18
42	49487	APRETUDE ER 600 MG/3 ML VIAL	3	2	$11,157.90
43	43222	DUPIXENT 300 MG/2 ML SYRINGE	3	1	$10,720.71
44	36716	JARDIANCE 10 MG TABLET	18	7	$10,514.79
45	36999	TRIUMEQ 600-50-300 MG TABLET	3	1	$10,445.40
46	28530	XIFAXAN 550 MG TABLET	3	1	$9,388.62
47	48574	TRULICITY 3 MG/0.5 ML PEN	10	4	$9,113.92
48	25200	FREESTYLE LITE TEST STRIP	82	50	$8,424.12
49	34076	ALOGLIPTIN 25 MG TABLET	49	22	$8,388.99
50	49090	CABENUVA ER 400 MG-600 MG SUSP	2	1	$8,312.64
TOTAL			**964**	**488**	**$1,227,621.49**

Medi-Cal Top 50 Drugs by Cost for 2nd Quarter 2023

- The top 50 drugs accounted for **28,648 claims** for **24,488 members** and cost **$39,740,857.16,** which is an increase of $2,732,910.41 in spend from the previous quarter and **$12,026,834.98** in spend compared to a quarter before Medi-Cal Rx conversion.
- Ozempic has risen from the number 6 to number 5, with 1181 claims for 1001 members.
- Vemlidy is down to number 7 with 346 claims for 307 members. This is a decrease of 8 claims since last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	44426	BIKTARVY 50-200-25 MG TABLET	670	525	$4,502,328.87
2	43506	HUMIRA(CF) PEN 40 MG/0.4 ML	121	95	$2,094,063.87
3	28159	STELARA 90 MG/ML SYRINGE	48	42	$2,075,726.07
4	36723	JARDIANCE 25 MG TABLET	1222	1129	$1,662,338.12
5	53536	OZEMPIC 0.25-0.5 MG/DOSE PEN	1181	1001	$1,582,382.90
6	36716	JARDIANCE 10 MG TABLET	975	890	$1,242,757.23
7	42624	VEMLIDY 25 MG TABLET	346	307	$1,177,516.70
8	97400	JANUVIA 100 MG TABLET	716	649	$999,593.66
9	49591	SKYRIZI 150 MG/ML PEN	49	35	$958,938.18
10	48208	OZEMPIC 1 MG/DOSE (4 MG/3 ML)	536	455	$930,352.33
11	40133	TAGRISSO 80 MG TABLET	31	21	$915,365.88
12	97005	HUMIRA PEN 40 MG/0.8 ML	58	48	$910,912.41
13	37789	COSENTYX SNRDY 300MG DOSE-2PEN	68	49	$886,339.58
14	40092	GENVOYA TABLET	109	84	$828,914.01
15	97724	ENBREL 50 MG/ML SURECLICK	68	54	$825,216.25
16	48277	DUPIXENT 300 MG/2 ML PEN	108	84	$783,464.35

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
17	25200	FREESTYLE LITE TEST STRIP	3929	3612	$770,902.31
18	27418	INVEGA SUSTENNA 234 MG/1.5 ML	142	95	$748,738.17
19	33935	ELIQUIS 5 MG TABLET	665	544	$727,266.28
20	46965	RYBELSUS 7 MG TABLET	352	322	$697,641.01
21	98637	BASAGLAR 100 UNIT/ML KWIKPEN	1308	1089	$679,771.75
22	47136	TRIKAFTA 100-50-75 MG/150 MG	11	10	$672,575.01
23	40953	DESCOVY 200-25 MG TABLET	177	137	$662,084.38
24	37171	TRULICITY 1.5 MG/0.5 ML PEN	351	294	$654,385.86
25	47258	IBRANCE 125 MG TABLET	20	15	$611,636.33
26	47426	VYONDYS-53 100 MG/2 ML VIAL	4	2	$608,070.35
27	43968	SYMTUZA 800-150-200-10 MG TAB	79	62	$598,608.27
28	22913	ALBUTEROL HFA 90 MCG INHALER	12018	10136	$554,826.09
29	44014	HUMIRA(CF) PEN 80 MG/0.8 ML	14	12	$538,659.79
30	37169	TRULICITY 0.75 MG/0.5 ML PEN	319	274	$536,453.97
31	34394	FARXIGA 10 MG TABLET	385	336	$512,992.77
32	37633	ODEFSEY TABLET	84	63	$511,672.89
33	36999	TRIUMEQ 600-50-300 MG TABLET	74	61	$503,541.22
34	37682	ABILIFY MAINTENA ER 400 MG SYR	106	74	$481,035.89
35	43699	MAVYRET 100-40 MG TABLET	24	24	$469,256.05
36	38702	INVEGA TRINZA 819 MG/2.63 ML	45	45	$463,614.72

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
37	54456	FERRIPROX 1,000 MG TAB(2X/DAY)	7	4	$444,209.67
38	43916	VERZENIO 150 MG TABLET	19	14	$441,883.67
39	43924	ENBREL 50 MG/ML MINI CARTRIDGE	33	26	$432,262.80
40	49099	CABENUVA ER 600 MG-900 MG SUSP	50	47	$410,324.46
41	30819	XARELTO 20 MG TABLET	358	302	$405,824.67
42	43222	DUPIXENT 300 MG/2 ML SYRINGE	59	50	$392,612.16
43	36172	OTEZLA 30 MG TABLET	48	42	$386,325.78
44	49055	TAKHZYRO 300 MG/2 ML SYRINGE	6	3	$376,890.45
45	52125	OZEMPIC 2 MG/DOSE (8 MG/3 ML)	191	158	$359,543.83
46	46966	RYBELSUS 14 MG TABLET	162	146	$351,328.47
47	97472	ZINC SULFATE POWDER	554	351	$345,366.79
48	94200	DEXCOM G6 SENSOR	314	296	$341,667.80
49	48574	TRULICITY 3 MG/0.5 ML PEN	178	147	$338,338.19
50	05679	HUMALOG 100 UNIT/ML VIAL	256	227	$334,334.90
TOTAL			**28,648**	**24,488**	**$39,740,857.16**

636 IHSS Top 50 Prior Authorization Requests by Volume for 2nd Quarter 2023

- Top 50 PA requests = 162. There were 251 total PA requests for quarter 2.
  - 55 requests (34%) were approved. This approval rate is lower, by 19%, than what was observed last quarter.
  - 107 requests (66%) were denied or partially approved.
- Wegovy 0.25mg/0.5ml is new at number one and had a total of 21 requests for that strength, which is the starting dose.
  - There were 35 total requests for this medication in the top 50, for the various strengths.
    - There were 26 denials and 4 partial approvals.
  - Wegovy requires a diagnosis of obesity or history of heart attack, despite diet and exercise, and requires trial and failure of, or reason not to use Qsymia and Contrave.
- Jardiance 10mg is at number 2 with 13 requests (along with the 25mg tablet, in total it had 18 requests) with 2 approvals.
  - The formulary alternative is Steglatro, with trial and failure of metformin.
- Ozempic 0.25-0.5mg/dose pen is at number 3 with 10 requests for that strength, which is the starting dose.
  - Ozempic requires a trial and failure of metformin.
- Vemlidy is at number 4, with 9 requests. Five of those were approved.
  - Vemlidy requires trial and failure of entecavir.
- Lidocaine 5% patch is at number 5 and had 8 requests with 3 approvals.
  - This medication requires a diagnosis of neuropathic pain and a trial and failure of gabapentin or pregabalin and one other formulary alternative used for neuropathic pain or morphine MME $\leq$ 50 for 3 months.

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
1	WEGOVY 0.25 MG/0.5 ML PEN	21	3	14.3%	17	81.0%	1	4.8%
2	JARDIANCE 10 MG TABLET	13	2	15.4%	11	84.6%	0	0.0%
3	OZEMPIC 0.25-0.5 MG/DOSE PEN	10	4	40.0%	4	40.0%	2	20.0%
4	VEMLIDY 25MG TABLET	9	5	55.6%	1	11.1%	3	33.3%
5	LIDOCAINE 5% PATCH	8	3	37.5%	5	62.5%	0	0.0%
6	WEGOVY 0.5 MG/0.5 ML PEN	7	1	14.3%	4	57.1%	2	28.6%
7	EMGALITY 120 MG/ML PEN	6	2	33.3%	2	33.3%	2	33.3%
8	JARDIANCE 25 MG TABLET	5	1	20.0%	1	20.0%	3	60.0%
9	WEGOVY 1 MG/0.5 ML PEN	5	0	0.0%	4	80.0%	1	20.0%
10	ENTECAVIR 0.5 MG TABLET	4	1	25.0%	0	0.0%	3	75.0%
11	FARXIGA 10 MG TABLET	4	3	75.0%	1	25.0%	0	0.0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
12	HYDROCODONE-ACETAMIN 5-325 MG	3	3	100.0%	0	0.0%	0	0.0%
13	SKYRIZI 150 MG/ML PEN	3	3	100.0%	0	0.0%	0	0.0%
14	STEGLATRO 5 MG TABLET	3	1	33.3%	0	0.0%	2	66.7%
15	TRANEXAMIC ACID 650 MG TABLET	3	1	33.3%	0	0.0%	2	66.7%
16	XIIDRA 5% EYE DROPS	3	0	0.0%	3	100.0%	0	0.0%
17	ALTACE 1.25 MG CAPSULE	2	1	50.0%	1	50.0%	0	0.0%
18	ATOVAQUONE-PROGUANIL 250-100	2	1	50.0%	1	50.0%	0	0.0%
19	CONTRAVE ER 8-90 MG TABLET	2	1	50.0%	1	50.0%	0	0.0%
20	DEFERASIROX 360 MG TABLET	2	1	50.0%	1	50.0%	0	0.0%
21	ENDOMETRIN 100 MG VAG INSERT	2	0	0.0%	1	50.0%	1	50.0%
22	FARXIGA 5 MG TABLET	2	0	0.0%	1	50.0%	1	50.0%
23	LUMIGAN 0.01% EYE DROPS	2	0	0.0%	2	100.0%	0	0.0%
24	MAVYRET 100-40 MG TABLET	2	0	0.0%	1	50.0%	1	50.0%
25	METHADONE HCL 10 MG TABLET	2	1	50.0%	0	0.0%	1	50.0%
26	METHADONE HCL 5 MG TABLET	2	2	100.0%	0	0.0%	0	0.0%
27	OXYCODONE HCL (IR) 10 MG TAB	2	0	0.0%	2	100.0%	0	0.0%
28	PHENTERMINE 37.5 MG TABLET	2	0	0.0%	0	0.0%	2	100.0%
29	PILOCARPINE HCL 5 MG TABLET	2	2	100.0%	0	0.0%	0	0.0%
30	SCOPOLAMINE 1 MG/3 DAY PATCH	2	0	0.0%	2	100.0%	0	0.0%
31	STEGLATRO 15 MG TABLET	2	1	50.0%	0	0.0%	1	50.0%
32	TACROLIMUS 0.1% OINTMENT	2	1	50.0%	1	50.0%	0	0.0%
33	TALTZ 80 MG/ML AUTOINJECTOR	2	2	100.0%	0	0.0%	0	0.0%
34	TRETINOIN 0.05% CREAM	2	0	0.0%	2	100.0%	0	0.0%
35	TRULICITY 1.5 MG/0.5 ML PEN	2	2	100.0%	0	0.0%	0	0.0%
36	WEGOVY 1.7 MG/0.75 ML PEN	2	1	50.0%	1	50.0%	0	0.0%
37	XOLAIR 150 MG/ML SYRINGE	2	0	0.0%	2	100.0%	0	0.0%
38	ABIRATERONE ACETATE 250 MG TAB	1	0	0.0%	0	0.0%	1	100.0%
39	ACETAMINOPHEN ER 650 MG TABLET	1	0	0.0%	1	100.0%	0	0.0%

RANK	DRUGS	Total	Approved		Denied		Partially Approved	
40	ACTEMRA ACTPEN 162 MG/0.9 ML	1	0	0.0%	0	0.0%	1	100.0%
41	ACULAR LS 0.4% OPHTH SOL	1	0	0.0%	1	100.0%	0	0.0%
42	ADDERALL XR 20 MG CAPSULE	1	1	100.0%	0	0.0%	0	0.0%
43	ALLI 60 MG CAPSULE	1	1	100.0%	0	0.0%	0	0.0%
44	ALOGLIPTIN-METFORMIN 12.5-1000MG TABLET	1	1	100.0%	0	0.0%	0	0.0%
45	ALVESCO 160 MCG INHALER	1	0	0.0%	1	100.0%	0	0.0%
46	AZELAIC ACID 15% GEL	1	1	100.0%	0	0.0%	0	0.0%
47	BASAGLAR 100 UNIT/ML KWIKPEN	1	1	100.0%	0	0.0%	0	0.0%
48	BELBUCA 150 MCG FILM	1	1	100.0%	0	0.0%	0	0.0%
49	BETAMETHASONE DP AUG 0.05% OIN	1	0	0.0%	1	100.0%	0	0.0%
50	BRIMONIDINE-TIMOLOL 0.2%-0.5%	1	0	0.0%	0	0.0%	1	100.0%
TOTAL		**162**	**55**		**76**		**31**	

Medi-Cal Top 50 Prior Authorization Requests by Volume for 2nd Quarter 2023

- The top 50 drugs accounted for **175,083 claims** for **155,526 members** and cost **$3,805,809.48.**
- Ibuprofen moved down to number 4 from number 2 with 7642 claims for 6897 members. This is a decrease of 33 claims from last quarter.
- Fluticasone has risen to number 2 from number 3 with 9506 claims for 8741 members. This is an increase of 1,985 claims from last quarter.
- Aspirin has risen from number 4 to number 3 with 7650 claims for 7063 members. This is an increase of 344 claims from last quarter.
- Loratadine remains at the number 5 spot with 7642 claims for 6897 members. This is an increase of 1,322 claims from last quarter.

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
1	22913	ALBUTEROL HFA 90 MCG INHALER	12018	10136	$554,826.09
2	62263	FLUTICASONE PROP 50 MCG SPRAY	9506	8741	$180,344.48
3	00161	ASPIRIN EC 81 MG TABLET	7650	7063	$80,863.00
4	35742	IBUPROFEN 600 MG TABLET	7642	6897	$108,086.54
5	60563	LORATADINE 10 MG TABLET	6186	5582	$99,515.09
6	49291	CETIRIZINE HCL 10 MG TABLET	5664	5202	$91,016.93
7	43721	ATORVASTATIN 20 MG TABLET	4967	4697	$75,840.28
8	02683	AMLODIPINE BESYLATE 5 MG TAB	4659	4256	$63,057.75
9	43722	ATORVASTATIN 40 MG TABLET	4527	4178	$74,137.04
10	02682	AMLODIPINE BESYLATE 10 MG TAB	4347	3928	$59,873.28
11	16965	ACETAMINOPHEN 500 MG CAPLET	4106	3726	$52,766.59
12	04348	OMEPRAZOLE DR 20 MG CAPSULE	4018	3448	$61,862.65
13	25200	FREESTYLE LITE TEST STRIP	3929	3612	$770,902.31
14	00781	GABAPENTIN 300 MG CAPSULE	3858	3150	$73,676.81

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
15	10857	METFORMIN HCL 1,000 MG TABLET	3707	3443	$61,612.77
16	45680	DICLOFENAC SODIUM 1% GEL	3671	3179	$97,512.63
17	10810	METFORMIN HCL 500 MG TABLET	3630	3214	$56,058.61
18	46430	FAMOTIDINE 20 MG TABLET	3455	3056	$50,153.80
19	39661	AMOXICILLIN 500 MG CAPSULE	3136	2925	$40,146.73
20	12486	HYDROCODONE-ACETAMIN 5-325 MG	3131	2327	$41,392.59
21	70330	HYDROCODONE-ACETAMIN 10-325 MG	3126	1387	$58,960.32
22	43720	ATORVASTATIN 10 MG TABLET	3123	2900	$44,868.52
23	40120	PANTOPRAZOLE SOD DR 40 MG TAB	3116	2635	$48,909.11
24	94422	VITAMIN D2 1.25MG(50,000 UNIT)	3064	2831	$43,399.07
25	86212	POLYETHYLENE GLYCOL 3350 POWD	2802	2601	$71,241.73
26	35744	IBUPROFEN 800 MG TABLET	2730	2360	$44,013.36
27	09101	DOCUSATE SODIUM 100 MG SOFTGEL	2658	2362	$34,514.05
28	20045	ONDANSETRON ODT 4 MG TABLET	2655	2454	$37,790.37
29	04695	FEROSUL 325 MG TABLET	2643	2375	$34,498.18
30	16391	TRAZODONE 50 MG TABLET	2521	1975	$40,160.63
31	31242	TRIAMCINOLONE 0.1% OINTMENT	2499	2327	$48,500.76
32	00223	VITAMIN D3 25 MCG TABLET	2467	2320	$29,150.40
33	14851	LOSARTAN POTASSIUM 50 MG TAB	2446	2228	$37,044.20
34	35793	NAPROXEN 500 MG TABLET	2387	2100	$40,401.12

Rank	GCN	Label Name	Claims	Unique Members	Total Cost
35	99882	VITAMIN D3 50 MCG SOFTGEL	2267	2170	$28,757.48
36	94781	FOLIC ACID 1 MG TABLET	2253	1945	$37,355.99
37	94200	FREESTYLE 28G LANCETS	2249	2144	$44,005.28
38	29840	BENZONATATE 100 MG CAPSULE	2228	2020	$31,253.84
39	34824	HYDROCHLOROTHIAZIDE 25 MG TAB	2228	2032	$29,531.32
40	48191	TAMSULOSIN HCL 0.4 MG CAPSULE	2161	1891	$36,556.91
41	14850	LOSARTAN POTASSIUM 25 MG TAB	2149	1981	$31,105.67
42	16965	ACETAMINOPHEN 500 MG TABLET	2051	1888	$19,287.39
43	14853	LOSARTAN POTASSIUM 100 MG TAB	2044	1875	$32,687.87
44	39802	CEPHALEXIN 500 MG CAPSULE	2042	1935	$28,919.75
45	30952	HYDROCORTISONE 2.5% OINTMENT	1948	1840	$33,483.13
46	35930	IBUPROFEN 100 MG/5 ML SUSP	1925	1811	$33,830.89
47	00780	GABAPENTIN 100 MG CAPSULE	1918	1642	$30,636.50
48	46431	FAMOTIDINE 40 MG TABLET	1905	1672	$28,704.49
49	13943	HYDROXYZINE HCL 25 MG TABLET	1853	1494	$30,410.70
50	42193	FLUCONAZOLE 150 MG TABLET	1818	1571	$22,184.48
TOTAL			**175,083**	**155,526**	**$3,805,809.48**

Macrolides

Executive Summary

CLASS OVERVIEW

Macrolides are a class of antibiotics used to treat a wide variety of infections caused by a range of susceptible bacteria including types of gram-positive and gram-negative aerobes, anaerobes, and other types of bacteria (e.g. mycobacteria species, H. pylori, etc.). Indications vary by product but include various URI and lower respiratory tract infections, urogenital infections, GI infections, OM (in children), and systemic infections. They are also indicated to treat SSSI although they are uncommonly used in practice in this setting due to high rates of resistance. Macrolide antibiotics are bacteriostatic. Common side effects include GI upset, diarrhea, abnormal taste, and rash; macrolides have been associated with prolonged cardiac repolarization and QTc interval. Azithromycin has a long half-life allowing for convenient dosing and a relatively low rate of drug interactions. Fidoxamicin (Dificid) is indicated only for Clostridioides (formerly Clostridium) difficile infection (CDI).

UTILIZATION FINDINGS

There were 77 claims for 73 members, for a total cost of $1,906, and an average cost per claim of $25. The most highly utilized medication was azithromycin (Zithromax®, Zithromax Z-Pak®, Zithromax TRI-PAK®) tablet, with 67 claims. There were no prior authorization requests.

RECOMMENDATIONS

- No changes

PRODUCT TABLE (4/1/2023 to 6/30/2023)

Medication	Rx	Current Status	Recommendation
Macrolides			
clarithromycin 125 mg/5 mL, 250 mg/5mL oral suspension	0	NF	No change
clarithromycin ER 500 mg tablet,extended release 24 hr	0	NF	No change
clarithromycin 250mg, 500 mg tablet	5	F	No change
erythromycin lactobionate (Erythrocin™) 500 mg intravenous solution	0	NF	No change
erythromycin ethylsuccinate (E.E.S. Granules®, EryPed®) 200 mg/5 mL oral suspension	0	F	No change
erythromycin ethylsuccinate (EryPed®) 400 mg/5 mL oral suspension	0	F	No change
erythromycin ethylsuccinate (E.E.S®) 400 mg tablet	0	F	No change
Erythrocin™ (as stearate) (erythromycin) 250 mg tablet	0	NF	No change
erythromycin 250 mg capsule,delayed release	0	F	No change
erythromycin 250 mg, 500mg tablet	4	F	No change
erythromycin 250 mg, 333 mg, 500mg (Ery-Tab®) tablet, delayed release	0	F	No change
Dificid® (fidaxomicin) 40 mg/mL oral suspension	0	NF	No change
Dificid® (fidaxomicin) 200 mg tablet	0	NF	No change
azithromycin (Zithromax®) 1 gram oral packet	0	F	No change
azithromycin (Zithromax®) 100 mg/5 mL, 200 mg/5 mL oral suspension	1	F	No change
azithromycin (Zithromax®, Zithromax Z-Pak®, Zithromax TRI-PAK®) 250 mg, 500 mg, 600 mg tablet	67	F 600mg: F-AL (min 21 yrs)	No change
azithromycin (Zithromax®) 500 mg intravenous solution	0	NF	No change

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

CLINICAL SUMMARY

Macrolides are a class of antibiotics used to treat a wide variety of infections caused by a range of susceptible bacteria including types of gram-positive and gram-negative aerobes, anaerobes, and other types of bacteria (e.g. mycobacteria species, H. pylori, etc.). Indications vary by product but include various URI and lower respiratory tract infections, urogenital infections, GI infections, OM (in children), and systemic infections. They are also indicated to treat SSSI although they are uncommonly used in practice in this setting due to high rates of resistance. Macrolide antibiotics are bacteriostatic. Common side effects include GI upset, diarrhea, abnormal taste, and rash; macrolides have been associated with prolonged cardiac repolarization and QTc interval. Azithromycin has a long half-life allowing for convenient dosing and a relatively low rate of drug interactions. Fidoxamicin (Dificid) is indicated only for CDI.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Azithromycin (Zithromax®)	Labeled Treatment of COPD exacerbations (due to *H. influenzae*, *M. catarrhalis*, or *S. pneumonia*) MAC: In adults (labeled)[#] and children (off-label) with advanced HIV infection, prevention of MAC (alone or in combination with rifabutin), treatment of disseminated MAC (in combination with ethambutol) Acute OM due to *H. influenzae*, *M. catarrhalis*, or *S. pneumonia* in children ≥ 6 months Acute bacterial sinusitis in children ≥ 6 months (FDA approved but not IDSA recommended due to *S. pneumonia* resistance) CAP due to *Chlamydophila pneumoniae*, *H. influenzae*, *Legionella pneumophila*, *M. catarrhalis*, *Mycoplasma pneumoniae*, or *S. pneumonia* Uncomplicated SSSI due to *S. aureus*, *S. pyogenes*, or *S. agalactiae*	Treatment of COPD exacerbations: 500 mg in a single loading dose on day 1, followed by 250 mg QD on days 2 to 5 or 500 mg QD for 3 days MAC[#]: – Prevention: • Primary (CD4 <50 cells/mm^3): 1,200 mg QW (preferred) or 600 mg BIW (d/c when CD4 >100 cells/mm^3 for ≥ 3 months on ART)[§] • Secondary (as part of a combination regimen): 500 to 600 mg QD (d/c after completing ≥ 12 months therapy, no signs/symptoms of MAC disease, and sustained (> 6 months) CD4 >100 cells/mm^3 in response to ART) • Children – (20 mg/kg [maximum 1,200 mg], adolescents 1200 mg) QW or 5 mg/kg (maximum 250 mg) QD – Treatment of disseminated MAC: • Adults (labeled) and adolescents (off-label) – 500 to 600 mg QD • Children (off-label) – 10 to 12 mg/kg (maximum 500 mg) QD Acute OM: – 1-day regimen: 30 mg/kg as a single dose (maximum dose: 1,500 mg) – 3-day regimen: 10 mg/kg QD for 3 days (maximum: 500 mg daily) – 5-day regimen: 10 mg/kg on day 1 (maximum: 500 mg daily) followed by 5 mg/kg/day QD on days 2 to 5 (maximum: 250 mg daily) Acute bacterial sinusitis: 10 mg/kg QD for 3 days (maximum 500 mg/day) CAP: – Adult, outpatient: 500 mg on day 1, followed by 250 mg QD for 4 days or 500 mg QD for 3 days – Adult, inpatient: 500 mg QD for ≥ 3 days – Children (≥ 6 months [labeled], > 3 months [off-label]): 10 mg/kg (maximum 500 mg) as a single dose on day 1 followed by 5 mg/kg/day (maximum 250 mg) on days 2 through 5 Uncomplicated SSSI: 500 mg on day 1, followed by 250 mg QD on days 2 through 5

Medication	Indications	Dosing/Administration
Azithromycin (Zithromax®) (*continued…*)	Pharyngitis/tonsillitis due to *S. pyogenes* (as an alternative to first-line therapy)	Pharyngitis/tonsillitis: – Group A Streptococcal pharyngitis (adults): 500 mg on day 1, followed by 250 mg QD on days 2 through 5 or 500 mg QD for 3 days – Group A Streptococcal tonsillopharyngitis (children): • Labeled: 12 mg/kg/dose QD for 5 days (maximum 500 mg/day) • Off-label, IDSA: 12 mg/kg (maximum 500 mg/dose) on day 1 followed by 6 mg/kg/dose (maximum 250 mg/dose) QD on days 2 through 5 • Off-label, 3 day regimen (not for use in infants): 20 mg/kg/dose QD for 3 days (maximum 1,000 mg/dose)
	Cervicitis, empiric	Cervicitis (empiric): 1 g as a single dose (in combination with ceftriaxone if patient risk for or local prevalence of gonorrhea is high, or follow-up is a concern)
	Urethritis and cervicitis due to *C. trachomatis* or *N. gonorrhoeae*[#]	Urethritis or cervicitis: – Due to *C. trachomatis* • Adult: 1 g as a single dose • Children and adolescents ≥ 45 kg (off-label): 1 g as a single dose – Due to *N. gonorrheoae* • 1 g as a single dose in combination with ceftriaxone[#]

Medication	Indications	Dosing/Administration
Azithromycin (Zithromax®) (*continued…*)	Off-label Acne vulgaris Babesiosis	 Acne vulgaris‖: 500 mg QD for 4 consecutive days/month for 3 months (adults and adolescents); 500 mg QD for 3 days in the first week, followed by 500 mg QW until week 10 (adults and adolescents); or 500 mg QD for 3 consecutive days each week in month 1, followed by 500 mg QD for 2 consecutive days each week in month 2, then 500 mg QD for 1 day each week in month 3 (adults only); re-evaluate at 3 to 4 months Babesiosis: – Adult, mild to moderate: 500 mg on day 1, followed by 250 mg QD in combination with atovaquone for 7 to 10 days in immunocompetent patients; higher doses of may be used in immunocompromised patients (600 to 1,000 mg/day) – Adult, severe disease: use IV formulation, may switch to oral following improvement on IV therapy) – Children: 10 mg/kg on day 1 (maximum 500 mg), followed by 5 mg/kg daily thereafter (maximum 250 mg/dose); in combination with atovaquone for 7 to 10 days as initial therapy for active disease

Medication	Indications	Dosing/Administration
Azithromycin (Zithromax®) (*continued…*)	Bronchiectasis (non-CF), prevention of pulmonary exacerbations (for patients with ≥2-3 exacerbations/year; for those who do not have P. aeruginosa infection, have P. aeruginosa but cannot take inhaled abx, or continue to have exacerbations despite inhaled abx)¶	Bronchiectasis (non-CF), prevention of pulmonary exacerbations: 500 mg TIW or 250 mg QD
	Bronchiolitis obliterans syndrome	Bronchiolitis obliterans syndrome: 250 mg QD for 5 days, followed by 250 mg TIW for at least a 3-month trial or indefinitely
	Campylobacter infection	Campylobacter infection: 1 g as a single dose or 500 mg QD for 3 days (if symptoms have not resolved after 24 hours of single-dose therapy, continue with 500 mg QD for 2 more days); for HIV-infected patients, 500 mg QD for 5 days
	Cat scratch disease	Cat scratch disease: – Adult: 500 mg as a single dose, then 250 mg QD for 4 days – Children ≥ 45.5 kg: 500 mg on day 1 followed by 250 mg QD days 2 to 5 – Children < 45.5 kg: 10 mg/kg on day 1 followed by 5 mg/kg QD days 2 to 5
	C. trachomatis: conjunctivitis (infants), infection of the pharynx, expedited partner therapy	*C. trachomatis*: – conjunctivitis: 20 mg/kg QD for 3 days – infection of the pharynx: 1 g as a single dose – expedited partner therapy: 1 g as a single dose
	Cholera	Cholera: 1 g as a single dose
	Prevention of COPD exacerbations	Prevention of COPD exacerbations: 250 to 500 mg TIW or 250 mg QD
	CF, anti-inflammatory¶	CF, anti-inflammatory: 250 mg (<40 kg) or 500 mg (≥40 kg) TIW or 250 mg QD
	Endocarditis prophylaxis (dental or invasive respiratory tract procedure)	Endocarditis prophylaxis: 500 mg (adults) or 15 mg/kg (children, maximum 500 mg) single dose 30 to 60 minutes prior to procedure
	Gonococcal infection: disseminated (arthritis, arthritis-dermatitis syndrome, meningitis, and endocarditis), uncomplicated (rectum, or pharynx; conjunctivitis), expedited partner therapy	Gonococcal infection: – disseminated (adults and adolescents): 1 g as a single dose in combination with ceftriaxone – uncomplicated proctitis or pharyngitis (adults and adolescents); conjunctivitis (adolescents): 1 g as a single dose in combination with ceftriaxone – expedited partner therapy (adults): 1 g as a single dose in combination with cefixime
	Granuloma inguinale	Granuloma inguinale: 1 g QW or 500 mg QD for ≥ 3 weeks and until lesions have healed (if symptoms do not improve within the first few days, consider adding gentamicin)
	Lyme disease	Lyme disease: 500 mg (adults) or 10 mg/kg (children, maximum 500 mg) QD for 7 to 10 days

Medication	Indications	Dosing/Administration
Azithromycin (Zithromax®) (*continued…*)	MAC pulmonary disease (nodular/bronchiectatic, in patients with CF), as part of an appropriate combination regimen	MAC pulmonary disease: – nodular/bronchiectatic: 500 to 600 mg TIW continue treatment until culture negative on therapy for ≥1 year – severe nodular/bronchiectatic: 250 to 500 mg QD continue treatment until culture negative on therapy for ≥1 year (some experts recommend checking levels and/or using higher doses due to data suggesting a relationship between peak concentration and clinical outcome) – in patients with CF: 250 to 500 mg QD continue treatment until culture negative on therapy for ≥1 year (intermittent dosing (i.e. TIW) is not recommended in CF)
	Mycobacterium abscessus infection	Mycobacterium abscessus infection: 250 to 500 mg QD, as part of an appropriate combination regimen, for ≥6 to 12 months (pulmonary and bone) and ≥4 months for (skin/soft tissue)
	Mycoplasma genitalium	Mycoplasma genitalium: (consider alternate therapy due to rapid emergence of resistance) 1 g as a single dose or 500 mg on day 1, followed by 250 mg QD on days 2 through 5
	Pertussis	Pertussis: 500 mg on day 1, followed by 250 mg QD on days 2 to 5
	STI, prophylaxis following sexual assault	STI prophylaxis (adults and adolescents): 1 g as a single dose in combination with ceftriaxone (plus metronidazole or tinidazole)
	Shigella infection	Shigella infection: 500 mg QD for 3 days (5 days for *Shigella dysenteriae* type 1 or for patients with HIV coinfection)
	Syphilis, primary and secondary	Syphilis, primary and secondary: (consider alternate therapy due to rapid emergence of resistance; do not use in patients with HIV, pregnant women, or MSM) 2 g as a single dose
	Travelers' diarrhea, empiric treatment	Travelers' diarrhea: 1 g as a single dose or 500 mg QD for 3 days (if symptoms have not resolved after 24 hours of single-dose therapy, continue with 500 mg QD for 2 more days); for dysentery or febrile diarrhea, 500 mg QD for 3 days
	Urethritis, empiric	Urethritis, empiric: 1 g as a single dose (in combination with ceftriaxone if microscopic evidence of gonococcal urethritis or high clinical suspicion for gonococcal infection)

Medication	Indications	Dosing/Administration
Clarithromycin	<u>Labeled</u> Acute bacterial exacerbation of chronic bronchitis in adults due to susceptible *H. influenzae*, *H. parainfluenzae*, *M. catarrhalis*, or *S. pneumonia*	Acute bacterial exacerbation of chronic bronchitis: – *H. influenza*: • IR tablets/oral suspension – 500 mg q12 hours for 7-14 days • ER tablets: 1000 mg for 7 days – *H. parainfluenzae*: • IR tablets/oral suspension – 500 mg q12 hours for 7 days • ER tablets: 1000 mg for 7 days – *M. catarrhalis* or *S. pneumonia*: • IR tablets/oral suspension – 250 mg q12 hours for 7-14 days • ER tablets: 1000 mg for 7 days
	Acute maxillary sinusitis (FDA approved but not IDSA recommended due to S. pneumonia resistance)	Acute maxillary sinusitis: IR tablets – 500 mg q12 hours for 14 days
	Eradication of *H. pylori* to reduce the risk of duodenal ulcer recurrence as a component of combination therapy in adults with active or 5-year history of duodenal ulcer disease[#]	*H. pylori*[#]: – Clarithromycin triple therapy: 500 mg BID + a standard- or double-dose PPI + (amoxicillin 1 g BID or metronidazole 500 mg TID) for 14 days (avoid in patients at risk for macrolide resistance) – Concomitant regimen: 500 mg BID + amoxicillin 1 g BID + a standard-dose PPI BID + (metronidazole or tinidazole 500 mg BID) for 10 to 14 days – Sequential regimen: amoxicillin 1 g BID + a standard-dose PPI BID for 5 to 7 days; then follow with clarithromycin 500 mg BID + a standard-dose PPI BID + (metronidazole or tinidazole 500 mg BID) for 5 to 7 days – Hybrid regimen: amoxicillin 1 g BID + a standard-dose PPI BID for 7 days; then follow with amoxicillin 1 g BID + clarithromycin 500 mg BID + a standard-dose PPI BID + (metronidazole or tinidazole 500 mg BID) for 7 days
	Prophylaxis and treatment of disseminated mycobacterial infections due to MAC in patients with advanced HIV infection[#]	Prophylaxis of disseminated MAC in patients with advanced HIV infection[#]: – Primary prevention, adults (CD4 <50 cells/mm^3): 500 mg BID (d/c when CD4 >100 cells/mm^3 for ≥ 3 months on ART)§ – Primary prevention, adolescents: 500 mg BID (d/c when CD4 >100 cells/mm^3 for ≥ 3 months on ART) – Primary or secondary prevention, infants and children: 7.5 mg/kg/dose (maximum 500 mg/dose) BID (for secondary prophylaxis use with ethambutol +/- rifampin)

Medication	Indications	Dosing/Administration
Clarithromycin (*continued…*)	Prophylaxis and treatment of disseminated mycobacterial infections due to MAC in patients with advanced HIV infection[#]	Treatment of disseminated mycobacterial infections due to MAC in patients with advanced HIV infection[#] – Treatment, adults and adolescents: 500 mg BID + ethambutol; consider additional agents (e.g. rifabutin, aminoglycoside, fluoroquinolone) for CD4 < 50 cells/mm^3, high mycobacterial load, or ineffective ART; may d/c if no signs/symptoms of MAC disease, CD4 > 100 cells/mm^3 has been maintained for > 6 months in response to ART, and completed ≥ 12 months of therapy – Treatment, infants and children: 7.5 to 15 mg/kg/dose (maximum 500 mg/dose) BID + ethambutol (+ rifabutin for severe disease)
	Acute OM in pediatric patients ≥ 6 months due to susceptible *H. influenzae*, *M. catarrhalis*, or *S. pneumonia*	Acute OM: 7.5 mg/kg q12 hours for 10 days (maximum 500 mg/dose)
	Pharyngitis/tonsillitis due to susceptible *S. pyogenes* (alternative agent)	Pharyngitis/tonsillitis (IR tablets, oral suspension): 250 mg (adults) or 7.5 mg/kg (children) q12 hours for 10 days
	CAP due to susceptible *M. pneumoniae*, *S. pneumoniae*, or *C. pneumoniae* (adult and pediatric patients) and *H. influenzae*, *H. parainfluenzae*, or *M. catarrhalis* (adults)	CAP: – *M. pneumoniae*, *S. pneumoniae*, *C. pneumoniae*: • Adult – IR tablets/oral suspension – 250 mg q12 hours for 7-14 days • Adult – ER tablets: 1000 mg for 7 days • Children ≥ 6 months (labeled), ≥ 3 months (off-label, *M. pneumoniae* and *C. pneumoniae* only, excludes *S. pneumoniae*) – 7.5 mg/kg BID for 10 days (maximum 500 mg/day) – *H. parainfluenzae*, *M. catarrhalis*: • ER tablets: 1000 mg for 7 days – *H. influenza*: • IR tablets/oral suspension – 250 mg q12 hours for 7 days • ER tablets: 1000 mg for 7 days – Empiric (off label): • Adult – 500 mg BID + beta-lactam for 5 days • Children – Outpatient , < 5 years old – 7.5 mg/kg (maximum 500 mg/day) BID for 7-14 days Outpatient, ≥ 5 years old – 7.5 mg/kg (maximum 1 g/day), duration not specified
	Uncomplicated SSSIs due to susceptible *S. aureus* or *S. pyogenes*	Uncomplicated SSSIs: IR tablets/oral suspension – 250 mg (adults) or 7.5 mg/kg (children) q12 hours for 7-14 days

Medication	Indications	Dosing/Administration
Clarithromycin (*continued…*)	Off-label Bartonellosis infection (treatment/long-term suppressive therapy) in HIV-infected adolescents and adults (excluding CNS infections and endocarditis) Bartonellosis infection (treatment/secondary prophylaxis) in HIV-exposed/-positive infants and children (excluding CNS infections and endocarditis) Infective endocarditis prophylaxis in patients allergic to PCN or oral ampicillin Pertussis (whooping cough) Lyme disease (early) Pharyngitis, group A streptococci in PCN-allergic patients (children) Rosacea	Bartonellosis infection, HIV-infected adolescents/adults: – Treatment: 500 mg BID for ≥ 3 months – Long-term suppression: 500 mg BID; may d/c if completed 3 to 4 months therapy and CD4 > 200 cells/mm^3 for ≥ 6 months (some clinicians would d/c only if Bartonella titers have also decreased 4-fold) Bartonellosis infection, HIV-exposed/-positive infants/children – Treatment/secondary prophylaxis: 7.5 mg/kg BID (maximum 1 g/day) for ≥ 3 months Infective endocarditis prophylaxis: 500 mg (adults) or 15 mg/kg (children) 30 to 60 minutes before procedure Pertussis: 500 mg (adults, adolescents) BID for 7 days Lyme disease: 500 mg BID for 14 to 21 days Group A streptococci pharyngitis: 7.5 mg/kg q12 hours for 7 days (maximum 500 mg/day) Rosacea: 50 mg BID for 4 weeks, followed by 250 mg QD for another 4 weeks

Medication	Indications	Dosing/Administration
Erythrocin™ (erythromycin) Erythromycin (EryPed®) Erythromycin base Ery-Tab® (erythromycin base) E.E.S.® (erythromycin ethyl succinate)	**By oral route unless otherwise noted** Labeled (covered by "Usual Dosage") Diphtheria caused by *C. diphtheria*† Erythrasma caused by *C. minutissimum*† Listeriosis caused by *Listeria monocytogenes* Prophylaxis of initial (treatment of S. pyogenes URI in PCN-allergic patients) attacks of rheumatic fever† Respiratory tract infections: – Caused by *Mycoplasma pneumonia*†‡ – Mild to moderate lower respiratory tract infections caused by *S. pneumoniae* or *S. pyogenes*†‡ – Mild to moderate URIs caused by *S. pyogenes*, *S. pneumoniae*, or *H. influenza* (in combination with sulfonamides) †‡ SSSIs of mild to moderate severity caused by *S. pyogenes* or *S. aureus*†‡ Labeled (with indication-specific dosages) Acute PID caused by *N. gonorrhoeae* in females sensitive to PCN Conjunctivitis of the newborn, pneumonia of infancy, and urogenital infections during pregnancy; treatment of uncomplicated urethral, endocervical, or rectal infections in adults caused by *C. trachomatis** Intestinal amebiasis caused by *Entamoeba histolytica* Legionnaires disease caused by *Legionella pneumophila*† Nongonococcal urethritis caused by *Ureaplasma urealyticum**†	**400 mg EES produces the same serum levels as 250 mg erythromycin base or stearate** Usual Dosage Adults: Base and stearate: 250 mg q6 hours, 333 mg q8 hours (base only), or 500 mg q12 hours (BID dose not recommended for doses > 1 g/day) EES: 400 to 800 mg every 6 to 12 hours Children: 30 to 50 mg/kg/day in 2 to 4 divided doses (may double dose, up to maximum of 4g/day, for severe infections) (Max 4 g/day relative to infection severity) Indication-specific Dosages PID: 500 mg erythromycin injection q6 hours for 3 days, followed by 500 mg erythromycin (base) PO q12 hours, 333 mg (base) PO q8 hours or 250 mg (base) PO q6 hours for 7 days Conjunctivitis of the newborn: 50 mg/kg/day in 4 divided doses for at least 2 weeks Pneumonia of infancy: 50 mg/kg/day in 4 divided doses for at least 3 weeks Urogenital infections during pregnancy: 250 mg (base) QID for 14 days or 500 mg (base) QID for 7 days** C. trachomatis infection, uncomplicated: – Lymphogranuloma venereum (alternative therapy to doxycycline), off-label: 500 mg (base) QID for 21 days – Urogenital infection, off-label: 500 mg (base) QID or 800 mg (EES) QID for 7 days Intestinal amebiasis: – Adult: 500 mg (base or stearate) q12 hours, 333 mg (base) q8 hours, 250 mg (base or stearate) q6 hours, or 400 mg (EES) QID for 10 to 14 days – Children: 30 to 50 mg/kg/day in divided doses for 10 to 14 days Legionnaires: 1 to 4 g (base or stearate) daily or 1.6 to 4 g (EES) daily in divided doses Nongonococcal urethritis: 500 mg (base) QID or 800 mg (EES) QID for 7 days

Medication	Indications	Dosing/Administration
Erythrocin™ (erythromycin) Erythromycin (EryPed®) Ery-Tab® (erythromycin base) E.E.S.® (erythromycin ethyl succinate) Erythromycin base (*continued…*)	Labeled (with indication-specific dosages) (*continued…*) Pertussis (whooping cough) caused by *Bordetella pertussis* (not preferred agent in children < 1 month) Prophylaxis of recurrent (in PCN- and sulfonamide-allergic patients) attacks of rheumatic fever† Pre-operative, prophylactic colorectal decontamination (off-label in children ≥ 1 year) Primary syphilis caused by *Treponema pallidum*^ Off-label Acne vulgaris *Bartonella* spp. infections including cutaneous BA and BA, PH, bacteremia, osteomyelitis, and other severe infections (excluding CNS infections or endocarditis) in HIV-infected patients Chancroid due to H. ducreyi Impetigo Prevention of COPD exacerbations Gastroparesis Granuloma inguinale when azithromycin is not appropriate Lyme disease	Indication-specific Dosages (*continued…*) Pertussis: – Adult: 500 mg (base) q6 hours for 14 days – Children: 40 to 50 mg/kg/day in 4 divided doses for 14 days Rheumatic fever – Prevention of recurrent attacks: 250 mg (base or stearate) or 400 mg (EES) BID Pre-operative, prophylactic colorectal decontamination: – Adult: 1 g (base) per dose at 1 PM, 2 PM, and 11 PM on the day before surgery – Children: 20 mg (base)/kg at 1 PM, 2 PM, and 11 PM on the day before surgery Syphilis: 30 to 40 g (base or stearate) or 48 to 64 g (EES) in divided doses over a period of 10 to 15 days Acne vulgaris‖: 250 to 500 mg (base) BID initially, followed by 250 to 500 mg (base) QD (re-evaluate at 3 to 4 months) Bartonella spp. infections: – Non-HIV-infected adults: 500 mg (base) QID for 3 months (BA) or 4 months (PH) – Non-HIV-infected children: 40 mg/kg/day (EES) in 4 divided doses (maximum 2 g/day) for 3 months (BA) or 4 months (PH) – HIV-infected adults and adolescents: 500 mg (base) q6 hours (BA, PH, bacteremia, and osteomyelitis); 500 mg (base) q6 hours + rifampin (other severe infections excluding CNS infections or endocarditis); continue for ≥ 3 months depending on relapse occurrence and clinical condition) Chancroid: 500 mg (base) TID for 7 days Impetigo: – Adult: 250 mg (base) or 400 mg (EES) QID for 7 days – Children: 40 mg/kg/day in 3 to 4 divided doses for 7 days COPD exacerbation prophylaxis: 200 to 400 mg/day (formulation not specified) or 250 mg (stearate) BID Gastroparesis: 250 to 500 mg (base) TID before meals (limit duration, tachyphylaxis may occur after 4 weeks) Granuloma inguinale: 500 mg (base) QID for at least 3 weeks or until lesion is healed Lyme disease: 500 mg (base) QID for 14 to 21 days

Medication	Indications	Dosing/Administration
Dificid® (fidaxomicin)	CDI	200 mg BID for 10 days

*When TCNs are contraindicated or not tolerated
^Not recommended by the Center for Disease Control
†Oral and injection routes
‡In children by injection route of administration only
**Current practice, not from prescribing information which is inconsistent with current clinical practice
§Some experts do not recommend routine initiation of MAC primary prophylaxis, regardless of initial CD4 count in the setting of prompt ART initiation and subsequent viral suppression
‖Use shortest duration possible to minimize bacterial resistance
¶ Patients should be screened for NTM; if positive, azithromycin should not be given
# Indication is labeled but dosing listed is off-label due to labeled dosing inconsistent with best clinical practice

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Azithromycin (Zithromax®)	None	All: Hypersensitivity to the active ingredient (azithromycin – angioedema, anaphylaxis, SJS, TEN, DRESS have been reported; clarithromycin – SJS, TEN, DRESS, Henoch-Schönlein purpura [IgA vasculitis], and acute generalized exanthematous pustulosis have been reported), other macrolide or ketolide, or any component of the formulation Azithromycin and clarithromycin: History of cholestatic jaundice/hepatic dysfunction associated with prior use Clarithromycin and erythromycin: Concurrently with drugs metabolized by CYP3A4 (e.g. cisapride, pimozide, ergotamine, dihydroergotamine, lovastatin, simvastatin) Azithromycin: pimozide is not listed as a contraindication in the azithromycin PI, but azithromycin is listed as a contraindication in the pimozide PI due to the potential for CYP3A4 inhibition Clarithromycin: together with colchicine in patients with renal or hepatic impairment
Clarithromycin		
Erythrocin™ (erythromycin) Erythromycin (EryPed®) Ery-Tab® (erythromycin base) E.E.S.® (erythromycin ethyl succinate) Erythromycin base		
Dificid® (fidaxomicin)		Hypersensitivity to fidaxomicin

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Azithromycin (Zithromax®) Clarithromycin Erythrocin™ (erythromycin) Erythromycin (EryPed®) Ery-Tab® (erythromycin base) E.E.S.® (erythromycin ethyl succinate) Erythromycin base	Concerns related to AEs: – Altered cardiac conduction: Macrolides (especially erythromycin) have been associated with QT prolongation and infrequent cases of arrhythmias, including torsades de pointes (may be fatal) – Use may result in fungal or bacterial superinfection, including CDI (>2 months post-treatment) and pseudomembranous colitis – Azithromycin only: Possibility of increased cardiac mortality associated with higher baseline CV risk in some studies but not others – Clarithromycin, erythromycin: Elevated LFTs and hepatitis have been reported; usually reversible upon discontinuation. May lead to hepatic failure or death (rarely) Disease-related concerns: – Caution in myasthenia gravis; exacerbation and new onset of symptoms have occurred – Caution in hepatic impairment – Azithromycin only: May mask or delay symptoms of gonorrhea or syphilis, appropriate culture and susceptibility tests should be performed prior to initiating treatment – Clarithromycin only: Caution in patients with CAD; possible increased in risk of all-cause mortality ≥1 year after the end of treatment – Azithromycin, clarithromycin: Caution in severe renal impairment (clarithromycin requires dose adjustment) Concurrent drug therapy issues: – Potentially significant DDIs may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy – Avoid in patients receiving Class IA or Class III antiarrhythmic agents or other drugs known to prolong the QT interval – Erythromycin: Major inhibitor of CYP3A4, high potential for DDIs; caution with agents substantially metabolized by CYP3A4; avoid concurrent use with strong CYP3A4 inhibitors, may increase the risk of sudden cardiac death Special populations: – Elderly: Caution, increased risk of QT prolongation or torsades de pointes and hearing loss (erythromycin only) – Azithromycin, erythromycin: Has been associated with IHPS in neonates, infants – Clarithromycin: Decreased survival has been observed in HIV patients with MAC receiving clarithromycin doses exceeding the recommended maximum Dosage form specific issues: – Clarithromycin: • ER tablets have been reported present in the stool, particularly in patients with anatomic or functional GI disorders with decreased transit times; consider alternative dosage forms or an alternative antimicrobial • Some dosage forms may contain propylene glycol large amounts of which may be toxic and have been associated hyperosmolality, lactic acidosis, seizures, and respiratory depression – Some dosage forms may contain benzyl alcohol large amounts of which have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates Other warnings/precautions: – Clarithromycin: *H. pylori*: Short-term combination therapy (≤7 days) has been associated with a higher incidence of treatment failure
Dificid® (fidaxomicin)	Other warnings/precautions: – Do not use for systemic infections; systemic absorption is negligible

PRACTICE GUIDELINES

Archived IDSA guidelines for Streptococcal Pharyngitis (published 2012) were not included. No corresponding, current guidelines in the United States or internationally are available.

Metlay JP, Waterer GW, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019 Oct 1;200(7):e45-e67. doi: 10.1164/rccm.201908-1581ST. PMID: 31573350; PMCID: PMC6812437.

Antibiotics recommended for empiric treatment of community acquired pneumonia (CAP) in adults in the outpatient setting:

For healthy outpatient adults without comorbididies or risk factors for antibiotic resistant pathogens:

- amoxicillin 1 g three times daily (strong recommendation, moderate quality of evidence), or
- doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence), or
- a macrolide (azithromycin 500 mg on first day then 250 mg daily or clarithromycin 500 mg twice daily or clarithromycin extended release 1,000 mg daily) only in areas with pneumococcal resistance to macrolides <25% (conditional recommendation, moderate quality of evidence).

For outpatient adults with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes; alcoholism; malignancy; or asplenia:

- combination therapy with amoxicillin/clavulanate 500 mg/125 mg three times daily, or amoxicillin/clavulanate 875 mg/125 mg twice daily, or 2,000 mg/125 mg twice daily, or a cephalosporin (cefpodoxime 200 mg twice daily or cefuroxime 500 mg twice daily); AND macrolide (azithromycin 500 mg on first day then 250 mg daily, clarithromycin [500 mg twice daily or extended release 1,000 mg once daily]) (strong recommendation, moderate quality of evidence for combination therapy), or doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence for combination therapy); OR
- monotherapy with a respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily, or gemifloxacin 320 mg daily) (strong recommendation, moderate quality of evidence).

Antibiotic regimens recommended for empiric CAP treatment in adults in the inpatient setting without risk factors for MRSA and P. aeruginosa:

In inpatient adults with nonsevere CAP without risk factors for MRSA or *P. aeruginosa:*

- combination therapy with a β-lactam (ampicillin + sulbactam 1.5–3 g every 6 h, cefotaxime 1–2 g every 8 h, ceftriaxone 1–2 g daily, or ceftaroline 600 mg every 12 h) and a macrolide (azithromycin 500 mg daily or clarithromycin 500 mg twice daily) (strong recommendation, high quality of evidence), or
- monotherapy with a respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily) (strong recommendation, high quality of evidence).

An option for adults with CAP who have contraindications to both macrolides and fluoroquinolones:

- combination therapy with a β-lactam (ampicillin + sulbactam, cefotaxime, ceftaroline, or ceftriaxone, doses as above) and doxycycline 100 mg twice daily (conditional recommendation, low quality of evidence).

In inpatient adults with severe CAP without risk factors for MRSA or *P. aeruginosa*:

- a β-lactam plus a macrolide (strong recommendation, moderate quality of evidence); or
- a β-lactam plus a respiratory fluoroquinolone (strong recommendation, low quality of evidence).

Recommendation Definitions:

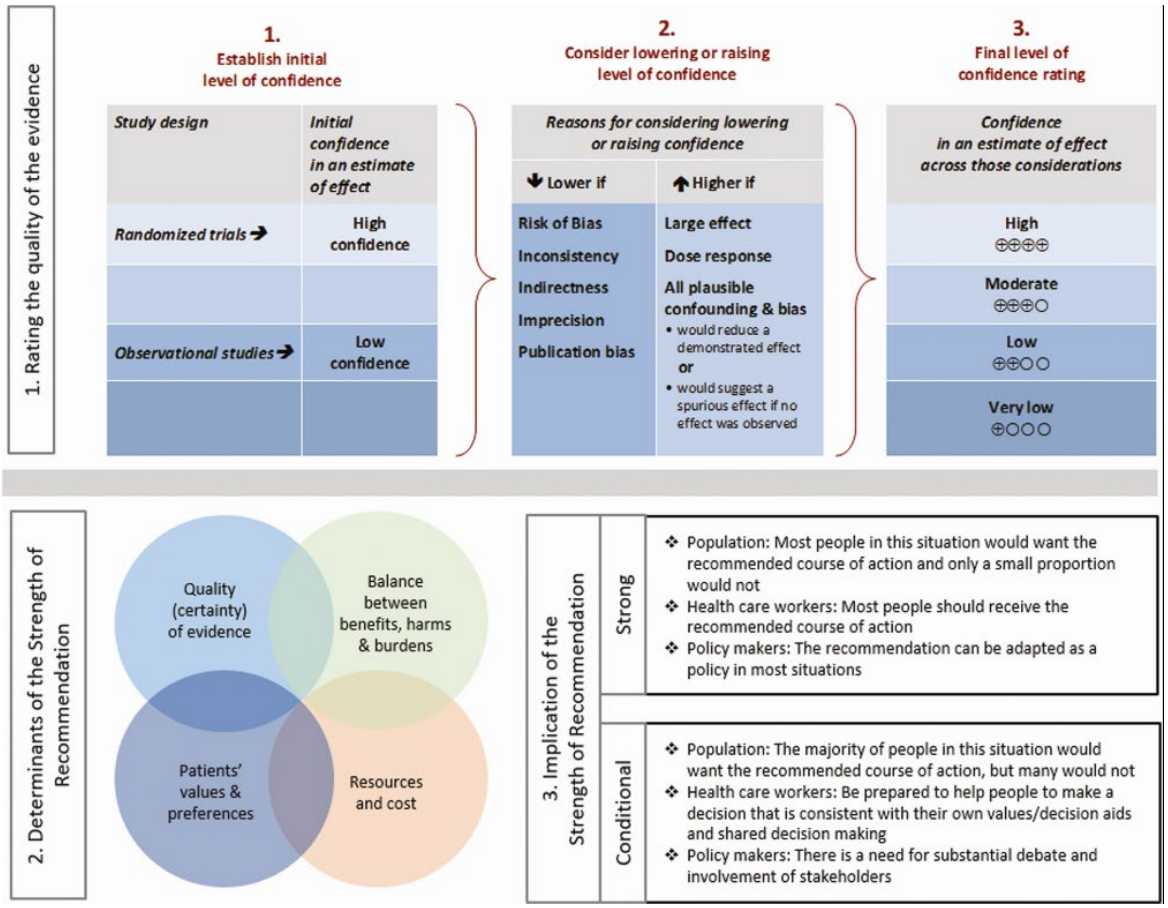
"We followed the GRADE standards for evaluating the evidence for each Population, Intervention, Comparison, Outcome (PICO)and assigned a quality of evidence rating of high, moderate, low, or very low. On the basis of the quality of evidence, recommendations were assigned as strong or conditional. In some cases, strong recommendations were made in the setting of low or very low quality of evidence in accordance with the GRADE rules for when such recommendations are allowable (e.g., when the consequences of the recommendation were high, such as preventing harm or saving life). In all other cases,

recommendations that were based on low or very low quality of evidence and not believed to represent standards of care were labeled as conditional recommendations. Statements in favor of strong recommendations begin with the words "We recommend . . ."; statements in favor of conditional recommendations begin with the words "We suggest . . . ." Although we specified pairwise PICO questions for all antibiotic options in the outpatient and inpatient settings, we summarized the recommendations using lists of treatment options, in no preferred order, rather than retain the PICO format for this section."

Johnson S, Lavergne V, Skinner AM, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. 2021; 73(5):e1029-e1044

- For patients with an initial CDI episode, we suggest using fidaxomicin rather than a standard course of vancomycin (conditional recommendation, moderate certainty of evidence). Comment: This recommendation places a high value in the beneficial effects and safety of fidaxomicin, but its implementation depends upon available resources. Vancomycin remains an acceptable alternative.
- In patients with recurrent CDI episodes, we suggest fidaxomicin (standard or extended-pulsed regimen) rather than a standard course of vancomycin (conditional recommendation, low certainty evidence). Comment: Vancomycin in a tapered and pulsed regimen or vancomycin as a standard course are acceptable alternatives for a first CDI recurrence. For patients with multiple recurrences, vancomycin in a tapered and pulsed regimen, vancomycin followed by rifaximin, and fecal microbiota transplantation are options in addition to fidaxomicin.
    - The opinion of the panel is that appropriate antibiotic treatments for at least 2 recurrences (i.e., 3 CDI episodes) should be tried prior to offering fecal microbiota transplantation.

Recommendation Definitions



Workowski KA, Bachmann LH, Chan PA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2021. MMWR Recomm Rep. 2021;70(RR-03):1-192. Available at: https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

Diseases Characterized by Genital, Anal, or Perianal Ulcers

- Chancroid
  - Azithromycin 1 g orally in a single dose
    OR
  - Ceftriaxone 250 mg IM in a single dose
    OR
  - Ciprofloxacin 500 mg orally two times a day for 3 days
    OR
  - Erythromycin base 500 mg orally three times a day for 7 days
- Granuloma inguinale (donovanosis)
  - Recommended Regimen
    - Azithromycin 1 g orally once per week or 500 mg daily for at least 3 weeks and until all lesions have completely healed
  - Alternative Regimens
    - Doxycycline 100 mg orally BID for at least 3 weeks and until all lesions have completely healed
    - Erythromycin base 500 mg orally QID for at least 3 weeks and until all lesions have completely healed
      OR
    - Trimethoprim-sulfamethoxazole one double-strength (160 mg/800 mg) tablet orally BID for at least 3 weeks and until all lesions have completely healed
- Lymphogranuloma Venereum
  - Recommended Regimen
    - Doxycycline 100 mg orally BID for 21 days
  - Alternative Regimen
    - Erythromycin base 500 mg orally QID for 21 days

Syphilis

- Primary and Secondary Syphilis
  - Recommended Regimen for Adults
    - Benzathine penicillin G 2.4 million units IM in a single dose
  - Recommended Regimen for Infants and Children
    - Benzathine penicillin G 50,000 units/kg IM, up to the adult dose of 2.4 million units in a single dose
  - PCN allergy
    - Doxycycline (100 mg orally 2 times/day for 14 days) and tetracycline (500 mg orally 4 times/day for 14 days) have been used for years and can be effective. Compliance is likely to be better with doxycycline than tetracycline because tetracycline can cause more gastrointestinal side effects and requires more frequent dosing. Limited clinical studies, along with biologic and pharmacologic evidence, indicate that ceftriaxone (1 g daily either IM or IV for 10 days) is effective for treating primary and secondary syphilis; however, the optimal dose and duration of ceftriaxone therapy have not been defined. Azithromycin as a single 2-g oral dose has been effective for treating primary and secondary syphilis among certain populations. However, because of T. pallidum chromosomal mutations associated with azithromycin and other macrolide resistance and documented treatment failures in multiple U.S. geographic areas, azithromycin should not be used as treatment for syphilis.

Diseases Characterized by Urethritis and Cervicitis

- Nongonococcal Urethritis
  - Recommended Regimens
    - Doxycycline 100 mg orally 2 times/day for 7 days
  - Alternative Regimens
    - Azithromycin 1 g orally in a single dose
      OR
    - Azithromycin 500 mg orally in a single dose; then 250 mg orally daily for 4 days
- Cervicitis
  - Recommended Regimens for Presumptive Treatment (consider concurrent treatment for gonococcal infection if patient is at risk for gonorrhea or lives in a community where the prevalence of gonorrhea is high)
    - Azithromycin 1 g orally in a single dose
      OR
    - Doxycycline 100 mg orally 2 times/day for 7 days

Chlamydia

- Non-pregnant adults
  - Recommended Regimen
    - Doxycycline 100 mg orally 2 times/day for 7 days
  - Alternative Regimens
    - Levofloxacin 500 mg orally QD for 7 days
      OR
    - Azithromycin 1 g orally in a single dose

- Pregnancy
  - Recommended Regimens
    - Azithromycin 1 g orally in a single dose
  - Alternative Regimens
    - Amoxicillin 500 mg orally TID for 7 days

  *An association between oral erythromycin and azithromycin and IHPS has been reported in infants aged <6 weeks. Infants treated with either of these antimicrobials should be followed for signs and symptoms of IHPS.
- Infant Pneumonia Caused by C. trachomatis
  - Recommended Regimen
    - Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days
  - Alternative Regimen
    - Azithromycin 20 mg/kg/day orally, 1 dose QD for 3 days
- Chlamydial Infections Among Infants and Children
  - Recommended Regimen for Infants and Children Who Weigh <45 kg
    - Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into 4 doses daily for 14 days
      (Data are limited on the effectiveness and optimal dose of azithromycin for the treatment of chlamydial infection in infants and children who weigh <45 kg)
  - Recommended Regimen for Children Who Weigh ≥45 kg but Who Are Aged <8 Years
    - Azithromycin 1 g orally in a single dose
  - Recommended Regimens for Children Aged ≥8 years
    - Azithromycin 1 g orally in a single dose
      OR
    - Doxycycline 100 mg orally BID for 7 days

<u>Gonococcal Infections in Adolescents and Adults</u>

- Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum
  - Recommended Regimen
    - Ceftriaxone 500 mg IM in a single dose for persons weighing <150 kg
    - If chlamydial infection has not been excluded, treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days
    - For persons weighing >150 kg, 1 g ceftriaxone should be administered
  - Alternative Regimens (if ceftriaxone is not available)
    - Gentamicin 240 mg IM in a single dose
      PLUS
    - Cefixime 800 mg orally in a single dose
      OR
    - Azithromycin 2 g orally in a single dose
- Uncomplicated Gonococcal Infections of the Pharynx
  - Recommended Regimen
    - Ceftriaxone 500 mg IM in a single dose for persons weighing <150 kg
    - For persons weighing >150 kg, 1 g ceftriaxone should be administered

- Gonococcal Conjunctivitis
  - Recommended Regimen
    - Ceftriaxone 1 g IM in a single dose
- Disseminated Gonococcal Infection (DGI)
  Treatment of Arthritis and Arthritis-Dermatitis Syndrome
  - Recommended Regimen
    - Ceftriaxone 1 g IM or IV every 24 hours
    - If chlamydia infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days
  - Alternative Regimens
    - Cefotaxime 1 g IV every 8 hours
      OR
    - Ceftizoxime 1 g IV every 8 hours

  Treatment of Gonococcal Meningitis and Endocarditis
  - Recommended Regimen
    - Ceftriaxone 1–2 g IV every 12–24 hours
    - If chlamydia infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally 2 times/day for 7 days

<u>Gonococcal Infections among Neonates</u>

- Ophthalmia Neonatorum
  Prophylaxis
  - Recommended Regimen
    - Erythromycin (0.5%) ophthalmic ointment in each eye in a single application at birth

  Treatment
  - Recommended Regimen
    - Ceftriaxone 25-50 mg/kg IV or IM in a single dose, not to exceed 250 mg
- DGI and Gonococcal Scalp Abscesses in Neonates
  - Recommended Regimens
    - Ceftriaxone 25–50 mg/kg/day IV or IM in a single daily dose for 7 days, with a duration of 10–14 days if meningitis is documented
    - OR
    - Cefotaxime 25 mg/kg IV or IM every 12 hours for 7 days, with a duration of 10–14 days if meningitis is documented
- Neonates Born to Mothers Who Have Gonococcal Infection
  - Recommended Regimen in the Absence of Signs of Gonococcal Infection
    - Ceftriaxone 25–50 mg/kg IV or IM in a single dose, not to exceed 250 mg

<u>Gonococcal Infections among Infants and Children</u>

  - Recommended Regimen for Infants and Children Who Weigh ≤45 kg and Who Have Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis
    - Ceftriaxone 25–50 mg/kg IV or IM in a single dose, not to exceed 250 mg IM
  - Recommended Regimen for Children Who Weigh >45 kg and Who Have Uncomplicated Gonococcal Vulvovaginitis, Cervicitis, Urethritis, Pharyngitis, or Proctitis
    - Treat with one of the regimens recommended for adults (see Gonococcal Infections)
  - Recommended Regimen for Children Who Weigh ≤45 kg and Who Have Bacteremia or Arthritis
    - Ceftriaxone 50 mg/kg (maximum dose: 2 g) IM or IV in a single dose daily for 7 days
  - Recommended Regimen for Children Who Weigh >45 kg and Who Have Bacteremia or Arthritis
    - Ceftriaxone 1 g IM or IV in a single dose daily every 24 hours for 7 days

<u>Pelvic Inflammatory Disease (PID)</u>

- Recommended Parenteral Regimens for PID

- Ceftriaxone 1 g every 24 hours
  PLUS
- Doxycycline 100mg orally or IV every 12 hours
  PLUS
- Metronidazole 500 mg orally or IV every 12 hours
  OR
- Cefotetan 2 g IV every 12 hours
  PLUS
- Doxycycline 100 mg orally or IV every 12 hours
  OR
- Cefoxitin 2 g IV every 6 hours
  PLUS
- Doxycycline 100 mg orally or IV every 12 hours

- Alternative Parenteral Regimens
  - Ampicillin-sulbactam 3 g IV every 6 hours
    PLUS
  - Doxycycline 100 mg orally or IV every 12 hours
    OR
  - Clindamycin 900 mg IV every 8 hours
    PLUS
  - Gentamicin loading dose IV or IM (2mg/kg body weight) followed by a maintenance dose (1.5mg/kg body weight) every 8 hours
- Recommended Intramuscular or Oral Regimens for PID
  - Ceftriaxone 500 mg IM in a single dose
    PLUS
  - Doxycycline 100 mg orally 2 times/day for 14 days with metronidazole 500 mg orally 2 times/day for 14 days
    OR
  - Cefoxitin 2 g IM in a single dose and probenecid 1 g orally administered concurrently in a single dose
    PLUS
  - Doxycycline 100 mg orally 2 times/day for 14 days with metronidazole 500 mg orally 2 times/day for 14 days
    OR
  - Other parenteral third-gen cephalosporin (e.g. ceftizoxime or cefotaxime)
    PLUS
  - Doxycycline 100 mg orally 2 times/day for 14 days with metronidazole 500 mg orally 2 times/day for 14 days

Recommendation Definitions

Class/Level	Definition	Suggestion for this Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.

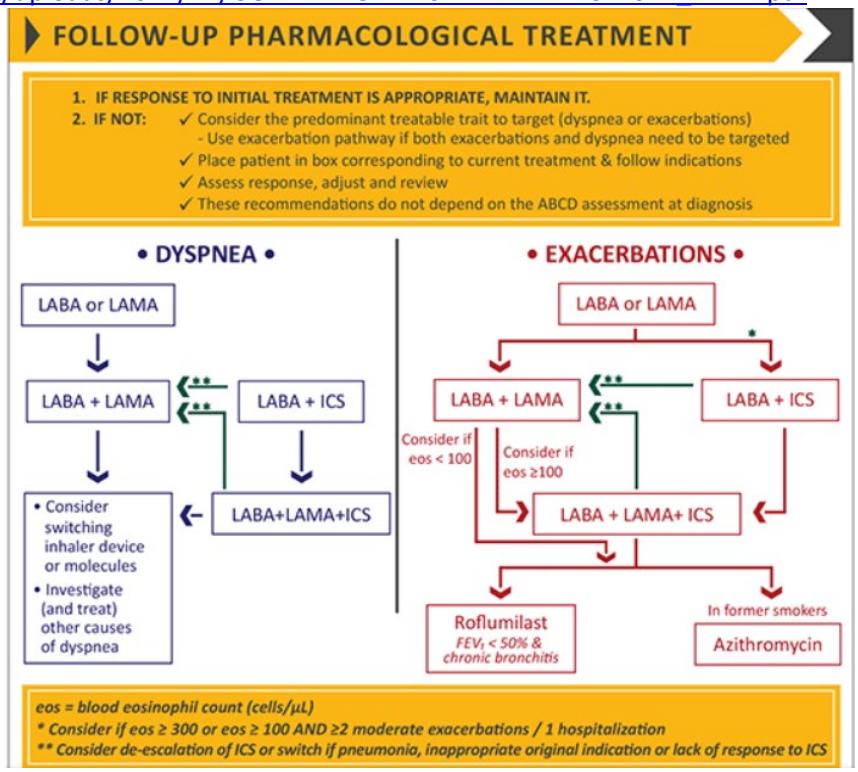
Class/Level	Definition	Suggestion for this Practice
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I (statement)	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

Class/Level	Definition
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: • The number, size, or quality of individual studies. • Inconsistency of findings across individual studies. • Limited generalizability of findings to routine primary care practice. • Lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies. • Important flaws in study design or methods. • Inconsistency of findings across individual studies. • Gaps in the chain of evidence. • Findings not generalizable to routine primary care practice. • Lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.

*The USPSTF defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of chronic obstructive pulmonary disease: 2022 Report. https://goldcopd.org/wp-

content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf



Recommendation Definitions

Recommendations		
	Sources of Evidence	**Definition**
A	Randomized controlled trials (RCTs) Rich body of high quality evidence without any significant limitation or bias	Evidence is from endpoints of well-designated RCTs that provide consistent findings in the population for which the recommendation is made without any important limitations. Requires high evidence from >2 clinical trials involving a substantial number of subjects, or a single high quality RCT involving substantial numbers of patient without any bias.
B	Randomized controlled trials (RCTs) Limited body of evidence	Evidence is from RCTs that include only a limited number of patients, post hoc or subgroup analyses of RCTs or meta analyses of RCTs. Also pertains when few RCTs exist, or important limitations are evident (methodologic flaws, small numbers, short duration, undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent).
C	Non-randomized trials Observational studies	Evidence is from outcomes of uncontrolled or non-randomized trials or from observational studies.
D	Panel consensus judgement	Provision of guidance is deemed valuable but clinical literature addressing the subject is insufficient. Panel consensus is based on clinical experience or knowledge that does not meet the above stated criteria.

Papi A, Rabe KF, Rigau D, et al. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J 2017; 49: 1600791. https://doi.org/10.1183/13993003.00791-2016.

- Should antibiotics be administered to ambulatory patients who are having a COPD exacerbation? ERS/ATS recommendation

For ambulatory patients having a COPD exacerbation, we suggest the administration of antibiotics (conditional recommendation, moderate quality of evidence). Antibiotic selection should be based upon local sensitivity patterns.

Recommendation Definitions

Recommendation	Definition
Strong	For an intervention when the panel was certain that the desirable consequences of the intervention outweighed the undesirable consequences or against an intervention if the panel was certain that the undesirable consequences of the intervention outweigh the desirable consequences. A strong recommendation indicates that most well-informed patients would choose to have or not to have the intervention.
Conditional	For an intervention when the panel was uncertain that the desirable consequences of the intervention outweighed the undesirable consequences or against an intervention if the panel was uncertain that the undesirable consequences of the intervention outweigh the desirable consequences. A conditional recommendation indicates that well-informed patients may make different choices regarding whether to have or not have the intervention.

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

^ From the GRADE series of papers.

Daley CL, Iaccarino JM, Lange C, et al. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. Clinical Infectious Diseases. 2020; 71(4):905-913.
https://doi.org/10.1093/cid/ciaa1125

- Mycobacterium avium Complex
  - In patients with macrolide-susceptible MAC pulmonary disease we suggest azithromycin-based treatment regimens rather than clarithromycin-based regimens (conditional recommendation, very low certainty in estimates of effect).
    - The panel felt that azithromycin was preferred over clarithromycin because of better tolerance, less drug-interactions, lower pill burden, single daily dosing, and equal efficacy. However, when azithromycin is not available or not tolerated, clarithromycin is an acceptable alternative.

Recommendation Definitions

Recommendations		
	Strong	**C**onditional
Patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the intervention. Adherence to the recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at ta management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their values and preferences.
Policy makers	The recommendation can be adopted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.

Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf.

- Disseminated MAC Disease
  Preferred Therapy
  - At Least 2 Drugs as Initial Therapy With:
    - Clarithromycin 500 mg PO BID (AI) + ethambutol 15 mg/kg PO daily (AI), or
    - (Azithromycin 500–600 mg + ethambutol 15 mg/kg) PO daily (AII) if drug interaction or intolerance precludes the use of clarithromycin
  - Duration:
    - At least 12 months of therapy, can discontinue if no signs and symptoms of MAC disease and sustained (>6 months) CD4 count >100 cells/µL in response to ART
- Alternative Therapy
  - Addition of a third or fourth drug should be considered for patients with advanced immunosuppression (CD4 counts <50 cells/µL), high mycobacterial loads (>2 log CFU/mL of blood), or in the absence of effective ART (CIII).
  - Third or Fourth Drug Options May Include:
    - RFB 300 mg PO daily (dosage adjustment may be necessary based on drug interactions) (CI),
    - Amikacin 10–15 mg/kg IV daily (CIII) or Streptomycin 1 g IV or IM daily (CIII)], or
    - Moxifloxacin 400 mg PO daily (CIII) or Levofloxacin 500 mg PO daily (CIII)
- Other Comments
  - Testing of susceptibility to clarithromycin and azithromycin is recommended (BIII).

Recommendation Definitions

Strength of Recommendation	Definition	Quality of Evidence	Definition
A	Strong recommendation for the statement	I	One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
B	Moderate recommendation for the statement	II	One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
C	Optional recommendation for the statement	III	Expert opinion

Stevens DL, Bisno AL, Chambers HF, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases, Volume 59, Issue 2, 15 July 2014, Pages e10–e52, https://doi.org/10.1093/cid/ciu296.

- Patients with Recurrent Cellulitis: What Is the Preferred Evaluation and Management of Patients With Recurrent Cellulitis?
  - Identify and treat predisposing conditions such as edema, obesity, eczema, venous insufficiency, and toe web abnormalities (strong, moderate). These practices should be performed as part of routine patient care and certainly during the acute stage of cellulitis (strong, moderate).
  - Administration of prophylactic antibiotics, such as oral penicillin or erythromycin bid for 4–52 weeks, or intramuscular benzathine penicillin every 2–4 weeks, should be considered in patients who have 3–4 episodes of cellulitis per year despite attempts to treat or control predisposing factors (weak, moderate). This program should be continued so long as the predisposing factors persist (strong, moderate).
- Evaluation and Treatment of Bacillary Angiomatosis and Cat Scratch Disease: What Is the Appropriate Approach for the Evaluation and Treatment of Bacillary Angiomatosis and Cat Scratch Disease?

- Azithromycin is recommended for cat scratch disease (strong, moderate) according to the following dosing protocol:
  - Patients >45 kg: 500 mg on day 1 followed by 250 mg for 4 additional days (strong, moderate).
  - Patients <45 kg: 10 mg/kg on day 1 and 5 mg/kg for 4 more days (strong, moderate).
- Erythromycin 500 mg QID or doxycycline 100 mg bid for 2 weeks to 2 months is recommended for treatment of bacillary angiomatosis (strong, moderate).

Recommendation Definitions

Strength of Recommendation and Quality of Evidence	Clarity of Balance Between Desirable and Undesirable Effects	Methodological Quality of Supporting Evidence (Examples)	Implications
Strong recommendation, high-quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research is unlikely to change our confidence in the estimate of effect
Strong recommendation, moderate quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Strong recommendation, low-quality quality evidence	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence	Recommendation may change when higher-quality evidence becomes available. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Strong recommendation, very low-quality evidence (very rarely applicable)	Desirable effects clearly outweigh undesirable effects, or vice versa	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher-quality evidence becomes available; any estimate of effect for at least 1 critical outcome is very uncertain
Weak recommendation, high-quality evidence	Desirable effects closely balanced with undesirable effects	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patient's or societal values. Further research is unlikely to change our confidence in the estimate of effect
Weak recommendation, moderate-quality evidence	Desirable effects closely balanced with undesirable effects	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Weak recommendation, low-quality evidence	Uncertainty in the estimates of desirable effects, harms, and burden; desirable effects, harms, and burden may be closely balanced	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Weak recommendation, very low-quality evidence	Major uncertainty in the estimates of desirable effects, harms, and burden; desirable effects may or may not be balanced with undesirable effects	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least 1 critical outcome, is very uncertain

Lieberthal AS, Carroll AE, Chonmaitree T, et al. The Diagnosis and Management of Acute Otitis Media. Pediatrics. 2013 Mar;131(3):e964-99. doi: 10.1542/peds.2012-3488.

- Clinicians should prescribe amoxicillin for AOM when a decision to treat with antibiotics has been made and the child has not received amoxicillin in the past 30 days or the child does not have concurrent purulent conjunctivitis or the child is not allergic to penicillin. Evidence Quality: Grade B. Strength: Recommendation.
- Clinicians should prescribe an antibiotic with additional β-lactamase coverage for AOM when a decision to treat with antibiotics has been made, and the child has received amoxicillin in the last 30 days or has concurrent purulent conjunctivitis, or has a history of recurrent AOM unresponsive to amoxicillin. Evidence Quality: Grade C. Strength: Recommendation.
- Note: Macrolides, such as erythromycin and azithromycin, have limited efficacy against both *H. influenzae* and *S. pneumoniae*

Recommendation Definitions

Class/Level	Definition	Implication
Strong Recommendation	A strong recommendation in favor of a particular action is made when the anticipated benefits of the recommended intervention clearly exceed the harms (as a strong recommendation against an action is made when the anticipated harms clearly exceed the benefits) and the quality of the supporting evidence is excellent. In some clearly identified circumstances, strong recommendations may be made when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
Recommendation	A recommendation in favor of a particular action is made when the anticipated benefits exceed the harms, but the quality of evidence is not as strong. Again, in some clearly identified circumstances, recommendations may be made when high-quality evidence is impossible to obtain but the anticipated benefits outweigh the harms	Clinicians would be prudent to follow a recommendation but should remain alert to new information and sensitive to patient preferences
Option	Options define courses that may be taken when either the quality of evidence is suspect or carefully performed studies have shown little clear advantage to 1 approach over another	Clinicians should consider the option in their decision-making, and patient preference may have a substantial role
No Recommendation	No recommendation indicates that there is a lack of pertinent published evidence and that the anticipated balance of benefits and harms is presently unclear	Clinicians should be alert to new published evidence that clarifies the balance of benefit versus harm

Class/Level	Definition
A	Well-designed RCTs or diagnostic studies on relevant populations
B	RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, reasoning from first principles
X	Exceptional situations in which validating studies cannot be performed and there is a clear preponderance of benefit or harm

Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. Circulation. 2009 Mar 24;119(11):1541-51. doi: 10.1161/CIRCULATIONAHA.109.191959.

- Prevention of Initial Attacks (Primary Prevention)
  - The use of an oral macrolide (erythromycin or clarithromycin) or azalide (azithromycin) is reasonable for patients allergic to penicillins (Class IIa, LOE B). Ten days of therapy is indicated, except for azithromycin, which is given for 5 days.
- Prevention of Recurrent Attacks of Rheumatic Fever (Secondary Prevention)

- For the patient who is allergic to both penicillin and sulfisoxazole, an oral macrolide (erythromycin or clarithromycin) or azalide (azithromycin) is recommended (Class I, LOE C).

Recommendation Definitions

Class/Level	Definition
Class I	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa	Weight of evidence/opinion is in favor of usefulness/efficacy.
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.
Class III	Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

Level of Evidence	Definition
A	Data derived from multiple randomized clinical trials or meta-analyses
B	Data derived from a single randomized trial or nonrandomized studies
C	Only consensus opinion of experts, cases studies, or standard of care

Floto RA, Olivier KN, Saiman L et al. US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis. Thorax. 2016 Jan;71 Suppl 1:i1-22. doi: 10.1136/thoraxjnl-2015-207360.

- The CF Foundation and the ECFS recommend that individuals receiving azithromycin as part of their CF medical regimen who have a positive NTM culture should not continue azithromycin treatment while evaluation for NTM disease is underway as azithromycin monotherapy may lead to resistance. A macrolide agent may be included in a multidrug treatment regimen if criteria are met for NTM disease (consensus 89%)
- The CF Foundation and the ECFS recommend that the intensive phase should include a daily oral macrolide (preferably azithromycin) in conjunction with 3–12 weeks of intravenous amikacin and one or more of the following: intravenous tigecycline, imipenem or cefoxitin, guided but not dictated by drug susceptibility testing. The duration of intensive phase therapy should be determined by the severity of infection, the response to treatment and the tolerability of the regimen (consensus 83%)
- The CF Foundation and the ECFS recommend that the continuation phase should include a daily oral macrolide (preferably azithromycin) and inhaled amikacin, in conjunction with 2–3 of the following additional oral antibiotics: minocycline, clofazimine, moxifloxacin and linezolid, guided but not dictated by drug susceptibility testing (consensus 89%)
- The CF Foundation and the ECFS recommend that monotherapy with a macrolide or other antimicrobial should never be used in the treatment of *M. abscessus* complex pulmonary disease (consensus 100%)
- The CF Foundation and the ECFS recommend that clarithromycin-sensitive MAC pulmonary disease should be treated with a daily oral antibiotic regimen containing a macrolide (preferably azithromycin), rifampin and ethambutol (consensus 89%)
- The CF Foundation and the ECFS recommend that monotherapy with a macrolide or other antimicrobial agent should never be used in the treatment of MAC pulmonary disease (consensus 100%)

Recommendation Definitions – Not Applicable: These recommendations were based on voting consensus of 19 invited committee members. The committee set the threshold for acceptance of a recommendation at 80% and expressly decided not to use the GRADE system of evaluating published evidence, given the paucity of clinical trial data.

Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al. Pulmonary Clinical Practice Guidelines Committee. Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health. Am J Respir Crit Care Med. 2013 Apr;187(7):680-9.

- For individuals with CF, 6 years of age and older, with *P. aeruginosa* persistently present in cultures of the airways, the CF Foundation recommends the chronic use of azithromycin to improve lung function and reduce exacerbations (Certainty of Net Benefit: High; Estimate of Net Benefit: Moderate; Recommendation B)
- For individuals with CF, 6 years of age and older, without *P. aeruginosa* persistently present in cultures of the airways, the CF Foundation recommends the chronic use of azithromycin should be considered to reduce exacerbations (Certainty of Net Benefit: Moderate; Estimate of Net Benefit: Small; Recommendation C)
- Note: Due to concern that the chronic use of azithromycin in individuals with occult or active NTM infection could lead to resistance and complicate NTM treatment, the committee suggests that patients be screened for NTM before initiating azithromycin and reassessed periodically at 6- to 12-month intervals. Additionally, this monotherapy should be withheld in those infected with NTM.

Recommendation Definitions

	Magnitude of Net Benefit (Benefit Minus Harms)			
Certainty of Net Benefit	**Substantial**	**Moderate**	**Small**	**Zero/Negative**
High	A	B	C	D
Moderate	B	B	C	D
Low	I (insufficient evidence)			

Strength of Recommendation	Definition
A	The committee strongly recommends that clinicians routinely provide this therapy. There is high certainty that the net benefit is substantial.
B	The committee recommends that clinicians routinely provide this therapy. There is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial.
C	The committee recommends that clinicians consider providing this therapy to selected patients depending on individual circumstances. However, for most individuals without signs or symptoms there is likely to be only a small benefit from this service
D	The committee recommends against the therapy. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits. Clinicians should discourage the use of this service.
I	The committee concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.

Quality of Evidence	Definition
High	The available evidence includes consistent results from well designed, well conducted studies in representative populations. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies; inconsistency of findings across individual studies; limited generalizability of findings to routine primary care practice; lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: limited number or size of studies; important flaws in study design or methods; inconsistency of findings across individual studies; gaps in the chain of evidence; findings not generalizable; lack of information on important health outcomes. More information may allow estimation of effects on health outcomes.

Tiwari T, Murphy TV, Moran J; National Immunization Program, CDC. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC Guidelines. MMWR Recomm Rep. 2005 Dec 9;54(RR-14):1-16. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5414a1.htm.

- Post-exposure prophylaxis and Treatment. The macrolide agents erythromycin, clarithromycin, and azithromycin are preferred for the treatment of pertussis in persons aged >1 month. For infants aged <1 month, azithromycin is preferred; erythromycin and clarithromycin are not recommended. For treatment of persons aged >2 months, an alternative agent to macrolides is TMP/SMX

Recommended antimicrobial treatment and postexposure prophylaxis for pertussis, by age group

Age group	Primary agents			Alternate agent*
	Azithromycin	Erythromycin	Clarithromycin	TMP-SMZ
<1 month	Recommended agent. 10 mg/kg per day in a single dose for 5 days (only limited safety data available.)	Not preferred. Erythromycin is associated with infantile hypertrophic pyloric stenosis. Use if azithromycin is unavailable; 40–50 mg/kg per day in 4 divided doses for 14 days	Not recommended (safety data unavailable)	Contraindicated for infants aged <2 months (risk for kernicterus)
1–5 months	10 mg/kg per day in a single dose for 5 days	40–50 mg/kg per day in 4 divided doses for 14 days	15 mg/kg per day in 2 divided doses for 7 days	Contraindicated at age <2 months. For infants aged ≥2 months, TMP 8 mg/kg per day, SMZ 40 mg/kg per day in 2 divided doses for 14 days
Infants (aged ≥6 months) and children	10 mg/kg in a single dose on day 1 then 5 mg/kg per day (maximum: 500 mg) on days 2–5	40–50 mg/kg per day (maximum: 2 g per day) in 4 divided doses for 14 days	15 mg/kg per day in 2 divided doses (maximum: 1 g per day) for 7 days	TMP 8 mg/kg per day, SMZ 40 mg/kg per day in 2 divided doses for 14 days
Adults	500 mg in a single dose on day 1 then 250 mg per day on days 2–5	2 g per day in 4 divided doses for 14 days	1 g per day in 2 divided doses for 7 days	TMP 320 mg per day, SMZ 1,600 mg per day in 2 divided doses for 14 days

* Trimethoprim sulfamethoxazole (TMP–SMZ) can be used as an alternative agent to macrolides in patients aged ≥2 months who are allergic to macrolides, who cannot tolerate macrolides, or who are infected with a rare macrolide-resistant strain of *Bordetella pertussis*.

Recommendation Definitions – Not applicable

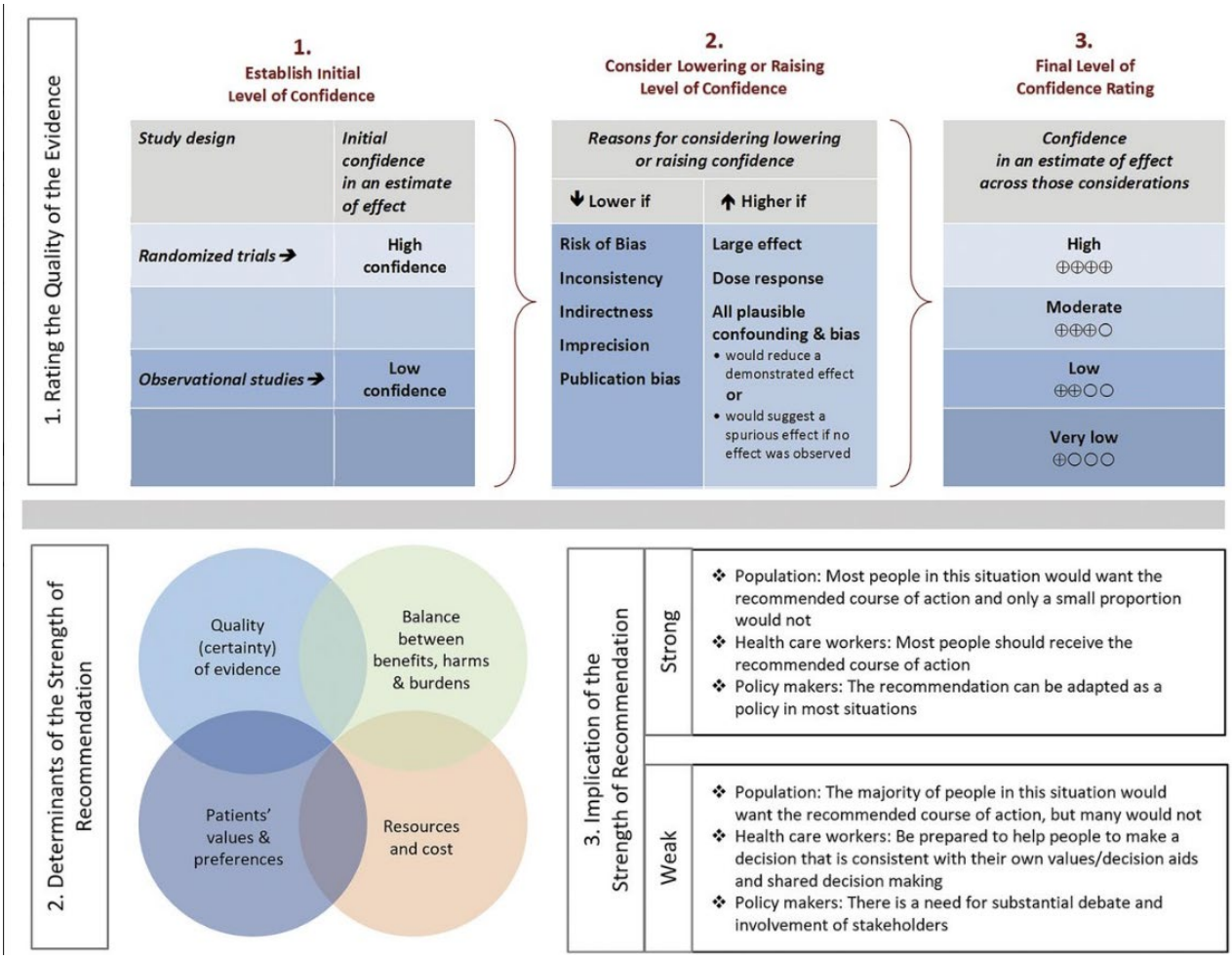
Lantos PM, Rumbaugh J, Bockenstedt LK, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America, American Academy of Neurology, and American College of Rheumatology: 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease. Neurology. 2021 Feb 9;96(6):262-273. doi: 10.1212/WNL.0000000000011151. Epub 2020 Nov 30. Erratum in: Neurology. 2021 Feb 9;96(6):296. PMID: 33257476.

- Recommended Antibiotic Regimens for the Chemoprophylaxis of Lyme Disease Following a High-Risk Tick Bite: For high-risk *Ixodes* spp. bites in all age groups, we recommend the administration of a single dose of oral doxycycline within 72 hours of tick removal over observation (strong recommendation, moderate-quality evidence). **Comment:** Doxycycline is given as a single oral dose, 200 mg for adults and 4.4 mg/kg (up to a maximum dose of 200 mg) for children.
- Recommended Antibiotic Regimens for the Treatment of Erythema Migrans: For patients with erythema migrans, we recommend using oral antibiotic therapy with doxycycline, amoxicillin, or cefuroxime axetil (strong recommendation; moderate quality of evidence). **Comment:** For patients unable to take both doxycycline and beta-lactam antibiotics, the preferred secondline agent is azithromycin. We recommend that patients with erythema migrans be treated with either a 10-day course of doxycycline or a 14-day course of amoxicillin or cefuroxime axetil rather than longer treatment courses (strong recommendation, moderate quality of evidence). **Comment:** If azithromycin is used, the indicated duration is 5–10 days, with a 7-day course preferred in the United States, as this duration of therapy was used in the largest clinical trial performed in the United States
- Recommended Antibiotic Regimens for Treatment of Acute Neurologic Manifestations of Lyme Disease Without Parenchymal Involvement of the Brain or Spinal Cord: In patients with Lyme disease–associated meningitis, cranial neuropathy, radiculoneuropathy, or with other peripheral nervous system (PNS) manifestations, we recommend using IV ceftriaxone, cefotaxime, penicillin G, or oral doxycycline over other antimicrobials (strong recommendation, moderate-quality evidence). **Comment:** Decisions about the choice of antibiotic among these, including the route of administration, should primarily be made based on individual factors such as side effect profile, ease of administration, ability to tolerate oral medication, and concerns about compliance unrelated to

effectiveness. Treatment route may be changed from IV to oral during treatment. The preferred antibiotic duration is 14–21 days.

- Recommended Antibiotic Regimens for the Treatment of Lyme Carditis: For the treatment of Lyme carditis, we suggest 14–21 days of total antibiotic therapy over longer durations of treatment (weak recommendation, very-low-quality evidence). **Comment:** Oral antibiotic choices for Lyme carditis are doxycycline, amoxicillin, cefuroxime axetil, and azithromycin.

Recommendation Definitions:



Approach and Implications to Rating the Quality of Evidence and Strength of Recommendations Using the GRADE Methodology (Unrestricted use of the Figure Granted by the US GRADE Network)[1,2]
GRADE = Grading of Recommendations Assessment, Development, and Evaluation.

Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2017 Feb;112(2):212-239. doi: 10.1038/ajg.2016.563.

- What are evidence-based first-line treatment strategies for providers in North America?
  - Clarithromycin triple therapy consisting of a PPI, clarithromycin, and amoxicillin or metronidazole for 14 days remains a recommended treatment in regions where H. pylori clarithromycin resistance is known to be <15% and in patients with no previous history of macrolide exposure for any reason (Conditional recommendation; low quality of evidence (for duration: moderate quality of evidence)).
  - Bismuth quadruple therapy consisting of a PPI, bismuth, tetracycline, and a nitroimidazole for 10–14 days is a recommended first-line treatment option. Bismuth quadruple therapy is particularly attractive in patients

with any previous macrolide exposure or who are allergic to penicillin (strong recommendation; low quality of evidence).
    - Concomitant therapy consisting of a PPI, clarithromycin, amoxicillin and a nitroimidazole for 10–14 days is a recommended first-line treatment option (strong recommendation; low quality of evidence (for duration: very low quality of evidence)).
    - Sequential therapy consisting of a PPI and amoxicillin for 5–7 days followed by a PPI, clarithromycin, and a nitroimidazole for 5–7 days is a suggested first-line treatment option (conditional recommendation; low quality of evidence (for duration: very low quality of evidence)).
    - Hybrid therapy consisting of a PPI and amoxicillin for 7 days followed by a PPI, amoxicillin, clarithromycin and a nitroimidazole for 7 days is a suggested first-line treatment option (conditional recommendation; low quality of evidence (For duration: very low quality of evidence)).
    - Levofloxacin triple therapy consisting of a PPI, levofloxacin, and amoxicillin for 10–14 days is a suggested first-line treatment option (conditional recommendation; low quality of evidence (For duration: very low quality of evidence)).
    - Fluoroquinolone sequential therapy consisting of a PPI and amoxicillin for 5–7 days followed by a PPI, fluoroquinolone, and nitroimidazole for 5–7 days is a suggested first-line treatment option (conditional recommendation; low quality of evidence (for duration: very low quality of evidence)).
- When first-line therapy fails, what are the options for salvage therapy?
    - In patients with persistent H. pylori infection, every effort should be made to avoid antibiotics that have been previously taken by the patient (unchanged from previous ACG guideline) (Strong recommendation; moderate quality of evidence).
    - Bismuth quadruple therapy or levofloxacin salvage regimens are the preferred treatment options if a patient received a first-line treatment containing clarithromycin. Selection of best salvage regimen should be directed by local antimicrobial resistance data and the patient's previous exposure to antibiotics (Conditional recommendation; for quality of evidence see individual statements below).
    - Clarithromycin or levofloxacin-containing salvage regimens are the preferred treatment options, if a patient received first-line bismuth quadruple therapy. Selection of best salvage regimen should be directed by local antimicrobial resistance data and the patient's previous exposure to antibiotics (Conditional recommendation; for quality of evidence see individual statements below).

  The following regimens can be considered for use as salvage treatment:
    - Bismuth quadruple therapy for 14 days is a recommended salvage regimen. (Strong recommendation; low quality of evidence)
    - Levofloxacin triple regimen for 14 days is a recommended salvage regimen. (Strong recommendation; moderate quality of evidence (For duration: low quality of evidence)
    - Concomitant therapy for 10–14 days is a suggested salvage regimen. (conditional recommendation; very low quality of evidence)
    - Clarithromycin triple therapy should be avoided as a salvage regimen. (conditional recommendation; low quality of evidence)
    - Rifabutin triple regimen consisting of a PPI, amoxicillin, and rifabutin for 10 days is a suggested salvage regimen (conditional recommendation; moderate quality of evidence (For duration: very low quality of evidence)).
    - High-dose dual therapy consisting of a PPI and amoxicillin for 14 days is a suggested salvage regimen (conditional recommendation; low quality of evidence (For duration: very low quality of evidence)).

Recommendation Definitions

Class/Level	Definition
Strong	The strength of recommendations was determined to be "strong" or "conditional" based on the quality of evidence, the certainty about the balance between desirable and undesirable effects of the intervention, the certainty about patients' values and preferences, and the certainty about whether the recommendation represents a wise use of resources.
Conditional	

Class/Level	Definition
High	Further research is unlikely to change the confidence in the estimate of effect
Moderate	Further research would be likely to have an impact on the confidence in the estimate of effect
Low	Further research would be expected to have an impact on the confidence in the estimate of effect
Very Low	Any estimate of effect is very uncertain

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Vardakas KZ, Trigkidis KK, Falagas ME. Fluoroquinolones or macrolides in combination with β-lactams in adult patients hospitalized with community acquired pneumonia: a systematic review and meta-analysis. Clin Microbiol Infect. 2017 Apr;23(4):234-241. doi: 10.1016/j.cmi.2016.12.002.	Data bases searched: PubMed, Scopus and the Cochrane Library Study types included in search: observational cohort studies, non-randomized trials and RCTs of patients with CAP receiving BLM or BLFQ. Data quality assessment: MINORS and GRADE Study type performed: meta-analysis N = 17 studies (16,684 patients)	• Primary: mortality
Results: No RCTs were identified, and the body of evidence was overall low in quality. In the meta-analysis of adjusted mortality data, a non-significant difference between the two regimens was observed (adjusted risk ratio 1.26, 95% CI 0.95–1.67, I2 43%). **Conclusion**: No determination or recommendation can be made in terms of a preferred regimen (BLM or BLFQ) for reducing mortality in hospitalized patients with CAP. In order to make a recommendation, RCTs would be needed.		

Citation	Design	Endpoints
Skalsky K, Yahav D, Lador A, Eliakim-Raz N, Leibovici L, Paul M. Macrolides vs. quinolones for community-acquired pneumonia: meta-analysis of randomized controlled trials. Clin Microbiol Infect. 2013 Apr;19(4):370-8. doi: 10.1111/j.1469-0691.2012.03838.x.	Data bases searched: PubMed, the Cochrane Library, and LILACS databases Study types included in search: RCTs comparing any quinolone vs. any macrolide, administered as monotherapies or both in combination with a beta-lactam antibiotic for the treatment of CAP in adult inpatients or outpatients Data quality assessment: A domain-based method, recommended by the Cochrane handbook, was used to assess risk of bias. Allocation concealment and generation were graded as low, high or unknown risk of bias. Study type performed: meta-analysis using the Mantel–Haenszel fixed-effects model N = 16 studies (4,989 patients)	• Primary: 30-day all-cause mortality and treatment failure
Results: While all-cause mortality (event rate 2%) was not significantly different for macrolides vs. quinolones, RR 1.03 (0.63–1.68, seven trials), treatment failure (RR 0.78 [0.67–0.91, 16 trials]) and microbiologic failure (RR 0.63 [0.49–0.81, 13 trials]) were significantly lower with quinolones. All AEs, including those requiring discontinuation, were significantly more frequent with macrolides and gastrointestinal in nature. **Conclusion**: There appears to be an advantage to using quinolones in the treatment of CAP in terms of treatment failure and adverse events, but no advantage in terms of all-cause mortality, when compared to macrolides.		

Citation	Design	Endpoints
Wu Q, Shen W, Cheng H, Zhou X. Long-term macrolides for non-cystic fibrosis bronchiectasis: a	Data bases searched: MEDLINE, EMBASE, ClinicalTrials.gov, the Cochrane Library, CINAHL, AMED, PsycINFO and major China databases as well as hand-searching of respiratory journals and meeting abstracts	• Primary: RR of exacerbations • Secondary: health-related QOL (SGRQ scores), dyspnea scale (the British

systematic review and meta-analysis. Respirology. 2014 Apr;19(3):321-9. doi: 10.1111/resp.12233.	Study types included in search: RCTs comparing long-term macrolides with placebo and/or usual medical care in non-CF bronchiectasis Data quality assessment: Jadad's scale Study type performed: meta-analysis using a fixed-effects (in the setting of substantial heterogeneity) or random-effects model to estimate RR and WMD and 95% CI N = 9 studies (530 patients)	Medical Research Council), 24-h sputum volume, lung function (change in FEV1 from baseline to the end of the study), eradication of the common respiratory pathogens, AEs, macrolide resistance and airway inflammatory parameters
Results: Compared with placebo and/or usual medical care, long-term macrolides significantly reduced the risk of the exacerbations (number of participants with exacerbations (RR = 0.70, 95% CI 0.60–0.82, P < 0.00001); average exacerbations per participant (WMD = −1.01, 95% CI −1.35 to −0.67, P < 0.00001), the SGRQ total scores (WMD = −5.39 95% CI −9.89 to −0.88, P = 0.02), dyspnea scale (WMD = −0.31 95% CI −0.42 to −0.20, P < 0.00001), 24-h sputum volume (P < 0.00001), and attenuated the decline of FEV1 (WMD 0.02 L, 95% CI 0.00–0.04, P = 0.01). Eradication of pathogens (P = 0.06), overall rate of AEs (P = 0.61), and emergence of new pathogens (P = 0.61) were not elevated, while GI events increased significantly with macrolides (P = 0.0001). A meta-analysis of macrolide resistance could not be performed due to data heterogeneity. **Conclusion**: Long-term treatment of non-CF bronchiectasis with macrolides is a viable treatment option.		

Citation	Design	Endpoints
Fan LC, Lu HW, Wei P, Ji XB, Liang S, Xu JF. Effects of long-term use of macrolides in patients with non-cystic fibrosis bronchiectasis: a meta-analysis of randomized controlled trials. BMC Infect Dis. 2015 Mar 27;15:160. doi: 10.1186/s12879-015-0872-5.	Data bases searched: Embase, Pubmed, the Cochrane Library and Web of Science Study types included in search: RCTs assessing the efficacy or safety of macrolides in comparison with placebo, another class of antibiotic or blank control in the treatment of patients with non-CF bronchiectasis Data quality assessment: Cochrane Collaboration tool in the Review Manager software for selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias Study type performed: meta-analysis using Review Manager software and Stata Statistical software N = 10 studies (601 patients)	• Primary: improvement of exacerbations of bronchiectasis • Secondary: changes of microbiology, lung function, QOL, sputum volume, AEs and macrolide resistance
Results: Macrolides reduced the rate of acute exacerbations per patient to a statistically-significant degree (Rate Ratio = 0.55, 95% CI: 0.47, 0.64, P < 0.001), increased the number of patients free from exacerbations (OR = 2.81, 95% CI: 1.85, 4.26, P < 0.001), and prolonged time to a first exacerbation (HR = 0.38, 95% CI: 0.28, 0.53, P < 0.001). Macrolides maintenance treatment was superior to control with respect to attenuating FEV1 decline (p = 0.02), improving sputum volume (p = 0.009) and SGRQ total scores (p = 0.02), but showed a statistically significantly higher risk of AEs, especially diarrhea. Although eradication of pathogens was improved in the macrolide group, it was accompanied by a dramatic and statistically significant increase in pathogen resistance to macrolides. There was no significant difference between groups in terms of new appearance of a microbiologic profile or AE-related discontinuation. **Conclusion**: Macrolide maintenance treatment of non-CF bronchiectasis can effectively reduce frequency of exacerbations, attenuate lung function decline, decrease sputum volume, and improve QOL, but at the expense of increased AEs (especially diarrhea) and pathogen resistance.		

Citation	Design	Endpoints
Gao YH, Guan WJ, Xu G, et al. Macrolide therapy in adults and children with non-cystic fibrosis bronchiectasis: a systematic review	Data bases searched: PubMed, EMBASE, CENTRAL databases Study types included in search: RCTs of patients (children and adults) with clinically stable non-CF bronchiectasis treated with long-term macrolide therapy (≥2 months) compared placebo or usual care	• Primary: number of bronchiectasis exacerbations

and meta-analysis. PLoS One. 2014 Mar 6;9(3):e90047. doi: 10.1371/journal.pone.0090047.	Data quality assessment: Jadad scoring system Study type performed: meta-analysis using Review Manager software and Stata Statistical software; RR for dichotomous variables and WMD or SMD for continuous variables with 95% CI were calculated N = 9 studies (559 patients)	• Secondary: exacerbation-related admissions, QOL, spirometry, 6MWT and AEs
Results: Macrolide therapy significantly reduced the number of patients experiencing ≥ 1 exacerbation in adults [RR = 0.59; 95% CI, 0.40–0.86; P = 0.006] and children [RR = 0.86; 95% CI, 0.75–0.99; P = 0.04], but not the number of patients with admissions for exacerbation. Macrolide therapy was also associated with reduced frequency of exacerbations in adults (RR = 0.42; 95% CI, 0.29 to 0.61; P<0.001) and children (RR = 0.50; 95% CI, 0.35 to 0.71; P<0.001). Pooled analyses suggested that spirometry, including FEV1 and FVC, were significantly improved in adults but not in children. Macrolide therapy improved the QOL (WMD, −6.56; 95% CI, −11.99 to −1.12; P = 0.02; I2 = 86%) but not performance on 6MWT. There was no difference in overall AEs in adults although reports of diarrhea and abdominal discomforts were higher with macrolide therapy. **Conclusion**: Macrolide maintenance therapy in adults and children was effective and safe in reducing bronchiectasis exacerbations, but not related admissions. In addition, macrolide therapy in adults was associated with improvement in QOL and spirometry.		

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (4/1/2023 to 6/30/2023)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Macrolides								
clarithromycin 125 mg/5 mL, 250 mg/5mL oral suspension	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
clarithromycin ER 500 mg tablet, extended release 24 hr	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
clarithromycin 250mg, 500 mg tablet	5	5	$74.12	$14.82	0	0 (0%)	F	No change
erythromycin lactobionate (Erythrocin™) 500 mg intravenous solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
erythromycin ethylsuccinate (E.E.S. Granules®, EryPed®) 200 mg/5 mL oral suspension	0	0	$0.00	$0.00	0	0 (0%)	F	No change
erythromycin ethylsuccinate (EryPed®) 400 mg/5 mL oral suspension	0	0	$0.00	$0.00	0	0 (0%)	F	No change
erythromycin ethylsuccinate (E.E.S®) 400 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Erythrocin™ (as stearate) (erythromycin) 250 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
erythromycin 250 mg capsule, delayed release	0	0	$0.00	$0.00	0	0 (0%)	F	No change
erythromycin 250 mg, 500mg tablet	4	2	$1,486.40	$371.60	0	0 (0%)	F	No change
erythromycin 250 mg, 333 mg, 500mg (Ery-Tab®) tablet, delayed release	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Dificid® (fidaxomicin) 40 mg/mL oral suspension	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Dificid® (fidaxomicin) 200 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
azithromycin (Zithromax®) 1 gram oral packet	0	0	$0.00	$0.00	0	0 (0%)	F	No change
azithromycin (Zithromax®) 100 mg/5 mL, 200 mg/5 mL oral suspension	1	1	$17.96	$17.96	0	0 (0%)	F	No change
azithromycin (Zithromax®, Zithromax Z-Pak®, Zithromax TRI-PAK®) 250 mg, 500 mg, 600 mg tablet	67	65	$328.20	$4.90	0	0 (0%)	F 600mg: F-AL (min 21 yrs)	No change
azithromycin (Zithromax®) 500 mg intravenous solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Total	**77**	**73**	**$1,906.68**	**$24.76**	**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

GLOSSARY

6MWT – 6-minute walk test
abx – antibiotics
AE – adverse effect/event
ART – antiretroviral therapy
BA – bacillary angiomatosis
BID – twice daily
BIW – twice weekly
BLFQ – β-lactam/fluoroquinolone
BLM - β-lactam/macrolide
CAD – coronary artery disease
CAP – community acquired pneumonia
CDI – *Clostridioides* (formerly *Clostridium*) *difficile* infection
CF – cystic fibrosis
CI – confidence interval
CV – cardiovascular
d/c – discontinue
DDIs – drug-drug interactions
DRESS – drug rash with eosinophilia and systemic symptoms
ECFS – European Cystic Fibrosis Society
EES – erythromycin ethylsuccinate
FEV1 – forced expiratory volume in 1 second
FVC – forced vital capacity
GI – gastrointestinal
GRADE – Grading of Recommendations Assessment, Development and Evaluation
HR – hazard ratio
IDSA – Infectious Disease Society of America
IHPS – infantile hypertrophic pyloric stenosis
LFT – liver function test
LILACS – Literatura Latino Americana em Ciências da Saúde (Latin American Literature in Health Sciences)
MAC – Mycobacterium avium complex
MINORS – methodological index for non-randomized studies
MSM – men who have sex with men
NTM – nontuberculous mycobacteria
OM – otitis media
OR – odds ratio
PCN – penicillin
PH – peliosis hepatis
PI – prescribing information/package insert
PID – pelvic inflammatory disease
PO – by mouth/orally
PPI – proton pump inhibitor
QD – once daily
QOL – quality of life
QW – once weekly
QID – 4 times per day
RGM – rapidly growing mycobacteria
RR – relative risk
SGRQ – St. George's Respiratory Questionnaire
SJS – Stevens-Johnson syndrome
SMD – standard mean difference
SSSI – skin and skin structure infection
STI – sexually transmitted infections
TCN – tetracycline
TEN – toxic epidermal necrolysis
TID – 3 times per day
TIW – 3 times weekly
TMP/SMX – trimethoprim-sulfamethoxazole
URI – upper respiratory tract infections
USPSTF – United States Preventive Services Task Force
WMD – weighted mean difference

REFERENCES

1. Drug Facts and Comparisons. Facts & Comparisons. St. Louis, MO: Wolters Kluwer Health, Inc; March 2005. Available at: http://www.wolterskluwercdi.com/. Accessed February 10, 2023.
2. Lexicomp Online, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2018. Available at: online.lexi.com. Accessed February 10, 2023.UpToDate, Waltham, MA: UpToDate Inc., http://www.uptodate.com. Accessed February 10, 2023.
3. Mofenson LM, Brady MT, Danner SP, et al. Guidelines for the Prevention and Treatment of Opportunistic Infections among HIV-exposed and HIV-infected children: recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. MMWR Recomm Rep. 2009 Sep 4;58(RR-11):1-166. Accessed February 10, 2023.
4. Bradley JS, Byington CL, Shah SS, et al. The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America, Clinical Infectious Diseases, Volume 53, Issue 7, 1 October 2011, Pages e25–e76, https://doi.org/10.1093/cid/cir531. Accessed February 10, 2023.
5. Workowski KA, Bachmann LH, Chan PA; Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2021. MMWR Recomm Rep. 2021;70(RR-03):1-192. Available at: https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf. Accessed February 9, 2023.
6. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of chronic obstructive pulmonary disease: 2022 Report. https://goldcopd.org/wp-content/uploads/2021/12/GOLD-REPORT-2022-v1.1-22Nov2021_WMV.pdf. Accessed February 9, 2023.
7. Papi A, Rabe KF, Rigau D, et al. Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J 2017; 49: 1600791. https://doi.org/10.1183/13993003.00791-2016. Accessed February 10, 2023.
8. Criner GJ, Bourbeau J, Diekemper R, et al. Prevention of acute exacerbations of COPD: American College of Chest Physicians and Canadian Thoracic Society Guideline. Chest. 2015 Apr;147(4):894-942. doi: 10.1378/chest.14-1676. doi:10.1378/chest.14-1676. Accessed February 10, 2023.
9. Daley CL, Iaccarino JM, Lange C, et al. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline. Clinical Infectious Diseases. 2020; 71(4):905-913. https://doi.org/10.1093/cid/ciaa1125. Accessed February 9, 2023.
10. Stevens DL, Bisno AL, Chambers HF, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases, Volume 59, Issue 2, 15 July 2014, Pages e10–e52, https://doi.org/10.1093/cid/ciu296. Accessed February 10, 2023.Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Accessed February 10, 2023.
11. Lieberthal AS, Carroll AE, Chonmaitree T, et al. The Diagnosis and Management of Acute Otitis Media. Pediatrics. 2013 Mar;131(3):e964-99. doi: 10.1542/peds.2012-3488. Accessed February 10, 2023.
12. Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute Streptococcal pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. Circulation. 2009 Mar 24;119(11):1541-51. doi: 10.1161/CIRCULATIONAHA.109.191959. Accessed February 10, 2023.
13. Floto RA, Olivier KN, Saiman L et al. US Cystic Fibrosis Foundation and European Cystic Fibrosis Society consensus recommendations for the management of non-tuberculous mycobacteria in individuals with cystic fibrosis. Thorax. 2016 Jan;71 Suppl 1:i1-22. doi: 10.1136/thoraxjnl-2015-207360. Accessed February 10, 2023.
14. Mogayzel PJ Jr, Naureckas ET, Robinson KA, et al. Pulmonary Clinical Practice Guidelines Committee. Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health. Am J Respir Crit Care Med. 2013 Apr;187(7):680-9. Accessed on January 28, 2019.
15. Tiwari T, Murphy TV, Moran J; National Immunization Program, CDC. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis: 2005 CDC Guidelines. MMWR Recomm Rep. 2005 Dec 9;54(RR-14):1-16. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5414a1.htm. Accessed February 10, 2023.
16. Lantos PM, Rumbaugh J, Bockenstedt LK, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America, American Academy of Neurology, and American College of Rheumatology: 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease. Neurology. 2021 Feb 9;96(6):262-273. doi: 10.1212/WNL.0000000000011151. Epub 2020 Nov 30. Erratum in: Neurology. 2021 Feb 9;96(6):296. PMID: 33257476. Accessed February 9, 2023.
17. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2017 Feb;112(2):212-239. doi: 10.1038/ajg.2016.563. Accessed February 10, 2023.
18. Vardakas KZ, Trigkidis KK, Falagas ME. Fluoroquinolones or macrolides in combination with β-lactams in adult patients hospitalized with community acquired pneumonia: a systematic review and meta-analysis. Clin Microbiol Infect. 2017 Apr;23(4):234-241. doi: 10.1016/j.cmi.2016.12.002. Accessed February 10, 2023.
19. Skalsky K, Yahav D, Lador A, Eliakim-Raz N, Leibovici L, Paul M. Macrolides vs. quinolones for community-acquired pneumonia: meta-analysis of randomized controlled trials. Clin Microbiol Infect. 2013 Apr;19(4):370-8. doi: 10.1111/j.1469-0691.2012.03838.x. Accessed February 10, 2023.

20. Wu Q, Shen W, Cheng H, Zhou X. Long-term macrolides for non-cystic fibrosis bronchiectasis: a systematic review and meta-analysis. Respirology. 2014 Apr;19(3):321-9. doi: 10.1111/resp.12233. Accessed February 10, 2023.
21. Fan LC, Lu HW, Wei P, Ji XB, Liang S, Xu JF. Effects of long-term use of macrolides in patients with non-cystic fibrosis bronchiectasis: a meta-analysis of randomized controlled trials. BMC Infect Dis. 2015 Mar 27;15:160. doi: 10.1186/s12879-015-0872-5. Accessed February 10, 2023.
22. Gao YH, Guan WJ, Xu G, et al. Macrolide therapy in adults and children with non-cystic fibrosis bronchiectasis: a systematic review and meta-analysis. PLoS One. 2014 Mar 6;9(3):e90047. doi: 10.1371/journal.pone.0090047. Accessed February 10, 2023.Johnson S, Lavergne V, Skinner AM, et al. Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults. 2021; 73(5):e1029-e1044. Accessed February 10, 2023.
23. Metlay JP, Waterer GW, et al. Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019 Oct 1;200(7):e45-e67. doi: 10.1164/rccm.201908-1581ST. PMID: 31573350; PMCID: PMC6812437. Accessed February 10, 2023.

Bowel Preparatory Agents

Executive Summary

CLASS OVERVIEW

Bowel preparation ("prep") regimens are most commonly used in the setting of colonscopy but also prior to planned elective colon resection, procedures with the potential to injure the bowel (e.g. advanced endometriosis, staging for gynecologic malignancies), and barium enema x-ray examinations. The purpose of bowel prep in the setting of colonoscopy is clear visualization and accurate diagnosis; in the surgical setting, bowel prep is used to reduce the risk of resultant infection. There are various formulations available on the market, most of which are orally administered solutions for reconstitution or dilution – hypertonic [e.g. Suprep (sodium, potassium and magnesium sulfates)]; isotonic [e.g. polyethylene glycol-electrolyte (PEG-ES) solutions]; hypotonic [e.g. over-the-counter Miralax (PEG3350) + bisacodyl + magnesium citrate, this regimen is not Food and Drug Administration (FDA) approved]. Two regimens (Osmoprep, Sutab) are in tablet form with instructions to drink with large volumes of clear liquid. Additionally, sodium phosphate (Fleet) enemas are commonly used as a preparation for sigmoidoscopy.

There are three US-based guidelines related to the use of bowel preparations prior to colonoscopy: the American Society for Gastrointestinal Endoscopy (ASGE) Guideline for Bowel Preparation before Colonoscopy (2015); American College of Gastroenterology (ACG)/American Gastroenterological Association (AGA)/ASGE: Optimizing Adequacy of Bowel Cleansing for Colonoscopy – Recommendations from the US Multi-Society Task Force on Colorectal Cancer (2014); and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN): Report on Bowel Preparation for Pediatric Colonoscopy.

There are no bowel prep products in the pipeline anticipated to be approved within the next 6 months. Many products in this class are available generically.

UTILIZATION FINDINGS

There were 102 claims for 102 members, for a total cost of $2,470, and an average cost per claim of $24. The most highly utilized medication was PEG-ES (Na2SO4, NaHCO3, NaCl, KCl) (Golytely®) 236 g powder for reconstitution, with 79 claims. There were no prior authorization requests.

RECOMMENDATIONS

- No changes

PRODUCT TABLE (4/1/2023 to 6/30/2023)

Medication	Rx	Current Status	Recommendation
Bowel Prep Agents-Rx			
OsmoPrep® (sodium phosphate) 1.5 gram tablet	0	NF	No change
peg-electrolyte (NaCl, NaHCO3, KCl) (NuLYTELY®) solution 420 gram oral solution	18	F	No change
PEG-Prep [PEG-ES (NaCL, NaHCO3, KCl, Bisac)](Halflytely® with bisacodyl and flavor pack) 5 mg-210 gram oral kit†	0	NF	No change
Sodium, potassium and magnesium sulfates (Suprep®) Bowel Prep Kit 17.5 gram-3.13 gram-1.6 gram oral solution	0	NF	No change
Clenpiq™ (sodium picosulfate, magnesium oxide, ascorbic acid) 10 mg-3.5 g-12 g/160 mL solution	0	NF	No change
Plenvu® [PEG-ES (Na2SO4, NaCl, KCl, sodium ascorbate, ascorbic acid)] 140 gram-9 gram-5.2 gram powder pack	0	NF	No change
Sutab® (sodium sulfate, potassium chloride, and magnesium sulfate) 1.479-0.188-0.225 gram tablet	0	NF	No change
[PEG-ES (NaSO4, NaCL, KCl; ascorbic acid, sodium ascorbate)] (MoviPrep®) 100 g powder for reconstitution	0	NF	No change
PEG-ES (Na2SO4, NaHCO3, NaCl, KCl) (Golytely®) 236 g powder for reconstitution	79	F-QL (4000/90)	No change
PEG-ES ((Na2SO4, NaHCO3, NaCl, KCl) (Colyte® w/Flavor packs)) 240 g powder for reconstitution	5	F-QL (4000/90)	No change

Abbreviations: PEG = polyethylene glycol; PEG-ES = polyethylene glycol-electrolye solution
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

CLINICAL SUMMARY

Bowel prep regimens are most commonly used in the setting of colonscopy but also prior to planned elective colon resection, procedures with the potential to injure the bowel (e.g. advanced endometriosis, staging for gynecologic malignancies), and barium enema x-ray examinations. The purpose of bowel prep in the setting of colonoscopy is clear visualization and accurate diagnosis; in the surgical setting, bowel prep is used to reduce the risk of resultant infection. There are various formulations available on the market, most of which are orally administered solutions for reconstitution or dilution – hypertonic [e.g. Suprep (sodium, potassium and magnesium sulfates)]; isotonic [e.g. polyethylene glycol-electrolyte (PEG-ES) solutions]; hypotonic [e.g. over-the-counter Miralax (PEG3350) + bisacodyl + magnesium citrate, this regimen is not Food and Drug Administration (FDA) approved]. Two regimens (Osmoprep, Sutab) are in tablet form with instructions to drink with large volumes of clear liquid. Additionally, sodium phosphate (Fleet) enemas are commonly used as a preparation for sigmoidoscopy.

There are three US-based guidelines related to the use of bowel preparations prior to colonoscopy: the American Society for Gastrointestinal Endoscopy (ASGE) Guideline for Bowel Preparation before Colonoscopy (2015); American College of Gastroenterology (ACG)/American Gastroenterological Association (AGA)/ASGE: Optimizing Adequacy of Bowel Cleansing for Colonoscopy – Recommendations from the US Multi-Society Task Force on Colorectal Cancer (2014); and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN): Report on Bowel Preparation for Pediatric Colonoscopy.

PRACTICE GUIDELINES

ASGE Standards of Practice Committee, Saltzman JR, Cash BD, et al. Bowel preparation before colonoscopy. Gastrointest Endosc. 2015 Apr;81(4):781-94. doi: 10.1016/j.gie.2014.09.048. Epub 2015 Jan 14.

- We recommend that bowel preparations be individualized by the prescribing provider for each patient based on efficacy, cost, safety, and tolerability considerations balanced with the patient's overall health, comorbid conditions, and preferences. ⊕⊕⊕⊕
- We suggest intensive education and more aggressive than standard bowel preparation regimens be considered for patients with predictors for inadequate preparation. ⊕⊕◯◯
- We recommend a low-residue diet be used in conjunction with FDA-approved purgatives for bowel preparation before colonoscopy. ⊕⊕⊕◯
- We recommend split-dose regimens for all patients and/or same day preparations for afternoon colonoscopies with a portion of the preparation taken within 3 to 8 hours of the procedure to enhance colonic cleansing and patient tolerance. ⊕⊕⊕◯
- We recommend that sodium phosphate and magnesium citrate preparations not be used in the elderly or patients with renal disease or taking medications that alter renal blood flow or electrolyte excretion. ⊕⊕⊕⊕
- We recommend against the use of metoclopramide as an adjunct to oral bowel preparation. ⊕⊕⊕◯

Recommendation Definitions

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

Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the US Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol. 2014 Oct;109(10):1528-45. doi: 10.1038/ajg.2014.272. Epub 2014 Sep 16.

Dosing and Timing of Colon Cleansing Regimens

- Use of a split-dose bowel cleansing regimen is strongly recommended for elective colonoscopy (Strong recommendation, high-quality evidence).
- A same-day regimen is an acceptable alternative to split dosing, especially for patients undergoing an afternoon examination (Strong recommendation, high-quality evidence).
- The second dose of split preparation ideally should begin 4–6 h before the time of colonoscopy with completion of the last dose at least 2 h before the procedure time (Strong recommendation, moderate-quality evidence).

FDA-approved Preparations

- Selection of a bowel-cleansing regimen should take into consideration the patient's medical history, medications, and, when available, the adequacy of bowel preparation reported from prior colonoscopies (Strong recommendation, moderate-quality evidence).
- A split-dose regimen of 4 l PEG-ELS provides high-quality bowel cleansing (Strong recommendation, high-quality evidence).
- In healthy nonconstipated individuals, a 4-L PEG-ELS formulation produces a bowel-cleansing quality that is not superior to a lower-volume PEG formulation (Strong recommendation, high-quality evidence).

OTC Non-FDA-approved Preparations

- The OTC bowel cleansing agents have variable efficacy that ranges from adequate to superior, depending on the agent, dose, timing of administration, and whether it is used alone or in combination; regardless of the agent,

the efficacy and tolerability are enhanced with a split-dose regimen (Strong recommendation, moderate-quality evidence).
- Although the OTC purgatives generally are safe, caution is required when using these agents in certain populations; for example, magnesium-based preparations (both OTC and FDA-approved formulations) should be avoided in patients with chronic kidney disease (Weak recommendation, very low quality evidence).

Adjuncts to Colon Cleansing Before Colonoscopy
- The routine use of adjunctive agents [e.g. simethicone, flavored electrolyte solutions (Gatorade), prokinetics, spasmolytics, bisacodyl, senna, olive oil, and probiotics] for bowel cleansing before colonoscopy is not recommended (Weak recommendation, moderate-quality evidence).

Differences in Patient Preference/Willingness to Repeat Comparisons
- Split-dose bowel cleansing is associated with greater willingness to repeat regimen compared with the day before regimen (Strong recommendation, high-quality evidence).
- The use of low-volume bowel cleansing agents is associated with greater willingness to undergo a repeat colonoscopy (Strong recommendation, high-quality evidence).

Selection of Bowel Preparation in Specific Populations
- There is insufficient evidence to recommend specific bowel preparation regimens for elderly persons; however, we recommend that sodium phosphate preparations be avoided in this population (Strong recommendation, low-quality evidence).
- There is insufficient evidence to recommend specific bowel preparation regimens for children and adolescents undergoing colonoscopy; however, we recommend that sodium phosphate preparations should not be used in children younger than age 12 or in those with risk factors for complications from this medication (Strong recommendation, very low quality evidence).
- Sodium phosphate should be avoided in patients with known or suspected inflammatory bowel disease (Weak recommendation, very low quality evidence).
- Additional bowel purgatives should be considered in patients with risk factors for inadequate preparation (e.g. patients with a prior inadequate preparation, history of constipation, use of opioids or other constipating medications, prior colon resection, diabetes mellitus, or spinal cord injury) (Weak recommendation, low-quality evidence).
- Low-volume preparations or extended time delivery for high-volume preparations are recommended for patients after bariatric surgery (Weak recommendation, very low quality evidence).
- Tap water enemas should be used to prepare the colon for sigmoidoscopy in pregnant women (Strong recommendation, very low quality evidence).
- There is insufficient evidence to recommend specific regimens for persons with a history of spinal cord injury; additional bowel purgatives should be considered (Weak recommendation, very low quality evidence).

Recommendation Definitions^

Recommendation Strength	Definition
Strong	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted. The less values and preferences vary, or the lesser the uncertainty in values and preferences, the higher the likelihood that a strong recommendation is warranted. The lower the costs of an intervention, the higher the likelihood that a strong recommendation is warranted.
Weak	The narrower the gradient between the desirable and undesirable effects, the higher the likelihood that a weak recommendation is warranted. The lower the quality of evidence, the higher the likelihood that a weak recommendation is warranted. The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted. The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted.

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

^*From the GRADE series of papers*

Pall H, Zacur GM, Kramer RE, et al. Bowel Preparation for Pediatric Colonoscopy: Report of the NASPGHAN Endoscopy and Procedures Committee. J Pediatr Gastroenterol Nutr. 2014 Sep;59(3):409-16. doi: 10.1097/MPG.0000000000000447.

NASPGHAN best practices cleanout regimens

Option 1: PEG-3350, 1-day cleanout	<50 kg = 4 g · kg^{-1} · day^{-1}* + bisacodyl 5 mg >50 kg = 238 g in 1.5 L sports drink* + bisacodyl 10 mg
Option 2: PEG-3350, 2-day cleanout	<50 kg = 2 g · kg^{-1} · day^{-1}* + bisacodyl 5 mg >50 kg = 2 g · kg^{-1} · day^{-1}* + bisacodyl 10 mg
Option 3: NG cleanout	PEG-ELS: 25 mL · kg^{-1} · h^{-1}, maximum 450 mL/h† Sulfate-free PEG-ELS: 25 mL · kg^{-1} · h^{-1}, maximum 450 mL/h†
Option 4: non-PEG cleanout	Magnesium citrate 4–6 mL · kg^{-1} · day^{-1} + bisacodyl 5–10 mg

The vast majority (>90%) of children should not need NG cleanout and inpatient stay unless persistent vomiting or history of failed procedure because of poor bowel preparation. Patients with significant stool burden may benefit from modified regimen, that is, doubling duration of cleanout in option 1. NG = nasogastric tube; PEG = polyethylene glycol; PEG-3350 = a specific polyethylene glycol product; PEG-ELS = PEG with electrolytes.

* Should be administered for 4 to 6 hours.

† Until effluent is clear or up to 4 L and then reassess.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (4/1/2023 to 6/30/2023)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Bowel Prep Agents-Rx								
OsmoPrep® (sodium phosphate) 1.5 gram tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
peg-electrolyte (NaCl, NaHCO3, KCl) (NuLYTELY®) solution 420 gram oral solution	18	18	$496.18	$27.57	0	0 (0%)	F	No change
PEG-Prep [PEG-ES (NaCL, NaHCO3, KCl, Bisac)](Halflytely® with bisacodyl and flavor pack) 5 mg-210 gram oral kit†	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sodium, potassium and magnesium sulfates (Suprep®) Bowel Prep Kit 17.5 gram-3.13 gram-1.6 gram oral solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Clenpiq™ (sodium picosulfate, magnesium oxide, ascorbic acid) 10 mg-3.5 g-12 g/160 mL solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Plenvu® [PEG-ES (Na2SO4, NaCl, KCl, sodium ascorbate, ascorbic acid)] 140 gram-9 gram-5.2 gram powder pack	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sutab® (sodium sulfate, potassium chloride, and magnesium sulfate) 1.479-0.188-0.225 gram tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
[PEG-ES (NaSO4, NaCL, KCl; ascorbic acid, sodium ascorbate)] (MoviPrep®) 100 g powder for reconstitution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
PEG-ES (Na2SO4, NaHCO3, NaCl, KCl) (Golytely®) 236 g powder for reconstitution	79	79	$1,905.74	$24.12	0	0 (0%)	F-QL (4000/90)	No change
PEG-ES ((Na2SO4, NaHCO3, NaCl, KCl) (Colyte® w/Flavor packs)) 240 g powder for reconstitution	5	5	$68.80	$13.76	0	0 (0%)	F-QL (4000/90)	No change
TOTAL	**102**	**102**	**$2,470.72**	**$24.22**	**0**	**0 (0%)**		

Abbreviations: PEG = polyethylene glycol; PEG-ES = polyethylene glycol-electrolye solution
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

REFERENCES

1. Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on July 14, 2020.
2. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: http://www.fda.gov/. Accessed on July 14, 2020.
3. DailyMed. U.S. National Library of Medicine. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed on February 1, 2023.
4. A-Rahim Y, Falchuk M. Bowel preparation before colonoscopy in adults. Saltzman JR, Robson KM, eds. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on February 1, 2023.
5. ASGE Standards of Practice Committee, Saltzman JR, Cash BD, et al. Bowel preparation before colonoscopy. Gastrointest Endosc. 2015 Apr;81(4):781-94. doi: 10.1016/j.gie.2014.09.048. Epub 2015 Jan 14. Accessed on July 14, 2020.
6. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the US Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol. 2014 Oct;109(10):1528-45. doi: 10.1038/ajg.2014.272. Epub 2014 Sep 16. Accessed on July 14, 2020.
7. Pall H, Zacur GM, Kramer RE, et al. Bowel Preparation for Pediatric Colonoscopy: Report of the NASPGHAN Endoscopy and Procedures Committee. J Pediatr Gastroenterol Nutr. 2014 Sep;59(3):409-16. doi: 10.1097/MPG.0000000000000447. Accessed on July 14, 2020.
8. BioMedTracker. New York, NY: Informa, PLC. Available at: www.biomedtracker.com. Accessed on February 1, 2023.
9. Guyatt GH, Oxman AD, Gunn E Vist, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008 Apr 26; 336(7650): 924–926. doi: 10.1136/bmj.39489.470347.AD. Accessed on August 15, 2018.

Alameda Medication Request Guidelines (MRGs) For Review Q3 2023 P&T: Consent Agenda

Recommendation:

- Minor wording update

Moxifloxacin Oral Tablet	
Therapeutic Classes (AHFS)	Quinolone antibiotics
Medications	Formulary, Step Therapy Moxifloxacin 400mg tablet ****Please Note: If the request is for moxifloxacin for the treatment of multi-drug resistant tuberculosis, refer to criteria for medications for the treatment of multi-drug resistant tuberculosis *****
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all of the criteria are met, approve ~~up~~ 1 fill up to FDA approved maximum dosing If the criteria is not met, the request will be referred to a clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for approval: • Appropriate diagnosis/indication AND • Appropriate dose of medication based on age (i.e. pediatric and elderly populations) and indication AND • Documented trial and failure or intolerance to up to two formulary antibiotics that are used to treat the documented diagnosis OR • No other formulary medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia. OR • Based on culture and sensitivity data, moxifloxacin is the only treatment option.
Criteria Statement	Moxifloxacin tablet is reserved for members who have used (or cannot/should not use) up to two formulary antibiotic medications (if available) that are used to treat the documented diagnosis or when moxifloxacin is the only treatment option, based on culture and sensitivity data.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Minor clarification update

Physician Administered Medication (PAD)/ Medical Benefit Guidelines	
Therapeutic Classes (AHFS)	N/A
Medications	Physician Administered Medications (PAD) under the medical benefit
Covered Uses	Medically accepted indications 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** Up to a 6 month duration depending upon the diagnosis and usual treatment therapies **Later Approvals** Up to a 12 month duration depending upon the diagnosis and usual treatment therapies If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.
PA Review Criteria	****Medications falling under the physician administered drug/ medical benefit will be reviewed by AAH. Forward requests to AAH for review**** **Initial Authorization:** • Approve if: ○ Medication or product is administered by a healthcare professional AND ○ The medication will be provided via the Medical Benefit AND ○ Appropriate diagnosis/indication for requested medication or meets criteria below AND ▪ Medication is being requested for an accepted off-label use and is listed in the standard clinical decision support resources (as noted in Diagnosis section above) OR ▪ Requested use can be supported by at least two published peer reviewed clinical studies which must be submitted along with request ○ Requested quantity does not exceed FDA approved or standard off-label dose OR • Member is new to the plan (within the last 6 months) and the request is for continuation of therapy. Approve if: ○ Continuation of therapy is clinically appropriate AND ○ Medication or product is administered by a healthcare professional AND ○ Prescriber attests that member has been on this medication continuously before joining AAH AND ○ Request is for generic or single source brand AND ○ The diagnosis and dosage provided meets FDA labeling and/or drug-specific criteria or off-label criteria **Reauthorization:** • Continuation of therapy is clinically appropriate AND • Medication or product is administered by a healthcare professional under the Medical Benefit
Criteria Statement	N/A
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Minor clarification update

Off-label uses	
Therapeutic Classes (AHFS)	N/A
Medications	Formulary, Formulary PA required, Formulary, ST required, or Non-formulary medications with off-label uses
Covered Uses	Off-Label indications (medically accepted indications are defined using the following sources: American Hospital Formulary Service-Drug Information (AHFS-DI), Truven Health Analytics Micromedex DrugDEX (DrugDEX), National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium, Wolters Kluwer Lexi-Drugs, and Elsevier/Gold Standard Clinical Pharmacology and/or positive results from two peer-reviewed published studies.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**Initial criteria for approval:**
	• One of the following:
	  ◦ Patient has had a documented trial and or intolerance with up to two preferred medications used to treat the documented diagnosis, or for medications where there is only one preferred agent, only that agent must have been ineffective or not tolerated.
	  ◦ No other formulary medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia
	AND
	• One of the following:
	  ◦ Medication is being requested for an accepted off-label use and is listed in the standard clinical decision support resources (as noted in Covered Uses section above)
	  ◦ Requested use can be supported by at least two published peer reviewed clinical studies which must be submitted along with request
	AND
	• Medication is being requested at an appropriate dose per literature
	
	Reauthorization criteria for approval:
	• Patient is stable and continuing the medication AND
	• Medication is used for appropriate indication and at appropriate dose

Criteria Statement	Medications for off-label use are reserved for members who have a medication being requested at an appropriate dose per the medical literature AND have used (or cannot should not use) up to two preferred medications to treat the diagnosis, or where there is no other formulary medication with a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia available AND the 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.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Minor clarification update

Non-Formulary and PA Required Medications without Drug-Specific Criteria	
Therapeutic Classes (AHFS)	N/A
Medications	Non-Formulary and PA Required Medications without Drug Specific Criteria ****Please Note: If the request is for a non-formulary brand with a generic, refer to Criteria for Brand Medications When Generic is Available*****
Covered Uses	Medically accepted indications 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 purposes/ indications (unless related to gender dysphoria, mental health, or substance use disorder)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	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	**Approval** Up to 12 months depending on diagnosis and usual treatment therapies If the criteria is not met, the request will be referred to a clinical reviewer for medical necessity review.
PA Review Criteria	****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**** **Criteria for approval:** • Appropriate diagnosis/Indication for requested non-formulary medication or meets off-label criteria below AND *Off-label criteria:* ○ One of the following: ▪ Patient has had a documented trial and or intolerance with up to two preferred medications used to treat the documented diagnosis, or for medications where there is only one preferred agent, only that agent must have been ineffective or not tolerated. ▪ No other formulary medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia **AND**

	○ One of the following: ▪ Medication is being requested for an accepted off-label use and is listed in the standard clinical decision support resources (as noted in Covered Uses section above) ▪ Requested use can be supported by at least two published peer reviewed clinical studies which must be submitted along with request • Appropriate dose of medication based on age (i.e. pediatric and elderly populations) and indication AND • In the absence of evidence supporting the use of the requested medication compared to the preferred agents, documented trial and failure or intolerance with at least three formulary medications (if available) that are used to treat the documented diagnosis (consideration will also be given to the route of administration, mechanism of action, and potency of the requested medication and the alternatives tried). For medications where there is only one formulary agent, only that agent must have been ineffective or not tolerated OR • No other formulary medication has a medically accepted use for the patient's specific diagnosis as referenced in the medical compendia. OR • All other formulary medications are contraindicated based on the patient's diagnosis, other medical conditions, or other medication therapy. OR • 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] • 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 used approved, dosed once daily.)
Criteria Statement	Non-formulary and prior authorization required medications are reserved for members who have used (or cannot/should not use) up to three formulary three formulary that are used to treat the documented diagnosis OR meet off-label criteria OR has tried and failed or is unable to use separate components (or therapeutic equivalents) of a combination medication or is unable to use a consolidated dose form.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Retacrit availability is no longer an issue, update preferred agents.
- Minor zidovudine clarification

Erythropoiesis-Stimulating Agents	
Therapeutic Classes (AHFS)	Erythropoiesis-Stimulating Agents
Medications	Formulary, PA required Retacrit (epoetin alfa-epbx) - **PREFERRED** Aranesp (darbepoetin alfa) Procrit (epoetin alfa) ~~– **PREFERRED** (if Retacrit is not available)~~ Epogen (epoetin alfa) ~~– **PREFERRED** (if Retacrit is not available)~~ Non-formulary Mircera (methoxy polyethylene glycol-epoetin beta)
Covered Uses	Medically accepted indications 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** If criteria are met, the request will be approved as follows: 1 month if the patient is deficient in iron, vitamin B12 or folate, and in the perisurgical setting 3 months for all other requests. If the provider attests that the preferred medication is for a chronic or long-term condition, reauthorization will be approved for 12 months If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**Criteria for authorization of existing epoetin users who are NEW to the plan:**
	• Documentation of current dose
	• Documentation of hemoglobin level results within 30 days or member has responded to therapy (≥1-2 g/dL increase in hemoglobin (HgB) or decrease in transfusion requirements)
	
	Requests for Initial Therapy:
	• All lab results submitted must have been drawn within 30 days of request:
	• The following lab values – hemoglobin (HgB) and hematocrit (HCT)
	• Normal lab results or, if abnormally low, appropriate supplementation as follows:
	  ○ serum ferritin level (normal is > 100 ng/mL)
	  ○ transferrin saturation (TSAT) (normal is > 20%)
	  ○ vitamin B12 level(> 223 pg/mL)
	  ○ folate level (> 3.1 ng/mL)
	• For requests for non-preferred ESAs, documentation must be provided as to why preferred are not medically appropriate for the member.
	• **For anemia of CKD:**
	  ○ HgB < 10 g/dL
	
	• **For anemia related to cancer:**

Erythropoiesis-Stimulating Agents	
	○ Receiving myelosuppressive therapy for palliative treatment (members receiving myelosuppressive therapy with curative intent should not receive ESAs) **AND** documented symptomatic anemia with HgB <10 g/dL **OR** ○ The member has symptomatic anemia related to myelodysplastic syndrome AND documented serum erythropoietin level ≤ 500 mU/mL • **For zidovudine-related anemia in members with HIV:** ○ The member must currently be receiving zidovudine-containing highly active antiretroviral therapy (HAART) (zidovudine ≤ 4200 mg/week) ○ Erythropoietin level ≤ 500 mU/mL • **For ribavirin-induced anemia:** ○ Documented attempt to reduce dose was made ○ HgB < 12 g/dL • **For members undergoing surgery to reduce the need for allogenic blood transfusion:** ○ Perioperative hemoglobin must be < 13 g/dL and > 10 g/dL. ○ The member is scheduled for an elective, non-cardiac, nonvascular surgery. **Reauthorization**: • Repeat normal labs within 30 days from date of request, or appropriate supplementation as follows: ○ serum ferritin level (> 100 ng/mL) ○ TSAT (> 20%) ○ vitamin B12 level (> 223 pg/mL) ○ folate level (> 3.1 ng/mL) • For anemia of CKD: HgB ≤ 11 g/dL • For anemia related to cancer: HgB ≤ 12 g/dL • For zidovudine-related anemia in members with HIV: HgB ≤ 12 g/dL • For ribavirin-induced anemia: HgB ≤ 12 g/dL • An increase in dose has not occurred more than once every 4 weeks • If the request is a non-preferred agent, documentation must be provided as to why preferred medications are not medically appropriate for the member
Criteria Statement	Mircera, Procrit, Epogen, or Aranesp are reserved for members who have used (or cannot/should not use) Retacrit., ~~Procrit, or Epogen,~~
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Minor wording clarifications

Vancomycin	
Therapeutic Classes (AHFS)	Antibacterials, miscellaneous
Medications	Formulary, with quantity limit Vancomycin 125, 250 mg capsules Firvanq 25, 50 mg/ml solution Non-Formulary Vancomycin 250mg/5ml (50mg/ml) 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), 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 only up to 10 day duration.~~ Durations exceeding 10 days are approvable if vancomycin was used for initial episode of Clostridium (or Clostridioides) difficile infection (CDI) and now pulsed-tapered regimen required. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	Requests for formulary agents above the quantity limit will be approved if: • Dosing requested is appropriate based on dosing guidelines AND • Treatment with vancomycin capsules or Firvanq is being requested for treatment of a first recurrence when vancomycin capsules or Firvanq was used for initial treatment and pulsed-tapered regimen is required OR • Treatment with vancomycin capsules or Firvanq is being requested for treatment of a second or subsequent recurrence and pulsed-tapered regimen is required Requests for vancomycin 250mg/5ml (50mg/ml) oral solution will be approved if: • Dose is appropriate per label or supported by compendia/standard of care guidelines for initial treatment OR first, second, or subsequent recurrence and pulsed-tapered regimen is required AND • The patient has tried and failed both formulary dosage forms, and/or has another documented medical reason (intolerance, hypersensitivity, contraindication, etc.) for not utilizing these medications to treat their medical condition.
Criteria Statement	Vancomycin capsules or Firvanq above the quantity limits are reserved for members with a first recurrence of Clostridium (or Clostridioides) difficile infection (CDI) after initial treatment with vancomycin capsules or Firvanq or members with a second recurrence in which pulsed-tapered regimen is required. Vancomycin 250mg/5ml (50mg/ml) oral solution is reserved for members who have used (or cannot/should not use) formulary vancomycin capsules and Firvanq.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Minor wording clarification

Scabicides and Pediculicides	
Therapeutic Classes (AHFS)	Scabicides and pediculicides
Medications	Formulary, Step therapy required Malathion (Ovide) 0.5% lotion Spinosad (Natroba) 0.9% suspension Ivermectin (Sklice) 0.5% lotion Non-Formulary Lindane 1% shampoo Crotan (crotamiton) 10% lotion Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial** If all conditions are met, the request will be approved for up to 1 treatment. **Re-approval** If conditions are met, the request will be approved for a maximum of 2 treatments in a 30 day period. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	INITIAL: **Head Lice:** For the approval of the formulary-step therapy required medications: • Diagnosis of pediculosis capitis (head lice and its eggs). • Documented intolerance or hypersensitivity to a first line agent, permethrin 1% OTC or pyrethrins/piperonyl butoxide OTC OR • Documented trial and failure of a first line agent, permethrin 1% OTC or pyrethrins/piperonyl butoxide OTC, within the previous 45 days, but no earlier than 7 days after the original fill. For the approval of the non-formulary medication: • All criteria above must be met AND documented trial and failure, intolerance, or reason not to use two of the following formulary medications: malathion (Ovide) 0.5% lotion or spinosad (Natroba) 0.9% suspension or ivermectin (Sklice) 0.5% lotion **Scabies:** For the approval of the formulary-step therapy required medications: • Diagnosis of scabies (Sarcoptes scabiei) • Documented trial and failure, intolerance, or hypersensitivity to the first line agent: permethrin 5% topical cream For the approval of the non-formulary medication: • All criteria above must be met AND documented trial and failure of: spinosad (Natroba) 0.9% suspension

	RENEWAL: • For head lice: spinosad can be approved for a second treatment if live lice are present 7 days after the initial treatment. • For head lice: malathion can be approved for a second treatment if live lice are present 7-9 days after the initial treatment. • For scabies: Crotan can be approved for a second treatment if itching still present or if new burrows or lesions continue to appear 2-4 weeks after the initial treatment & also the 2nd application 24 hours later ~~2nd application.~~
Criteria Statement	For the treatment of head lice, malathion (Ovide) 0.5% lotion, spinosad (Natroba) 0.9% suspension, and ivermectin (Sklice) 0.5% lotion are reserved for members who have used (or cannot/should not use) permethrin 1% OTC or pyrethrins/piperonyl butoxide OTC. For the treatment of head lice, Lindane lotion is reserved for members who have used (or cannot/should not use) permethrin 1% OTC or pyrethrins/piperonyl butoxide OTC AND two of the following formulary medications: malathion (Ovide) 0.5% lotion or spinosad (Natroba) 0.9% suspension or ivermectin (Sklice) 0.5% lotion. For the treatment of scabies, spinosad (Natroba) 0.9% suspension is reserved for members who have used (or cannot/should not use) permethrin 5% topical cream. For the treatment of scabies, Crotan lotion is reserved for members who have used (or cannot/should not use) permethrin 5% topical cream AND spinosad (Natroba) 0.9% suspension.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Minor spelling update

Dronabinol	
Therapeutic Classes (AHFS)	Antiemetics, Miscellaneous
Medications	Formulary, PA required Dronabinol (Marinol): pays at point of sale for members with diagnosis of HIV ICD 10 B20, for all other diagnoses, prior authorization is required Non-formulary Syndros 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), 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:
	• Patient has anorexia or weight loss associated with AIDS/HIV OR
	• Patient has nausea or vomiting due to chemotherapy AND documentation of trial and failure, contraindication, or intolerance to at least two of the following~~:~~
	  ○ 5-HT3 antagonists (ondansetron up to 8mg BID, granisetron)
	  ○ Dopamine receptor antagonists (e.g. ~~prochlorpherazine~~prochlorperazine, promethazine, or metoclopramide)
	  ○ Aprepitant
	  ○ Dexamethasone
	• OR Patient has anorexia or weight loss associated with cancer AND documentation of trial and failure, contraindication, or intolerance to megestrol or cyproheptadine.
	• If request is for Syndros, above criteria must be met AND documentation provided of inability to swallow dronabinol capsules must be provided

Criteria Statement	Dronabinol is reserved for members that have AIDS/HIV. For nausea or vomiting due to chemotherapy, dronabinol is reserved for members who have used (or cannot/should not use) ondansetron, granisetron, dexamethasone, or ~~prochlorpherazine~~prochlorperazine. For weight loss due to cancer, dronabinol is reserved for members who have used (or cannot/should not use) megestrol or cyproheptadine.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Constipation agents	
Therapeutic Classes (AHFS)	N/A
Medications	<u>Formulary, Prior Authorization Required</u> Linzess (linaclotide) capsule lubiprostone (Amitiza) Movantik (naloxegol) Relistor (methylnaltrexone) Symproic (naldemedine) Motegrity (prucalopride) Trulance (plecanatide) Ibsrela (tenapanor)
Covered Uses	Medically accepted indications 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"**
Age Restrictions	Patient must be ≥ 18 years of age
Prescriber Restrictions	None
Coverage Duration	**Initial Approval** 6 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	**INITIAL AUTHORIZATION for irritable bowel syndrome with constipation predominate (IBS-C):** • The patient has a clinical diagnosis of irritable bowel syndrome constipation predominate (IBS-C) • Medication is prescribed at an FDA approved dosage • Documentation of trial and failure, contraindication, or intolerance of a soluble fiber (e.g. psyllium) within the last 90 days • If the above criteria are met, for requests for Linzess, Trulance, or lubiprostone (Amitiza): approve. **OR** • For requests for other formulary, prior authorization required medications, the above criteria must be met, AND documentation of trial and failure, contraindication, or intolerance of Linzess, Trulance, or lubiprostone (Amitiza) within the last 90 days is required **INITIAL AUTHORIZATION for chronic idiopathic constipation (CIC):** • The patient has a clinical diagnosis of chronic idiopathic constipation (CIC) • Medication is prescribed at an FDA approved dosage • Documentation of trial and failure, intolerance, or inability to use a soluble fiber (e.g. psyllium) within the last 90 days • Documentation of trial and failure, contraindication, or intolerance, to at least 2 formulary alternative laxatives (example: milk of magnesia, polyethylene glycol, docusate sodium, senna) within the last 90 days

	• If the above criteria are met, for requests for Linzess, Trulance, Motegrity, or lubiprostone (Amitiza): approve. **OR** • For requests for other formulary, prior authorization required medications, the above criteria must be met, AND documentation of trial and failure, contraindication, or intolerance to Linzess, Trulance, Motegrity, or lubiprostone (Amitiza) within the last 90 days is required **INITIAL AUTHORIZATION FOR DIAGNOSIS OPIOID-INDUCED CONSTIPATION (OIC) with chronic non-cancer pain:** • The patient has a clinical diagnosis of opioid-induced constipation with chronic non-cancer pain • Medication is being prescribed at an FDA approved dosage • Documentation of trial and failure contraindication, or intolerance to at least 2 formulary alternative laxatives (example: milk of magnesia, polyethylene glycol, docusate sodium, senna) within the last 90 days • If the above criteria are met, for requests for Movantik, Symproic, or lubiprostone (Amitiza): approve **OR** • For requests for other formulary, prior authorization required medications, the above criteria must be met, AND documentation of trial and failure, contraindication, or intolerance to Movantik, Symproic, or lubiprostone (Amitiza) within the last 90 days is required **INITIAL AUTHORIZATION FOR DIAGNOSIS OPIOID-INDUCED CONSTIPATION (OIC) with advanced illness:** • The patient has a clinical diagnosis of opioid-induced constipation with advanced illness • Medication is being prescribed at an FDA approved dosage • Documentation of trial and failure contraindication, or intolerance to at least 2 formulary alternative laxatives (example: milk of magnesia, polyethylene glycol, docusate sodium, senna) within the last 90 days • If the above criteria are met, for requests for Relistor injectable (e.g. vial or syringe) approve. **OR** • For requests for other formulary, prior authorization required medications, the above criteria must be met, AND documentation of trial and failure, contraindication, or intolerance to Relistor injectable (e.g. vial or syringe) within the last 90 days is required **PA CRITERIA FOR REAUTHORIZATION (IBS-C, CIC, opioid-induced constipation):** • Documentation of continued clinical benefit from treatment. • Medication is being prescribed at an FDA approved dosage
Criteria Statement	For the diagnosis of irritable bowel syndrome with constipation, lubiprostone (Amitiza), Linzess, and Trulance are reserved for members who have used (or cannot/should not use) a soluble fiber (example: psyllium) within the last 90 days. Ibsrela is reserved for members who have also used lubiprostone (Amitiza), Linzess, or Trulance within the last 90 days. For the diagnosis of chronic idiopathic constipation, lubiprostone (Amitiza), Linzess, Motegrity, and Trulance are reserved for members who have used (or

	cannot/should not use) a soluble fiber (example: psyllium) AND at least 2 formulary alternative laxatives (example: milk of magnesia, polyethylene glycol, docusate sodium, senna) within the last 90 days. For the diagnosis of opioid-inducted constipation with chronic non-cancer pain, lubiprostone (Amitiza), Symproic, and Movantik are reserved for members who have used (or cannot/should not use) at least 2 formulary alternative laxatives (example: milk of magnesia, polyethylene glycol, docusate sodium, senna) within the last 90 days. Relistor is reserved for members who have also used lubiprostone (Amitiza), Symproic, or Movantik within the last 90 days. For the diagnosis of opioid-inducted constipation with advanced illness, Relistor injectable is reserved for members who have used (or cannot/should not use) at least 2 formulary alternative laxatives (example: milk of magnesia, polyethylene glycol, docusate sodium, senna) within the last 90 days.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Multaq (dronedarone)	
Therapeutic Classes (AHFS)	Antiarrhythmic agents
Medications	Formulary, PA required Multaq (dronedarone)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to 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** • Diagnosis of paroxysmal or persistent atrial fibrillation (AF) or atrial flutter. • Attestation that the patient does not have NYHA (New York Heart Association) Class III or IV heart failure or symptomatic heart failure with recent decompensation in the last 4 weeks requiring hospitalization. • Attestation that the patient does not have permanent atrial fibrillation (AF) that will not or cannot be cardioverted or restored to normal sinus rhythm.
Criteria Statement	Multaq is reserved for members who have paroxysmal or persistent atrial fibrillation or atrial flutter without NYHA (New York Heart Association) class III or IV heart failure or symptomatic heart failure with recent decompensation in the last 4 weeks requiring hospitalization. Members must also not have permanent atrial fibrillation that cannot be cardioverted to normal sinus rhythm.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Safety Edit Exception	
Therapeutic Classes (AHFS)	N/A
Medications	Formulary drugs and non-formulary drugs (non-formulary and formulary drug criteria must also be met): • Exceeding the Food and Drug Administration (FDA) or compendia max dose recommendations • Exceeding the FDA dosing or compendia administration frequency recommendations • Exceeding the FDA or compendia duration of therapy recommendations • Duplication of therapy error at Point of Service (POS) • Age Restriction error at POS • Day Supply Limit error at POS
Covered Uses	Medically accepted indications 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** One month approval for duplication of therapy when transitioning from one agent to another and day supply limit due to a dose increase . All other scenarios: 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	**Exceeding the Food and Drug Administration (FDA) or compendia maximum dose, administration frequency or duration of therapy recommendations.** • The member must have a documented treatment failure with the drug at the maximum tolerated dose or maximum dose (whichever is the lesser dose), administration frequency or duration of therapy. AND • The provider must submit a medical reason why the maximum dose, administration frequency or duration of therapy needs to be exceeded based on the member's condition or treatment history. **Duplication of therapy** <u>Transition from one agent to another</u> • If a provider has outlined a plan to transition a member to a similar drug or provided a dose titration schedule, the requested drug is approved for one month*. <u>Concurrent Therapy with two similar agents</u> • The provider must submit a medical reason why treatment with more than one drug in the same class is required based on the member's condition and treatment history. OR • The provider must submit disease state specific standard of care guidelines supporting concurrent therapy.

	Age Restriction • The provider must submit a medical reason why the drug is needed for a member whose age is outside of the plan's minimum or maximum age limit. AND • The indication and dose requested is supported by the Medical Compendia or current treatment guidelines. **Day Supply Limit** • An additional fill exceeding the day supply limit is needed based on a dose increase or is needed to achieve a total daily dose OR • The provider must submit a medical reason why an additional fill is needed outside of the plan's day supply limit. AND • The indication and dose requested is supported by the Medical Compendia or current treatment guidelines.
Criteria Statement	N/A
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Quantity Limit Exception	
Therapeutic Classes (AHFS)	N/A
Medications	Formulary drugs exceeding the Alameda Alliance's published quantity limits A quantity limit is defined as a limitation in the amount of medication per fill or time period and/or limitation in the amount of fills per calendar year or other time period.
Covered Uses	Medically accepted indications 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 has submitted justification for the approval of doubling (or higher) of the number of tablets/capsules per prescription for a medication that has a higher strength tablet/capsule available, stating why that higher dose tablet/capsule cannot be used (e.g. two lorazepam 0.5mg tablets to equal the dose of lorazepam 1mg, when lorazepam 1mg tablet exists). AND • The dose requested is supported by the Medical Compendia or current treatment guidelines. OR • 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	N/A
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Atovaquone-proguanil (Malarone)	
Therapeutic Classes (AHFS)	Antimalarials
Medications	Formulary, PA required: Atovaquone-proguanil (Malarone) 62.5-25 mg tablet Atovaquone-proguanil (Malarone) 250-100 mg tablet
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage duration	For prophylaxis: If all of the conditions are met, the request will be approved for up to 3 months. If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review. For treatment: If all of the conditions are met, the request will be approved for one time fill. 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 THE USE OF ATOVAQUONE/PROGUANIL FOR MALARIA PROPHYLAXIS • The medication is being prescribed at a dose that is within FDA approved guidelines. • Member is traveling to a country with mefloquine resistant malaria (see CDC website at http://www.cdc.gov/malaria/travelers/country_table/a.html) OR • Member is traveling to a country with known malaria risk and due to time constraints is unable to start prophylaxis with preferred agents 1-2 weeks prior to departure OR • Member has underlying neuropsychiatric conditions (as shown through clinical notes and/or claims history) such as: active and/or recent history of depression, chronic anxiety disorders, psychosis, and/or schizophrenia. **CRITERIA FOR THE USE OF ATOVAQUONE/PROGUANIL FOR MALARIA TREATMENT** • Diagnosis of malaria
Criteria Statement	For prophylaxis, atovaquone-proguanil is reserved for members traveling to a country with mefloquine resistance, member is unable to start therapy 1 to 2 weeks prior to travel departure, or member has condition such as depression, anxiety, psychosis, or schizophrenia.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Santyl Ointment	
Therapeutic Classes (AHFS)	Collagenase (enzymatic debriding ointment)
Medications	**Formulary, PA required** Santyl ointment
Covered Uses	Medically accepted indications 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** 3 months **Later Approvals** 3 months If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**Criteria for initial approval of Santyl ointment**
	• Santyl ointment requests may be approved for up to 3 months
	  ○ For requests greater than 3 months, the provider must submit a medical reason of necessity
	• Type of wound is one of the following:
	  ○ Wounds to be debrided, severe burns, or chronic dermal ulcers
	• Verification that the requested amount does not exceed the amount on the Santyl dosing calculator: **https://www.santyl.com/hcp/dosing**
	  ○ Dimension of wound and duration of treatment required for calculation of dose and amount
	
	Criteria for reauthorization:
	• Documentation submitted indicates a clinical benefit was observed (e.g., reduction in wound size, decrease in wound-related pain, etc.)
	• Duration of time requested as therapy extension
	• Verification that the requested amount does not exceed the amount on the Santyl dosing calculator: **https://www.santyl.com/hcp/dosing**
	  ○ Dimension of wound and duration of treatment required for calculation of dose and amount

Criteria Statement	Santyl ointment is reserved for members who are undergoing wound care treatment requiring enzymatic debridement therapy.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Spravato (esketamine) Intranasal	
Therapeutic Classes (AHFS)	N/A
Medications	Spravato (esketamine) intranasal
Covered Uses	Medically accepted indications 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** 4 weeks **Later Approvals** 6 months If criteria is not met, request will be sent to a clinical reviewer for medical necessity review.

PA Review Criteria	**Initial Authorization:**
	• The member has a diagnosis of at least one of the following:
	  ○ Major depressive disorder with treatment-resistant depression.
	  ○ Major depressive disorder with acute suicidal ideation or behavior.
	• Medication will be used in conjunction with an oral antidepressant.
	• Medication is being prescribed at an FDA approved dosage.
	
	Additionally, if member has diagnosis for major depressive disorder with treatment-resistant depression only (i.e. without suicidal ideation or behavior):
	• Documented trial and failure of three preferred oral antidepressants (eg. SSRIs, SNRIs, TCAs) of at least a minimum effective dose for four (4) weeks or longer OR; a medical justification as to why the patient cannot use preferred alternative(s).
	
	Re-authorization:
	• Medication is prescribed at an FDA-approved dosage.
	• Medication is being used in conjunction with an oral antidepressant.
	• Documentation was submitted indicating the member has clinically benefited from therapy.

Criteria Statement	Spravato is reserved for members who have treatment-resistant depression who have tried and failed (or cannot use) three other preferred oral antidepressants for 4 weeks or longer and who will use Spravato along with another oral antidepressant. Spravato is reserved for members who have depression with acute suicidal ideation and who will use Spravato along with another oral antidepressant.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Topical Acne Agents	
Therapeutic Classes (AHFS)	Cell stimulants and proliferants
Medications	Formulary restricted to members ≤ 21 years and quantity limit #45 g/30 days; prior authorization required for members > 21 years Tretinoin (Retin-A) 0.01%, 0.025%, 0.05% gel Tretinoin (Retin-A) 0.1%, 0.025%, 0.05% cream
Covered Uses	Medically accepted indications 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	Tretinoin criteria for approval: For members ≤ 21 years of age: • Documentation of trial and failure, intolerance, contraindication, or inability to use the following formulary alternative: Differin 0.1% gel OTC For members > 21 years of age • Diagnosis of acne vulgaris • Documentation of trial and failure, intolerance, contraindication, or inability to use the following formulary alternatives: Differin 0.1% gel OTC AND topical antibiotics
Criteria Statement	For members ≤ 21 years of age, tretinoin gel or cream are reserved for members who have used (or cannot/should not use) Differin 0.1% OTC gel. For members > 21 years of age, tretinoin gel or cream are reserved for members who have acne, who have used (or cannot/should not use) Differin 0.1% OTC gel and topical antibiotics.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Memantine ER (Namenda XR)	
Therapeutic Classes (AHFS)	Central Nervous System Agents, Misc
Medications	Formulary, step therapy required memantine ER (Namenda XR)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to 12 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	Criteria for approval • Documented trial and failure, intolerance, or contraindication to use donepezil AND memantine IR OR • Documentation member unable to adhere to twice daily dosing due to caregiver limitations
Criteria Statement	Memantine ER is reserved for members who have used (or cannot/should not use) donepezil AND memantine IR or for members unable to comply with twice daily dosing due to caregiver limitations.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Tranexamic acid (Lysteda)	
Therapeutic Classes (AHFS)	Hemostatics
Medications	PA required, quantity limit (30/5), fill limit (1 fill per 28 days) Tranexamic acid (Lysteda) 650mg tablet
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Patients who are pregnant
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	None
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	Criteria for initial authorization: • Diagnosis of cyclic heavy menstrual bleeding (HMB) • The medication is used at the FDA-approved dose of 1,300 mg 3 times daily (3,900 mg/day) for a maximum of 5 days during monthly menstruation • Documented contraindication to or trial and failure of the use of a formulary combined oral estrogen-progestin contraceptive OR an oral progestin only contraceptive AND a formulary non-steroidal anti-inflammatory agent. Criteria for re-authorization: • Patient is stable and has a reduction of heavy menstrual bleeding **Criteria for Quantities and Fills Greater Than Allowed:** If the patient requires doses greater than the set limits after meeting approval the following conditions must be met: • The provider has submitted a medical reason why the plan's quantity or fill limit will be inadequate based on the member's condition and treatment history
Criteria Statement	Tranexamic acid (Lysteda) is reserved for members who are experiencing heavy menstrual bleeding and have tried and failed or are unable to take oral contraceptives and non-steroidal anti-inflammatory agents (NSAIDs). 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	~~9/2022~~9/2023

Recommendation:

- No changes

Biologic Agents for Nasal Polyposis	
Therapeutic Classes (AHFS)	SKIN AND MUCOUS MEMBRANE AGENTS, MISC.; RESPIRATORY TRACT AGENTS, MISCELLANEOUS
Medications	Formulary, PA required Dupixent (dupilumab) Xolair (omalizumab) Nucala (mepolizumab)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Use of Dupixent, Nucala, or Xolair concomitantly or with another pulmonary biologic (e.g. Fasenra, Cinqair)
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Patients must be 18 years age or older Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be an allergist/immunologist or otolaryngologist
Coverage Duration	**Initial Approval** If the criteria are met, the initial request may be approved for up to a 6-month duration. **Reauthorization** Reauthorization requests may be approved for 6 months. If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	****Xolair: For asthma and urticaria, please refer to the "Xolair for Asthma and Urticaria" policy**** ****Dupixent: For atopic dermatitis, please refer to the "Agents for Atopic Dermatitis" policy; For asthma, please refer to the "Pulmonary Biologics for Asthma and Eosinophilic Conditions**** ****Nucala: For asthma or other eosinophilic conditions, please refer to the "Pulmonary Biologics for Asthma and Eosinophilic Conditions" policy**** **Initial Authorization:** • Diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) • Medication is being prescribed at an FDA approved dosage • Patient is currently using an intranasal corticosteroid and will continue therapy, will be prescribed an intranasal corticosteroid with request, or has a medical reason for not using an intranasal corticosteroid • Documentation of ONE of the following: o Trial and failure or intolerance or has a medical reason for not using ALL of the following therapies: ▪ an intranasal corticosteroid ▪ a systemic corticosteroid o Prior surgery for nasal polyps **Re-authorization:** • Member will continue to use intranasal corticosteroid, or has a medical reason for not using an intranasal corticosteroid • Documentation has been provided that demonstrates a clinical benefit (e.g. improvements in symptom severity, nasal polyp score [NPS], sino-nasal

	outcome test-22 [SNOT-22], nasal congestion score [NCS]), nasal obstruction symptom visual analogue scale [VAS]) • Medication is being prescribed at an FDA-approved dosage
	When used for chronic rhinosinusitis with nasal polyps, Xolair, Nucala, or Dupixent are reserved for members who have used (or cannot/should not use) an intranasal steroid (and will continue using it) and additionally, who have used (or cannot/should not use) all of the following: intranasal corticosteroids and a systemic corticosteroid, OR has had prior surgery for nasal polyps.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes.
- A full insulin class review will be presented during Q4 2023 P&T to review and analyze upcoming insulin price 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 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 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	~~6/2022~~9/2023

Recommendation:

- No changes

Antiemetics	
Therapeutic Classes (AHFS)	5-HT3 Receptor Antagonists, Neurokinin-1 receptor antagonists
Medications	Formulary ondansetron (Zofran) tablet 4mg, 8mg (quantity limit) ondansetron (Zofran) ODT (quantity limit) Formulary, Prior Authorization Required ondansetron (Zofran) tablet 24mg (quantity limit) palonosetron (Aloxi) IV solution 0.25mg/5ml vial palonosetron (Aloxi) IV solution 0.25mg/2ml vial, 0.25mg/5ml syringe granisetron (Kytril) oral tablet, IV solution Zuplenz (ondansetron) oral film aprepitant (Emend) capsule Non-Formulary ondansetron (Zofran) oral solution, IV solution, injection (IV/SQ) solution Anzemet (dolasetron) tablet Sustol (granisetron ER) SQ injection Sancuso (granisetron ER) transdermal patch fosaprepitant (Emend) IV emulsion Emend (fosaprepitant) powder packet Cinvanti (aprepitant) IV emulsion Varubi (rolapitant) oral capsule Akynzeo (fosnetupitant/palonosetron) capsule, IV solution Any other newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** If all of the conditions are met, the request will be approved for up to a 6 month duration, as per chemotherapy cycle, or as recommended per FDA approved indications and/or defined medical compendium and/or per the NCCN, ASCO, NCI, or MASCC standard of care guidelines. 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 (Pediatric Population): • Check AAH active CCS cases for members < 21 years of age Criteria for approval (Adult Population): • Prescribed dosing is within FDA approved indications and limitations and/or supported by medical compendium and NCCN, ASCO, NCI, or MASCC standard of care guidelines, and is within quantity limits, if applicable. • Patients receiving an antineoplastic agent = HIGH or MODERATE emetic risk per the NCCN Practice guidelines can receive palonosetron hydrochloride

	(Aloxi) and aprepitant (Emend) capsule, as first line antiemetic agents **For reference, please consult the most recent NCCN guidelines for Antiemesis which can be located under NCCN Guidelines for Supportive Care: Antiemesis* @ https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf • For all other patients, if the request is for a formulary, prior authorization required or non-formulary agent, the patient has a documented treatment failure after receiving an adequate trial of formulary 5HT-3 RA (ondansetron) and/or has another documented medical reason (intolerance, hypersensitivity, contraindication, etc.) for not utilizing these medications to treat their medical condition. • The medication is recommended and prescribed by a specialist in the field to treat the patient's respective medical condition. 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	Antiemetics other than ondansetron tablets and ODT are reserved for members who have used (or cannot/should not use) oral ondansetron 4mg or 8 mg oral tablets or oral disintegrating tablets for the respective mechanism of action requested. Palonosetron (Aloxi) or aprepitant (Emend) capsule are reserved for members who are using a high or moderate emetic risk antineoplastic.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Rifabutin (Mycobutin)	
Therapeutic Classes (AHFS)	Antitubercular agents
Medications	Formulary, PA required Rifabutin (Mycobutin) 150 mg capsule
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber is an infectious disease specialist or working in consultation with infectious disease specialist
Coverage Duration	**Initial Approval** **Diagnosis of tuberculosis** If all of the conditions are met, the request will be approved for up to 26 weeks. If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review. **Prophylaxis of disseminated mycobacterium avium complex (MAC) disease** If all of the conditions are met, the request will be approved for up to a 12 month duration. If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	For prophylaxis of disseminated mycobacterium avium complex (MAC) disease, approve if: • Documentation of advanced HIV • Documentation that the patient does not have active tuberculosis • Documented trial and failure, contraindication, intolerance, or inability to use azithromycin or clarithromycin • Requested dose is within recommended dosing guidelines For diagnosis of tuberculosis, approve if: • Documented contraindication, intolerance, or inability to use rifampin. • Requested dose is within recommended dosing guidelines
Criteria Statement	For prophylaxis of disseminated mycobacterium avium complex (MAC) disease, rifabutin is reserved for members who have used (or cannot/should not use) azithromycin or clarithromycin and do not have active tuberculosis. For tuberculosis, rifabutin is reserved for members who have used (or cannot/should not use) rifampin
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Topical Antibiotics	
Therapeutic Classes (AHFS)	ANTIBACTERIALS (SKIN, MUCOUS MEMBRANE)
Medications	Formulary, with quantity limits clindamycin phosphate topical gel 1% (60/30, 6 fills per 12 months) clindamycin phosphate (Cleocin T) topical lotion 1% (6 fills per 12 months) clindamycin phosphate (Cleocin T) topical solution 1% (6 fills per 12 months) clindamycin phosphate topical swab 1% (6 fills per 12 months) erythromycin-benzoyl peroxide (Benzamycin) topical gel 3-5% (6 fills per 12 months) Ery Pads (erythromycin) topical swab 2% (6 fills per 12 months) erythromycin with ethanol (Erygel) topical gel 2% (6 fills per 12 months) erythromycin with ethanol topical solution 2% (6 fills per 12 months) gentamicin topical cream 0.1% (2 fills per 12 months) gentamicin topical ointment 0.1% (2 fills per 12 months) A quantity limit is defined as a limitation in the amount of medication per fill or time period and/or limitation in the amount of fills per calendar year or other time period.
Covered Uses	Medically accepted indications 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** (request for more than 6 fills in 12 months, or 2 fills in 12 months for gentamicin) 3 months **Later Approvals** 6 months If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Formulary step therapy required topical antibiotic criteria for approval: • Documentation that patient has had sufficient prior trial/failure or contraindication/inability to use the required step therapy drug topical benzoyl peroxide (this can be taken OTC, paid claims not required) Initial Approval: Topical antibiotic request for exceeding quantity or fill limit • The member must have a documented clinical benefit and need to continue the drug prescribed over the health plan's quantity or fill limit OR • The member requires a dose within prescribing guidelines that exceeds the plan's quantity or fill limit. Later Approval: Topical antibiotic request: continues to exceed quantity or fill limit • Documentation that condition has improved or stabilized with therapy and the prescriber recommends continuation of therapy
Criteria Statement	Formulary topical antibiotic <insert drug> is reserved for members who have used (or cannot/should not use) topical benzoyl peroxide. Formulary topical antibiotic <insert drug> is reserved for members who have used (or cannot/should not use) quantities within the quantity and/or fill limits.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Fertility Agents	
Therapeutic Classes (AHFS)	Estrogen agonists-antagonists, gonadotropins, antigonadotropins
Medications	Cetrotide (cetrorelix), ganirelix (Fyremadel), clomiphene (Serophene, Clomid), choriogonadotropin alfa (Pregnyl), chorionic gonadotropin (Novarel), Ovidrel (choriogonadotropin alfa), Follistim AQ (follitropin beta), Gonal-F, Gonal-F RFF, Gonal-F RFF Rediject (follitropin alfa), Menopur (menotropins) Any other newly approved medication for fertility ***Requests for non-fertility related indications: refer to the Non-Formulary and PA Required Medications without Drug-Specific Criteria**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Pregnancy
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber is experienced in fertility treatment, such as OB/GYN, fertility specialist, endocrinologist, etc.
Coverage Duration	If the criteria are met, the request will be approved for 12 months If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**For authorization of fertility agents:**
	• The request is for **iatrogenic infertility** (infertility caused directly or indirectly by surgery, chemotherapy, radiation, or other medical treatment)
	  ○ Requests for other causes of infertility will be denied
	• Medication is prescribed for an FDA-approved indication for treatment of infertility.
	• Medication is prescribed at an FDA approved or compendia supported dose and duration of therapy.
	• Requests for Novarel or Ovidrel:
	  ○ Documentation of a trial and therapy failure, intolerance, or medical reason why patient cannot use Pregnyl.
	• Requests for Cetrotide:
	  ○ Documentation of a trial and therapy failure, intolerance, or medical reason why patient cannot use ganirelix.

Criteria Statement	Medications used for infertility are reserved for members who have a diagnosis of iatrogenic infertility. Novarel or Ovidrel are reserved for members who have used (or cannot/ should not use) Pregnyl. Cetrotide is reserved for members who have used (or cannot/ should not use) ganirelix.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Erectile Dysfunction Medications	
Therapeutic Classes (AHFS)	Phosphodiesterase type 5 inhibitors, vasodilating agents, miscellaneous
Medications	Sildenafil (Viagra), tadalafil (Cialis), vardenafil (Staxyn), vardenafil (Levitra), Stendra (avanafil), Caverject (alprostadil), Edex (alprostadil), Muse (alprostadil), IFE-BiMix (papaverine/phentolamine/water), IFE-PG20 (alprostadil in sodium chloride), Tri-Mix (papaverine/phentolamine/alprostadil) Any other medication for erectile dysfunction
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber is experienced in fertility treatment, such as OB/GYN, fertility specialist, endocrinologist, etc.
Coverage Duration	If the criteria are met, the request will be approved for 12 months If conditions are not met, the request will be sent to a clinical reviewer.

PA Review Criteria	**Authorization criteria:**
	• Medication is prescribed for erectile dysfunction
	• Medication is prescribed at an FDA approved dose
	• The request is for **iatrogenic infertility** (infertility caused directly or indirectly by surgery, chemotherapy, radiation, or other medical treatment)
	  ○ Requests for other causes of infertility or erectile dysfunction not associated with iatrogenic infertility will be denied
	• Requests for sildenafil (Viagra):
	  ○ Approve
	• Requests for medications other than sildenafil (Viagra):
	  ○ Documentation of a trial and therapy failure, intolerance, or medical reason why patient cannot use sildenafil (Viagra):

Criteria Statement	Medications used to treat erectile dysfunction are reserved for members who have a diagnosis of erectile dysfunction associated with iatrogenic infertility. Medications other than sildenafil (Viagra) are reserved for members who have used (or cannot/ should not use) sildenafil (Viagra).
Last P&T Review Date	~~9/2022~~9/2023

Alameda Medical PAD Policies for Review Q3 2023 P&T: Consent Agenda

Recommendation:

- Minor wording update

Exondys 51	
Medications	Exondys 51 (eteplirsen) injection
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), 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	Prescribed by neurologist or provider who specializes in the treatment of DMD
Coverage Duration	If the criteria are met, the initial request will be approved for a maximum 6 month duration. Further authorizations will be for 6 months.
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** Exondys 51 is approved when all of the following criteria are met: • Documentation of a diagnosis of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping • Dose is within FDA approved dosing • Member has been on a stable dose of corticosteroids for at least 6 months • Baseline dystrophin levels are provided • 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), or Time to Climb 4 Steps Test (TTCLIMB)] • The member is ambulatory (e.g. able to walk with our without assistance, and not wheelchair dependent) **Criteria for Re-Authorization:** **Documentation of all of the following:** • The member is ambulatory • Improvement or stabilization demonstrated by scores of motor function tests [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)] • Improvement in dystrophin level from baseline • Documentation of tolerability • Dose is within FDA approved dosing If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.
Last Review Date	~~9/2022~~9/2023

Recommendation:

- Remove duplicate Procrit
- Minor zidovudine clarification

Erythropoiesis-Stimulating Agents	
Medications	Retacrit (epoetin alfa-epbx) - biosimilar Procrit (epoetin alfa) ~~Procrit (epoetin alfa)~~ Epogen (epoetin alfa) Mircera (methoxy polyethylene glycol-epoetin beta) Aranesp (darbepoetin alfa) Any other newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age ~~for MCAL~~
Prescriber Restrictions	N/A
Maximum Billable Units	variable
Coverage Duration	**Initial Approval** If criteria are met, the request will be approved as follows: 1 month if the patient is deficient in iron, vitamin B12 or folate, and in the perisurgical setting 3 months for all other requests. If the provider attests that the preferred medication is for a chronic or long-term condition, reauthorization will be approved for 12 months

Other Criteria	**** When this biosimilar is indicated, and available, 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.**
	
	Criteria for authorization of existing epoetin users who are NEW to the plan:
	• Documentation of current dose
	• Documentation of hemoglobin level results within 30 days or member has responded to therapy (≥1-2 g/dL increase in hemoglobin (HgB) or decrease in transfusion requirements)
	
	Requests for Initial Therapy:
	• All lab results submitted must have been drawn within 30 days of request:
	• The following lab values – hemoglobin (HgB) and hematocrit (HCT)
	• Normal lab results or, if abnormally low, appropriate supplementation as follows:
	  ○ serum ferritin level (normal is > 100 ng/mL)
	  ○ transferrin saturation (TSAT) (normal is > 20%)
	  ○ vitamin B12 level(> 223 pg/mL)
	  ○ folate level (> 3.1 ng/mL)

Erythropoiesis-Stimulating Agents	

	• **For anemia of CKD:**
	  ○ HgB < 10 g/dL
	
	• **For anemia related to cancer:**
	  ○ Receiving myelosuppressive therapy for palliative treatment (members receiving myelosuppressive therapy with curative intent should not receive ESAs) **AND** documented symptomatic anemia with HgB <10 g/dL
	  OR
	  ○ The member has symptomatic anemia related to myelodysplastic syndrome AND documented serum erythropoietin level ≤ 500 mU/mL
	
	• **For zidovudine-related anemia in members with HIV:**
	  ○ The member must currently be receiving zidovudine-containing highly active antiretroviral therapy (HAART) (zidovudine ≤ 4200 mg/week)
	  ○ Erythropoietin level ≤ 500 mU/mL
	
	• **For ribavirin-induced anemia:**
	  ○ Documented attempt to reduce dose was made
	  ○ HgB < 12 g/dL
	
	• **For members undergoing surgery to reduce the need for allogenic blood transfusion:**
	  ○ Perioperative hemoglobin must be < 13 g/dL and > 10 g/dL.
	  ○ The member is scheduled for an elective, non-cardiac, nonvascular surgery.
	
	Reauthorization:
	• Repeat normal labs within 30 days from date of request, or appropriate supplementation as follows:
	  ○ serum ferritin level (> 100 ng/mL)
	  ○ TSAT (> 20%)
	  ○ vitamin B12 level (> 223 pg/mL)
	  ○ folate level (> 3.1 ng/mL)
	• For anemia of CKD: HgB ≤ 11 g/dL
	• For anemia related to cancer: HgB ≤ 12 g/dL
	• For zidovudine-related anemia in members with HIV: HgB ≤ 12 g/dL
	• For ribavirin-induced anemia: HgB ≤ 12 g/dL
	• An increase in dose has not occurred more than once every 4 weeks
	• Dose continues to be appropriate per label or supported by compendia/standard of care guidelines
	
	If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review

Last Review Date	~~9/2022~~9/2023

Recommendation:

- No changes

Adakveo	
Medications	Adakveo (crizanlizumab-tmca)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL Member must be 16 years of age or older
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	If the criteria are met, the initial request will be approved for up to a 12 month duration; reauthorization requests will be approved for up to 12 months.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	• Member has a confirmed diagnosis of sickle cell disease
	• Documentation was provided that the member has had 2 or more pain crises in the last 12 months
	• Documentation was provided that the member has been taking hydroxyurea at the maximum tolerated dose and has been compliant within the last 6 months (or a medical reason was provided why the patient is unable to use hydroxyurea)
	• Documentation of the member's current weight
	• Request is for an FDA-approved dose
	
	Reauthorization:
	• Documentation has been submitted that the member has demonstrated or maintained ONE of the following changes from baseline:
	  ○ Reduction in pain crises
	  ○ Increased time between crises
	  ○ Decrease in days hospitalized
	• Documentation of the member's current weight
	• Request is for an FDA-approved dose
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.

Last Review Date	~~9/2022~~9/2023

Alameda Alliance for Health (IHSS)

Q3 2023 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
Trikafta 80-40-60 mg (d)/59.6 mg (n) granule pack, Trikafta 100-50-75 mg (d)/75 mg (n) granule pack	NF to F-PA
Lupron Depot-Ped 45 mg intramuscular syringe kit	NF to F-PA
Abilify Asimtufii 720 mg/2.4 mL suspension, extend .rel. IM syringe, Abilify Asimtufii 960 mg/3.2 mL suspension, extend. rel. IM syringe	NF to F-PA
Kalydeco 13.4 mg oral granules in packet	NF to F-PA
Udenyca Autoinjector 6 mg/0.6 mL subcutaneous auto-injector	NF to F-PA
Liqrev 10 mg/mL oral suspension	NF to F-PA
Zeposia Starter Kit (28-day) 0.23 mg-0.46 mg-0.92 mg capsules dosepack	NF to F-PA
Flucelvax Quad 2023-2024	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Fluad Quad 2023-2024	NF to F-AL-QL (65 years and up) (1 fill per 270 days)
Afluria Quad 2023-2024	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Flublok Quad 2023-2024	NF to F-AL-QL (18 years and up) (1 fill per 270 days)
Fluzone Quad 2023-2024	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Fluzone High-Dose Quad 2023-2024	NF to F-AL-QL (65 years and up) (1 fill per 270 days)
Flumist Quad 2023-2024	NF to F-AL-QL (12-49 years) (1 fill per 270 days)
Flulaval Quad 2023-2024	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Fluarix Quad 2023-2024	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Afluria Quad 2023-2024	NF to F-AL-QL (12 years and up) (1 fill per 270 days)
Mycozyl (tolnaftate) AC External Cream 1 %	F to NF (no past 6 month utilization)
FaStep COVID-19 Antigen Test In Vitro Kit	NF to F-QL (8 per 30 days)

Alameda Alliance for Health (Medi-Cal & IHSS)

Q3 2023 Physician Administered Drug (PAD) Prior authorization (PA) list Updates

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.

HCPCS Code	Product Name (Generic Name, Brand Name)	PA Action
J9160	ONTAK (DENILEUKIN DIFTITOX) 300 MCG	Addition
J2503	MACUGEN (PEGAPTANIB SODIUM) 0.3 MG	Addition
J2504	ADAGEN (PEGADEMASE BOVINE) 25 IU	Addition
J0135	HUMIRA (ADALIMUMAB) 20MG	Addition
J3490	UNCLASSIFIED Drug	Addition

POLICY AND PROCEDURE

Policy Number	RX-002
Policy Name	Pharmacy Benefit Prior Authorization Review Process
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	Group Care (IHSS)
Effective Date	12/01/1997
Approval / Revision Date	9/26/2023~~6/20/2023~~

POLICY STATEMENT

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

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

PROCEDURE

I. Prior Authorization Process Guidelines

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

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

II. Submitting a Prior Authorization (PA) or Appeal

Prior authorizations and appeals may be filed either orally or in writing by the member or the member's provider/provider's office authorized representative. Prior Authorizations and appeals are received by telephone via PerformRx help desk, PerformRx PA fax number or our direct pharmacy telephone number.

The Alliance provides a prompt review of prior authorizations and appeal requests (24 hours for prior authorizations and up to 30 days for an appeal).

III. Prior Authorization Requirements and Processes

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

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

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

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

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

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

G. Outreach calls (up to 2 attempts within 24-hr TAT) may be made to the requesting provider to request reasonably necessary clinical information when needed to make a PA decision for medication requests. For each outreach attempt, the reviewer is to document the following:
   a) Name and title of person spoken to
   b) Phone number called (if different from one already noted in the PA system)
   c) What specific information was requested

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

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

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

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

L. If a reviewer is not able to review a request using the MRG based on individual needs or delivery system considerations the request will be considered an Exception Request (***see RX-003 Exception Review Process***). The reviewer then adheres to the following process:
   1. The reviewer documents the reason why the MRG cannot be used and refers the case to a pharmacist for review.
   2. The pharmacist reviews the case and background materials. When appropriate, the pharmacist can approve the request, documenting the rationale for the authorization.
   3. The pharmacist can modify or deny the request for the following reasons:
      a) **Insufficient information** was received to make a decision (as determined by the Alliance Medication Request Guidelines, national standard guidelines, prescribing information, or other sources of standard prescribing information).
      b) **Not a covered benefit:** The requested medication is not a covered benefit (unless treating gender dysphoria or alleviating mental health or substance use):
         (1) The product requested is a dietary supplement, Medical Food, or other products not approved by the FDA.
         (2) The product requested is being used for a cosmetic purpose.
         (3) Appetite/weight suppressants being used for cosmetic purposes and with no medical necessity (as documented by clinic notes)
         (4) The product requested is being used to aid/improve hair growth or impair/stop/reduce hair growth.

(5) The product requested is to be used by the member as part of a medical or clinical study protocol. Note that supporting medications that may be needed for the study (but are not directly a part of the study) are covered by Alameda Alliance.

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

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

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

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

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

h) **Medical Necessity**: Use of the requested product does not meet medical necessity. To meet medical necessity, the treatment must be ~~ALL of~~ALL the following:

(1) Safe, effective, and within national standards of practice.
(2) Not experimental or part of a current clinical trial or study.
(3) Specific and treat the identified condition.
(4) Expected to improve health or prevent or delay progression of the condition from getting worse.
(5) Not primarily for convenience.
(6) Not being used to avoid legal consequences.
(7) Not ~~be~~to be contraindicated, dangerous to the patient, or have other reasons why the requested drug should not be used.

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

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

k) Request for additional clinical information goes unanswered

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

M. Of the above listed denial reasons, the pharmacist will review the requests for medical necessity (essentially becoming an ***Exception Request***, refer to ***RX-003 Exception Review Process***) if:

1. Clinical information provided does not meet criteria for use based on ~~MRG~~MRG.
2. The member has not tried and failed the initial treatment option for drugs that require step ~~therapy~~therapy.

3. Benefit rules cannot be applied AND there is no ~~MRG~~MRG.

N. The pharmacist will defer cases that cannot be denied based on the above listed denial reasons (and do not qualify as an ***Exception Request, see RX-003 Exception Review Process)***. These requests and any other highly complicated cases will be sent to an Alliance board-certified Medical Director for review.

1. The Alliance Medical Director reviews the background of the case and, if needed, contacts the requesting provider for any additional information needed for the review.
2. The Medical Director may render one of 3 decisions: approve, deny, or modify.
3. The Medical Director finalizes the review and returns the case to the reviewing pharmacist with documentation of their decision and the rationale.

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

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

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

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

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

A. Prospective Standard Requests

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

V. Provision of Drugs during Emergency Circumstances

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

A. Alliance providers are informed of this policy via the Alliance's Provider Manual.

B. Alliance members are informed of this policy via member's Explanation of Coverage.

C. Alliance providers are responsible for following the prior authorization process for the remainder of the prescription.

D. The Alliance allows for payment of the three (3) day supply of the drugs even ~~in the event that~~if the prior authorization request is subsequently denied.

~~C.~~

~~D.~~E. The Alliance allows for payment of the three (3) day supply of the drugs even ~~in the event that~~if the prior authorization request is subsequently denied.

~~E.~~F. Continuity of care requirements do not require the Alliance to continue coverage of drugs dispensed under this provision if they are not found to be medically necessary.

VI. Provision of Contraceptive Drugs

A. The Alliance covers all FDA approved contraceptive drugs, devices, and other products,

Formatted: Font: Bold

including all FDA-approved contraceptive drugs, ~~devices~~devices, and products available ~~over the counter~~over the counter, as prescribed by the member's provider.

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

Formatted: Indent: Left: 0.81", No bullets or numbering

~~VI.~~VII. Annual Review of Pharmacy Prior Authorization and UM Criteria

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

~~VII.~~VIII. Monitoring of the PA process

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

---

DEFINITIONS / ACRONYMS

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

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

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

NCQA: National Committee on Quality Assurance

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Pharmacy Benefit Manager (Currently PerformRx)

RELATED POLICIES AND PROCEDURES

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

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

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

REVISION HISTORY

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

REFERENCES

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

MONITORING

This P&P is reviewed annually to ensure effectiveness.

APPENDIX

Table 1: Decision Types

a. IHSS

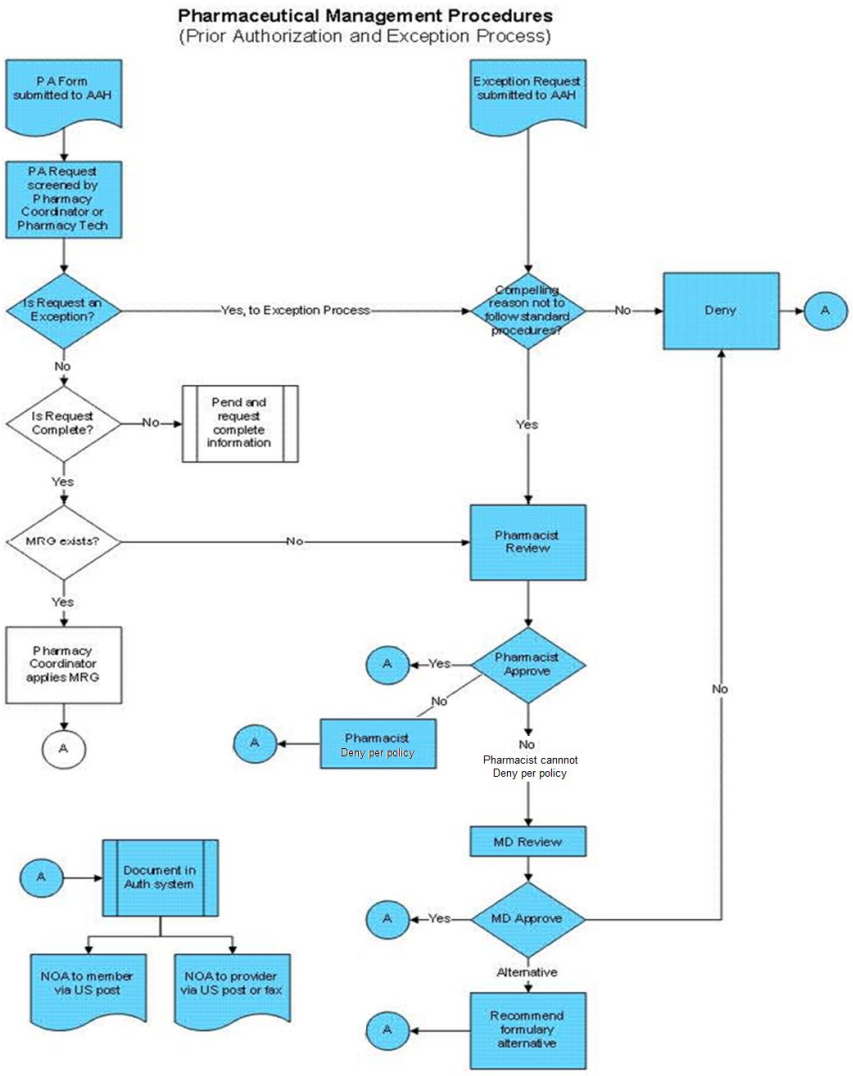
Reviewer Type	Approval	Denial	Modification	Deferral
PBM Clinicians	Yes	Yes	Yes	N/A
Plan Pharmacist	Yes	Yes	Yes	N/A
Plan Medical Director	Yes	Yes	Yes	N/A

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

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

Table 3: Decision & Notification Time Frames

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


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

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

POLICY AND PROCEDURE

Policy Number	RX-003
Policy Name	Exception Review Process
Department Name	Pharmacy Services
Department Officer	Chief Medical Officer
Policy Owner	Senior Director, Pharmacy Services
Line(s) of Business	Group Care (IHSS)
Effective Date	6/16/2020
Approval / Revision Date	9/26/2023~~6/20/2023~~

POLICY STATEMENT

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

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

PROCEDURE

I. Exception Process Guidelines

A. Members and their providers are expected to follow pharmaceutical management procedures set forth by the Alliance. However, in some cases a member or provider may opt to seek an exception based on medical necessity. Examples of exception requests include (but are not limited to):
   1. A request for coverage of a non-formulary item with no existing Medication Review Guidelines (MRG)
   2. A request to bypass an implemented formulary management program, such as step therapy

3. A request to authorize a greater supply than standard quantity limits
4. Any request outside the existing pharmaceutical management procedure and authorization process

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

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

II. Exception Review Requirements and Process

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

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

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

C. Types of Exception Requests – All Exception requests must be reviewed by an appropriate healthcare professional and decisions shall be made based on the available clinical evidence in the medical literature as well as any patient-specific

factors. Types of Exceptions include (but are not limited to):

1. **Quantity Limit (QL) Override**
   a) Quantity limits are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.
   b) Providers must provide documentation for why the quantity limit is insufficient for the member and why formulary alternatives or alternate doses cannot be used. Potential QL override requests may involve:
      i. Split dosing for tolerability
      ii. One-time dose titration
      iii. Requirement of a higher dose for efficacy (must be supported by clinical evidence)
2. **Step Therapy (ST) Override**
   a) Step Therapy protocols are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.
   b) Providers must submit necessary justification and supporting clinical documentation~~document~~ (through clinic notes documenting previous medication trials including dose/duration/time frame and/or pharmacy fill history) supporting the provider's determination that the required prescription drug is inconsistent with good professional practice for provision of medically necessary covered services to the member, taking into consideration the member's needs and medical history, along with the professional judgment of the member's provider. The basis of the provider's determination may include, but is not limited to, any of the following criteria:
      i. The required prescription drug is contraindicated or is likely, or expected, to cause an adverse reaction or physical or mental harm to the member, in comparison to the requested prescription drug, based on the known clinical characteristics of the member, and the known characteristics and history of the member's prescription drug regimen.
      ii. The required prescription drug is expected to be ineffective based on the known clinical characteristics of the member, and the known characteristics and history of the member's prescription drug regimen.
      iii. The member has tried the required prescription drug while covered by their current or previous health coverage or Medicaid, and that prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse reaction. The health care service plan may require the submission of documentation demonstrating that the member tried the required prescription drug before it was discontinued.
      iv. The required prescription drug is not clinically appropriate for the member because the required drug is expected to do any of the following, as determined by the member's prescribing provider:
         (1) Worsen a comorbid condition.
         (2) Decrease the capacity to maintain a reasonable functional ability in performing daily activities.
         (3) Pose a significant barrier to adherence to, or compliance with, the member's drug regimen or plan of care.

Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt, Not Bold
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt
Formatted: Font: (Default) Times New Roman, 12 pt

v. The member is stable on a prescription drug selected by the member's prescribing provider for the medical condition under consideration while covered by their current or previous health coverage or Medicaid. ~~why the preferred formulary first line agent cannot or should not be used.~~

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

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

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

(a) Patient name

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

(c) Quantity distributed

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

~~b)~~c) The Alliance provides coverage for prescription drugs may require step therapy i~~I~~f there is more than one drug that is clinically appropriate for the treatment of a medical condition~~, a health care service plan that provides coverage for prescription drugs may require step therapy~~.

~~c) If there are not MRG's to specify the agents that must be used prior to approval, at least three (3) formulary alternatives (either within the same mechanism of action, same therapeutic class, or that treat the same condition in accordance with nationally accepted clinical guidelines) must be tried before the requested product can be approved.~~

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

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

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

Formatted: Font: (Default) Times New Roman, 12 pt

Formatted: Font: (Default) Times New Roman, 12 pt

Formatted

Formatted

Formatted: Normal, No bullets or numbering

~~i. Patient name~~
~~ii.i. Medication name, dose, and route of administration~~
~~iii.i. Quantity distributed~~
~~iv.i. Date medication was started and date last given/filled~~

3. **Age Limit (AL) Override**
   a) Age Limits are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.
   b) For override of Age Limits, the provider must submit clinic notes, any relevant labs, and supporting clinical evidence (e.g., national guidelines, primary literature) that the drug being requested is safe and effective for the patient and why formulary alternatives cannot or should not be used.
4. **Fill Limit (FL) Override**
   a) Fill limits (a maximum number of fills over a certain period of time) are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.
   b) For override of Fill Limits, the provider must submit documentation for why the member requires additional medication beyond the limit in place, why formulary alternatives cannot or should not be used in the patient, and any relevant labs results and/or other clinical references, national guidelines, or primary literature to support continued use of the drug requested~~.~~.
5. **Maximum Dose Exceeded Override**
   a) Maximum doses are set by the prescribing information/package insert for the medication upon FDA approval or by national guidelines for the condition being treated.
   b) For use of doses beyond the maximum labeled dose, the provider must submit any relevant labs results, clinical references, national guidelines, and/or primary literature to support the use of a dose beyond the standard dose and justification for why a formulary alternative cannot be used in place of a higher dose of the requested medication.
6. **Dose Consolidation Override**
   a) Quantity limits are established through the P&T Committee and are a part of the Medication Request Guidelines for that drug/class.
   b) For approval of a doubling (or higher) of the number of tablets/capsules per prescription for a medication that has a higher strength tablet/capsule available, justification must be submitted for why that higher dose tablet/capsule cannot be used.
7. Partial Fill
   a) The Alliance has availability of prescription partial fills of approved medically necessary medications.
8. **Lost/Stolen Medication Override**
   a) Requests for non-controlled medications can be approved by Alliance pharmacy technicians upon request by the member, pharmacy, or provider.
   b) For Lost/Stolen controlled medications, the member or provider must submit a police report to the plan that documents which medications were taken and the date the event occurred.

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

9. Refill-Too-Soon Override

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

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

10. Vacation Override

a) Vacation Overrides for up to 3 months (90 days) for travel outside California can be approved by the PBM or by the Alliance pharmacy technicians upon request by the member, pharmacy, or provider when documentation of the departure date, destination, and return date are provided for the following:
   i. Non-specialty medications
   ii. Non-single-source medications, and/or
   iii. Non-controlled medications

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

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

11. Member Reimbursements

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

b) Reimbursements are not valid and will not be approved when the following criteria exclusions apply:
   i. If the request is made before the 180 days accepted time frame per EOC requirement.
   ii. If the drug was not covered and required a Prior Authorization and Perform PA does not show any active approval for the date paid

out of pocket.
iii. If the required documents are not submitted (Note: re-review can be considered once all documents are received).
iv. If the request is made for pharmaceutical services received outside of the United States.

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

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

12. Continuation of Therapy Override

a) The Alliance shall allow continuation of therapy for members using medically necessary drugs when it can be shown through clinic notes/provider attestation for OTC products or prescription fill history that the member has been taking the medication prior to enrollment.
b) For non-transitioning members who are already established with Alliance, the Alliance does not consider use of medication samples provided through a physician office as a valid reason for approval/continuation of that medication, or as an acceptable step therapy to another medication.
c) For non-transitioning members who are already established with Alliance, the Alliance shall allow provider attestation for OTC products that the member has been taking.
d) For transitioning members until the Beneficiary can be seen by a Plan provider to establish a care plan, as required by Welfare & Institutions (W&I) Code, Section 14185(b), the Alliance will allow for continuation of medically necessary medications, including medication samples, if provided clinic notes showing all the following:
   i. Patient name
   ii. Medication name, dose, and route of administration
   iii. Quantity distributed
   iv. Date medication was started and date last given/filled
e) For override of the formulary based on continuation of therapy the provider must submit clinical documentation showing the member has previously tried without success or cannot/should not take formulary alternatives, including any relevant labs.

13. Discharge Medication Override

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

14. Therapeutic Duplication Override

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

15. Day Supply Limit

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

D. Exception Requests Based on Medical Necessity:

1. Since exception requests, by definition, do not have a MRG in place, the Pharmacy Technician will not be able to approve the request.
2. The reviewer documents the reason why the request qualifies as an Exception request and refers the case to a pharmacist for review.
3. The pharmacist reviews the case and background materials. The pharmacist can approve Exception Requests when ALL the following criteria are met:
   a) History of failure, contraindication, or intolerance to all formulary alternatives, or no formulary alternatives exist (if applicable)
   b) The treatment plan is:
      i. Safe, effective, and within national standards of practice.
      ii. Not experimental or part of a current clinical trial or study.
      iii. Specific and treats the identified condition.
      iv. Expected to improve health or prevent or delay progression of the condition from getting worse.
      v. Not primarily for convenience.
      vi. Not being used to avoid legal consequences.
      vii. Not contraindicated or have other reasons why use of the drug should not be used.
   c) One of the following:
      i. Requested drug is FDA-approved for the condition being ~~treated~~treated.
      ii. If requested for an off-label indication, the use is supported in compendia.
      iii. If the off-label use is supported by nationally recognized treatment guidelines or by two (2) peer reviewed articles.
3. The pharmacist will defer cases that cannot be denied based on the above listed denial reasons. These requests and any other highly complicated cases will be sent to an Alliance board-certified Medical Director for review.
   a) The Alliance Medical Director reviews the background of the case and, if needed, contacts the requesting provider for any additional information needed for the review.

b) The Medical Director may render one of 3 decisions: approve, deny, or modify.
c) The Medical Director finalizes the review and returns the case to the reviewing pharmacist with documentation of their decision and the rationale.

4. The reviewer documents the criteria and rationale for the decision in the pharmacy authorization system.
5. A pharmacist or a medical director can use nationally recognized treatment guidelines and other clinical information in support of making the decision.
6. Members receive a notice of action (NOA) letter with the outcome of the request and their rights and the process to appeal the decision. The provider also receives an identical copy of the NOA via fax or regular mail. All NOA letters sent to members and providers include their rights and the process to appeal the decision.

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

E. **External Review**

A request for an external review when the Alliance denies a prior authorization (PA) can be made for a drug that is not covered by the plan or for an investigational drug or therapy. A request for an external review will not prevent the filing of a grievance or Independent Medical Review (IMR) with the California Department of Managed Health Care (DMHC). Requests for external review will be made and completed in the Alliance Grievances and Appeals Department.

III. Pain Medication Requests for the Terminally Ill

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

approved based on medical necessity.

G. The pharmacy department shall keep a log of any requests for pain medication that are deemed to be for a terminally ill member.
   1. The log shall be reviewed on a weekly basis for any denials.
   2. Pain medication requests for terminally ill members shall be tracked monthly and any trends shall be reported on to the Health Care Quality Committee (HCQC) on a quarterly basis.

A. All other medication requests for the terminally ill members

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

IV. Provision of Drugs during Emergency Circumstances

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

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

VI. **Monitoring Process**

F. The Alliance provides oversight of its PBM through an annual audit of the PA review process.
G. The Senior Director of Pharmacy Services or designee reviews a monthly authorization report, which provides statistics on all approvals, denials, and modifications to ensure that providers and members have been notified in accordance within the mandated turnaround times.
H. Inter-rater Reliability Review (IRR)
   1. The **Senior Director of** Pharmacy Services **or designee** will conduct IRR annually for clinical pharmacists who review and make determinations for the exceptions requests.
   2. 8 cases will be pulled and reviewed. If 100% clinical pharmacist agreement is

not found in all 8 cases then another 22 will be pulled and reviewed for a total of 30 cases.

3. When a total of 30 cases are reviewed, at least 90% agreement between the clinical pharmacists will be attained. Otherwise, additional sessions will be held until the 90% agreement threshold is reached in a total of 30 cases.
4. The Alliance will immediately supply remediation if the passing threshold is not met.
5. New staff require testing prior to conducting utilization review without supervision.
6. Results of the IRR will be reported to UM Committee.

DEFINITIONS / ACRONYMS

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

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

HCQC: Health Care Quality and Compliance Committee

NCQA: National Committee on Quality Assurance

AFFECTED DEPARTMENTS/PARTIES

Pharmacy Services
Pharmacy Benefit Manager (Currently PerformRx)

RELATED POLICIES AND PROCEDURES

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

RELATED WORKFLOW DOCUMENTS OR OTHER ATTACHMENTS

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

REVISION HISTORY

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

REFERENCES

- California Code of Regulations (CCR), Health & Safety Code, §§1367.01, 1367.21, 1367.22, 1367.24, 1367.206 and 1373.96
- CCR, Welfare & Institutions Code, §14185

- CCR, Title 22, §§51003, 51014.1, 51014.2, 53854 and 53894
- CCR Title 28 §1300.67.24
- MMCD Policy Letter 08-013
- NCQA, 2016 HP Standards & Guidelines, UM 13 (Procedures for Pharmaceutical Management), Element E (Considering Exceptions)
- DHCS All Plan Letter 20-020 Governor's Executive Order N-01-19, regarding Transitioning Medi-Cal Pharmacy Benefits from Managed Care to Medi-Cal Rx
- DMHC APL 20-035 (OPL): Medi-Cal Pharmacy Benefit Carve Out – Medi-Cal Rx
- DMHC APL 18-001 (OPL): Newly Enacted Statutes Impacting Health Plan License Filings

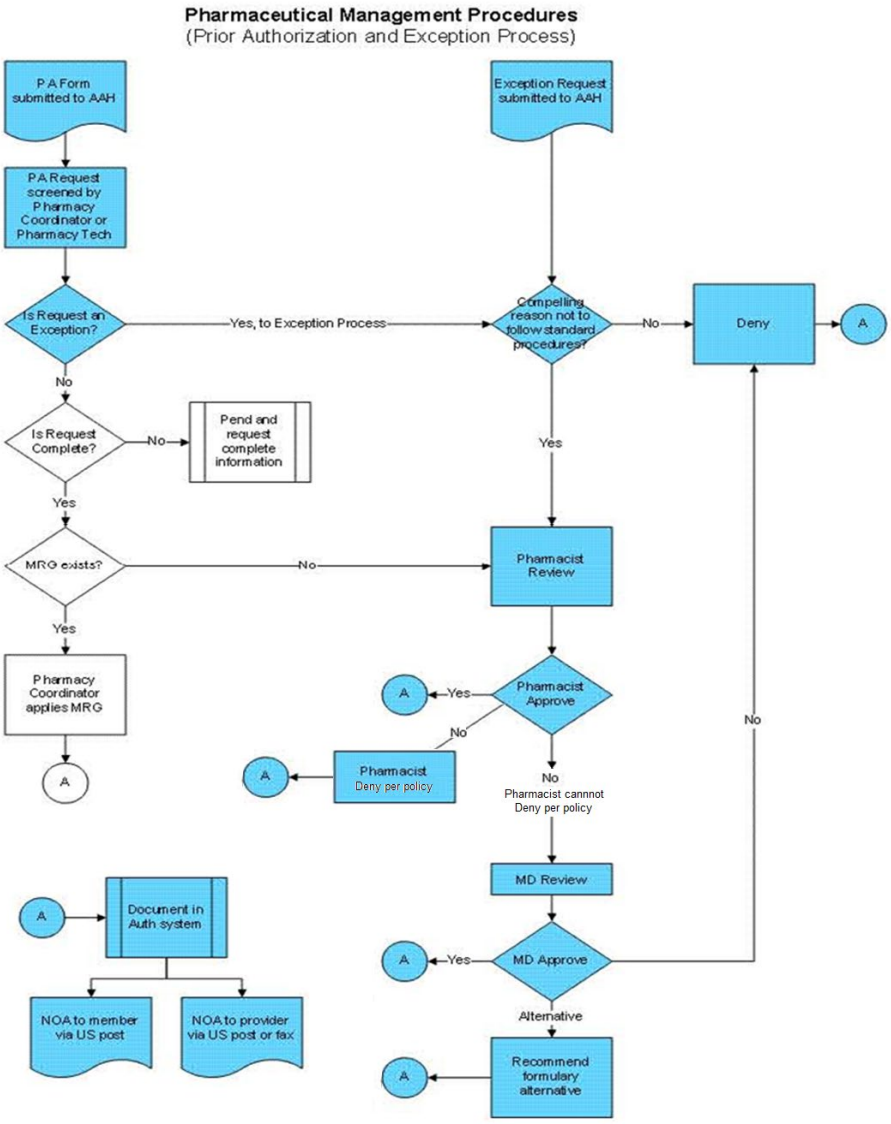
MONITORING

This P&P is reviewed annually to ensure effectiveness.

APPENDIX

Table 1: Decision & Notification Time Frames

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


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

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

www.alamedaalliance.org

90-Day Supply on Maintenance Medications

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

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

Asthma & COPD

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

Blood Pressure & Heart Health

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

Blood Pressure & Heart Health (cont.)

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

Blood Pressure & Heart Health (cont.)
Eprosartan/HCTZ
Felodipine
Flecainide
Fosinopril
Furosemide
Guanfacine
Hydralazine
Hydrochlorothiazide
Indapamide
Irbesartan
Irbesartan/HCTZ
Isoproterenol
Isosorbide Dinitrate
Isosorbide Mononitrate
Labetalol
Lisinopril
Lisinopril/HCTZ
Methyldopa
Methyldopa/HCTZ
Metolazone
Metoprolol Succinate
Metoprolol Tartrate
Mexiletine
Midodrine
Minodixidil
Nadolol
Niacin
Nicardipine
Nifedipine
Nitroglycerin
Olmesartan

Blood Pressure & Heart Health (cont.)
Pentoxifyline
Pindolol
Prazosin
Propafenone
Propranolol
Propranolol/HCTZ
Quinidine gluconate
Quinidine sulfate
Ramipril
Reserpine
Sotalol
Spironolactone
Spironolactone/HCTZ
Telmisartan
Telmisartan/HCTZ
Terazosin
Triamterene/HCTZ
Valsartan/HCTZ
Verapamil
Warfarin

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

Diabetes (cont.)
Pioglitazone
Rosiglitazone
Rosiglitazone/Metformin
Tolazamide
Tolbutamide

Gastrointestinal Health
Balsalazide
Sulfasalazide
Ursodiol

Gout
Allopurinol
Probenecid

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

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

Men's Health
Alfuzosin
Doxazosin
Finasteride
Tamsulosin
Terazosin

Mental Health
Bupropion
Duloxetine
Escitalopram
Fluoxetine
Mirtazapine
Paroxetine
Sertraline
Trazodone

Miscellaneous
Cabergoline
Fludrocortisone
Hydroxychloroquine
Hydroxyurea
Leflunomide
Methazolamide

Miscellaneous
Methotrexate
Methylsulfate
Neostigmine

Myasthenia Gravis
Edrophonium Chloride
Physostigmine Salicylate
Pyridostigmine Bromide

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

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

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

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

Thyroid Conditions
Armour Thyroid
Levothyroxine
Liothyronine
Methimazole
Propylthiouracil

Transplant
Azathioprine
Mycophenolate Mofetil
Mycophenolate Sodium
Tacrolimus

Urinary Incontinence & Retention
Bethanechol
Desmopressin
Oxybutinin

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

3/8

Vitamins & Nutritional Health

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

Women's Health

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

4/8

ALAMEDA Alliance FOR HEALTH

Up to 365~~90~~-Day Supply on Contraceptives

~~Products shaded in grey require prior authorization.~~ Generic products are listed under **LABEL NAME** by their ingredient components.

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

Formatted Table

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

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

Formatted Table

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

Formatted Table

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

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

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

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

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

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

PHARMACY & THERAPEUTICS COMMITTEE

Record of Committee Meeting Minutes

Tuesday, June 20, 2023 | 5:00pm – 7:00pm

Status	Voting Committee Members	Organization	Initials	Officer / Notes
P	Steve O'Brien, MD	CMO - Alliance	SO	Chairman
P	Helen Lee, PharmD	Senior Director of Pharmacy Services – Alliance	HL	Co-Chair
P	Aaron Basrai, PharmD	Haller's Pharmacy	AB	BOG
P	Paul Bayard, MD	La Clinica de la Raza (CHCN)	PB	
P	Pamela Gumbs, PharmD	United Pharmacy	PG	
P	Ivan Lee, MD	Private Practice	IL	
P	Bao Dao, MD	Epic Care	BD	
P	Donna Carey, MD	Medical Director of Case Management- Alliance	DC	

P=Present; PH=Call-in; A=Absent; CMO = Chief Medical Officer; DOPS=Director of Pharmacy Services; BOG = Board of Governors Representative

Status	Regular Guests	Organization	Role / Department
P	Natalee Felten	PerformRx	Formulary Management & Drug Utilization Review
P	Todd Lebowkins	PerformRx	Pharmacy Account Executive
A	Pat DeHoratius	PerformRx	Manager Formulary/DUR
P	Barrie Cheung	PerformRx	Regional Pharmacy Director
P	Ayoola Ayeni	PerformRx	Pharmacy Account Executive
P	Rahel Negash, PharmD	Alameda Alliance	Pharmacy Supervisor
P	Ramon Tran Tang, PharmD	Alameda Alliance	Clinical Pharmacist
P	Jefferey Bencini, Pharm D	Alameda Alliance	Clinical Pharmacist
P	Timothy Tong, Pharm D	Alameda Alliance	Clinical Pharmacist
A	Beverly Juan, MD	Alameda Alliance	Medical Director
A	Sanjay Bhatt, MD	Alameda Alliance	Medical Director
A	Darryl Crowder	Alameda Alliance	Provider Relations
A	Bibek Sandhu, PharmD, MBA	PillarRX	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	S. O'Brien	Call to Order • Agenda Overview	Called to order at 5:00PM	
II) Informational Updates	S. O'Brien H. Lee	Informational Updates • CalAIM Updates (ECM, CS x 12, TCS, LTC, ICF-DD, BH/ABA) – Our ECM which is our Enhanced Case Management is expanding significantly coming July 1st. We currently have about 13,000 members who are eligible. We are adding kids in a variety of categories. That will be another almost 9,000 people. So almost doubled in the ECM population. We have multiple new providers in a community base organization. As well as providers like the CHCN clinic who are going to be providing those services to kids. – We are also expanding our communities support portfolio. We currently have 3 housing communities for those members who are in lieu of services, asthma remediation, medical food, medical respite. We also have a get out of SNF, LTC pilot and a get out of LTC pilot. – We are starting 3 more coming July 1st, personal caregiver services, so services like IHSS services but before you get them so like a bridge. Caregiver respite, for people who are the primary caregivers, for members who are ill it will be important for the pediatric population CCS population. Home modifications, where you can do a limited number of home modifications. Like a wheelchair ramp or grab bar things like that. And coming next January will be adding sobering centers this will be something to expand hopefully some of the work they will be doing at Cherry Hill that will take us up to 12 community supports by January. – We are also transitional care services, currently providing to those who are high risk members we are only two plans in the state providing the full panel of transitional care services the state has requested this far. We are working on getting the staffing. This coming January they want to do all members who have been in the hospital this will be a very significant expansion for transitional care services. We will also be welcoming with in our LTC population group homes for kids and young adults with developmental delay and other issues and that's going to be another LTC population. – Our BH office went live April 1st with our insourcing of behavioral health from Beacon. Beacon who used to be our delegate and provided that service. We now provide this service ourselves with our own internal coordination and contracting with providers. Everything is going well, and we do have a little backlog on some of our BHT or autism services we are actively addressing. We are working on a variety of correction plans for this. Otherwise, things are going well. • CEO & COO Transition – We also had a very significant transition come June 1st Scott Coffin our long time CEO retired, and our former COO Matt Woodruff is now our CEO. • DHCS Audit results – Our DHCS Audit results were really good in April. They come annually, we have three main credentialling bodies NCQA which is voluntary, DMHC, and DHCS. This year we got really good results, there were no findings in UM. Helen will talk to us about any findings in Pharmacy or not. – Once again, as Dr. O'Brien said, we went through very smooth audit period. There were zero findings for pharmacy. But as you know pharmacy does support PAD which is the physician administered drug. We will continue to collaborate with UM. • PAD Updates – Starting this month pharmacy went through transition with UM department as so now pharmacy technicians and pharmacists will handle end to end process.		

- The same PA entry, fax, phone number, email will still come in as a UM benefit. However, as soon as we identify this is a pharmaceutical it will come through the pharmacy department.
- Technicians will be checking eligibility, LOB, then it will go through clinical review process. Of course, if we need to make any denial, determination will go through the medical director as we have done before.
- So, no change internally from a provider's perspective, same entry system, same workflow but internally at the Alliance pharmacy team will own this process working with our UM team and medical directors.
- Later we will talk about our single PAD PA list that we had went over in June 2022.

- Medi-Cal Rx MCDAC Drugs
  - MCDAC (Medical Drug Advisory Committee) drug recommendation.
  - There were two drugs.
  - Amjevita which is prefilled syringes and comes as auto injector for various arthritis, ulcerative colitis, and plaque psoriasis. Formulary when this was on under our medical LOB it was not available in 2021. Based on the safety and efficacy, essential need, and misuse potential we recommend keeping it as formulary with prior authorization requirement for their formulary known as the Contract Drug List.
  - Also, for our group care currently this same drug is on formulary with PA required.
  - Austedo which is a treatment for Tardive dyskinesia, Chorea associated Huntington's Disease. Once again before Medi-Cal Rx conversion it was a non-formulary drug and based on further review we are recommending making it formulary for Austedo. And for Austedo XR we will require a PA.

MCDAC Drug	Indication	CDL Status	Recommendation Based on - Safety, Efficacy, Essential Need, Misuse Potential, etc.	Previous MCAL Status
Amjevita (adalimumab-atto) 20mg/0.4ml, 40mg/0.8ml pre-filled syringe and 40mg/0.8ml pre-filled sureclick autoinjector	Rheumatoid Arhritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylosis, Crohn's Disease, Ulcerative Colitis and Plaque Psoriasis	F-PA	Keep F-PA	N/A, F-PA in GC
Austedo (deutetrabenazine) 6mg, 9mg and 12mg tablets; Austedo XR (deutetrabenazine) 6mg, 12mg and 24mg tablets	Tardive Dyskinesia, Chorea associated Huntington's Disease	F (Austedo) and F-PA (Austedo XR)	Keep F-PA	NF

III) Pharmacy Utilization Reports (Quarter 2, 2022) — H. Lee

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

- **Top 50 Drugs by Cost (IHSS)**
  - 636 IHSS
  - Reporting period, 1st quarter 2023 which is January until March 2023
  - 530 members
  - 1,025 claims
  - cost $1,150,629,
  - increase of $61,761 in spending from the previous quarter.
  - Tagrisso has moved up to the number one spot once again with 6 claims for 2 members.
  - Vemlidy is down to number 2 with 48 claims for 19 members.

- This is a decrease of 2 claims for 1 member since the previous quarter. This medication is managed via the Hepatitis B MRG guideline.
- Biktarvy appears at the number three spot, down from number 2 during the last quarter. The number of claims has increased by 1.
- Jakafi is at number 4 with 3 claims for 1 member, which is the same amount of claims as the previous quarter. Recently a new MRG was implemented during Q4 2022 P&T to review requests for the graft versus host disease indication of this medication. The oncology-related indications for this medication are reviewed via the oncology MRG.
- Cabometyx is at number 5, and Piqray is at number 6, both with only 2 claims for 1 member. Requests for these medications are reviewed via the oncology MRG.

Questions

PB – is there a reason specifically for Ozempic, are people trying to use this for weight loss?

HL: It is actually for type II diabetes; we are getting increased PA requests simply because there are more commercial running and it's getting a lot of attention. It's pretty costly drug. There are PA requirements for diabetes and other indications, but it is defiantly off label use.

RN: I would agree that it makes sense that people are trying to use this for weight loss. If it is often confused with Rigovy, for weight management, we will direct them to Rigovy.

SO: Also, our number 11 drug is also Ozempic if you add those together then it's really like number 4. I think we will definitely see an increase in use of Ozempic and Rigovy, keep in mind that morbid obesity is very expensive.

HL: Other plans are also considering to allow Ozempic to be used for obesity. Simply because as you said morbid obesity can cause more issues and costs. We might need to revisit in the future.

AB: Is it step therapy on Ozempic at all or only PA it will go through?

RN: Its step with Metformin.

AB: I just worry that it can be used for weight loss if a prescriber writes a prescription for Metformin, then all of a sudden step therapy will be there and then they will get their metformin afterwards. Could be something to look at for audits and focus in and see.

HL: We can certainly do that Dr. Basrai.

- **Top 50 Drugs by Cost (Medi-Cal)**
  - 28,797 claims
  - 24,664 members
  - Cost $37,007,946.75
  - increase of $9,293,924.57
  - The drug composition is slightly different than group care.
  - The number 1 was Biktarvy total cost $4,391,262.22
  - Number 2 Humira cost $2,214,075.74
  - Number 3 Stelara cost $2,096,012.90
  - Number 4 Jardiance 25mg cost $1,458,712.85
  - Number 5 Vemlidy cost $1,176,709.99

		– Number 6 Ozempic cost $1,122,917.35 – Number 7 Jardiance 10mg cost $1,075,977.59 – Number 8 Tagrisso cost $1,046,167.66 – Number 9 Januvia cost$1,005,854.56 – Number 10 Genvoya cost $846,827.56 **Questions** PB: I'm trying to understand that these are patients that are in AAH members and that they switched to Medi-Cal Rx and the cost went up 9 million dollars. Is that what happened with the conversion? HL: Yes, correct. PB: Is the reason because it is just a more open formulary? It allows more expensive drugs to be prescribed. Is that one of the reasons? HL: Number one they do have actually closed formulary known as the contract drug list (CDL) however, as you said they used to not required PA they had no edits to stop or having restrictions. Then finally they started to gradually bring back those edits and start to add PA. Their PA volume, phone call volume is going up significantly. Then this particular data is for the beginning of this year. The reason why they are having a lot of dollars spent is because their CDL is their rebate driven formulary. It's not by cost or necessarily efficacy quote end quote, it's really about maximizing rebate opportunities with the pharmaceuticals. So, you will see a huge jump. What does this mean? They are spending over one thousand five hundred dollars per person per member whose using pharmacy benefit for top 50 drugs. On our end the claim cost $1285 per claim. SO: If that is the cost, again as you mentioned the rebates they may be getting on the back end and how it all maps out is harder for us to see and they will be much less transparent about. HL: They will not share per member per month costs. We used to track them. SO: Also, important for us to know those rebates, some portion of those used to remain in the community as 340-B for pharmacies associated with clinics at CHCN or the EVAC pharmacy that I started or a variety of other pharmacies that have 340- B again don't have that safe keeping for all of those rebates. That is a fair amount of money to offset some of these costs. But they did it, that is the cost of letting the guards off for the most part. It's starting to come down some, definitely reinstate. • **Top 50 PA Requests by Volume (IHSS)** – Top 50 PA requests = 110. There were 174 total PA requests for quarter 1. – 59 requests (53%) were approved. This approval rate is higher, by 16%, than what was observed last quarter. – 51 requests (47%) were denied or partially approved. – Jardiance 10mg is at the top with 9 requests (along with the 25mg tablet, in total it had 11 requests) with 6 approvals. The formulary alternative is Steglatro. – Vemlidy shares the top spot, also with a total of 9 requests. Six of those were approved. Vemlidy requires trial and failure of entecavir. – Basaglar had 6 requests with 1 approval. The formulary alternatives are insulin glargine-yfgn and the newly approved biosimilar Rezvoglar (insulin glargine-aglr).		

		– Wegovy also had a total of 10 requests in the top 50, with 3 approvals, for the various strengths. Both Saxenda and Wegovy require a diagnosis of obesity or history of heart attack, despite diet and exercise, and require trial and failure of, or reason not to use Qsymia and Contrave. – Lidocaine 5% patch is at number 5 and had 4 requests with 2 approvals. • **Top 50 Drugs by Volume (Medi-Cal)** – The top 50 drugs accounted for 170,352 claims for 151,063 members and cost $3,933,493.40. – Most of the drugs are generic or OTC products. – Number 1 was Albuterol cost $595,600.46 – Number 2 Ibuprofen cost $108,176.21 – Number 3 Fluticasone cost $142,907.00 – Number 4 Aspirin EC cost $75,625.91 – Number 5 Loratadine cost $77,586.02 – Number 6 Atorvastatin cost $74,053.71 – Number 7 Amlodipine cost $63,195.48 – Number 8 Atorvastatin 40mg cost $75,625.91 – Number 9 Diclofenac Sodium Gel cost 1% $121,924.13 – Number 10 Amlodipine 10mg cost $59,405.59		

IV) E-Voting Material/Consent Agenda

H. Lee
B. Ochoa

E-Voting Material/Consent Agenda

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

Helen Lee, PharmD, MBA, Senior Pharmacy Director – Alameda Alliance
Benita Ochoa, CPhT – 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**
Opioids and Opioid Combinations Class Review	• No change
Contraceptive Foams, Devices Class Review	• No change
Diuretics Class Review	• No change
Gaucher Disease Class Review	• No change
Sucraid Monograph	• No change
Ridaura Monograph	• No change
Provenge Monograph	• No change
Medication Request Guidelines	**Changes**
Short acting opioids (part of opioid class review)	• Policy name update
Long acting opioids (part of opioid class review)	• Policy name update
Butorphanol (part of opioid class review)	• No change
Diuretics (part of diuretics class review)	• No change
Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	• Add new medication Briumvi to policy
Pregabalin (Lyrica and Lyrica CR)	• Update Lyrica CR brand/generic status
vigabatrin (Sabril)	• Update criteria statement to align with criteria
Hereditary Angioedema (HAE)	• Update criteria statement to align with criteria
Topiramate (Topamax) sprinkles	• Minor wording update
Emflaza (deflazacort)	• Minor wording update
febuxostat (Uloric)	• No change

Approved via e-voting:
Yes: 8
No: 0
Abstained: 0

		Formulary, step therapy required *For drugs without specific criteria	• No change			
		Non-formulary and prior authorization required oral liquid formulations	• No change			
		Calcitonin Gene-Related Peptide (CGRP) Antagonists for Headache Prevention	• No change			
		Lamotrigine ER	• No change			
		Levalbuterol (Xopenex/Xopenex HFA)	• No change			
		Lidocaine Patch	• No change			
		Potassium-removing agents	• No change			
		Fenofibrates	• No change			
		Nutritional formulas, infant formulas (STC C5F C5C)	• No change			
		Serotonin Receptor Agonists (Triptans)	• No change			
		Rufinamide (Banzel)	• No change			
		Tiagabine (Gabitril)	• No change			
		Phosphate Binders	• No change			
		Movement Disorders	• No change			
		Aptiom (eslicarbazepine)	• No change			
		Alprazolam (Xanax)	• No change			
		Rectiv (nitroglycerin) ointment	• No change			
		Acute Migraine Treatments	• No change			
		Palforzia	• No change			
		Lupkynis	• No change			
		Physician Administered Drug (PAD) Guidelines	**Changes**			
		Healthcare professional (HCP) administered/IV Disease Modifying Therapies (DMTs) for Multiple Sclerosis (MS)	• Add new medication Briumvi to policy			
		Naglazyme	• No change			

Calcitonin Gene-Related Peptide (CGRP) Antagonists for Headache Prevention	• No change
Interim Formulary Updates	
• See p. 156 in packet	
Pharmacy Policy & Procedure Updates	
• RX-002 – PA Review Process	• Update TAT section
• RX-003 - Exception Review	• Medical necessity NOA language update
• RX-005 - P&T Committee Roles	• Stipend language update
• RX-013 – Physician Facility-Administered Drugs (PAD) Prior Authorization Review Process	• Updates with 7/172023 go-live
ED Oversight	
• No updates	
90 Day Maintenance List updates	
• No updates	
P&T Meeting Minutes	
• P&T Meeting Minutes Q1 March 28, 2023	

Comments:

HL: One of the things I want to highlight is for one of the pharmacy policy and procedure that you guys evoted for RX-013 which was the policy we created June of 202 for Physician facility administered drugs and PA review process. The actual Rx conversion date from UM team to Pharmacy is updated to July 17 instead of June 19th. The reason is we want to make sure there is more ample training by UM department to pharmacy team.

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
Oxbryta 300mg tablet	NF to F-PA
Sunlenca 309mg/ml subcutaneous solution, Sunlenca 300mg tablet	NF to F
Colchicine 0.6 mg capsules	F-QL (30/30) to F-PA (authorizations placed for 2 utilizing members)
Clindamycin palmitate HCL oral solution 75 mg/5 ml	F-AL (max 12) to F-PA (no members under 12 years on IHSS)
Orenitram month 2 titration 0.125mg-0.25mg ER tablet, Orenitram month 3 titration 0.125-0.25mg-1mg ER tablet, Orenitram month 1 titration 0.125mg-0.25mg ER tablet	NF to F-PA
Flurazepam 30mg capsule	F-QL (30/30) (generics no longer available, no past 6 month utilization)
Fluticasone propionate 45 mcg-salmeterol (Advair HFA) 21 mcg/actuation HFA inhaler, Fluticasone propionate 115 mcg-salmeterol (Advair HFA) 21 mcg/actuation HFA inhaler, Fluticasone propionate 230 mcg-salmeterol (Advair HFA) 21 mcg/actuation HFA inhaler	Remove brands from formulary, authorized generics remain on formulary as F-PA
Misoprostol 100mcg & 200mcg tablet	Formulary status remains F, change to $0 copay
All contraceptives	Per APL 22-031 and SB 523 (Contraceptive Equity Act of 2022) and SB 245: • All contraceptives on formulary at F status, with no utilization management. (If a generic exists, the generic can be on formulary) • All contraceptives change to $0 copay • All contraceptives pay for up to a 12 month supply in one fill
Mifepristone 200mcg	NF to F, $0 copay
Rezvoglar (Insulin glargine-aglr) 100 units/ml Kwikpen	NF to F-QL (30/30)
Cyclogyl (cyclopentolate HCL) 2% drops, Cyclogyl (cyclopentolate HCL) 0.5% drops	F to NF (generics no longer available, no past 6 month utilization)
Remove all monovalent covid vaccines	F to NF (EUA revoked)

V) New Business	N. Felten	**AAH UM Medication PA List & Infusion Codes** – **HL:** As you might recall June 2022, we shared master list outpatient PAD medications that require prior authorization. Since then, further changes have been made with UM dept to include medical devices and infusion pumps/supplies. Changes are not comprehensive and further changes are expected. Tim to provide list of changes and what was added compared to last year. – **TT:** Here is the list of the updated changes. Added several Radiopharmaceuticals drugs, oncology, and CART drugs with PA requirement. Updated drug name Q5122 to correct biosimilar name. Added J7191 factor VIII to require PA to medical line. Following below are to include for infusion pump and infusion pump supplies by adding PA requirement and notifying P&T committee. Pause for Questions – **HL:** Drugs that come in as pharmacy benefit for PAD doesn't require code with HCPC code with NDC. HCPC code can get expired can expire or changed to something else. Any changes, we will let the committee know. Any changes such as adding, modifying, or deleting will notify the committee every quarter. A handful of codes not listed on table as of now, may change or expire or obsolete CPT code or codes did not cover my medical. In that case, any changes will be made by the beginning of September. So, we'll report back next September. Also, one more thing I would like to emphasize when some drugs come into the market may be covered by medical or group care, may not have a specific HCPC code and would need to submit as under "unspecified HCPC code". Once HCPC code becomes available, it is expected that prescribers will identify those HCPC codes and be able to submit with correct NDC. We will require PA for those "unspecified" codes starting in September. Pause for Questions – **SO**: We anticipate changes with infusion centers and will need to work with them by sending notifications – **HL:** We will give an announcement 30 days in advance and provide updated PAD PA list in our provider portal. **Comments:** **Radicava ORG MRG, Radicava injection PAD – new** – First policy on page 214. 1st of 2 policies that are new for edaravone. Pharmacy MRG policy for oral medication. Indicated for treatment of ALS. Mechanism is that it slows the decline of ALS is unknown. It's a free radical that prevents oxidated damage to cell membranes and contributes to inhibiting the progression of ALS. It is available with 105mg/5ML oral suspension and a starter kit. The price is $12,700 for 28-day maintenance treatment. Members must have a diagnosis of ALS, a documented baseline evaluation of functionality with revised ALS rating scale greater than or equal to 2. The disease's duration is 2 years or less, baseline forced vital capacity of less than 80%, and they should be on riluzole or Rilutek or have as an adjunct treatment. – Moving on to the corresponding medical PAD policy for the injectable version of the drug Radicava. The criteria is the same as for the oral formulation. **Comments:**	Move to approve: 1st: PG 2nd: AB	

VI) Class Reviews, Monographs, and Recommendations	N. Felten	**Filspari Monograph + new MRG** **Recommendation:** – Starting on page 216, we are not changing the formulary status of this new medication, but we are implementing a new MRG. Filspari or sparsentan is indicated to reduce proteinuria if adults with primary immunoglobulin A nephropathy or IgAN at risk of rapid disease progression, generally a urine protein to creatinine ration greater than or equal to 1.5g/g. This is a rare progressive autoimmune disease that can lead to kidney damage and eventually end stage renal disease characterized by the buildup of immunoglobulin A, which helps the body fight off infection in the kidneys. At present, management of this disease state focuses on supportive care such as blood pressure control, reduction of proteinuria, and lifestyle modifications. – Treatment also includes systemic corticosteroids. We do have one FDA approved treatment for this disease. The dosage is 200mg once daily and after 14 days dose can be increased to recommended dose of 400mg once daily. Price is $9,900 per month. – In our new policy we are going exclude pregnancy and coadministration with RAAS inhibitors, endothelin receptor antagonists, of aliskiren. Prescriber should be a nephrologist. As fo the criteria we would like the correct diagnosis verified by biopsy, total urine protein greater than 1g/day and eGFR greater than or equal to 30 mL/min as well as trial and failure with a maximized stable dose of ACE inhibitor or ARB. **Comments: N/A**		
		Daybue Monograph + new MRG **Recommendation:** – First FDA approved treatment of RETT syndrome the exact mechanism is unknown its believed to treat the core symptoms of Rett by potentially reducing neuroinflammation and supporting synoptic function. – It is a rare genetic neurodevelopmental disorder caused by mutations on the X chromosome of the MECP2 gene. It occurs almost exclusively in females although there are some cases of males have been reported, Current guidelines for disease primary focus of the management of symptoms. – Pharmaceutical therapy can be used to improve breathing, motor function and controlled seizures. Indicated for adults and PEDS 2 years or older. It is given as a twice daily oral liquid. – Dosage based on weight as an example 20kg patient weight. – Price is about $50,000 per month but can vary based on weight. Estimated 6000-9000 people with this disease in United States. About 4,500 are currently diagnosed. New MRG policy on page 231. – Specialist to be neurologist, diagnosis of Rett, documentation of specific mutation MECP2 gene, patient weight, documentation, or provider attestation of all of the following RTT clinical severity scale rating between 10-36, Clinical global impression severity score (CGI-S) of greater than or equal to 4, and baseline Rett syndrome behavior questionnaire score (RSBQ) **Comments:**		
		Joenja Monograph + new MRG		

		Recommendation: – 1st FDA approved medication for treatment of activated phosphoinositide 3-kinase syndrome or APDS in adult and pediatric patients 12 years and older and weighing 45kg or greater. It is used to treat the genetic disorder APDS and has a wide variety of clinical manifestations including routine and severe infections. – Current treatment includes supportive therapies, managing symptoms such as long term anti-biotic,propylaxis Immunoglobulin replacement therapy. – This disease is very rare. It is prevalent in 1 to 2 patients per 1 million so, it is suggested there is fewer than 500 affected individuals in United States. The disease was first characterized in 2013, so it is relatively newly identified. – Administered in 70mg tablet given by mouth twice daily. The cost is $45,000 per month. New MRG can be found on page 240. – Prescriber to be specialist, documentation of gene mutation confirmed by genetic testing. Documentation of lymphoproliferation, history of repeated infection, or organ dysfunction. – Patient can not taking any immunosuppressive medication and attestation that female patient to potential risk to fetus and have negative pregnancy test prior to initiation of treatment. **Comments: N/A**		
		Skyclarys Monograph + new MRG **Recommendation:** – Indicated for the treatment of Friedreich's ataxia in adults and adolescents aged 16 or older. The mechanism is unknown how it exerts its therapeutic effects. – This disease state is rare, progressive, recessive neuro degenerate genetic disorder caused by mutation FSX gene and impacts the function of the cerebellum spinal cord and personal nervous symptom. The symptoms and clinical findings result primarily from degenerative changes in sensory nerve fiber. – There is no cure for this. No effective therapies to prevent, delay, or reverse the damage associated with this disease state. Only supportive care was used. Affects about 5,000 patients in US. Recommended dose is 150mg once daily orally. – The cost is $30,000 a month and the new MRG can be found on page 247. Require prescriber specialist, diagnosis confirmed by genetic testing, modified mFARS score between 20 and 80, and appropriate dosage. **Comments:**		
		Attention Deficit Hyperactivity Disorder (ADHD) Class Review – 13 claims for 6 members with a total cost of $2,273 with average cost per claim of $175. The most utilized medication was Vyvanse followed by generic Adderall. There was one PA request which was approved.		

		Recommendation: – Change Vyvanse chewable tablets from non-formulary to non-formulary PA for consistency with non-chewable Vyvanse tablets PA criteria. – Would like to change the quantity limit of 30/30 of Metadate 10,20, and 30mg ER capsules for consistency with other strengths with same medication. – On page 272, there is MRG under review for this medication class with changes to remove the formulations of Tenex policy as only the long acting is labeled for this medication. **Comments:**		
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): **Gonadotropin Releasing Hormone Antagonist Combination Products:** – First, we are adding Orilissa to the policy. – Second, we are differentiating between history of hepatic impairment for Myfembree and Oriahnn and severe hepatic impairment for Orilissa. – We are just spelling out to obstetrician/gynecologist. Duration coverage is also getting updated, subsequent authorization is going from 12 to 6 months. – Require initial authorization for all requests. All requests need to have an appropriate dose, attestation from the provider that patient is not currently pregnant, no history of osteoporosis and liver function is being checked. – We are also separating the policy by diagnosis. First, diagnosis is for endometriosis is associated with moderate to severe pain, this correlates to Orilissa and Myfembree. Patients require to try analgesic first (e.g., NSAIDs, COX-2 inhibitors) and need to be on a combination of estrogen progestin oral contraceptive pills (OCPs). – OCPs route can be bypassed if they excluded from progestins, gonadotropin releasing homone (GnRH) agonists, danazol or aromatase inhibitors (e.g., anastrozole, letrozole). – Second diagnosis is for heavy menstrual bleeding associated with fibroids, this correlates to Oriahnn and Myfembree. – We also drawing on preferred approval request for Oriahnn. – Adding a line in reauthorization criteria for positive clinical response. We want to see that it is working for the member, appropriate dose, and indication. Guideline (Changes): **Orilissa (elagolix) - RETIRE** – No other changes. Guideline (Changes): **Sleep Disorder Therapy** – Make simple changes in medications section, we are doing Generic (Xyrem) Sodium oxybate. – Updating age restriction on Xyrem and Xywav are now approved in the pediatric populations. – Change the renewal criteria to 12 months for all products. – Will see generic language again for (Xyrem) Sodium oxybate..		

		Guideline (Changes): **Cholinesterase Inhibitors** – Adding a product called Adlarity (donepezil) patch to non- formulary, PA required. – We also put Adlarity (Donepezil) with Rivastigmine (Exelon) patch together. Essentially, the request needs to show that they cannot be on oral therapy to get these two products. **Comments/Questions:** **PB:** Is this specifically or broadly describe dementia? I've seen certainly for Alzheimer, and I also seen it used for vascular and I believe Rivastigmine is for Parkinson associated dementia. I just wasn't sure what the diagnosis requirement was or maybe there isn't one. **RN:** Yes, we don't have listed here a specific diagnosis that is required. But for the new product Adlarity we do want to see that they have Alzheimer disease. Yes, Rivastigmine is also for Parkinson disease dementia. Yes, that is true. **PB:** I think we tried it with vascular dementia to see if they help but I don't know. Sorry, we don't have the answer for that. Okay, thank you. **RN:** Are there any other questions for this policy? Guideline (Changes): **Daliresp (roflumilast)** – It is now available generic, so we are updating the medications section. – PA review criteria which is consolidating the diagnosis to the first bullet point so we can see it is striking out on the bronchitis. – Will see the update on third, fourth, and fifth bullet points. – Essentially, what we had before is we were requiring that there are 2 preferred long-acting inhalers used for 3 months. – Now, we are only requiring one preferred long-acting combination inhaler that is actually used for 4 weeks in the last 60 days. – It could be a combination of (LABA/LAMA) or it could be a combination of 3 (LABA/LAMA/ICS). Guideline (Changes): **Injectable Atypical Antipsychotic Medications** – In PA review criteria section, remove the first bullet point due to duplicative language. – The 2nd and 3rd bullet points already addressed for oral atypical antipsychotic used. – In criteria for reauthorization section, adding example of what kind of compliance fill history can be used. – If the reviewer sees a claim or a provider attest that the patient is taking a product, then we are considered that the criteria is met. – Looking for approved dose at appropriate strength and if member is tolerating well. Guideline (No Changes): **Hepatitis C Medications** – Update minor changes of the treatment experienced with and without compensated cirrhosis. – Patients with any genotype All on Mavyret and they failed the therapeutic Only with Mavyret, they can go on 16 weeks of Mavyret, Sovaldi and Ribavirin or 12 weeks of Vosevi. – Update is to concise with most guidelines that are recommended. Guideline (No Changes): **Hemlibra (emicizumab-kxwh)**		

		– In coverage duration section, updating initial approval from 3 to 6 months based on clinical trial, clinical benefit was studied after 24 weeks. – Simplified with diagnosis to state severe hemophilia A only and strike out all the other language because that diagnosis alone is sufficient. Guideline (No Changes): **Lipotropics** – Generic icosapent ethyl (Vascepa) 0.5mg capsule is now available and will see it throughout the policy. – The other change unrelated to generic availability is reauthorization section, to provide more clarity to state that when we receive labs and provider attestation, it should be sufficient for clinical benefit. Guideline (No Changes): **Sedative Hypnotics** – Made minor change in medications section, adding the word tablet since Doxepin is available in more than one form. – In PA review criteria, we are also adding ramelteon (Rozerem) for those who are over 65 years old. – If patients want to get Doxepin tablet and if they are over 65, they just need doxepin concentrate and ramelteon (Rozerem) in order to get approval. – For DayVigo, Quviviq, or Belsmra, will see the same language was used, that is for those who are 65 and older. – It is more reflect to another requirement for those who are over 65 and older, we just directing them to taper the medications for elderly. **Comments/Questions:** **PB:** So, I appreciate making it easier for elderly patients to get the ramelteon and just curious on the ones for the younger people. Do you have a sense of the overlap? Let's say someone has sleepwalking or has sleep behavior on zolpidem. Is it likely to happen on Lunesta or Sonata or is that for those independent events? **RN:** So, Lunesta does have that black box warning for sleep disturbance, sleep driving and waking. What was the other one that you mentioned? **PB:** I think it was for Sonata. Because you wanted them to try Sonata? I guess it's just one, never mind. Sorry about that. I thought it was two, just one. That's fine. Okay, thank you. **RN:** Oh no. it's fine. Thank you. Guideline (No Changes): **Epidiolex (cannabidiol)** – Made changes in PA review criteria, previously we had all of the indications listed in various bullet points, but we are putting in all in one. – Instead of listing all of the various essential products to treat each of those conditions, we are going to ask for treatment failure to at least two antiepileptic drugs in order to get approval. **Comment:** **SO:** Awesome! Thanks, Rahel! That is a full load of work. That is the voting item, right on those specific changes on the medication review guideline?		

		HL: Correct! **SO:** And also, the next item is also a voting item. Is there any other questions throughout the medication review guideline? If not, I will probably lump together two of those and we will talk about next which is physician administered drug policies. **RN**: Okay, sounds good! There is one more policy but there is no changes to the policy. Guideline (No Changes): **Agents for Atopic Dermatitis** – No changes. **Comments:**		
VIII) Physician Administered Drug (PAD) Policies	N. Felten	**<u>Complement Inhibitors</u>** – Recommendation is to add the newer medication to the class Syfovre (pegcetacopian injection) to the policy. – Recommend adding ophthalmologist as prescriber type and to revise the coverage duration to be longer for Syfovre up to 12 months. – Want to update the vaccination and antimicrobial prophylaxis requirements to apply only to the previously covered policy agents. Syfovre does not carry that requirement in the labeling. – Criteria for review of Syfovre that are aligned with the trial inclusion criteria in study population. – Geographic Atrophy is for those greater than or equal to age 60 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) greater than or equal to 24 letters Early Treatment Diabetic Retinopathy Study (ETDRS) – And GA lesion size greater than or equal to 2.5 and less than or equal to 17.5 mm2 with at least 1 lesion greater than or equal to 1.25 mm2 – Under Reauthorizations we want to look for slowing of the growth rate of the lesion. – Under this section for generalized myasthenia gravis separately we want to align that with the approved indications. **<u>Anti-CD19 CAR-T Immunotherapies</u>** – We want to correct the age restriction for Tecartus to 18 years and older and adjust the criteria for the new indications for Breyanzi and Yescarta. – For NHL previously all 3 agents required 2 or more lines of prior systemic therapy for NHL. Now only Kymriah requires that. – Both Yescarta and Breyanzi can be used after 1 line of therapy, so these language updates match the labeling and FDA indication. **<u>B-Cell Maturation Antigen (BCMA) Directed Chimeric Antigen Receptor (CAR) T-Cell Therapy</u>** – Recommendations are here to add new medication Carvykti to the policy.		

		– We want to add a bullet point about no previous BCMA therapy. While there's nothing on the label that refers to this, the patients in the clinical trial were excluded if they were previously treated with BCMA therapy. **SMN2 Splicing Modifiers for the Treatment of Spinal Muscular Atrophy (SMA)** – Recommendations are based on the newest trial data, so the updates include changing the exclusion criteria to apply to Spinraza only. Evrysdi now has safety data, and that restriction can be removed. – We want to update the general diagnosis requirement with mutation analysis to align with the guidelines stating that the SMN1 gene can be either deleted or mutated. – Update the drug specific genetic testing requirements to incorporate the new indication expansion for Evrysdi and pre symptomatic patients.		
IX) Informational Updates on New Developments in Pharmacy	N. Felten	New Product Review • New Products were discussed. See page 19.		

BRAND NAME	GENERIC NAME/DOSAGE FORM	RECOMMENDATION
Pradaxa	Dabigatran etexilate mesylate oral pellets in packet 20mg, 30mg, 40mg, 50mg, 110mg, 150mg	Non-formulary
Takhzyro	Lanadelumab-flyo 150 mg/mL subcutaneous syringe	Non-formulary
Rebinyn	Factor IX human rec, pegylated 3,000 (+/-) unit intravenous solution	Non-formulary
Vegzelma	Bevacizumab-adcd 25 mg/mL intravenous solution	Non-formulary
Lamzede	Velmanase alfa-tycv 10mg IV solution	Non-formulary
Syfovre	pegcetacoplan/pf 15 mg/0.1 mL intravitreal solution	Non-formulary (see PAD)
Filspari	sparsentan 200 mg, 400 mg talet	Non-formulary (see monograph)
Orenitram	treprostinil diolamine Month 1 Titration 0.125 mg (126)-0.25 mg (42) tablet,ER DsPk Month 2 Titration 0.125 mg (126)-0.25 mg (210) tablet,ER DsPk	F-PA (already added via CRF)

				Month 3 Titration 0.125mg(126)-0.25mg (42)-1mg tablet,ER DsPk				
			Erleada	apalutamide 240 mg tablet	Non-formulary			
			Konvomep	omeprazole/sodium bicarbonate 2mg – 84mg/mL oral suspension	Non-formulary			
			Clenpiq	sod picosulf/mag ox/citric ac 10 mg-3.5 gram-12 gram/175 mL oral solution	Non-formulary			
			Emerphed	ephedrine sulfate 50 mg/10 mL (5 mg/mL) intravenous syringe	Non-formulary			
			Ervebo	ebola (zaire)vacc,live,vero/pf 1mL intramuscular suspension	Non-formulary			
			Rezvoglar KwikPen	insulin glargine-aglr 100 unit/mL (3 mL) subcutaneous	F-QL (30/30) (already added via CRF)			
			cefazolin 3 gram intravenous solution	cefazolin 3 gram intravenous solution	Non-formulary			
			cefazolin 2 gram intravenous solution	cefazolin 2 gram intravenous solution	Non-formulary			
			Altuviiio	fviii rec,fc-vwf-xten,bdd-ehtl	Non-formulary			

				250 (+/-) unit IV solution 500 (+/-) unit IV solution 1,000 (+/-) unit IV solution 2,000 (+/-) unit IV solution 3,000 (+/-) unit IV solution 4,000 (+/-) unit IV solution				
			AtorvaliQ	atorvastatin calcium 20 mg/5 mL (4 mg/mL) oral suspension	Non-formulary			
			Lumakras	Sotorasib 320 mg tablet	Non-formulary			
			Daybue	Trofinetide 200 mg/mL oral solution	Non-formulary (see monograph)			
			Skyclarys	Omaveloxolone 50 mg capsule	Non-formulary (see monograph)			
			Zynyz	retifanlimab-dlwr 500 mg/20 mL intravenous solution	Non-formulary			
			Joenja	leniolisib phosphate 70 mg tablet	Non-formulary (see monograph)			
			Zolgensma	onasemnogene abeparvovec-xioi 2x10e13/ml kit	Non-formulary			

			Tirosint	levothyroxine sodium 37.5mg, 44mg, 62.5mg capsules	Non-formulary		
			Cuvrior	trientine tetrahydrochloride 300 mg tablet	Non-formulary		
			Iheezo (PF)	chloroprocaine hcl/pf 3% eye gel in a dropperette	Non-formulary		
			Gohibic (EUA)	vilobelimab 10mg/mL intravaneous solution	Non-formulary		
			Mircera	methoxy peg-epoetin beta 120 mcg/0.3 mL injection syringe	Non-formulary		
			Austedo XR	deutetrabenazine 6mg, 12mg, 24mg extended-release tablets	Non-formulary		
			Omisirge	omidubicel-onlv intravenous suspension	Non-formulary		
X) Old Business		– None					
XI) Public Comment	N. Felten	– No public comment					
XII) Adjournment	S. O'Brien	– Meeting adjourned at 6:28PM				None	

DocuSigned by:
Rahel Negash
B271482D55A648D...

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

07/17/2023
Date

DocuSigned by:
Steve O'Brien
B18599763E004BE...

Steve O'Brien, MD
CMO, Alameda Alliance for Health

07/18/2023
Date

DocuSigned by:
Helen Lee
B5335D0F01154D2...

Helen Lee, PharmD, MBA
Senior Director, Pharmacy Services,
Alameda Alliance for Health

07/18/2023
Date

New Medication Request Guidelines (MRGs) Alameda Q3 2023 P&T

New:

Specialty Biologic Agents	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	Step 1: Preferred (pays at point-of-sale) Hadlima (adalimumab-bwwd) Adalimumab-fkjp (Hulio) Step 2: Preferred (PA required) Enbrel (etanercept) Simponi, Simponi Aria (golimumab) Infliximab Inflectra (infliximab-dyyb) Avsola (infliximab-axxq) Renflexis (infliximab-abda) Orencia (abatacept) Xeljanz, Xeljanz XR (tofacitinib) Kineret (anakinra) Otezla (Apremilast) Siliq (brodalumab) Kevzara (sarilumab) Actemra (tocilizumab) Olumiant (baricitinib) Entyvio (vedolizumab) Step 3: Non-Preferred (PA required) Humira (adalimumab) Stelara (ustekinumab) Skyrizi (risankizumab) Arcalyst (rilonacept) Ilaris (canakinumab) Tremfya (guselkumab) Remicade (infliximab) Cosentyx (secukinumab) Zeposia (ozanimod) Taltz (ixekizumab) Tysabri (natalizumab) Cimzia (certolizumab) Rinvoq (upadacitinib) Ilumya (tildrakizumab-asmn) Sotyktu (deucravacitinib) All adalimumab biosimilar agents not listed in step 1(ex. Amjevita, Cyltezo, Hyrimoz, Yuflyma, etc.) Litfulo (ritlecitinib) Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines. **** Non-FDA approved (i.e. off-label) uses; refer to the "Off-Label Use" policy****
Exclusion Criteria	N/A

Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by a specialist in the field to treat the member's respective medical condition
Coverage Duration	If all of the conditions are met, requests will be approved for 12 months.

PA Review Criteria	**Initial Authorization:**
	• The drug is being requested for an appropriate use (per the references outlined in "Covered Uses")
	• The dose requested is appropriate for the requested use (per the references outlined in "Covered Uses")
	• If the request is for a preferred Step 2 agent, documentation has been provided that the member has tried and failed or has a medical reason why (e.g. intolerance, contraindication) they cannot use a preferred Step 1 agent appropriate for the requested use (per the references outlined in "Covered Uses")
	• If the request is for a non-preferred Step 3 agent, documentation has been provided that the member has tried and failed or has a medical reason why (e.g. intolerance, contraindication) they cannot use one preferred step 1 agent and one preferred step 2 agent appropriate for the requested use (per the references outlined in covered uses)
	AND:
	• If the request is for a reference biologic drug with a biosimilar or interchangeable biologic drug (ex. Humira, Remicade), documentation of one of the following:
	  • The provider has verbally, or in writing, submitted a member-specific reason why the reference biologic is required based on the member's condition or treatment history; AND if the member had side effects or a reaction to the biosimilar or interchangeable biologic, the provider has completed and submitted an FDA MedWatch form to justify the member's need to avoid these drugs. MedWatch form must also be included with the prior authorization request.
	Form FDA 3500 – Voluntary Reporting
	  • The currently available biosimilar product does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested
	*NOTE:
	• Requests for 80mg/0.8mL dose presentations of Humira or non-preferred biosimilar adalimumab agents:
	  ○ Documentation that member has tried 40mg dose presentations to achieve desired dose, or a medical reason must be provided why this cannot be used.
	• Requests for Humira 10 mg/0.1 mL in pediatric patients may be approved without a trial of a step 1 or step 2 agent, when requested for an appropriate use (per the references outlined in "Covered Uses")
	
	Reauthorization:
	• Documentation submitted indicates that the member has obtained clinical benefit from the medication.
	• The drug is being requested for an appropriate use and dose (per the references outlined in "Covered Uses")

Criteria Statement	Step 2 preferred prior authorization required medications are reserved for members with an appropriate indication and dose, who have used (or cannot/should not use) a preferred step 1 medication. Step 3 non-preferred prior authorization required medications are reserved for members with an appropriate indication and dose, who have used (or cannot/should

	not use) a preferred step 1 medication and a step 2 preferred prior authorization required medication.
Last P&T Review Date	9/2023

New:

Transthyretin-mediated Amyloidosis Agents	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS
Medications	**Preferred:** Amvuttra (vutrisiran) Cardiomyopathy – Vyndaqel (tafamidis meglumine), Vyndamax (tafamidis) **Non-preferred**: Polyneuropathy – Tegsedi (inoterson) Or any other newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be neurologist, cardiologist, or specialist in the treatment of amyloidosis
Coverage Duration	If all the criteria are met, the initial request will be approved for 6 months. For continuation of therapy, the request will be approved for 6 months.

PA Review Criteria	**Initial Authorization**:
	• Regimen does not exceed FDA-approved dose/frequency
	• Patient has not undergone a liver or heart transplant
	• Patient is not taking any of these agents concurrently: Tegsedi, Amvuttra, Vyndaqel or Vyndamax
	• If the request is for Amvuttra, or Tegsedi, patient has diagnosis of polyneuropathy of hereditary transthyretin-mediated amyloidosis as evidenced by:
	  ○ Documented transthyretin variant by genotyping
	  ○ One of the following:
	  ▪ Patient has baseline polyneuropathy disability (PND) score ≤ IIIb
	  ▪ Patient has a baseline FAP Stage 1 or 2
	  ▪ Patient has baseline neuropathy impairment (NIS) score ≥ 5 and ≤ 130
	  ○ Patient has clinical signs/symptoms of neuropathy
	  ○ For Tegsedi, patient has contraindication to/or previous trial and failure of use of Amvuttra
	• If the request is for Vyndaqel or Vyndamax, patient has diagnosis of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis as evidenced by all of the following:
	  ○ Documented transthyretin variant by genotyping or wild-type amyloidosis
	  ○ Documented amyloid deposit by biopsy or positive technetium 99m pyrophosphate (Tc 99m PYP) cardiac imaging
	  ○ Patient has New York Heart Association (NYHA) functional class I, II, or III heart failure symptoms.
	
	Re-authorization:
	• Patient's regimen does not exceed FDA-approved dose/frequency for the agent
	• Patient has not undergone a liver or heart transplant

	• Patient is not taking any of these agents concurrently: Tegsedi, Amvuttra, Vyndaqel or Vyndamax) • Documented positive clinical response to therapy from baseline (stabilization/slowing of disease progression, improved neurological impairment, motor functions, improved NIS score, stabilization/reduced rate of decline in 6 minute walk test, etc.) • If the request is for Vyndaqel/Vyndamax ○ Patient has continued NYHA functional class I, II, or III heart failure symptoms
Criteria Statement	Amvuttra, and Tegsedi are reserved for members with a diagnosis of polyneuropathy of hereditary transthyretin-mediated amyloidosis who have not undergone a liver transplant, with clinical signs or symptoms of neuropathy. Tegsedi is reserved for members who have used (or cannot/should not use) Amvuttra. Vyndaqel and Vyndamax are reserved for members with a diagnosis of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis who have not undergone a heart transplant.
Last P&T Review Date	9/2023

New:

Vowst	
Therapeutic Classes (AHFS)	OTHER MISCELLANEOUS THERAPEUTIC AGENTS
Medications	Vowst (fecal microbiota spores, live-brpk)
Covered Uses	Medically accepted indications 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	Treatment of Clostridioides difficile infection (CDI)
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	If all the criteria are met, the request will be approved for 1 treatment course.
PA Review Criteria	**Initial Authorization:** • Medication is prescribed at an FDA approved dose • Diagnosis of at least 1 recurrent episode of CDI (≥2 total CDI episodes) • Current episode of CDI must be controlled (<3 unformed/loose stools/day for 2 consecutive days) • Positive stool test for C. difficile within 30 days before prior authorization request • Administration will occur 24–72 hours following completion of antibiotic course for CDI treatment • Confirmation patient will bowel cleanse using magnesium citrate or polyethylene glycol electrolyte solution the day before the first dose of Vowst *Vowst is limited to 1 treatment course*
Criteria Statement	Vowst is reserved for members who have a diagnosis of at least 1 recurrent episode of CDI (≥2 total CDI episodes), with the current episode of CDI being controlled (<3 unformed/loose stools/day for 2 consecutive days) and a positive stool test for C. difficile within 30 days before prior authorization request. Administration must be24–72 hours following completion of antibiotic course for CDI treatment and the member must bowel cleanse using magnesium citrate or polyethylene glycol electrolyte solution the day before the first dose of Vowst.
Last P&T Review Date	9/2023

New:

Vyjuvek	
Therapeutic Classes (AHFS)	GENE THERAPY
Medications	Vyjuvek (beremagene geperpavec-svdt)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Other forms of epidermolysis bullosa, such as epidermolysis bullosa simplex, junctional epidermolysis bullosa, kindler epidermolysis bullosa
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 dermatologist, geneticist, or specialist experienced in the treatment of dystrophic epidermolysis bullosa.
Coverage Duration	If the criteria are met, the initial request will be approved for up to a 3 month duration; reauthorization requests will be approved for up to 6 months.
PA Review Criteria	**Initial Authorization:** • Patient has a diagnosis of dystrophic epidermolysis bullosa, with confirmed mutation(s) in the COL7A1 gene via genetic testing. • Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected • Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated • Medication is prescribed at an FDA approved dose, and maximum weekly dispensable amount is not exceeded **Re-Authorization:** • Documentation or provider attestation of positive clinical response (i.e. improvement in wound appearance, wound closure, healing, etc.) • Documentation indicating need for continued treatment is needed (either to partially healed wounds or to other wound sites) • Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected • Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated • Medication is prescribed at an FDA approved dose, and maximum weekly dispensing amount is not exceeded.
Criteria Statement	Vyjuvek is reserved for members who have a diagnosis of dystrophic epidermolysis bullosa (DEB), with confirmed mutation(s) in the COL7A1 gene, with wound(s) that are clean with adequate granulation tissue, excellent vascularization, and do not appear infected, and with no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated.
Last P&T Review Date	9/2023

New Physician Administered Drug (PAD) Guidelines Alameda Q3 2023 P&T

New:

Omisirge	
Medications	Omisirge (omidubicel-onlv)
Covered Uses	Medically accepted indications 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	Patient has previously received this medication
Required Clinical Information	See “other criteria”
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by an oncologist
Coverage Duration	If all the criteria are met, the initial request will be approved for a one-time treatment.
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Patient has a hematologic malignancy planned for umbilical cord blood transplantation (UCBT) following myeloablative conditioning • Prescriber attests that the patient is eligible for myeloablative allogeneic hematopoietic stem cell transplantation (HSCT) AND does not have a readily available matched related donor, matched unrelated donor, mismatched unrelated donor, or haploidentical donor • Patient has not received a prior allogenic HSCT • Patient does not have known allergy to dimethyl sulfoxide (DMSO), Dextran 40, gentamicin, human serum albumin, or bovine material **The safety and effectiveness of repeat administration of Omisirge have not been evaluated and will not be approved.**
Last Review Date	9/2023

New:

Qalsody (tofersen)	
Medications	Qalsody (tofersen)
Covered Uses	Medically accepted indications 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 “other criteria”
Required Clinical Information	See “other criteria”
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by a neurologist, neuromuscular specialist, or physician specializing in the treatment of amyotrophic lateral sclerosis (ALS)
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 6 months.
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Diagnosis of ALS • Documentation of genetic test confirming a mutation in the superoxide dismutase 1 (SOD1) gene • Member is not dependent on invasive ventilation or tracheostomy • Documentation of slow vital capacity (SVC) ≥ 50% • Medication is prescribed at an FDA approved dose **Re-Authorization:** • Documentation or provider attestation of positive clinical response (e.g., reduction in the mean concentration of neurofilament light [NfL] chains in the plasma, reduction in concentration of SOD1 in cerebrospinal fluid (CSF), or improvement in the Revised ALS Functional Rating Scale (ALSFRS-R) total score) • Member is not dependent on invasive ventilation or tracheostomy • Medication is prescribed at an FDA approved dose
Last Review Date	9/2023

New:

Lamzede	
Medications	Lamzede (velmanase alfa-tycv)
Covered Uses	Medically accepted indications 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	Prescribed by a specialist in the treatment of alpha-mannosidosis or other lysosomal storage disorders
Coverage Duration	If all of the criteria are met, the request will be approved for 12 months.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization**
	• Diagnosis of alpha-mannosidosis as confirmed by one of the following:
	  ○ Deficiency in alpha-mannosidase enzyme levels or activity in blood leukocytes
	  ○ DNA testing
	• Prescriber attests that medication will only be used to treat non-central nervous system manifestations of alpha-mannosidosis
	• Prescriber attests patient can walk without support
	• Patient’s weight
	• Dosing is consistent with FDA-approved labeling or is supported by compendia or standard of care guidelines
	
	Reauthorization
	• Patient has demonstrated a clinical response (i.e., reduction in serum oligosaccharide concentrations, stabilization or improvement in 3-minute stair climbing test [3MSCT], 6-minute walking test [6-MWT], forced vital capacity [FVC], etc.)
	• Prescriber attests that medication will only be used to treat non- central nervous system manifestations of alpha-mannosidosis
	• Prescriber attests patient can walk without support
	• Patient’s weight
	• Dosing is consistent with FDA-approved labeling or is supported by compendia or standard of care guidelines

Last Review Date	9/2023

New:

Enzyme Replacement Therapies for Fabry Disease	
Medications	Fabrazyme (agalsidase beta) Elfabrio (pegunigalsidase alfa)
Covered Uses	Medically accepted indications 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	Prescribed by a geneticist, cardiologist, nephrologist or specialist experienced in the treatment of Fabry disease
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:** • Male members must have a documented diagnosis of Fabry disease confirmed by one of the following: 1. An undetectable (<1%) alpha galactosidase A (alpha-Gal-A) activity level OR 2. A deficient alpha-Gal-A activity level AND a documented detection of pathogenic mutations in the galactosidase alpha (*GLA*) gene by molecular genetic testing • Female members must have a documented diagnosis of Fabry disease confirmed by detection of pathogenic mutations in the *GLA* gene by molecular genetic testing AND evidence of clinical manifestation of the disease (e.g. kidney, neurologic, cardiovascular, gastrointestinal) • Member must not be using concurrently with Galafold (migalastat) • Documentation of the member's current weight • Request is for an FDA-approved dose **Re-Authorization:** • Documentation that member has experienced an improvement in symptoms from baseline including but not limited to: decreased pain, decreased gastrointestinal manifestations, decrease in proteinuria, stabilization of increase in eGFR, reduction of left ventricular hypertrophy (LVH) on echocardiogram, or improved myocardial function, or has remained asymptomatic • Member must not be using concurrently with Galafold (migalastat) • Documentation of the member's current weight • Request is for an FDA-approved dose
Last Review Date	9/2023

New:

Vyjuvek	
Medications	Vyjuvek (beremagene geperpavec-svdt)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	Other forms of epidermolysis bullosa, such as epidermolysis bullosa simplex, junctional epidermolysis bullosa, kindler epidermolysis bullosa
Required Clinical Information	See “other criteria”
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a dermatologist, geneticist, or specialist experienced in the treatment of dystrophic epidermolysis bullosa.
Coverage Duration	If the criteria are met, the initial request will be approved for up to a 3 month duration; reauthorization requests will be approved for up to 6 months.
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Patient has a diagnosis of dystrophic epidermolysis bullosa, with confirmed mutation(s) in the COL7A1 gene via genetic testing. • Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected • Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated • Medication is prescribed at an FDA approved dose, and maximum weekly dispensable amount is not exceeded **Re-Authorization:** • Documentation or provider attestation of positive clinical response (i.e. improvement in wound appearance, wound closure, healing, etc.) • Documentation indicating need for continued treatment is needed (either to partially healed wounds or to other wound sites) • Documentation is provided that wound(s) to be treated are clean with adequate granulation tissue, excellent vascularization, and do not appear infected • Documentation is provided that there is no evidence of, or history of squamous cell carcinoma in the wound(s) to be treated • Medication is prescribed at an FDA approved dose, and maximum weekly dispensing amount is not exceeded.
Last Review Date	9/2023

New:

Elevidys	
Medications	Elevidys (delandistrogene moxeparvovec-rokl)
Covered Uses	Medically accepted indications 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	• Any deletion in exon 8 and/or exon 9 in the Duchenne muscular dystrophy (DMD) gene • Concurrent use with an exon skipping drugs (such as Exondys 51, Amondys 45, Vyondys 53, Viltepso)
Required Clinical Information	See “other criteria”
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescribed by neurologist or provider who specializes in the treatment of DMD
Coverage Duration	If all the criteria are met, the initial request will be approved for a **one-time** treatment.
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Medication is prescribed at an FDA approved dose • Documentation of weight • Diagnosis of DMD with a confirmed mutation in the *DMD* gene • Attestation patient is ambulatory • Member has been on a stable dose of corticosteroids for at least 3 months • Baseline micro-dystrophin protein level
Last Review Date	9/2023

New:

Specialty Biologic Agents for FDA approved indications	
Medications	Step 1: Hadlima (adalimumab-bwwd) Adalimumab-fkjp (Hulio) Step 2: Enbrel (etanercept) Simponi, Simponi Aria (golimumab) Infliximab Inflectra (infliximab-dyyb) Avsola (infliximab-axxq) Renflexis (infliximab-abda) Orencia (abatacept) Xeljanz, Xeljanz XR (tofacitinib) Kineret (anakinra) Otezla (Apremilast) Siliq (brodalumab) Kevzara (sarilumab) Actemra (tocilizumab) Olumiant (baricitinib) Entyvio (Vedolizumab) Step 3: Humira (adalimumab) Stelara (ustekinumab) Skyrizi (risankizumab) Arcalyst (rilonacept) Ilaris (canakinumab) Tremfya (guselkumab) Remicade (infliximab) Cosentyx (secukinumab) Zeposia (ozanimod) Taltz (ixekizumab) Tysabri (natalizumab) Cimzia (certolizumab) Rinvoq (upadacitinib) Ilumya (tildrakizumab-asmn) Sotyktu (deucravacitinib) All adalimumab biosimilar agents not listed in step 1(ex. Amjevita, Cyltezo, Hyrimoz, Yuflyma, etc.) Litfulo (ritlecitinib) Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “other criteria”
Age Restrictions	Check AAH active CCS cases for members < 21 years of age

Prescriber Restrictions	Prescribed by a specialist in the field to treat the member's respective medical condition
Coverage Duration	If all of the conditions are met, requests will be approved for 12 months.
Maximum Billable Units	Variable

Other Criteria	**Initial authorization:**
	• The drug is being requested for an appropriate use (per the references outlined in "Covered Uses")
	• The dose requested is appropriate for the requested use (per the references outlined in "Covered Uses")
	• If the request is for a preferred Step 2 agent, documentation has been provided that the member has tried and failed or has a medical reason why (e.g. intolerance, contraindication) they cannot use a preferred Step 1 agent appropriate for the requested use (per the references outlined in "Covered Uses")
	• If the request is for a non-preferred Step 3 agent, documentation has been provided that the member has tried and failed or has a medical reason why (e.g. intolerance, contraindication) they cannot use one preferred step 1 agent and one preferred step 2 agent appropriate for the requested use (per the references outlined in covered uses)
	AND:
	• If the request is for a reference biologic drug with a biosimilar or interchangeable biologic drug (ex. Humira, Remicade), documentation of one of the following:
	  • The provider has verbally, or in writing, submitted a member-specific reason why the reference biologic is required based on the member's condition or treatment history; AND if the member had side effects or a reaction to the biosimilar or interchangeable biologic, the provider has completed and submitted an FDA MedWatch form to justify the member's need to avoid these drugs. MedWatch form must also be included with the prior authorization request.
	Form FDA 3500 – Voluntary Reporting
	  • The currently available biosimilar product does not have the same appropriate use (per the references outlined in "Covered Uses") as the reference biologic drug being requested
	*NOTE:
	• Requests for 80mg/0.8mL dose presentations of Humira or non-preferred biosimilar adalimumab agents:
	  ○ Documentation that member has tried 40mg dose presentations to achieve desired dose, or a medical reason must be provided why this cannot be used.
	• Requests for Humira 10 mg/0.1 mL in pediatric patients may be approved without a trial of a step 1 or step 2 agent, when requested for an appropriate use (per the references outlined in "Covered Uses")
	
	Reauthorization:
	• Documentation submitted indicates that the member has obtained clinical benefit from the medication.
	• The drug is being requested for an appropriate use and dose (per the references outlined in "Covered Uses")

Last Review Date	9/2023

New:

Leqembi	
Medications	Leqembi (lecanemab-irmb)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	Patients with moderate to severe Alzheimer's Disease (AD) Patients with neurodegenerative disease caused by a condition other than AD
Required Clinical Information	See "other criteria"
Age Restrictions	age 50-90 years
Prescriber Restrictions	Prescriber must be a neurologist
Coverage Duration	For initial authorization: the request will be approved in accordance with the FDA-indicated titration schedule for up to 6 months For reauthorization: if all of the conditions are met, the request will be approved for 6 months.
Maximum Billable Units	Variable

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

	○ CDR-G score of 0.5-1.0 and a Memory Box score of 0.5 or greater ○ MMSE score of 22-30 ○ Wechsler Memory Scale IV-Logical Memory (subscale) II (WMS-IV LMII) score at least 1 standard deviation below age-adjusted mean • Provider attestation of safety monitoring and management of amyloid related imaging abnormalities (ARIA) and intracerebral hemorrhage, as recommended per the manufacturer's prescribing information. • Documentation that member has experienced clinical benefit from the medication (such as: stabilization or decreased rate of decline in symptoms from baseline on CDR-SB, ADAS-Cog14, or ADCS MCI-ADL scales) • No recent (past 1 year) history of stroke, seizures or TIA
Last Review Date	9/2023

New:

Gene Therapy for Regular Red Blood Cell (RBC) Transfusion Dependent Beta-Thalassemia	
Medications	Zynteglo (betibeglogene autotemcel)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “other criteria”
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	If all the criteria are met, the initial request will be approved for a one-time treatment
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	
	• Medication is prescribed at an FDA approved dose
	• Member has a diagnosis of transfusion dependent beta-thalassemia
	• Member requires regular RBC transfusions defined as ONE of the following:
	  ○ History of ≥100 mL/kg/year of packed red blood cell (pRBCs) in the past 2 years
	  ○ History of ≥8 transfusions of pRBCs per year in the past 2 years
	• Prescriber attests that the member does not have accessibility to a family matched hematopoietic stem-cell transplantation (HSCT)
	• Negative pregnancy test (if applicable)
	
	The safety and effectiveness of repeat administration of Zynteglo have not been evaluated and will not be approved.

Last Review Date	9/2023

New:

Roctavian	
Medications	Roctavian (valoctocogene roxaparvovec-rvox)
Covered Uses	Medically accepted indications 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	Prior use of gene therapy for Hemophilia A
Required Clinical Information	See "other criteria"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a hematologist
Coverage Duration	If all the criteria are met, the initial request will be approved for a one-time treatment
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Diagnosis of severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) • Documentation of a current prophylactic regimen of Factor VIII infusions or bispecific monoclonal antibodies (i.e. Hemlibra) • Documented FDA-approved anti-AAV5 antibody test showing the patient is negative for anti-AAV5 antibodies • Documented Factor VIII inhibitor titer test showing the patient is negative for Factor VIII inhibitors • Prescriber attestation of performed liver health assessments • Patient weight • Medication is prescribed at an FDA approved dose **The safety and effectiveness of repeat administration of Roctavian has not been evaluated and will not be approved.**
Last Review Date	9/2023

New:

Enzyme replacement therapy for acid sphingomyelinase deficiency (ASMD)	
Medications	Xenpozyme (olipudase alfa-rpcp)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “other criteria”
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Specialists experienced in the treatment of ASMD
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.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	• Medication is prescribed at an FDA approved dose
	• Member has a diagnosis of ASMD confirmed by one of the following:
	  ○ Deficiency in acid sphingomyelinase (ASM) enzyme activity (as measured by peripheral blood leukocytes, cultured skin fibroblasts, or dried blood spots)
	  ○ Sphingomyelin phosphodiesterase-1 (SMPD1) gene mutation
	• Member has a clinical presentation consistent with ASMD type B or type A/B
	• Documentation of members height and weight
	• Documentation of baseline ALT and AST within 1 month prior to initiation of treatment
	
	Re-Authorization:
	• Documentation or provider attestation of positive clinical response (i.e. improvement in splenomegaly, hepatomegaly, pulmonary function, etc.)
	• Medication is prescribed at an FDA approved dose

Last P&T Review Date	9/2023

New:

Generalized Pustular Psoriasis (GPP) Agents	
Medications	Spevigo (spesolimab-abzo)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See “other criteria”
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a dermatologist or geneticist
Coverage Duration	If all of the criteria are met, the request will be approved for up to 2 doses.
Maximum Billable Units	Variable

Other Criteria	• Diagnosis of generalized pustular psoriasis (GPP)
	• Member is experiencing an acute flare of GPP of moderate to severe intensity as defined by the patient having all of the following:
	  ○ Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) total score of 3 or greater
	  ○ Presence of fresh pustules (new appearance or worsening of pustules)
	  ○ GPPPGA pustulation sub score of 2 or greater
	  ○ At least 5% of body surface area covered with erythema and the presence of pustules
	• If member has previously received Spevigo treatment for a prior GPP flare, member must have achieved a clinical response, defined as achieving a GPPPGA score of 0 or 1, to previous treatment but is now experiencing a new flare
	• Medication is prescribed at an FDA approved dose

Last P&T Review Date	9/2023

Adalimumab

Proprietary Name	Non-proprietary Name	Designation (RS, B, I)
Humira	Adalimumab	RS
Amjevita	adalimumab-atto	B
Hadlima	Adalimumab-bwwd	B
Cyltezo	Adalimumab-adbm	I
Yusimry	Adalimumab-aqvh	B
Hulio	Adalimumab-fkjp	B
Hyrimoz	Adalimumab-adaz	B
Idacio	Adalimumab-aacf	B
Yuflyma	Adalimumab-aaty	B
Abrilada	Adalimumab-afzb	B

RS – Reference Standard, B – Biosimilar, I – Interchangeable

Clinical Summary

Pharmacologic Classification

Adalimumab binds specifically to TNF-alpha and blocks its interaction with the p55 and p75 cell surface TNF receptors. Adalimumab also lyses surface TNF expressing cells *in vitro* in the presence of complement. Adalimumab does not bind or inactivate lymphotoxin (TNF-beta). TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Elevated concentrations of TNF are found in the synovial fluid of patients with rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, and ankylosing spondylitis and play an important role in both the pathologic inflammation and the joint destruction that are hallmarks of these diseases. Increased concentrations of TNF are also found in psoriasis plaques. In psoriasis, treatment with adalimumab may reduce the epidermal thickness and infiltration of inflammatory cells. The relationship between these pharmacodynamic activities and the mechanism(s) by which adalimumab exerts its clinical effects is unknown.

Adalimumab also modulates biological responses that are induced or regulated by TNF, including changes in the concentrations of adhesion molecules responsible for leukocyte migration (ELAM-1, VCAM-1, and ICAM-1 with an IC50 of 1-2 X 10-10M).

Disease and Treatment Overview

Adalimumab is a recombinant human IgG1 monoclonal antibody that was initially indicated in the setting of rheumatoid arthritis in 2002. Over the past two decades, AbbVie's Humira has received approvals totaling nine indications and is

known as the best-selling drug in the world. Adalimumab can be used to treat adult patients with rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa and uveitis.

An aggressive pipeline strategy as well as development of different formulations, concentrations and devices contributed to AbbVie's success at maintaining market exclusivity for Humira for over 20 years. While products that target TNFα have been useful for treating several indications, the last decade has seen a rise in several new biologic drugs, such as IL inhibitors and Janus kinase (JAK) inhibitors, some of which have shown to be superior to adalimumab and other TNF inhibitors. Many of these newer biologic agents have also already expanded on and attained additional indications, thereby further complicating an already crowded landscape for the majority of these disease states. Despite this, adalimumab and other TNF inhibitors continue to see a place in therapy for many of these conditions due to their longevity on the market combined with the advent of less expensive biosimilars becoming available.

Future Landscape

Multiple launches for approved biosimilar adalimumab products occurred in July 2023, which should drastically alter the competitive landscape. A variety of products are available including high concentration, citrate-free, and one interchangeable product to reference standard Humira. Several recently launched biosimilars are seeking to gain interchangeability status to Humira from the FDA. Notably, indications for adolescent hidradenitis suppurativa, pediatric uveitis, and pediatric ulcerative colitis remain under patent protection for Humira, and thus all approved biosimilar agents launched will not have these indications included in their labeling until after their expiration. In late 2025, exclusivity will expire for pediatric uveitis and adolescent hidradenitis suppurativa. The pediatric ulcerative colitis indication's exclusivity will not expire until early 2028.

Product Table

Medication	GPI	DDID
Humira (adalimumab) 40 mg, 80 mg pen		
Humira pen 40 mg/0.8 ml	6627001500F420	187789
Humira pen crohn-uc-hs 40 mg	6627001500F420	187790
Humira pen ps-uv-adol hs 40 mg	6627001500F420	187793
Humira(cf) pen 40 mg/0.4 ml	6627001500F430	202545
Humira(cf) pen 80 mg/0.8 ml	6627001500F440	213269
Humira(cf) pen 80 mg/0.8 ml	6627001500F440	203547
Humira(cf) pen pedi uc 80 mg	6627001500F440	213931
Humira(cf) pen ps-uv-ahs 80-40	6627001500F450	212858
Humira (adalimumab) 10 mg, 20 mg, 40 mg, 80 mg syringe		
Humira(cf) 10 mg/0.1 ml syring	6627001500F804	202550
Humira 10 mg/0.2 ml syringe	6627001500F805	186083
Humira(cf) 20 mg/0.2 ml syring	6627001500F809	202549
Humira 20 mg/0.4 ml syringe	6627001500F810	187774
Humira 40 mg/0.8 ml syringe	6627001500F820	187775
Humira(cf) 40 mg/0.4 ml syring	6627001500F830	202548
Humira(cf) pedi crohn 80mg/0.8	6627001500F840	202551
Humira(cf) pedi crohn 80-40 mg	6627001500F880	202537
Idacio (adalimumab-aacf) 40 mg pen		
Idacio(cf) pen 40 mg/0.8 ml	6627001502F540	223364
Idacio(cf) pen crohns-uc 40 mg	6627001502F540	223424
Idacio(cf) pen psoriasis 40 mg	6627001502F540	223425
Idacio (adalimumab-aacf) 40 mg syringe		
Idacio(cf) 40 mg/0.8 ml syring	6627001502F840	223412
Yuflyma (adalimumab-aaty) 40 mg autoinjector		
Yuflyma(cf) 40mg/0.4ml autoinj	6627001503F530	223784
Yuflyma(cf) 40mg/0.4ml autoinj	6627001503F530	223782
Hyrimoz (adalimumab-adaz) 40 mg, 80 mg pen		
Adalimumab-adaz(cf) pen 40 mg	6627001504D515	223550
Hyrimoz(cf) pen 40 mg/0.4 ml	6627001504D515	223570
Hyrimoz(cf) pen 80 mg/0.8 ml	6627001504D540	223567
Hyrimoz(cf) pen crohn-uc 80 mg	6627001504D540	223568
Hyrimoz(cf) pen psoria 80-40mg	6627001504D560	223574
Hyrimoz (adalimumab-adaz) 10 mg, 20 mg, 40 mg, 80 mg syringe		

Hyrimoz(cf) 10 mg/0.1 ml syrng	6627001504E508	223573
Hyrimoz(cf) 20 mg/0.2 ml syrng	6627001504E513	223572
Adalimumab-adaz(cf) 40 mg syrg	6627001504E515	223556
Hyrimoz(cf) 40 mg/0.4 ml syrng	6627001504E515	223571
Hyrimoz(cf) pedi crohn 80 mg	6627001504E540	223569
Hyrimoz(cf) pedi crohn 80-40mg	6627001504E560	223575
Cyltezo (adalimumab-adbm) 40 mg pen		
Cyltezo(cf) pen 40 mg/0.8 ml	6627001505F520	223497
Cyltezo(cf) pen crh-uc-hs 40mg	6627001505F520	223499
Cyltezo(cf) pen psoriasis 40mg	6627001505F520	223498
Cyltezo (adalimumab-adbm) 10 mg, 20 mg, 40 mg syringe		
Cyltezo(cf) 10 mg/0.2 ml syrng	6627001505F805	223501
Cyltezo(cf) 20 mg/0.4 ml syrng	6627001505F810	223518
Cyltezo(cf) 40 mg/0.8 ml syrng	6627001505F820	223502
Yusimry (adalimumab-aqvh) 40 mg pen		
Yusimry(cf) 40 mg/0.8 ml pen	6627001509D240	223530
Amjevita (adalimumab-atto) 40 mg autoinjector		
Amjevita(cf) 40mg/0.8ml autoin	6627001510D520	221675
Amjevita (adalimumab-atto) 10 mg, 20 mg, 40 mg syringe		
Amjevita(cf) 10mg/0.2ml syring	6627001510E505	222871
Amjevita(cf) 20mg/0.4ml syring	6627001510E510	221681
Amjevita(cf) 40mg/0.8ml syring	6627001510E520	221679
Hadlima (adalimumab-bwwd) 40 mg autoinjector		
Hadlima(cf) pushtouch 40mg/0.4	6627001520D510	223535
Hadlima pushtouch 40 mg/0.8 ml	6627001520D520	214152
Hadlima (adalimumab-bwwd) 40 mg syringe		
Hadlima(cf) 40 mg/0.4 ml syrng	6627001520E510	223533
Hadlima 40 mg/0.8 ml syringe	6627001520E520	214149
Hulio (adalimumab-fkjp) 40 mg pen		
Adalimumab-fkjp(cf) pen 40 mg	6627001535F520	211493
Hulio(cf) pen 40 mg/0.8 ml	6627001535F520	223421
Hulio (adalimumab-fkjp) 20 mg, 40 mg syringe		
Adalimumab-fkjp(cf) 20 mg syrg	6627001535F810	211485
Hulio(cf) 20 mg/0.4 ml syringe	6627001535F810	218946
Adalimumab-fkjp(cf) 40 mg syrg	6627001535F820	211486
Hulio(cf) 40 mg/0.8 ml syringe	6627001535F820	213918

Prescribing Information

		Humira	Amjevita	Hadlima	Abrilada	Cyltezo	Yusimry	Hulio/ Adalimumab-fkjp	Hyrimoz/ Adalimumab-adaz	Idacio	Yuflyma
Indication	Rheumatoid Arthritis (adults)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Juvenile Idiopathic Arthritis (≥ 2 years)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Psoriatic Arthritis (adults)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Ankylosing Spondylitis (adults)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Crohn's Disease (adults)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Crohn's Disease (≥ 6 years)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Ulcerative Colitis (adults)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Ulcerative Colitis (≥ 5 years)	✓									
	Plaque Psoriasis (adults)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Hidradenitis Suppurativa (adults)	✓	✓	✓	✓	✓	✓	✓	✓		✓
	Hidradenitis Suppurativa (≥ 12 years)	✓									
	Uveitis (adults)	✓	✓	✓		✓					
	Uveitis (≥ 2 years)	✓									
Dosage and Administration	<u>Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis:</u> Adults: 40 mg every other week. Some patients with RA not receiving methotrexate may benefit from increasing the dosage to 40 mg every week or 80 mg every other week.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	<u>Juvenile Idiopathic Arthritis (≥ 2 years):</u> • 10 kg (22 lbs) to less than 15 kg (33 lbs): 10 mg every other week • 15 kg (33 lbs) to less than 30 kg (66 lbs): 20 mg every other week • 30 kg (66 lbs) and greater: 40 mg every other week. **Yusimry, Idacio and Yuflyma labeling only list dosing for children 30 kg and up. Hulio labeling only lists dosing for children 15 kg and greater.*	✓	✓	✓	✓	✓	✓*	✓*	✓	✓*	✓*
	<u>Crohn's Disease:</u> • Pediatrics (≥ 6 years): Pediatric Weight / Recommended Dosage	✓	✓	✓	✓	✓	✓**	✓	✓	✓**	✓**

	<table><tr><th></th><th>Days 1 and 15</th><th>Starting on Day 29</th></tr><tr><td>17 kg (37 lbs) to less than 40 kg (88 lbs)</td><td>Day 1: 80 mg Day 15: 40 mg</td><td>20 mg every other week</td></tr><tr><td>40 kg (88 lbs) and greater</td><td>Day 1: 160 mg (single dose or split over two consecutive days) Day 15: 80 mg</td><td>40 mg every other week</td></tr></table> ***Yusimry, Idacio and Yuflyma labeling only list dosing for children 40 kg and up and adults.* • Adults: 160 mg on Day 1 (given in one day or split over two consecutive days); 80 mg on Day 15; and 40 mg every other week starting on Day 29.										
	<u>Ulcerative Colitis (Adults):</u> 160 mg on Day 1 (given in one day or split over two consecutive days), 80 mg on Day 15 and 40 mg every other week starting on Day 29. Discontinue in patients without evidence of clinical remission by eight weeks (Day 57).	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	<u>Ulcerative Colitis (Pediatrics ≥ 5 years):</u> <table><tr><th>Pediatric Weight</th><th colspan="2">Recommended Dosage</th></tr><tr><th></th><th>Days 1 through 15</th><th>Starting on Day 29*</th></tr><tr><td>20 kg (44 lbs) to less than 40 kg (88 lbs)</td><td>Day 1: 80 mg Day 8: 40 mg Day 15: 40 mg</td><td>40 mg every other week or 20 mg every week</td></tr><tr><td>40 kg (88 lbs) and greater</td><td>Day 1: 160 mg (single dose or split over two consecutive days) Day 8: 80 mg Day 15: 80 mg</td><td>80 mg every other week or 40 mg every week</td></tr><tr><td colspan="3">* Continue the recommended pediatric dosage in patients who turn 18 years of age and who are well-controlled on their HUMIRA regimen.</td></tr></table>	✓									
	<u>Plaque Psoriasis:</u>	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

<table>
<tr><td></td><td>• Adults: 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose.</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td><u>Hidradenitis Suppurativa:</u>
• Adults:
○ Day 1: 160 mg (given in one day or split over two consecutive days)
○ Day 15: 80 mg
○ Day 29 and subsequent doses: 40 mg every week or 80 mg every other week</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td></td><td>✓</td></tr>
<tr><td></td><td><u>Hidradenitis Suppurativa:</u>
• Adolescents (≥ 12 years):
<table><tr><th>Adolescent Weight</th><th>Recommended Dosage</th></tr><tr><td>30 kg (66 lbs) to less than 60 kg (132 lbs)</td><td>Day 1: 80 mg
Day 8 and subsequent doses: 40 mg every other week</td></tr><tr><td>60 kg (132 lbs) and greater</td><td>Day 1: 160 mg (given in one day or split over two consecutive days)
Day 15: 80 mg
Day 29 and subsequent doses: 40 mg every week or 80 mg every other week</td></tr></table></td><td>✓</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td><u>Uveitis:</u>
• Adults: 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose.</td><td>✓</td><td>✓</td><td>✓</td><td></td><td>✓</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td><u>Uveitis:</u>
• Pediatrics (≥ 2 years):
○ 10 kg (22 lbs) to less than 15 kg (33 lbs): 10 mg every other week
○ 15 kg (33 lbs) to less than 30 kg (66 lbs): 20 mg every other week
○ 30 kg (66 lbs) and greater: 40 mg every other week</td><td>✓</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table>

Black Box Warning	Increased risk of serious infections leading to hospitalization or death	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Occurrence of lymphoma or other related malignancies	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Warnings/Precautions	Serious infections	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Malignancies	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Hypersensitivity reactions (anaphylaxis and angioneurotic edema)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Hepatitis B virus reactivation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Neurologic reactions (optic neuritis, multiple sclerosis, Guillain-Barre syndrome)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Hematological reactions (pancytopenia, aplastic anemia)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Increased risk of infection when used with anakinra	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Heart Failure (new or worsening)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Autoimmunity (developing autoantibodies or lupus-like syndrome)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Immunizations (avoid live vaccines)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Increased risk of infection when used with abatacept	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Trade Name		Humira	Amjevita	Hadlima	Abrilada±	Cyltezo	Yusimry	Hulio Adalim-fkjp	Hyrimoz Adalim-adaz	Idacio	Yuflyma
Details	Manufacturer	AbbVie	Amgen	Samsung Bioepis	Pfizer	Boehringer Ingelheim	Coherus	Mylan/Viatris/ Biocon	Sandoz	Fresenius	Celltrion
	Interchangeable Status	N/A	No, unclear if seeking	Seeking	Seeking	Yes	No	Seeking	No	No	Seeking
	Citrate-free?	Yes	Yes	No/ Yes (HC)	Yes	Yes	Yes	Yes	No/ Yes (HC)	Yes	Yes
Presentation & Price	**Single-dose prefilled syringe:**										
	80 mg/0.8 mL*	$6922.64							$6576.51◊ ✓		
	40 mg/0.8 mL	$3461.31	$3288.24	$519	✓	$3288.24	✓	$3288.24 $497.50	✓	$3288.24	
	40 mg/0.4 mL*	$3461.31		$519					$3288.25 $657.65		$3288.25
	20 mg/0.4 mL	✓ (no active NDCs)	$3288.24		✓	$3288.24		$3288.24 $497.50	✓		
	20 mg/0.2 mL*	$3461.31							$3288.25 ✓		
	10 mg/0.2 mL	✓ (no active NDCs)	$3288.24		✓	$3288.24			✓		
	10 mg/0.1 mL*	$3461.31							$3288.25 ✓		
	Single-dose prefilled device (ie Autoinjector, Pen):										
	80 mg/0.8 mL*	$6922.64							$6576.51 ✓		
	40 mg/0.8 mL	$3461.31	$3288.24 or $1557.59	$519	✓	$3288.24	$497.50	$3288.24 $497.50	✓	$3288.24	
	40 mg/0.4 mL*	$3461.31		$519					$3288.25 $657.65		$3288.25
	Single-dose glass vial for institutional use only:										
	40 mg/0.8 mL	✓		✓	✓						

*^Drug pricing is based on wholesale acquisition cost (WAC) for a single dose of the listed strength. * Items in blue or with an asterisk denote a high concentration product/presentation. Not all listed presentations per the manufacturer package insert may launch, and pricing is entered for known launched products. ◊Only available in a 3-pack starter kit labeled for pediatric Crohn's Disease. ±Abrilada is FDA approved but not yet launched.*

Clinical Studies

Completed

Amjevita

Citation	Design	Endpoints
Cohen S, Genovese MC, Choy E, et al. Efficacy and safety of the biosimilar ABP 501 compared with adalimumab in patients with moderate to severe rheumatoid arthritis: a randomized, double-blind, phase III equivalence study. *Ann Rheum Dis*. 2017;76(10):1679-1687. doi:10.1136/annrheumdis-2016-210459	A phase 3, randomized, double-blind, active comparator-controlled, 26-week equivalence study comparing efficacy, safety and immunogenicity between Amjevita and adalimumab in patients with moderate to severe active rheumatoid arthritis (RA) despite methotrexate. A total of 526 patients were randomized 1:1 to either Amjevita or Humira 40 mg every 2 weeks.	Primary: Risk ratio (RR) of ACR20 between groups at week 24. Equivalence would be confirmed if the 90% CI for RR of ACR20 at week 24 fell between 0.738 and 1.355. Secondary: Disease Activity Score 28-joint count-C reactive protein (DAS28-CRP). Safety was assessed via adverse events (AEs) and laboratory evaluations. Antidrug antibodies were assessed to determine immunogenicity.
Results: ACR20 response at week 24 was 74.6% (Amjevita) and 72.4% (adalimumab). At week 24, the RR of ACR20 (90% CI) between groups was 1.039 (0.954, 1.133), confirming the primary hypothesis. Changes from baseline in DAS28-CRP, ACR50 and ACR70 were similar. There were no clinically meaningful differences in AEs and laboratory abnormalities. A total of 38.3% (Amjevita) and 38.2% (adalimumab) of patients tested positive for binding antidrug antibodies. **Conclusion:** The authors concluded Amjevita is similar to Humira in terms of safety, clinical efficacy, and immunogenicity in patients with moderate to severe RA.		
Citation	**Design**	**Endpoints**
Papp K, Bachelez H, Costanzo A, et al. Clinical similarity of the biosimilar ABP 501 compared with adalimumab after single transition: long-term results from a randomized controlled, double-blind, 52-week, phase III trial in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2017;177(6):1562-1574. doi:10.1111/bjd.15857	A randomized controlled, double-blind, 52-week, phase 3 trial demonstrating similarity in efficacy, safety and immunogenicity of Amjevita vs. adalimumab for moderate-to-severe plaque psoriasis. Patients were randomized 1:1 to Amjevita or Humira 40 mg every 2 weeks. At 16 weeks, patients with ≥50% improvement in PASI score could continue to week 52. Continuing subjects on Amjevita stayed on Amjevita, while Humira patients were randomized 1:1 to either continue Humira or switch to Amjevita. 308 subjects were randomized at week 16 (152 stayed on Amjevita, 79 stayed on Humira, 77 switched from Humira to Amjevita).	Percentage PASI improvement from baseline, PASI responders and mean change in affected body surface area from baseline to weeks 16, 32 and 50. Safety was monitored via adverse events (AEs) and antidrug antibodies (ADAs).

Results: PASI percentage improvements from baseline were similar across groups for weeks 16, 32 and 50 (range: 85·8-88·2%), with no significant differences detected across groups in percentages of PASI 50, 75, 90 and 100 responders. Changes from baseline in percentage body surface area affected were similar across groups and time points. No new safety signals were detected. AEs were balanced between groups. Percentages of patients with binding and neutralizing ADAs were similar across treatments. **Conclusion:** The authors concluded Amjevita and Humira have similar clinical efficacy, safety and immunogenicity over 52 weeks, even in patients who switch.

Hadlima

Citation	Design	Endpoints
Study SB5-G31-RA: A Randomized, Double-blind, Parallel Group, Multicenter Clinical Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics and Immunogenicity of SB5 Compared to Humira® in Subjects With Moderate to Severe Rheumatoid Arthritis Despite Methotrexate Therapy	A randomized, double-blind, parallel-group, multicenter study to evaluate the efficacy, safety, tolerability, PK, and immunogenicity of SB5 compared to EU-Humira. Patients have been diagnosed with RA for at least 6 months, active disease despite methotrexate therapy, and have no prior history of TNF inhibitor exposure. A total of 544 subjects were randomized in a 1:1 ratio to receive either SB5 40 mg every other week (eow) or EU-Humira 40 mg eow. At Week 24, subjects receiving EU-Humira were re-randomized in a 1:1 ratio to either continue on EU-Humira or transition to SB5 40 mg eow up to Week 50. Subjects originally randomized to SB5 continued to receive SB5 40 mg eow to Week 50. All subjects also received a stable dose of oral or parenteral MTX (10-25 mg/week) from four weeks prior to screening through Week 52.	Primary: ACR20 at week 24. The prespecified similarity margin for the proportion of subjects with ACR20 response at week 24 was ±15%, using a 95% confidence interval (CI) of the difference of the proportions in treatment groups. Secondary: ACR20 at week 52, ACR50 at weeks 24 and 52, DAS28 at week 24 and 52
Results: Primary: Approximately 68.0% of subjects randomized to SB5 and 67.4% of subjects randomized to EU-Humira remained in the study and achieved an ACR20 response at Week 24, for an estimated absolute difference between treatments of 0.76% (90% CI: (-5.78%, 7.30%), 95% CI: (-7.03%, 8.56%)). Of the subjects who did not have a major protocol violation and adhered to study visits and treatment (PPS1), 73.4% of subjects achieved ACR20 response on the SB5 treatment arm and 72.2% achieved ACR20 response on the EU-Humira arm at Week 24 (90% CI: (-6.55%, 6.85%), 95% CI: (-7.83%, 8.13%)). Secondary: The proportion of patients with ACR20, ACR50, and ACR70 response over time were similar across treatment arms for Week 0 to Week 24. Furthermore, at Week 24, ACR50 and ACR70 responses were similar, and the confidence intervals were appropriately small for SB5 and EU-Humira, using both the per-protocol set 1 and the full analysis set. For each analysis, the difference between SB5 and EU-Humira was less than 2%. Mean changes from baseline in the components of the ACR endpoint and the disease activity score (DAS28) were also similar between the two treatment arms. **Conclusion:** The FDA determined In SB5-G31-RA, the were no meaningful differences in terms of efficacy between SB5 and EU-Humira, and the frequency of treatment emergent adverse events, serious events, and events leading to discontinuation of study drug had no meaningful differences between the treatment arms. Given the scientific bridge was established (based on the analytical and PK comparisons) between SB5, US-Humira, and EU-Humira to justify the relevance of data generated with EU-		

Humira as the comparator the collective evidence from submitted clinical studies, including the comparative clinical study SB5-G31-RA, supports a demonstration of no clinically meaningful differences between SB5 and US-Humira in the studied indication (RA).

Abrilada

Citation	Design	Endpoints
Study B5381002: A Phase III, Randomized, Double-blind Study Comparing The Efficacy, Safety, Pharmacokinetics And Pharmacodynamics Of Pf-06410293 And Adalimumab In Subjects With Moderate To Severe, Active Rheumatoid Arthritis On A Background Of Methotrexate	A randomized, double-blind, two-arm parallel-group study to compare the efficacy, safety, population PK, and immunogenicity between PF06410293 and EU-Humira in combination with methotrexate in patients with moderately to severely active RA for at least 4 months who have had an inadequate response to methotrexate. A total of 597 subjects were randomized. 297 received Abrilada and 299 received EU-approved Humira. Of the 552 subjects re-randomized in Treatment Period 2 (at 26 weeks), 283 subjects continued Abrilada, 135 subjects continued EU-Humira and 134 subjects previously in the EU-Humira group were re-randomized to receive Abrilada. At week 52, the remaining patients on EU-Humira were crossed over to Abrilada. All patients received concurrent methotrexate through week 52. All adalimumab dosing was 40 mg sc every 2 weeks.	Primary: ACR20 response at Week 12. The agreed upon margin to establish similarity was set at -12% and +15%.
Results: At Week 12, 71.3% of the patients randomized to EU-Humira and 68.4% of the patients randomized to PF-0610293 were ACR20 responders who stayed on randomized treatment; the estimated difference on the absolute scale comparing PF-06410293 relative to EU-Humira was -2.98% (90% exact confidence interval (CI): -9.3%, 3.3%). Overall, there were no major differences in deaths, SAEs, TEAEs, AEs leading to discontinuation, and AESI between the treatment groups. **Conclusion:** The FDA determined in Study B5381002, there were no meaningful differences in terms of efficacy between Abrilada and EU-Humira, and the frequency of treatment emergent adverse events, serious events, and events leading to discontinuation of study drug had no meaningful differences between the treatment arms.		

Cyltezo

Citation	Design	Endpoints

Study 1297.2: Comparative efficacy, safety and immunogenicity of BI 695501 versus Humira US (VOLTAIRE®-RA)	A 48-week, randomized, double-blind, active comparator study of efficacy, safety and immunogenicity of BI 695501 compared to US-licensed Humira in subjects with moderately to severely active rheumatoid arthritis for at least 6 months receiving methotrexate therapy for at least 12 weeks. Patients (n=645) were randomized 1:1 to either Cyltezo or Humira 40 mg sc every 2 weeks for 48 weeks, Patients on Humira were re-randomized at 24 weeks and either switched to Cyltezo or remained on Humira.	Primary: ACR20 response at week 12 and week 24. Similarity was demonstrated if the 90% CI of the estimate of treatment difference was contained within the prespecified similarity margin of -12% to 15% at Week 12 and the 95% CI for the estimate of treatment difference was contained within the prespecified similarity margin of -15% to 15% at Week 24.
Results: Study 1297.2 met its primary objective of demonstrating that the proportion of subjects achieving the ACR20 response criteria was similar between BI 695501 and US-licensed Humira at Week 12 (66.4% and 60.5% respectively) and at Week 24 (68.4% and 64.0% respectively). After multiple doses of SC injection, the ADA formation was comparable between BI 695501 (43.2%) and US-licensed Humira (47.8%) at Week 24 in patients with RA. After re-randomization for the purpose of evaluating a single transition from US-licensed Humira to BI 695501, no further increase in the proportion of patients with ADA positive response was observed in the group transitioned from US-licensed Humira to BI 695501 when compared to the US-licensed Humira group by Week 40. No difference in safety was identified between BI 695501 and US licensed Humira treated subjects and there was no evidence of an effect of a single transition from US-licensed Humira to BI 695501 compared to continuous US-licensed Humira treatment in terms of safety or immunogenicity. **Conclusion:** The FDA determined this comparative clinical study provided the PK, safety, efficacy, and immunogenicity data to support the demonstration of no clinically meaningful differences between BI 695501 and US-licensed Humira.		

Yusimry

Citation	Design	Endpoints
Study CHS-1420-02: A Double-Blind, Randomized, Parallel-Group, Active-Control Study to Compare the Efficacy and Safety of CHS-1420 Versus Humira in Subjects With Chronic Plaque Psoriasis	A double-blind, randomized, active control, efficacy and safety study in subjects with moderate to severe psoriasis. Patients were 18 years of age or older, with PASI ≥12, moderate to severe disease, and total BSA involvement ≥10%. No prior TNF exposure was allowed. In Treatment period 1, 545 subjects were randomized to either CHS-1420 or U.S.-Humira in a 1:1 ratio and were treated for 15 weeks. In Treatment period 2, subjects originally randomized to CHS-1420 in Treatment period 1 continued to receive CHS-1420. Subjects originally randomized to U.S.-Humira were randomized to receive CHS-1420 or U.S.-Humira in a 1:1	Primary: Difference between the percentage of subjects in each treatment group achieving a 75% improvement in Psoriasis Area and Severity Index (PASI-75) at Week 12. Similarity is demonstrated if 90% CI for the treatment difference based on the proportion of subjects with PASI 75 at Week 12 for both the FAP and PPP fall within the prespecified margins of ±15.

	ratio. In Treatment period 3, all subjects who completed Treatment Periods 1+2 and achieved at least a 50% improvement in PASI (PASI-50) score at Week 24 received 23 weeks of open label CHS-1420 QOW from Week 25 through Week 47.	
Results: Overall, the mean percent change from baseline in PASI at Week 16 was -83.1% for the CHS-1420 group and -82.3% for the U.S.-Humira group, with an estimated treatment difference (weighted) of -0.9%. The 90% CI for treatment differences was (-4.78%, 3.01%), which is fully contained within the FDA recommended margin of -10% to +10%; thus, no clinically meaningful differences between treatment groups for the FDA recommended primary efficacy endpoint is demonstrated. **Conclusion:** In Study CHS-1420-02 on patients with plaque psoriasis, no clinically meaningful differences were observed between the immunogenicity of CHS-1420 and U.S.-Humira, or the impact of immunogenicity on efficacy, PK, and safety.		

Hulio

Citation	Design	Endpoints
Study FKB327-002: A Randomized, Blinded, Active-Controlled Study to Compare FKB327 Efficacy and Safety With the Comparator Humira® in Rheumatoid Arthritis Patients Inadequately Controlled on Methotrexate	A randomized, double-blind, parallel arm, active-comparator study, designed to assess relative efficacy, safety, immunogenicity, and multi-dose PK of FKB327 compared to US-Humira in patients with RA. 730 adult patients with active RA for at least 3 months despite stable doses of methotrexate were randomized 1:1 to either FKB327 or US-Humira at a dose of 40 mg every other week for 22 weeks. Patients had no prior treatment with adalimumab, cyclophosphamide or with more than 1 biologic or 1 protein kinase inhibitor DMARD for RA.	Primary: ACR20 response at Week 24. The prespecified similarity margin for the proportion of subjects with ACR20 response at week 24 was -12% to +15%. Secondary: DAS28-CRP score at Week 24
Results: Primary: The primary efficacy analysis of the primary endpoint, ACR20 response rate, showed that US-Humira treatment group had slightly higher response rate compared to FKB327 treatment group (74.3% vs 72.5%). However, the 90% CI of the difference between FKB327 and US-Humira ACR20 response rates was (-7.3%, 3.6%), and contained within the FDA recommended margin of (-12% to +15%). Secondary: DAS28-CRP scores at Week 24 were similar in the FKB327 and US-Humira treatment (3.43 and 3.42 respectively) with a treatment difference of 0.01 with 95% CI for the difference of (- 0.16, 0.18). **Conclusion:** The FDA concluded the collective evidence from this comparative clinical study in rheumatoid arthritis supports the conclusion of no clinically meaningful differences between FKB327 and US-Humira. The adjusted treatment difference in ACR20 response rates between the FKB327 and US-Humira treatment groups in the FAS population was -1.8 with a 90% CI of (-7.3%, 3.6%), which was contained within the similarity margin [-12%, +15%] recommended by FDA. Furthermore, ACR20, ACR50, and ACR70 responses over time, mean changes from baseline in the components of the ACR composite endpoint and the disease activity score (DAS28), and other secondary efficacy endpoint results, showed no obvious differences between FKB327 and US-Humira.		

Hyrimoz

Citation	Design	Endpoints
Study 301: A Randomized, Double-blind, Multicenter Study to Demonstrate Equivalent Efficacy and to Compare Safety and Immunogenicity of a Biosimilar Adalimumab (GP2017) and Humira® in Patients With Moderate to Severe Chronic Plaque-type Psoriasis	A multicenter, randomized, double-blind study in 465 male and female patients with chronic plaque-type psoriasis with treatment duration of up to 51 weeks comparing GP2017 with Humira. Patients had at least 10% BSA involvement, PASI ≥12 (moderate-severe), and previously received or were eligible to receive phototherapy or systemic therapy. Patients may not have prior exposure to adalimumab. Patients were randomized at Day 1 to receive GP2017 or Humira and were administered a loading dose of 80 mg sc, followed by 40 mg doses sc every other week from Week 1 up to Week 49. At Week 17, patients with a PASI50 response were re-randomized in a 2:1 ratio into continued (1a: continued GP2017 or 2a: continued Humira) or switched treatment groups (1b: GP2017 to Humira or 2b: Humira to GP2017).	Primary: PASI 75 response rate at week 16. Similarity was established if 90% confidence intervals are contained within ±18%, the pre-specified similarity criterion.

Results:

Table 5: PASI 75 Response Rates at Week 16

	GP2017	Humira	Difference	90% CI
PPS				
Overall	N=197 66.8%	N=196 65.0%	1.8	(-6.0, 9.7)
US	N=157 68.0%	N=157 62.6%	5.3	(-3.5, 14.1)
US excluding r 1268	N=143 74.5%	N=143 68.9%	5.6	(-4.5, 15.7)
FAS				
Overall	N=231 58.1%	N=234 55.9%	2.2	(-5.4, 9.7)
US	N=188 57.9%	N=190 53.2%	4.7	(-3.6, 13.1)
US excluding r 1268	N=174 62.6%	N=171 59.1%	3.5	(-4.9, 12.0)

Source: DDDP Statistics Reviewer

Table 5 presents the results for the overall population (all subjects), the subset of US subjects, and the subset of US subjects excluding Center 1268 for both the per-protocol set and the full-analysis set. In each case, the results are generally consistent and the 90% confidence intervals are contained within ±18%, the pre-specified similarity criterion. The secondary endpoints of percent change in PASI and IGA success are consistent with the results of the primary endpoint analysis. **Conclusion:** The FDA determined from a clinical standpoint, the clinical pharmacology, efficacy, safety, and immunogenicity data submitted to this 351(k) BLA from the clinical development program of GP2017, support the demonstration of no clinically meaningful difference between GP2017 and US-licensed Humira in the indication studied, i.e., plaque psoriasis.

Idacio

Citation	Design	Endpoints
Study EMR200588-002: A Randomized, Double-blind Trial to Evaluate the Efficacy, Safety and Immunogenicity of MSB11022 Compared With Humira® in Subjects With Moderate to Severe Chronic Plaque Psoriasis	A double-blind, randomized, multi-center, parallel-group, efficacy and safety study in subjects with moderate to severe chronic plaque psoriasis during 52 weeks of treatment. Patients were adults with PASI ≥12, PSGA ≥3, and BSA ≥10% diagnosed with psoriasis at least 6 months. In the Core Treatment Period, 443 subjects were randomized to either sc MSB11022 or EU- Humira in a 1:1 ratio. After completion of the Core Treatment Period at the Week 16 visit, subjects who achieved PASI 50 entered a 37-week double-blind Extended Period. Subjects who were initially randomized to the EU-Humira group were re-randomized 1:1 to receive either MSB11022 or EU-Humira starting with the Week 16 treatment for an additional 37 weeks. Subjects who were initially randomized to the MSB11022 group remained on MSB11022 throughout the entire study.	Primary: PASI 75 at week 16, evaluated using a 90% confidence interval with margins of ± 10% in the per-protocol analysis set.
Results: Overall, the mean percent change from baseline in PASI at Week 16 was -92.14% for the MSB11022 group and - 93.02% for the EU-Humira group, with an estimated treatment difference of 0.88%. The 90% CI for treatment differences was (-0.87%, 2.64%), which is fully contained within the FDA recommended margin of -10% to +10%. **Conclusion:** No meaningful differences between treatment groups for the FDA recommended primary efficacy endpoint is demonstrated based on the primary analysis.		

Yuflyma

Citation	Design	Endpoints

CT-P17 3.1: A Randomized, Active-Controlled, Double-Blind, Phase 3 Study to Compare Efficacy and Safety of CT-P17 With Humira When Co-administered With Methotrexate in Patients With Moderate to Severe Active Rheumatoid Arthritis	A Phase 3, randomized, active controlled, double-blind, comparative clinical study of either CT-P17 or EU-Humira co-administered with MTX in patients with moderate to severe active rheumatoid arthritis receiving concomitant methotrexate. Subjects (n=648) were randomized 1:1 to either EU-Humira or CT-P17 for 24 weeks (treatment period 1), then subjects in the Humira group were re-randomized 1?1 to either continue on Humira or transition to CT-P17 starting at week 26, through week 48.	Primary: clinical response according to ACR20 at Week 24. The 90% confidence interval (CI) for the difference in proportion between the CT-P17 and EU-Humira treatment groups were analyzed with therapeutic similarity of clinical response according to ACR20 criteria being concluded if the 90% CI for the treatment difference was entirely within the limits of -12% to 15% at Week 24.
Results: Approximately 83% of subjects randomized to CT-P17 and 83% of subjects randomized to EU-Humira achieved an ACR20 response (responder) at Week 24, for an estimated proportion difference of 0 (90% CI: -4.98, 4.98). The 90% CI ruled out the similarity margin of (-12%, 15%) proposed by the applicant, which demonstrated therapeutic similarity between the two treatment arms. In a supportive analysis of ACR20 response in the subset of subjects who completed the study and adhered to the protocol (PP population), 87% and 87% responded on CT-P17 and EU-Humira, respectively, for an estimated difference of 0.06% (90% CI: -4.70%, 4.86%) meeting the similarity margin of -12% to 15%. **Conclusion: T**he collective evidence from submitted clinical studies, including the comparative clinical study CT-P17 3.1 in patients with rheumatoid arthritis (RA), supports a demonstration of no clinically meaningful differences between CT-P17 and US-Humira.		

Clinical Opinions

Limited data is available to assess bioequivalence between Humira and biosimilar adalimumab products. Equivalency studies that are available primarily evaluate biosimilars to Humira in the setting of rheumatoid arthritis and psoriasis; in general, efficacy and safety markers are very similar and unlikely to generate clinically meaningful differences in most patients. Due to highly successful life cycle management strategies by manufacturers, biosimilars have taken significant time to become available on the market despite receiving FDA approval. Cost of available products will play a pivotal factor for formulary decision making, as well as available product presentations (strengths, citrate-free, pens or syringes). Humira's ability to maintain market share with the potential for continued rebate agreements and multiple biosimilar players entering the market will generate considerable change in the TNF treatment landscape in 2023 and beyond. Strategies will likely differ considerably depending on the type of market (Medicare, Medicaid, commercial).

References

1. Amjevita [prescribing information]. Amgen, Thousand Oaks, CA; August 2022.
2. Humira [prescribing information]. AbbVie, North Chicago, IL; February 2021.
3. Hadlima [prescribing information]. Organon, Jersey City, NJ; July 2023.
4. Abrilada [prescribing information]. Pfizer, New York, NY; June 2023.
5. Cyltezo [prescribing information]. Boehringer Ingelheim, Ridgefield, CT; June 2023.
6. Yusimry [prescribing information]. Coherus, Redwood City, CA; March 2023.
7. Hulio [prescribing information]. Mylan, Morgantown, WV; March 2023.
8. Hyrimoz [prescribing information]. Sandoz, Princeton, NJ; April 2023.
9. Idacio [prescribing information]. Fresenius Kabi, Lake Zurich, IL; December 2022.
10. Yuflyma [prescribing information]. Celltrion, Jersey City, NJ; May 2023.
11. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: https://clinicaltrials.gov/. Accessed on February 15, 2023.
12. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: https://www.ncbi.nlm.nih.gov/pubmed. Accessed on February 15, 2023.
13. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on February 15, 2023.
14. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: http://www.fda.gov/. Accessed on August 15, 2023.
15. Biomedtracker. Cambridge, MA: Informa Business Intelligence, Inc. https://www.biomedtracker.com/. Accessed on August 15, 2023.
16. IPD Analytics. Bay Harbor Islands, Florida: IPD Analytics, LLC. http://www.ipdanalytics.com. Accessed on August 15, 2023.
17. Turner, S. Humira: the highs and lows of the world's best-selling drug. Pharmaceutical Technology. Available at: https://www.pharmaceutical-technology.com/features/humira-abbvie-drug/. Accessed on February 15, 2023.
18. Cohen S, Genovese MC, Choy E, et al. Efficacy and safety of the biosimilar ABP 501 compared with adalimumab in patients with moderate to severe rheumatoid arthritis: a randomized, double-blind, phase III equivalence study. Ann Rheum Dis. 2017;76(10):1679-1687. doi:10.1136/annrheumdis-2016-210459.
19. Papp K, Bachelez H, Costanzo A, et al. Clinical similarity of the biosimilar ABP 501 compared with adalimumab after single transition: long-term results from a randomized controlled, double-blind, 52-week, phase III trial in patients with moderate-to-severe plaque psoriasis. Br J Dermatol. 2017;177(6):1562-1574. doi:10.1111/bjd.15857.
20. US Food and Drug Administration. Drug approval package: Hadlima (adalimumab) injection (Application No 761059Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/761059Orig1s000MultidisciplineR.pdf.
21. US Food and Drug Administration. Drug approval package: Abrilada (adalimumab) injection (Application No 761118Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/761118Orig1s000MultidisciplineR.pdf.
22. US Food and Drug Administration. Drug approval package: Cyltezo (adalimumab) injection (Application No 761058Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/761058Orig1s000MedR.pdf.
23. US Food and Drug Administration. Drug approval package: Yusimry (adalimumab) injection (Application No 761216Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2022/761216Orig1s000MultidisciplineR.pdf.
24. US Food and Drug Administration. Drug approval package: Hulio (adalimumab) injection (Application No 761154Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/761154Orig1s000MultidisciplineR.pdf.
25. US Food and Drug Administration. Drug approval package: Hyrimoz (adalimumab) injection (Application No 761071Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/761071Orig1s000MedR.pdf.
26. US Food and Drug Administration. Drug approval package: Idacio (adalimumab) injection (Application No 761255Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/761255Orig1s000MultidisciplineR.pdf.
27. US Food and Drug Administration. Drug approval package: Yuflyma (adalimumab) injection (Application No 761219Orig1s000). https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/761219Orig1s000MultidisciplineR.pdf.

Drug Name: Abrysvo (respiratory syncytial virus vaccine) **Manufacturer:** Pfizer

Approval Date: 5/31/2023 **Marketing Date:** 7/14/2023

Recommendation

- Change from NF to F-QL (1 dose per lifetime)
  - (DDID: 223691)

Prescribing Information

Indication

Indicated for:

- Active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older.
- Active immunization of pregnant individuals at 32 through 36 weeks' gestational age (GA) for the prevention of LRTD and severe LRTD cause by RSV in infants from birth through 6 months of age.

Mechanism of Action

Abrysvo™ induces an immune response against RSV pre F that protects against lower respiratory tract disease caused by RSV.

Dosage and Administration

Administer Abrysvo as a single approximately 0.5 mL dose. For intramuscular use only.

Black Box Warning

None

Adverse Reactions

Most common: fatigue, headache, pain at injection site, and muscle pain.

Serious: management of acute allergic reactions, syncope, altered immunocompetence, limitation of vaccine effectiveness.

Use in Specific Populations, Pregnancy

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4%, and 15% to 20%, respectively, and the estimated background risk of fetal deaths after 20 weeks is 0.6%. Abrysvo is not approved for use in individuals younger than 60 years of age. Data from a clinical trial (NCT04424316) that enrolled pregnant individuals who were randomly assigned 1:1 to receive Abrysvo or placebo (0.5 mL dose, containing the same buffer ingredients in the same quantities as in a single dose of Abrysvo at 24 through 36 weeks’ gestation revealed no evidence

for vaccine-associated increase in the risk of congenital anomalies or fetal deaths. In this study, there was a numerical imbalance in preterm births, with more preterm infants born to individuals in the Abrysvo group compared to individuals in the placebo group.

Drug Interactions

None

How Supplied

Solution for injection. A single dose after reconstitution is 0.5 mL.

Price

$295

(Per dose, based on WAC.)

Clinical Studies

Completed

Title	Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults (RENOIR) NCT: 05035212 PMID: 37018468
Design	Phase 3, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of Abrysvo™ in individuals 60 years of age and older.
Population	Abrysvo™ (n=17,197) Placebo (n=17,186) Of the participants in the study, 51% were male and 78% were White, 13% were Black or African American, and 37% were Hispanic/Latino. The median age of participants was 67 years (range 59-97 years)
Arms	Patients were randomized 1:1 to receive either: • A single intramuscular injection of Abrysvo™ vaccine at a dose of 120 mcg/0.5ml (RSV subgroups A and B, 60 mcg each) • Placebo
Endpoint(s)	Primary: • Vaccine efficacy against seasonal RSV-associated lower respiratory tract illness with at least two or at least three signs or symptoms

<table>
<tr><td>Inclusion Criteria</td><td>

Adults ≥60 years of age who are ambulatory and live in the community, or in assisted living or long-term care residential facilities that provide minimal assistance, such that the participant is primarily responsible for self-care and activities of daily living.
Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, frequent symptom assessment by mobile device application, and other study procedures, including collection of nasal swabs by themselves and by study staff when indicated.

</td></tr>
<tr><td>Exclusion Criteria</td><td>

Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.
Serious chronic disorder including metastatic malignancy, end-stage renal disease with or without dialysis, clinically unstable cardiac disease, or any other disorder that, in the investigator's opinion, excludes the participant from participating in the study.
Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.

</td></tr>
<tr><td>Results</td><td>Primary:

Table 3 Vaccine Efficacy of ABRYSVO Against RSV-LRTD - Individuals 60 years of Age and Older (Study 1)[a]
<table>
<tr><th>Efficacy Endpoint</th><th>ABRYSVO N=16,306[b] n</th><th>Placebo N=16,308[b] n</th><th>VE (%) (96.66% CI)</th></tr>
<tr><td>First episode of RSV-associated lower respiratory tract disease with ≥2 symptoms</td><td>11</td><td>33</td><td>66.7 (28.8, 85.8)</td></tr>
<tr><td>First episode of RSV-associated lower respiratory tract disease with ≥3 symptoms</td><td>2</td><td>14</td><td>85.7 (32.0, 98.7)</td></tr>
</table>
CI – confidence interval; N – number of participants; n = number of cases; RSV – respiratory syncytial virus; VE – vaccine efficacy (VE based on case count ratio is calculated as 1-(P/[1-P]), where P is the number of RSVpreF cases divided by the total number of cases)
[a] NCT05035212
[b] Evaluable efficacy population
</td></tr>
<tr><td>Conclusion</td><td>The vaccine candidate prevented RSV-associated lower respiratory tract illness and RSV-associated acute respiratory illness in adults (≥60 years of age), without evident safety concerns.</td></tr>
<tr><td>Interpretation</td><td>The RENOIR trial evaluated Abrysvo™ versus placebo in ~30,000 adults who were at least 60 years old. Protection against RSV-associated lower respiratory tract illness (LRTI-RSV) defined by two or more symptoms demonstrated vaccine efficacy of 66.7%; efficacy in protection against LRTI-RSV defined by three or more symptoms was 85.7%. Abrysvo™ was well tolerated. Abrysvo™, an un-adjuvanted vaccine, is the second vaccine to be approved for older adults, after GSK's Arexvy, an adjuvanted vaccine.</td></tr>
</table>

Guidelines

Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4.

Recommendations for Use of RSV Vaccines in Older Adults

On June 21, 2023, the Advisory Committ on Immunization Practices (ACIP) recommended that adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making.

Clinical Guidance

Shared Clinical Decision-Making for Adults Aged ≥60 years. Unlike routine and risk-based vaccine recommendations, recommendations based on shared clinical decision-making do not target all persons in a particular age group or an identifiable risk group. For RSV vaccination, the decision to vaccinate a patient should be based on a discussion between the health care provider and the patient, which might be guided by the patient's risk for disease and their characteristics, values, and preferences; the provider's clinical discretion; and the characteristics of the vaccine.

As part of this discussion, providers and patients should consider the patient's risk for severe RSV-associated disease. Epidemiologic evidence indicates that persons aged ≥60 years who are at highest risk for severe RSV disease and who might be most likely to benefit from vaccination include those with chronic medical conditions such as lung diseases, including chronic obstructive pulmonary disease and asthma; cardiovascular diseases such as congestive heart failure and coronary artery disease; moderate or severe immune compromise (either attributable to a medical condition or receipt of immunosuppressive medications or treatment); diabetes mellitus; neurologic or neuromuscular conditions; kidney disorders, liver disorders, and hematologic disorders; persons who are frail; persons of advanced age; and persons with other underlying conditions or factors that the provider determines might increase the risk for severe RSV-associated respiratory disease. Adults aged ≥60 years who are residents of nursing homes and other long-term care facilities are also at risk for severe RSV disease. It should be noted that the numbers of persons enrolled in the trials who were frail, were of advanced age, and lived in long-term care facilities were limited, and persons with compromised immunity were excluded (some of whom might have an attenuated immune response to RSV vaccination). However, adults aged ≥60 years in these populations may receive vaccination using shared clinical decision-making given the potential for benefit.

RSV Vaccination Timing

RSV vaccination is currently approved and recommended for administration as a single dose; sufficient evidence does not exist at this time to determine the need for revaccination. Optimally, vaccination should occur before the onset of the RSV season; however, typical RSV seasonality was disrupted by the COVID-19 pandemic and has not returned to prepandemic patterns. For the 2023–24 season, clinicians should offer RSV vaccination to adults aged ≥60 years using shared clinical decision-making as early as vaccine supply becomes available and should continue to offer vaccination to eligible adults who remain unvaccinated.

Vaccine Administration, Including Coadministration with Other Vaccines

Coadministration of RSV vaccines with other adult vaccines during the same visit is acceptable. Available data on immunogenicity of coadministration of RSV vaccines and other vaccines are currently limited. Coadministration of RSV and seasonal influenza vaccines met noninferiority criteria for immunogenicity with the exception of the FluA/Darwin H3N2 strain when the GSK RSV vaccine was co-administered with adjuvanted quadrivalent inactivated influenza vaccine. RSV and influenza antibody titers were somewhat lower with coadministration; however, the clinical significance of this is unknown.

Administering RSV vaccine with one or more other vaccines at the same visit might increase local or systemic reactogenicity. Data are only available for coadministration of RSV and influenza vaccines, and evidence is mixed regarding increased reactogenicity. Data are lacking on the safety of coadministration with other vaccines that might be

recommended for persons in this age group, such as COVID-19 vaccines; pneumococcal vaccines; adult tetanus, diphtheria, and pertussis vaccines; and the recombinant zoster vaccine (the recombinant zoster vaccine and GSK's RSV vaccine contains the same adjuvant). When deciding whether to co-administer other vaccines with an RSV vaccine, providers should consider whether the patient is up to date with currently recommended vaccines, the feasibility of the patient returning for additional vaccine doses, risk for acquiring vaccine-preventable disease, vaccine reactogenicity profiles, and patient preferences. Post licensure efficacy and safety monitoring of co-administered RSV vaccines with other vaccines will further direct guidance.

Clinical Opinions

Respiratory syncytial virus (RSV) is a single-stranded, negative-sense ribonucleic acid (RNA) respiratory virus that infects the lungs and airways. RSV affects patients of all ages, but the elderly and infants are at risk for developing more severe disease. Among adults infected with RSV, symptoms are usually consistent with an upper respiratory infection and the virus lasts less than five days. Some adults may have more severe symptoms consistent with a LRTI such as pneumonia. RSV can also lead to exacerbations of serious underlying conditions such as asthma, chronic obstructive pulmonary disease (COPD), and congestive heart failure. In adults 65 years and older, RSV leads to approximately 177,000 hospitalizations and 14,000 deaths per year. The mortality rate among hospitalized adults 50 years and older is 6 to 8%. RSV causes seasonal outbreaks throughout the world. In the United States, RSV primarily occurs during the fall, winter, and spring months, but the timing and severity of RSV season can vary from year to year. Disruption of the typical seasonal pattern, such as during the coronavirus disease 2019 (COVID-19) pandemic, may result in off season outbreaks.

There are no FDA approved agents for the treatment of RSV. Until recently, Synagis® (palivizumab), a recombinant humanized monoclonal antibody, was the only FDA approved agent for the prevention of RSV. Synagis® is not recommended or FDA approved for RSV prevention in adults. Abrysvo™ represents one of the first vaccine options indicated as a preventative measure against LRTD caused by RSV in adults 60 years and older. Abrysvo™ will compete with GSK's vaccine, Arexvy, which was approved shortly before Abrysvo™ for the same indication. Moderna has a similar vaccine in development, mRNA-1345, which would compete with both Arexvy and Abrysvo™. However, Moderna's vaccine candidate is unlikely to be approved in time for the 2023-2024 RSV season.

In June of 2023, the ACIP voted 9 to 5 to recommend that adults 65 years of age and older **may** receive a single dose of RSV vaccine, using shared clinical decision-making. An identical recommendation was made for adults 60 to 64 years of age, with a vote of 13 to 0. This recommendation was an amendment to the original recommendation made in February 2023 in which the ACIP suggested all adults 65 years of age and older **should** receive an RSV vaccination.

Abrysvo™ is also being studied under the name RSVpreF as a vaccine for the prevention of medically attended lower respiratory tract illness (MA-LRTI) and severe MA-LRTI caused by RSV in infants from birth up to 6 months of age by active immunization of pregnant individuals. If approved, RSVpreF will compete with the recently approved monoclonal antibody Beyfortus™ (nirsevimab).

Alternatives

Drug Name^	Formulary Status	Dosage Form	Price*
Arexvy (respiratory syncytial virus vaccine, adjuvanted)	NF	120 mcg/0.5 mL	$280

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

References

1. Abrysvo (respiratory syncytial virus vaccine). [prescribing information]. Pfizer, New York, NY; May, 2023.
2. AMCP eDossier System. Dymaxium Healthcare Innovations, Ltd. Available at: https://amcp.edossiers.com/. Accessed on June 6, 2023.
3. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: https://clinicaltrials.gov/. Accessed on June 6, 2023.
4. Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on June 6, 2023.
5. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: https://www.ncbi.nlm.nih.gov/pubmed. Accessed on June 6, 2023.
6. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on June 6, 2023.
7. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: http://www.fda.gov/. Accessed on June 6, 2023.
8. Walsh EE, Pérez Marc G, Zareba AM, et al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. *N Engl J Med*. 2023;388(16):1465-1477. doi:10.1056/NEJMoa2213836
9. Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4.

Drug Name: Arexvy (respiratory syncytial virus vaccine, adjuvanted)

Manufacturer: GlaxoSmithKline Biologicals

Approval Date: 5/3/2023

Marketing Date: 7/20/2023

Recommendation

- Change from NF to F-QL (1 dose per lifetime)
  - (DDID: 223763)

Prescribing Information

Indication

Indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in individuals 60 years of age and older.

Mechanism of Action

Arexvy induces an immune response against RSVpreF3 that protects against LRTD caused by Respiratory Syncytial Virus (RSV).

Dosage and Administration

For intramuscular administration only. Administer a single dose (0.5 mL) as an intramuscular injection.

Black Box Warning

None

Adverse Reactions

The most commonly reported solicited local adverse reaction (≥10%) was injection site pain. The most reported solicited systemic adverse reactions (≥10%) were fatigue, myalgia, headache, and arthralgia.

Serious: allergic reactions, syncope, altered immunocompetence.

Use in Specific Populations, Pregnancy

Arexvy is not approved for use in persons <60 years of age. In a clinical study that enrolled pregnant individuals who received an investigational unadjuvanted RSV vaccine that contained the same RSVPreF3 antigen as Aerxvy, an increase in preterm births was observed compared to pregnant individuals who received placebo (sucrose reconstituted with saline)

Drug Interactions

Data are not available for concomitant administration with other vaccines.

How Supplied

0.5 mL intramuscular injection

Price

$280

(Per dose, based on WAC.)

Clinical Studies

Completed

Title	Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults NCT: 04886596 PMID: 36791160
Design	Phase 3, randomized, placebo-controlled, observer-blind, multi-country study to demonstrate the efficacy of a single dose and annual revaccination doses of GSK's investigational vaccine in adults 60 years and older.
Population	N= 24,960 51.7% female; 79.4% White, 8.7% Black, 7.6% Asian, and 4.3% of other racial/ethnic groups including American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander; 5.5% of Hispanic or Latino ethnicity. The median age of participants was 69 years.
Arms	Patients were randomized 1:1 to receive a single dose of: • an $AS01_E$-adjuvanted RSV prefusion F protein-based candidate vaccine (RSVPreF3 OA) (Arexvy) (n=12,466) • Placebo (n = 12,494)
Endpoint(s)	Primary: • The prevention of a first episode of confirmed RSV-A and/or B-associated LRTD during the first season.
Inclusion Criteria	• A male or female ≥ 60 years old at the time of first vaccination, who live in the community (community dwelling participants) or in a long-term care facility (LTCF) (LTCF participants). • Participants who, in the opinion of the investigator, can and will comply with the requirements of the protocol.
Exclusion Criteria	• Any confirmed or suspected immunosuppressive or immunodeficient condition resulting from disease or immunosuppressive/cytotoxic therapy, based on medical history and physical examination (no laboratory testing required).

<table>
<tr><td></td><td>

Serious or unstable chronic illness.
Any history of dementia or any medical condition that moderately or severely impairs cognition.

</td></tr>
<tr><td>Results</td><td>Primary:

Table 2. Efficacy Analysis: First Respiratory Syncytial Virus-associated Lower Respiratory Tract Disease Overall, by Age and Co-morbidity Subgroups in Study 1[a] (Modified Exposed Set)
<table>
<tr><th rowspan="2">Subgroup</th><th colspan="3">AREXVY</th><th colspan="3">Placebo</th><th rowspan="2">% Efficacy (CI)[b]</th></tr>
<tr><th>N</th><th>n</th><th>Incidence Rate per 1,000 Person-Years</th><th>N</th><th>n</th><th>Incidence Rate per 1,000 Person-Years</th></tr>
<tr><td>Overall (≥60 years)</td><td>12,466</td><td>7</td><td>1.0</td><td>12,494</td><td>40</td><td>5.8</td><td>82.6 (57.9, 94.1)</td></tr>
<tr><td>60 to 69 years</td><td>6,963</td><td>4</td><td>1.0</td><td>6,979</td><td>21</td><td>5.5</td><td>81.0 (43.6, 95.3)</td></tr>
<tr><td>70 to 79 years</td><td>4,487</td><td>1</td><td>0.4</td><td>4,487</td><td>16</td><td>6.5</td><td>93.8 (60.2, 99.9)</td></tr>
<tr><td>Participants with at least 1 comorbidity of interest</td><td>4,937</td><td>1</td><td>0.4</td><td>4,861</td><td>18</td><td>6.6</td><td>94.6 (65.9, 99.9)</td></tr>
</table>
</td></tr>
<tr><td>Conclusion</td><td>A single dose of the RSVPreF3 OA vaccine had an acceptable safety profile and prevented RSV-related acute respiratory infection and lower respiratory tract disease and severe RSV-related lower respiratory tract disease in adults 60 years of age or older, regardless of RSV subtype and the presence of underlying coexisting conditions.</td></tr>
<tr><td>Interpretation</td><td>Arexvy proved to be efficacious against LRTD in patients 60 years and older. Additionally, Arexvy demonstrated even great efficacy in individuals with more severe disease. There are no FDA approved agents for the treatment of RSV. Until the approval of Arexvy, Synagis® (palivizumab), a recombinant humanized monoclonal antibody, was the only FDA approved agent for the prevention of RSV. However, Synagis is indicated for the pediatric population only. Arexvy represents the first RSV vaccine.</td></tr>
</table>

Guidelines

Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4.

Recommendations for Use of RSV Vaccines in Older Adults

On June 21, 2023, the Advisory Committ on Immunization Practices (ACIP) recommended that adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making.

Clinical Guidance

Shared Clinical Decision-Making for Adults Aged ≥60 years. Unlike routine and risk-based vaccine recommendations, recommendations based on shared clinical decision-making do not target all persons in a particular age group or an identifiable risk group. For RSV vaccination, the decision to vaccinate a patient should be based on a discussion between the health care provider and the patient, which might be guided by the patient's risk for disease and their characteristics, values, and preferences; the provider's clinical discretion; and the characteristics of the vaccine.

As part of this discussion, providers and patients should consider the patient's risk for severe RSV-associated disease. Epidemiologic evidence indicates that persons aged ≥60 years who are at highest risk for severe RSV disease and who might be most likely to benefit from vaccination include those with chronic medical conditions such as lung diseases, including chronic obstructive pulmonary disease and asthma; cardiovascular diseases such as congestive heart failure and coronary artery disease; moderate or severe immune compromise (either attributable to a medical condition or receipt of immunosuppressive medications or treatment); diabetes mellitus; neurologic or neuromuscular conditions; kidney disorders, liver disorders, and hematologic disorders; persons who are frail; persons of advanced age; and persons with other underlying conditions or factors that the provider determines might increase the risk for severe RSV-associated respiratory disease. Adults aged ≥60 years who are residents of nursing homes and other long-term care facilities are also at risk for severe RSV disease. It should be noted that the numbers of persons enrolled in the trials who were frail, were of advanced age, and lived in long-term care facilities were limited, and persons with compromised immunity were excluded (some of whom might have an attenuated immune response to RSV vaccination). However, adults aged ≥60 years in these populations may receive vaccination using shared clinical decision-making given the potential for benefit.

RSV Vaccination Timing

RSV vaccination is currently approved and recommended for administration as a single dose; sufficient evidence does not exist at this time to determine the need for revaccination. Optimally, vaccination should occur before the onset of the RSV season; however, typical RSV seasonality was disrupted by the COVID-19 pandemic and has not returned to prepandemic patterns. For the 2023–24 season, clinicians should offer RSV vaccination to adults aged ≥60 years using shared clinical decision-making as early as vaccine supply becomes available and should continue to offer vaccination to eligible adults who remain unvaccinated.

Vaccine Administration, Including Coadministration with Other Vaccines

Coadministration of RSV vaccines with other adult vaccines during the same visit is acceptable. Available data on immunogenicity of coadministration of RSV vaccines and other vaccines are currently limited. Coadministration of RSV and seasonal influenza vaccines met noninferiority criteria for immunogenicity with the exception of the FluA/Darwin H3N2 strain when the GSK RSV vaccine was co-administered with adjuvanted quadrivalent inactivated influenza vaccine. RSV and influenza antibody titers were somewhat lower with coadministration; however, the clinical significance of this is unknown.

Administering RSV vaccine with one or more other vaccines at the same visit might increase local or systemic reactogenicity. Data are only available for coadministration of RSV and influenza vaccines, and evidence is mixed regarding increased reactogenicity. Data are lacking on the safety of coadministration with other vaccines that might be

recommended for persons in this age group, such as COVID-19 vaccines; pneumococcal vaccines; adult tetanus, diphtheria, and pertussis vaccines; and the recombinant zoster vaccine (the recombinant zoster vaccine and GSK's RSV vaccine contains the same adjuvant). When deciding whether to co-administer other vaccines with an RSV vaccine, providers should consider whether the patient is up to date with currently recommended vaccines, the feasibility of the patient returning for additional vaccine doses, risk for acquiring vaccine-preventable disease, vaccine reactogenicity profiles, and patient preferences. Post licensure efficacy and safety monitoring of co-administered RSV vaccines with other vaccines will further direct guidance.

Clinical Opinions

Respiratory syncytial virus (RSV) is a single-stranded, negative-sense ribonucleic acid (RNA) respiratory virus that infects the lungs and airways. RSV affects patients of all ages, but the elderly and infants are at risk for developing more severe disease. Among adults infected with RSV, symptoms are usually consistent with an upper respiratory infection and the virus lasts less than five days. Some adults may have more severe symptoms consistent with a LRTI such as pneumonia. RSV can also lead to exacerbations of serious underlying conditions such as asthma, chronic obstructive pulmonary disease (COPD), and congestive heart failure. In adults 65 years and older, RSV leads to approximately 177,000 hospitalizations and 14,000 deaths per year. The mortality rate among hospitalized adults 50 years and older is 6 to 8%. RSV causes seasonal outbreaks throughout the world. In the United States, RSV primarily occurs during the fall, winter, and spring months, but the timing and severity of RSV season can vary from year to year. Disruption of the typical seasonal pattern, such as during the coronavirus disease 2019 (COVID-19) pandemic, may result in off season outbreaks.

There are no FDA approved agents for the treatment of RSV. Until the approval of Arexvy, Synagis® (palivizumab), a recombinant humanized monoclonal antibody, was the only FDA approved agent for the prevention of RSV. Because Synagis® is not recommended or FDA approved for RSV prevention in adults, Arexvy represents the first vaccine indicated as a preventative measure against LRTD caused by RSV in adults 60 years and older. Arexvy will compete with Pfizer's vaccine, Abrysvo, which was approved shortly after Arexvy for the same indication. Moderna has a similar vaccine in development, mRNA-1345, which would compete with both Arexvy and Abrysvo. However, Moderna's vaccine candidate is unlikely to be approved in time for the 2023-2024 RSV season.

In June of 2023, the ACIP voted 9 to 5 to recommend that adults 65 years of age and older **may** receive a single dose of RSV vaccine, using shared clinical decision-making. An identical recommendation was made for adults 60 to 64 years of age, with a vote of 13 to 0. This recommendation was an amendment to the original recommendation made in February 2023 in which the ACIP suggested all adults 65 years of age and older **should** receive an RSV vaccination.

Alternatives

Drug Name^	Formulary Status	Dosage Form	Price*
Abrysvo™	NF	120 mcg/0.5 mL	$295

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

References

1. Arexvy. [prescribing information]. GlaxoSmithKline Biologicals, Durhan, NC; May, 2023.
2. AMCP eDossier System. Dymaxium Healthcare Innovations, Ltd. Available at: https://amcp.edossiers.com/. Accessed on June 1, 2023.
3. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: https://clinicaltrials.gov/. Accessed on June 1, 2023.
4. Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on June 1, 2023.
5. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: https://www.ncbi.nlm.nih.gov/pubmed. Accessed on June 1, 2023.
6. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on June 1, 2023.
7. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: http://www.fda.gov/. Accessed on June 1, 2023.
8. Papi A, Ison MG, Langley JM, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. *N Engl J Med*. 2023;388(7):595-608. doi:10.1056/NEJMoa2209604
9. "Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection," American Academy of Pediatrics Committee on Infectious Diseases; American Academy of Pediatrics Bronchiolitis Guidelines Committee, *Pediatrics*, Vol 134, 2014, pp 620-638.
10. "Updated guidance: use of palivizumab prophylaxis to prevent hospitalization from severe respiratory syncytial virus infection during the 2022-2023 RSV season," American Academy of Pediatrics, November 17, 2022. https://www.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/interim-guidance-for-use-of-palivizumab-prophylaxis-to-prevent-hospitalization/.
11. Zoey Becker, "Beating its rivals, GSK nabs world-first approval for adult RSV vaccine Arexvy®," Fierce Pharma, May 3, 2023, https://www.fiercepharma.com/pharma/beating-rival-pfizer-gsk-nabs-world-first-approval-adult-rsv-vaccine-arexvy
12. Melgar M, Britton A, Roper LE, et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023. MMWR Morb Mortal Wkly Rep 2023;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4.

Ophthalmic Antibiotic and Antibiotic-Corticosteroid Combinations

Executive Summary

CLASS OVERVIEW

This review covers antibiotic products for ophthalmic use, with and without a corticosteroid. These preparations are only available as a prescription, and are used for various infectious and inflammatory indications involving the eye. Antibiotic preparations are typically selected empirically depending on the suspected causative bacterial organism. An ophthalmic antibiotic agent may also be used in ocular conditions or after procedures or injury where risk of bacterial infection is present. Judicious use of products containing ocular corticosteroids are generally recommended due to risks related to excessive exposure, such as cataracts and glaucoma. Preparations include as drops or ophthalmic ointments, and many agents in this category are available as generic.

UTILIZATION FINDINGS

There were 70 claims for 65 members, for a total cost of $1,170, and an average cost per claim of $16. The most highly utilized medication was erythromycin (Ilotycin®) 5 mg/gram (0.5 %) eye ointment, with 19 claims, followed by ofloxacin (Ocuflox®) 0.3 % eye drops, with 13 claims. There were no prior authorization requests.

RECOMMENDATIONS

- Change from F-QL (2 fills per 362 days) to F-PA. The cost is $257 per tube, which is above the cost of the other formulary medications in this class. This is not a chronic medication, so an authorization may not need to be placed for the one claim.
    - TobraDex® (tobramycin-dexamethasone) 0.3 %-0.1 % eye ointment

PRODUCT TABLE (4/1/2023 to 6/30/2023)

Medication	Rx	Current Status	Recommendation
Ophthalmic Antibiotic & Glucocorticoid Combinations			
Neomycin-bacitracin-polymyxin B-hydrocortisone (Neo Polycin HC®) 3.5 mg-400-10,000 unit/g-1 % eye ointment	0	F	No change
Neomycin -polymyxin B-dexamethasone (Maxitrol®) 3.5 mg/g-10,000 unit/g-0.1 % eye oint	4	F	No change
Neomycin-polymyxin-dexamethasone (Maxitrol®) 3.5 mg/mL-10,000 unit/mL-0.1% eye drops	8	F	No change
Zylet® (tobramycin-loteprednol etabonate) 0.3 %-0.5 % eye drops, suspension	0	NF	No change
Tobradex ST® (tobramycin / dexamethasone) 0.3 %-0.05 % eye drops, suspension	0	NF	No change
Blephamide S.O.P.® (sulfacetamide-prednisolone) 10 %-0.2 % eye ointment Note: Obsolete	0	NF	No change
Sulfacetamide-prednisolone (Vascocidin®) 10 %-0.23 % (0.25 %) eye drops	0	F	No change
Neomycin-polymyxin-hydrocortisone (Cortisporin®) 3.5 mg-10,000 unit-10mg/mL eye drop, susp	0	NF	No change
Pred-G® (gentamicin sulf-prednisolone) 0.3 %-1 % eye drops, suspension Note: obsolete	0	NF	No change
Pred-G S.O.P.® (gentamicin-prednisolone) 0.3 %-0.6 % eye ointment Note: obsolete	0	NF	No change
TobraDex® (tobramycin-dexamethasone) 0.3 %-0.1 % eye ointment	1	F-QL (2 fills per 365 days)	→ **F-PA**
Tobramycin-dexamethasone (TobraDex®) 0.3%-0.1% eye drops, suspension	0	NF	No change
Ophthalmic Antibiotics			
Sulfacetamide sodium (Sodium Sulamyd®) 10 % eye ointment	0	F	No change
Sulfacetamide sodium (Sodium Sulamyd®) 10 % eye drops	0	NF	No change
Ciloxan® (ciprofloxacin hcl) 0.3 % eye ointment	0	F-ST (ciprofloxacin 0.3% eye drops, ofloxacin eye drops, or moxifloxacin 0.5% eye drops	No change
Tobrex® (tobramycin) 0.3 % eye ointment	0	NF	No change

Tobramycin (Tobrex®) 0.3 % eye drops	1	F-QL (2 fills per 12 months)	No change
Neomycin-bacitracin-polymyxn (Neosporin®) 3.5 mg-400 unit-10,000 unit/gram eye oint	1	F	No change
Polymyxin B sulfate-trimethoprim (Polytrim®) 10,000 unit-1 mg/mL eye drops	3	F	No change
Moxifloxacin (Vigamox®) 0.5 % eye drops	12	F	No change
Besivance® (besifloxacin hcl) 0.6 % eye drops, suspension	0	NF	No change
Bacitracin-polymyxin B (Polysporin®) 500 unit-10,000 unit/gram eye ointment	0	F	No change
Gatifloxacin (Zymaxid®) 0.5 % eye drops	0	F-PA	No change
Moxifloxacin (Moxeza®) 0.5 % viscous eye drops	0	F-PA	No change
Erythromycin (Ilotycin®) 5 mg/gram (0.5 %) eye ointment	19	F-QL (2 fills per 365 days)	No change
Ciprofloxacin (Ciloxan®) 0.3 % eye drops	7	F-QL (2 fills per 365 days)	No change
Gentamicin (Garamycin®) 0.3 % (3 mg/gram) eye ointment Note: obsolete	0	NF	No change
Gentamicin (Garamycin®) 0.3 % eye drops	1	F-QL (2 fills per 365 days)	No change
Bacitracin (Baciguent®) 500 unit/gram eye ointment	0	F	No change
Ofloxacin (Ocuflox®) 0.3 % eye drops	13	F-QL (2 fills per 365 days)	No change
Levofloxacin (Quixin®) 0.5 % eye drops	0	NF	No change
Neomycin 1.75 mg-polymyxin 10,000 unit-gramicidin 0.025mg/mL (Neosporin®) eye drops	0	F	No change
Azasite® (azithromycin) 1 % eye drops	0	F-PA	No change
Levofloxacin 1.5 % eye drops	0	NF	No change

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

CLINICAL SUMMARY

This review covers antibiotic products for ophthalmic use, with and without a corticosteroid. These preparations are only available as a prescription, and are used for various infectious and inflammatory conditions involving the eye. Antibiotic preparations are typically selected empirically depending on the suspected causative bacterial organism. An ophthalmic antibiotic agent may also be used in ocular conditions or after procedures or injury where risk of bacterial infection is present. Judicious use of products containing ocular corticosteroids are generally recommended due to risks related to excessive exposure, such as cataracts and glaucoma. Preparations include as drops or ophthalmic ointments, and many agents in this category are available as generic.

PRACTICE GUIDELINES

American Academy of Ophthalmology Preferred Practice Pattern – Conjunctivitis (2018)
https://www.aao.org/preferred-practice-pattern/conjunctivitis-ppp-2018

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

- Conjunctivitis rarely causes permanent visual loss or structural damage, but the economic impact of conjunctivitis is considerable and largely due to lost work or school time and the cost of medical visits, testing and treatment.
- Chronic and/or recalcitrant conjunctivitis may be indicative of an underlying malignancy, such as sebaceous or squamous cell carcinoma.
- The ophthalmologist plays a critical role in breaking the chain of transmission of epidemic adenoviral conjunctivitis, primarily by educating the patient and family about proper hygiene. Infected individuals should be counseled to wash hands frequently and use separate towels, and to avoid close contact with others during the period of contagion.
- Dilute bleach soak (sodium hypochlorite) at 1:10 concentration is an effective disinfectant for tonometers. Notably, 70% isopropyl alcohol (e.g., alcohol wipes), 3% hydrogen peroxide, and ethyl alcohol are no longer recommended for tonometer disinfection.
- Surfaces should be disinfected with an EPA-registered hospital disinfectant in accordance with the directions and safety precautions on the label.
- Indiscriminate use of topical antibiotics or corticosteroids should be avoided. Viral conjunctivitis will not respond to anti-bacterial agents, and mild bacterial conjunctivitis is likely to be self-limited. No evidence exists demonstrating the superiority of any topical antibiotic agent. [I+, Good, Strong]
- In adults, conjunctivitis caused by ocular mucous membrane pemphigoid (OMMP), graft-versus-host disease (GVHD), gonococcus, and chlamydia are important to detect early because it is necessary to treat the concomitant systemic disorder. Diagnosis of superior limbic keratoconjunctivitis (SLK) may lead to further investigations that reveal a thyroid disorder. Early detection of conjunctivitis associated with neoplasms may be lifesaving.
- Herpes Zoster vaccination should be strongly recommended in patients 50 years or older.

American Academy of Ophthalmology Preferred Practice Pattern – Blepharitis (2018)
https://www.aao.org/preferred-practice-pattern/blepharitis-ppp-2018

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

- In the management of ocular surface disease, it is helpful to distinguish blepharitis and meibomian gland dysfunction (MGD) from aqueous deficient dry eye. Worsening of symptoms in the morning is typical of blepharitis, whereas worsening of the symptoms later in the day are typical of aqueous deficient dry eye.
- Blepharitis is typically a chronic condition that cannot be permanently cured, and successful management is dependent on patient compliance with a treatment regimen. This should be explained to the affected patient.
- Topical antibiotic ointments with or without corticosteroids or oral antibiotics can be used effectively in the treatment of blepharitis. Although azithromycin is used as a treatment for blepharitis, it may be hazardous when

used orally in patients with cardiovascular problems. Specifically, oral azithromycin may lead to abnormalities in the electrical activity of the heart, with the potential to create serious irregularities in heart rhythm.

- In patients with blepharitis who do not respond to therapy, the possibility of carcinoma or immune-mediated diseases should be considered, particularly if the blepharitis is associated with a loss of eyelashes and/or conjunctival cicatricial changes. Early diagnosis and appropriate treatment can prevent disfigurement and may be lifesaving.

American Academy of Ophthalmology Preferred Practice Pattern – Bacterial Keratitis (2018)
https://www.aao.org/preferred-practice-pattern/bacterial-keratitis-ppp-2018

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

- The majority of community-acquired cases of bacterial keratitis resolve with empiric therapy and are managed without smears or cultures. Smears and/or cultures are specifically indicated in the following circumstances: 1) a corneal infiltrate is central, large (>2 mm) and/or associated with significant stromal involvement or melting; 2) the infection is chronic in nature or unresponsive to broad-spectrum antibiotic therapy; 3) there is a history of corneal surgeries; 4) atypical clinical features are present that are suggestive of fungal, amoebic, or mycobacterial keratitis; or 5) infiltrates are in multiple locations on the cornea.
- Topical antibiotics should be prescribed to prevent acute bacterial keratitis in patients presenting with a contact lens-related corneal abrasion.
- Patching the eye in a patient who wears contact lenses and has a corneal abrasion is not advised because of the increased risk of bacterial keratitis. Bandage contact lens use in the management of these epithelial defects remains controversial.
- The use of a cycloplegic agent is an often-overlooked adjunctive treatment and may decrease pain as well as synechia formation in bacterial keratitis. It is indicated when substantial anterior chamber inflammation is present.
- Corticosteroids may be considered after 24 to 48 hours when the causative organism is identified and/or infection is responding to therapy. Corticosteroids should be avoided in cases of infection involving organisms like *Acanthamoeba, Nocardia,* and fungus.
- Awareness of the increased resistance of methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* to topical fluoroquinolones is important.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (4/1/2023 to 6/30/2023)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Ophthalmic Antibiotic & Glucocorticoid Combinations								
Neomycin-bacitracin-polymyxin B-hydrocortisone (Neo Polycin HC®) 3.5 mg-400-10,000 unit/g-1 % eye ointment	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Neomycin -polymyxin B-dexamethasone (Maxitrol®) 3.5 mg/g-10,000 unit/g-0.1 % eye oint	4	3	$38.42	$9.61	0	0 (0%)	F	No change
Neomycin-polymyxin-dexamethasone (Maxitrol®) 3.5 mg/mL-10,000 unit/mL-0.1% eye drops	8	7	$102.95	$12.87	0	0 (0%)	F	No change
Zylet® (tobramycin-loteprednol etabonate) 0.3 %-0.5 % eye drops, suspension	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Tobradex ST® (tobramycin / dexamethasone) 0.3 %-0.05 % eye drops, suspension	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Blephamide S.O.P.® (sulfacetamide-prednisolone) 10 %-0.2 % eye ointment Note: Obsolete	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sulfacetamide-prednisolone (Vascocidin®) 10 %-0.23 % (0.25 %) eye drops	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Neomycin-polymyxin-hydrocortisone (Cortisporin®) 3.5 mg-10,000 unit-10mg/mL eye drop, susp	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pred-G® (gentamicin sulf-prednisolone) 0.3 %-1 % eye drops, suspension Note: obsolete	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pred-G S.O.P.® (gentamicin-prednisolone) 0.3 %-0.6 % eye ointment Note: obsolete	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TobraDex® (tobramycin-dexamethasone) 0.3 %-0.1 % eye ointment	1	1	$257.66	$257.66	0	0 (0%)	F-QL (2 fills per 365 days)	→ **F-PA**
Tobramycin-dexamethasone (TobraDex®) 0.3%-0.1% eye drops, suspension	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Ophthalmic Antibiotics								
Sulfacetamide sodium (Sodium Sulamyd®) 10 % eye ointment	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Sulfacetamide sodium (Sodium Sulamyd®) 10 % eye drops	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Ciloxan® (ciprofloxacin hcl) 0.3 % eye ointment	0	0	$0.00	$0.00	0	0 (0%)	F-ST (ciprofloxacin 0.3% eye drops, ofloxacin eye drops, or moxifloxacin 0.5% eye drops	No change
Tobrex® (tobramycin) 0.3 % eye ointment	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

Tobramycin (Tobrex®) 0.3 % eye drops	1	1	$6.35	$6.35	0	0 (0%)	F-QL (2 fills per 12 months)	No change
Neomycin-bacitracin-polymyxn (Neosporin®) 3.5 mg-400 unit-10,000 unit/gram eye oint	1	1	$28.15	$28.15	0	0 (0%)	F	No change
Polymyxin B sulfate-trimethoprim (Polytrim®) 10,000 unit-1 mg/mL eye drops	3	3	$18.77	$6.26	0	0 (0%)	F	No change
Moxifloxacin (Vigamox®) 0.5 % eye drops	12	10	$239.40	$19.95	0	0 (0%)	F	No change
Besivance® (besifloxacin hcl) 0.6 % eye drops, suspension	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Bacitracin-polymyxin B (Polysporin®) 500 unit-10,000 unit/gram eye ointment	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Gatifloxacin (Zymaxid®) 0.5 % eye drops	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Moxifloxacin (Moxeza®) 0.5 % viscous eye drops	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Erythromycin (Ilotycin®) 5 mg/gram (0.5 %) eye ointment	19	19	$215.87	$11.36	0	0 (0%)	F-QL (2 fills per 365 days)	No change
Ciprofloxacin (Ciloxan®) 0.3 % eye drops	7	7	$85.10	$12.16	0	0 (0%)	F-QL (2 fills per 365 days)	No change
Gentamicin (Garamycin®) 0.3 % (3 mg/gram) eye ointment Note: obsolete	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Gentamicin (Garamycin®) 0.3 % eye drops	1	1	$6.06	$6.06	0	0 (0%)	F-QL (2 fills per 365 days)	No change
Bacitracin (Baciguent®) 500 unit/gram eye ointment	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Ofloxacin (Ocuflox®) 0.3 % eye drops	13	12	$171.27	$13.17	0	0 (0%)	F-QL (2 fills per 365 days)	No change
Levofloxacin (Quixin®) 0.5 % eye drops	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Neomycin 1.75 mg-polymyxin 10,000 unit-gramicidin 0.025mg/mL (Neosporin®) eye drops	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Azasite® (azithromycin) 1 % eye drops	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Levofloxacin 1.5 % eye drops	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Total	**70**	**65**	**$1,170.00**	**$16.71**	**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; Unlisted = Non-formulary

PRIOR AUTHORIZATION CRITERIA

Recommendation:

- Add medications criteria for antibiotic and glucocorticoid ointment combinations.
- Minor verbiage updates and clarifications.

Antibiotic Eye Medications	
Therapeutic Classes (AHFS)	Antibacterials (EENT)
Medications	Formulary • Ciprofloxacin 0.3% eye drops • Ofloxacin 0.3% eye drops • Moxifloxacin (Vigamox) 0.5% eye drops • Neomycin-bacitracin-polymyxin B-hydrocortisone (Neo Polycin HC) 3.5 mg-400-10,000 unit/g-1 % eye ointment • Neomycin -polymyxin B-dexamethasone (Maxitrol®) 3.5 mg/g-10,000 unit/g-0.1 % eye oint Formulary, Step Therapy Required • Ciloxan (ciprofloxacin) 0.3% eye ointment Formulary, PA required • Gatifloxacin (Zymaxid) ~~PREFERRED~~ • Moxifloxacin (Moxeza) • Azasite (azithromycin) • TobraDex (tobramycin-dexamethasone) 0.3 %-0.1 % eye ointment
Covered Uses	Medically accepted indications 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	None.
Coverage Duration	**Initial Approval** If the conditions are met, the request will be approved for 1 fill with a quantity limit of 1 bottle/tube. **Later Approvals** If criteria are not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	**For the formulary, step therapy required medication Ciloxan (ciprofloxacin) 0.3% eye ointment** • Documented contraindication to or trial and failure of one of the preferred antibiotic eye drops: ciprofloxacin, moxifloxacin (Vigamox), or ofloxacin **For gatifloxacin (Zymaxid) all of the following criteria must be met**: • For use after cataract surgery **AND** • Documented contraindication to or trial and failure of one of the preferred antibiotic eye drops: ciprofloxacin, moxifloxacin (Vigamox), or ofloxacin **For Azasite and moxifloxacin (Moxeza) all of the following criteria must be met:** • For use after cataract surgery **AND**

	• Documented contraindication to or trial and failure of one of the preferred antibiotic eye drops: ciprofloxacin, moxifloxacin (Vigamox), or ofloxacin **AND** • Documented contraindication to or trial and failure of gatifloxacin (Zymaxid) **For TobraDex (tobramycin-dexamethasone) 0.3 %-0.1 % eye ointment all of the following criteria must be met:** • Documented contraindication to or trial and failure of one of the preferred ophthalmic antibiotic & glucocorticoid combination eye ointments: neomycin-bacitracin-polymyxin B-hydrocortisone (Neo Polycin HC) eye ointment or neomycin -polymyxin B-dexamethasone (Maxitrol) eye ointment
Criteria Statement	Ciloxan (ciprofloxacin) eye ointment is reserved for members ~~who previously used other topical antibiotic eye drops which were ineffective, or~~ who cannot/should not take ciprofloxacin, moxifloxacin (Vigamox), or ofloxacin eye drops. Gatifloxacin (Zymaxid) is reserved for members who have had cataract surgery and ~~previously used other topical antibiotic eye drops which were ineffective, or~~ who cannot/should not take ciprofloxacin, moxifloxacin (Vigamox), or ofloxacin eye drops. Azasite or moxifloxacin (Moxeza) are reserved for members who have had cataract surgery and ~~previously used other topical antibiotic eye drops which were ineffective, or~~ who cannot/should not take ciprofloxacin, moxifloxacin (Vigamox), or ofloxacin eye drops AND gatifloxacin (Zymaxid)~~or moxifloxacin~~ eye drops. TobraDex (tobramycin-dexamethasone) eye ointment is reserved for members who cannot/should not take neomycin-bacitracin-polymyxin B-hydrocortisone (Neo Polycin HC) eye ointment or neomycin -polymyxin B-dexamethasone (Maxitrol) eye ointment.
Last P&T Review Date	~~3/2023~~9/2023

REFERENCES

1. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: http://www.fda.gov/. Accessed on 2/3/2023.
2. DailyMed. U.S. National Library of Medicine. Available at: https://dailymed.nlm.nih.gov/dailymed/. Accessed on 2/3/2023.
3. BioMedTracker. New York, NY: Informa, PLC. Available at: www.biomedtracker.com. Accessed on 2/3/2023.
4. Varu DM, Rhee MK, Akpek EK, et al. Conjunctivitis Preferred Practice Pattern®. *Ophthalmology*. 2019;126(1):P94-P169. doi:10.1016/j.ophtha.2018.10.020. Accessed on 2/3/2023.
5. Amescua G, Akpek EK, Farid M, et al. Blepharitis Preferred Practice Pattern®. *Ophthalmology*. 2019;126(1):P56-P93. doi:10.1016/j.ophtha.2018.10.019. Accessed on 2/3/2023.
6. Lin A, Rhee MK, Akpek EK, et al. Bacterial Keratitis Preferred Practice Pattern®. *Ophthalmology*. 2019;126(1):P1-P55. doi:10.1016/j.ophtha.2018.10.018. Accessed on 2/3/2023.

Ulcerative Colitis, Crohn's Disease
(Oral & Topical Agents)

Executive Summary

CLASS OVERVIEW

Ulcerative colitis (UC) and Crohn's Disease (CD) are two major disorders that involve chronic inflammation of the gastrointestinal (GI) tract. UC and CD both have distinct and overlapping pathologic and clinical features. UC is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon. It commonly involves the rectum and may extend to parts of or the entire colon. CD meanwhile, encompasses a multisystem group of disorders with specific clinical and pathological features. It is primarily characterized by transmural inflammation and may involve any portion of the entire GI tract from mouth to perianal area. Treatment of UC and CD is selected on the basis of disease location, severity, and goal of inducing or maintaining remission. Most patients will require maintenance therapy because of the high incidence of relapse after inducing remission. Surgical treatment is indicated for medically intractable disease or severe complications.

Oral and topical medications approved by the FDA for treatment of UC and CD primarily consist of 5-aminosalicylates (5-ASA) and corticosteroids, available in oral and rectal formulations. 5-ASA products are only indicated and recommended for use in inducing and maintaining remission in mildly or moderately active UC. Non-systemic corticosteroids such as budesonide are generally only recommended for UC in those unresponsive to 5-ASA, but it is recommended as first line in inducing remission in mild to moderately active CD. Patients who have failed to respond to conventional therapy with aminosalicylates and/or corticosteroids, and have more severe forms of UC and CD, are generally put on biologic therapies such as tumor necrosis factor inhibitors and other monoclonal antibody classes. This review only focuses on the oral and topical medications approved for use in UC and CD. It does not review any biologic treatments for UC and CD, or any oral medications used off-label (i.e., immunomodulators).

UTILIZATION FINDINGS

There were 16 claims for 10 members, for a total cost of $3,778, and an average cost per claim of $236. The most highly utilized medication was budesonide DR (Entocort® EC) 3 mg oral capsules, with 5 claims. There was one prior authorization request, which was not approved.

RECOMMENDATIONS

- No changes

PRODUCT TABLE (4/1/2023 to 6/30/2023)

Medication	Rx	Current Status	Recommendation
Oral 5-Aminosalicylate Agents			
Mesalamine ER (Apriso®) 0.375 g oral capsules	0	F-ST (t/f sulfasalazine, sulfasalazine DR, or balsalazide)	No change
Mesalamine DR (Asacol® HD) 800 mg oral tablets	3	F-PA	No change
Mesalamine DR (Lialda®) 1.2 g oral tablets	0	F-ST (t/f sulfasalazine, sulfasalazine DR, or balsalazide)	No change
Mesalamine DR (Delzicol®) 400 mg oral capsules	3	F-ST (t/f sulfasalazine, sulfasalazine DR, or balsalazide)	No change
Mesalamine ER (Pentasa®) 500 mg oral capsules	0	F-PA	No change
Pentasa® (mesalamine ER) 250 mg oral capsules	0	F-PA	No change
Dipentum® (olsalazine) 250 mg oral capsules	0	NF	No change
Sulfasalazine (Azulfidine®) 500 mg oral tablets	3	F	No change
Sulfasalazine DR (Azulfidine EN®) 500 mg oral tablets	2	F	No change
Balsalazide (Colazal®) 750 mg oral capsules	0	F	No change
Rectal 5-Aminosalicylate Agents			
Mesalamine (Canasa®) 1,000 mg rectal suppository	0	F	No change
Mesalamine (Rowasa®) 4 g/60 ml rectal enema	0	F	No change
Mesalamine (SFRowasa®) 4 g/60 mL rectal enema	0	F	No change
Oral Glucocorticoids			
Budesonide DR (Entocort® EC) 3 mg oral capsules	5	F-QL (540/365)	No change
Budesonide ER (Uceris®) 9 mg oral tablets	0	F-PA	No change
Ortikos™ (budesonide ER) 6 mg, 9 mg oral capsules	0	NF	No change
Rectal Glucocorticoids			
Cortifoam® (hydrocortisone acetate) 10% rectal foam	0	F-PA	No change
Hydrocortisone (Cortenema®) 100 mg/60 ml rectal enema	0	F	No change
Budesonide (Uceris®) 2mg rectal foam	0	F-PA	No change

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

CLINICAL SUMMARY

UC and CD are two major disorders that involve chronic inflammation of the GI tract. UC and CD both have distinct and overlapping pathologic and clinical features. UC is characterized by recurring episodes of inflammation limited to the mucosal layer of the colon. It commonly involves the rectum and may extend to parts of or the entire colon. Bowel movements tend to be frequent and small in volume due to rectal inflammation. Symptoms that are usually present in patients with UC include diarrhea, abdominal pain, urgency, and tenesmus, and incontinence. Patients with mainly distal disease may have constipation accompanied by frequent discharge of blood and mucus. Onset of symptoms are usually gradual, and symptoms are progressive over several weeks. Patients may also have systemic symptoms including fever, fatigue, and weight loss. They may also have dyspnea and palpitations due to anemia secondary to iron deficiency from blood loss, anemia of chronic disease, or autoimmune hemolytic anemia. The presence and severity of systemic symptoms depends on the clinical severity of the intestinal disease.

The severity of UC can predict long-term outcomes and can be objectively measured using a clinical disease activity index. The Montreal classification of severity of ulcerative colitis is one example that stratifies ulcerative colitis severity into mild, moderate, and severe based on the frequency and severity of diarrhea, as well as the presence of systemic symptoms and laboratory abnormalities. Patients with mild disease have 4 or fewer stools per day with or without blood, no signs of systemic toxicity (i.e., fever, tachycardia), and a normal C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR). Moderate disease is characterized by 4 to 6 loose bloody stools per day, mild anemia that does not require blood transfusions, and abdominal pain that is not severe. Patients with severe UC typically have ≥ 6 loose bloody stools per day with severe cramps and evidence of systemic toxicity as evidenced by a fever, tachycardia, anemia, or an elevated CRP or ESR. Additional terminology is often used to describe the extent of involvement of UC. Ulcerative proctitis refers to disease within 18 cm of the anal verge. Ulcerative proctosigmoiditis refers to disease limited to the rectum and sigmoid colon. Left-sided colitis refers to disease that extends beyond the colon and as far as the splenic flexure, while extensive colitis refers to disease extending proximal to the splenic flexure.

The use of aminosalicylates and non-systemic corticosteroids is generally only recommended to be used in mild to moderate UC. Topical (rectal) mesalamine is recommended as first-line treatment for inducing remission in mild to moderate ulcerative proctitis or proctosigmoiditis. Mesalamine suppositories are normally used for ulcerative proctitis, and mesalamine enemas for ulcerative proctosigmoiditis. Rectal glucocorticoids (i.e., hydrocortisone, budesonide) are recommended for patients who cannot tolerate topical mesalamine but can or are willing to use rectal therapy. Patients who are unwilling to use rectal agents can use oral 5-ASA agents, preferably mesalamine or diazo-bonded 5-ASA (i.e., balsalazide) with sulfasalazine considered as an alternative option. The selection of a specific formulation of mesalamine varies depending on insurance coverage/cost, product availability, convenience of dosing, and clinician preference, however, clinical guidelines prefer using oral mesalamine products with once daily dosing to optimize patient adherence. Left sided or extensive colitis is managed with a combination of oral 5-ASA agents plus rectal mesalamine. Budesonide multi-matrix (Uceris®), an oral formulation of budesonide that extends its delivery to the entire colon, is only recommended for those who do not respond to a combination of oral 5-ASA and topical mesalamine. Most patients who have achieved remission with mild to moderate UC, generally require some sort of maintenance therapy. Generally, the oral 5-ASA agent and/or topical mesalamine product used to achieve remission is normally continued. Steroids are not used for maintenance of remission due to lack of efficacy and risk of adverse effects.

CD is a disorder of uncertain etiology that is generally characterized by transmural inflammation of the GI tract and may involve any portion of the entire GI tract from mouth to the perianal area. The clinical manifestations of CD are more variable than those of UC. Patients can have symptoms for several years prior to diagnosis. The hallmark symptoms of CD include abdominal pain, diarrhea (with or without gross bleeding), fatigue, and weight loss. Common complications of CD include perianal disease, which include anal fissures, fistulas, and abscesses. Other complications of CD include intestinal obstruction, malabsorption, arthritis as a result of the inflammatory process, eye involvement (i.e., uveitis iritis, and episcleritis), skin lesions, and pulmonary complications such as chronic bronchitis and interstitial lung disease.

CD severity is commonly determined by utilizing the Crohn's Disease Activity Index (CDAI). Clinical remission is defined as a CDAI <150 and involves patients who are asymptomatic. Mild CD is defined as a CDAI between 150-220 and involves patients who are typically ambulatory and tolerating an oral diet. These patients have <10% weight loss and no symptoms

of systemic disease (i.e. fever, tachycardia). Moderate to severe CD involves a CDAI score between 220-450 and comprises patients who have failed treatment for mild to moderate disease or those who have prominent systemic symptoms. Severe-fulminant disease involves a CDAI score >450 and comprises of patients with persistent symptoms despite glucocorticoids or biologic agents, or those presenting with high fever, persistent vomiting, intestinal obstruction, peritoneal signs, cachexia, or evidence of an abscess.

The choice of therapy for CD varies depending on the anatomic location of the disease, disease severity, and whether the goal is to induce or maintain remission. The use of 5-ASA and glucocorticoids is primarily used for the treatment of mild (low risk) CD. Enteric coated budesonide (Entocort® EC, Ortikos™) is recommended as first line treatment for inducing remission in mild to moderately active CD of the ileum and proximal colon. Both Entocort® EC and Ortikos™ have the same label and dosing with the only difference between the two being that Ortikos™ comes as 6 mg and 9 mg extended-release capsules, whereas Entocort® EC is only available as 3 mg extended-release capsules. Alternative glucocorticoids like prednisone, can be used in CD patients who do not respond to budesonide. The use of 5-ASA products for CD is controversial and is generally not recommended to be used as studies evaluating the efficacy of 5-ASA in CD have had mixed results. Maintenance of remission of mild CD primarily revolves around tapering and discontinuing the glucocorticoid used, followed by clinical observation and ilecolonoscopy in 6 to 12 months. Conventional glucocorticoids are not recommended to be used to maintain remission given their side effect profile. Despite budesonide (Entocort® EC, Ortikos™) 6 mg daily being FDA approved for maintenance of remission in mild to moderate CD, there is limited data to support its use in the maintenance of remission beyond 4 months. Patients who initially respond to oral glucocorticoids but cannot tolerate gradual tapering should no longer be regarded as low-risk and are typically reassigned to the moderate/high risk category.

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Mesalamine ER (Apriso®) 0.375g oral capsules	Maintenance of remission of ulcerative colitis in adults	1.5 g orally once daily in the morning
Mesalamine DR (Asacol® HD) 800 mg oral tablets	Treatment of moderately active ulcerative colitis in adults	1.6 g orally 3 times daily for 6 weeks
Mesalamine DR (Delzicol®) 400 mg oral capsules	Treatment of mildly to moderately active ulcerative colitis in patients ≥5 years	800 mg orally 3 times daily for 6 weeks
	Maintenance of remission of ulcerative colitis in adults	1.6 to 2.4 g orally in 2 to 4 divided doses
Mesalamine DR (Lialda®) 1.2g oral tablets	Treatment of mildly to moderately active ulcerative colitis in patients weighing ≥24 kg	2.4 to 4.8 g orally once daily
	Maintenance of remission of mildly to moderately active ulcerative colitis in adults	2.4 to 3.6 g orally once daily
Pentasa® (mesalamine ER) 250, 500 mg oral capsules	Treatment and maintenance of remission of mildly to moderately active ulcerative colitis in adults	1 g orally 4 times daily (for both treatment and maintenance of remission)
Mesalamine (Canasa®) 1,000 mg rectal suppository	Treatment of mildly to moderately active ulcerative proctitis in adults	1,000 mg (1 suppository) rectally (retained for at least 1 to 3 hours) at bedtime for 3 to 6 weeks
Mesalamine (Rowasa®) 4 g/60 ml rectal enema Mesalamine (SFRowasa®) 4 g/60 mL enema	Treatment of active mild to moderate distal ulcerative colitis, proctosigmoiditis or proctitis in adults	Distal ulcerative colitis or proctosigmoiditis: - 4 g rectally at bedtime, retained overnight (duration of rectal therapy is 3 to 6 weeks) Ulcerative proctitis: - 4 g rectally at bedtime, retained overnight
Sulfasalazine (Azulfidine®) 500 mg oral tablets Sulfasalazine DR (Azulfidine EN®) 500 mg oral tablet	Treatment of mild to moderate ulcerative colitis; adjunctive therapy in severe ulcerative colitis; prolongation of the remission period between acute attacks of ulcerative colitis	Ulcerative colitis: - Initial: 3 to 4 g/day orally in divided doses at ≤8-hour intervals; may initiate therapy with 1 to 2 g/day to reduce GI intolerance - Maintenance: 2 g/day orally in divided doses at ≤8-hour intervals Crohn's disease ***(off label):*** - 3 to 6 g/day orally in divided doses for up to 16 weeks
	Treatment of rheumatoid arthritis in patients who have responded inadequately to salicylates or other NSAIDs	
	Treatment of pediatric patients with polyarticular-course juvenile rheumatoid arthritis who have responded inadequately to salicylates or other NSAIDs (Delayed release only)	
	Treatment of mild to moderately active Crohn disease (***off label)***	
Balsalazide (Colazal®) 750 mg oral capsule	Treatment of mildly to moderately active ulcerative colitis in patients ≥5 years of age	2.25 g orally 3 times daily for 8 to 12 weeks
	Remission maintenance of ulcerative colitis ***(off label)***	1.5 or 3 g orally twice daily for 6 to 12 months
Dipentum® (olsalazine) 250 mg oral capsule	Maintenance of remission of ulcerative colitis in patients intolerant to sulfasalazine	1 g/day orally in 2 divided doses

Medication	Indications	Dosing/Administration
	Treatment of ulcerative colitis ***(off label)***	2 to 3 g/day orally in 2 to 4 divided doses
Cortifoam® (hydrocortisone acetate) 10% rectal foam	Treatment of ulcerative colitis, especially distal forms including ulcerative proctitis, ulcerative proctosigmoiditis, and left-sided ulcerative colitis	One applicatorful (90 mg) rectally once or twice daily
Hydrocortisone (Cortenema®) 100 mg/60 ml rectal enema		One enema (100 mg) rectally once or twice daily
Budesonide DR (Entocort® EC) 3 mg oral capsule	Treatment of active Crohn disease (mild to moderate) involving the ileum and/or the ascending colon in patients ≥8 years of age	9 mg orally once daily in the morning for up to 8 weeks
Ortikos® (budesonide ER) 6 mg, 9 mg oral capsules	Maintenance of clinical remission (for up to 3 months) of Crohn disease (mild to moderate) involving the ileum and/or the ascending colon in adults	6 mg orally once daily for up to 3 months
Budesonide ER (Uceris®) 9 mg oral tablet	Induction of remission in patients with active ulcerative colitis (mild to moderate)	9 mg orally once daily in the morning for up to 8 weeks
Budesonide (Uceris®) 2mg rectal foam	Remission induction in patients with active mild to moderate distal ulcerative colitis extending up to 40 cm from the anal verge	Initial: 2 mg (one metered dose) rectally twice daily for 2 weeks Maintenance: 2 mg (one metered dose) rectally once daily for 4 weeks

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Dopamine Replacement		
Mesalamine (Apriso®, Asacol® HD, Canasa®, Delzicol®, Lialda®, Pentasa®, Rowasa®, SFRowasa®)	N/A	Hypersensitivity to mesalamine, aminosalicylates, salicylates, or any component of the formulation
Sulfasalazine (Azulfidine®, Azulfidine-EN®)		Hypersensitivity to sulfasalazine, its metabolites, sulfonamides, salicylates, or any component of the formulation; intestinal or urinary obstruction; porphyria
Balsalazide (Colazal®)		Hypersensitivity to balsalazide or its metabolites, aminosalicylates, salicylates, or any component of the formulation
Dipentum® (olsalazine)		Hypersensitivity to olsalazine, aminosalicylates, salicylates, or metabolites or any component of the formulation
Cortifoam® (hydrocortisone acetate) rectal foam		Hypersensitivity to hydrocortisone or any component of the formulation; obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses, extensive fistulas, and sinus tracts
Hydrocortisone (Cortenema®) 100 mg/60 ml rectal enema		Hypersensitivity to hydrocortisone or any component of the formulation; systemic fungal infections and ileocolostomy during the immediate or early postoperative period
Budesonide (Entocort® EC, Uceris®, Ortikos®)		Hypersensitivity to budesonide or any component of the formulation

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Mesalamine (Apriso®, Asacol® HD, Canasa®, Delzicol®, Lialda®, Pentasa®, Rowasa®, SFRowasa®)	Concerns related to adverse effects: - Photosensitivity: Use with caution in patients with pre-existing skin conditions, severe photosensitivity reactions have been reported Disease-related concerns: - Hepatic impairment - Renal impairment Special populations: - Elderly: Uncontrolled studies and post marketing reports suggest an increased incidence of blood dyscrasias (i.e., agranulocytosis, neutropenia, pancytopenia) in patients >65 years of age Dosage form specific issues: - Apriso®: Contains phenylalanine which can be harmful to patients with phenylketonuria (PKU) - Asacol® HD & Delzicol®: Intact, partially intact, and/or tablet shells have been reported in the stool - Canasa® suppositories: Contain saturated vegetable fatty acid esters (contraindicated in patients with allergy to these components) - Rowasa® enema: Contain metabisulfite salts that may cause severe hypersensitivity reactions (i.e., anaphylaxis) in patients with sulfite allergies - Tablets: Patients with pyloric stenosis or other organic or functional upper GI obstructive disorders may have prolonged gastric retention of tablets, delaying the release of mesalamine in the colon; avoid use in patients at risk of upper GI avoid obstruction Other warnings/precautions: - Bioequivalence: Asacol® HD 800 mg tablet has not been shown to be bioequivalent to two Delzicol® 400 mg capsules
Sulfasalazine (Azulfidine®, Azulfidine-EN®)	Concerns related to adverse effects: - CNS effects - Folate deficiency: May decrease folic acid absorption - Infections: Serious infections (some fatal), including sepsis and pneumonia, have been reported; infections may be associated with agranulocytosis, neutropenia, or myelosuppression - Sulfonamide ("sulfa") allergy Disease-related concerns: - Allergies/asthma - Hepatic impairment - Renal impairment Special populations: - Slow acetylators: Patients classified as slow acetylators may be at increased risk for adverse reactions due to a prolonged half-life of sulfapyrazine (metabolite of sulfasalazine) Dosage form specific issues: - Delayed release tablets (Azulfidine-EN®): Use in patients with UC who cannot take uncoated sulfasalazine tablets because of GI intolerance, and in whom there is evidence that this intolerance is not primarily the result of high blood levels of sulfapyridine and its metabolites (i.e., patients experiencing nausea and vomiting with the first few doses of the drug, patients in whom a reduction in dosage does not alleviate the adverse GI effects) - Delayed release tablets (Azulfidine-EN®): Discontinue if tablets are noted to pass without disintegrating Other warnings/precautions: - Skin/urine discoloration
Balsalazide (Colazal®)	Concerns related to adverse effects:

Medication	Warnings/Precautions
	- Dermatologic reactions: Severe cutaneous adverse reactions, including acute generalized exanthematous pustulosis, drug reaction with eosinophilia and systemic symptoms, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported - Hypersensitivity reactions - Intolerance syndrome: May cause an acute intolerance syndrome (cramping, acute abdominal pain, bloody diarrhea; sometimes fever, headache, rash) - Photosensitivity: Use with caution in patients with pre-existing skin conditions, severe photosensitivity reactions have been reported - Renal effects: Renal impairment (including minimal change disease, acute and chronic interstitial nephritis, and renal failure) has been reported; a renal function evaluation is recommended prior to initiation of therapy and periodically during treatment - Staining: May cause staining of teeth or tongue if capsule is opened and sprinkled on food - Sulfasalazine hypersensitivity Disease-related concerns: - GI tract obstruction: May cause prolonged gastric retention and delay release of drug in the colon - Hepatic impairment - Renal impairment Special populations: - Elderly: Uncontrolled studies and post marketing reports suggest an increased incidence of blood dyscrasias (i.e., agranulocytosis, neutropenia, pancytopenia) in patients >65 years of age
Dipentum® (olsalazine)	Concerns related to adverse effects: - Dermatologic reactions: Severe cutaneous adverse reactions, including acute generalized exanthematous pustulosis, drug reaction with eosinophilia and systemic symptoms, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported - Diarrhea: Commonly occurs and may be dose related - Hypersensitivity reactions - Intolerance syndrome: May cause an acute intolerance syndrome (cramping, acute abdominal pain, bloody diarrhea; sometimes fever, headache, rash) - Photosensitivity: Use with caution in patients with pre-existing skin conditions, severe photosensitivity reactions have been reported - Renal effects: Renal impairment (including minimal change disease, acute and chronic interstitial nephritis, and renal failure) has been reported; a renal function evaluation is recommended prior to initiation of therapy and periodically during treatment - Sulfasalazine hypersensitivity Disease-related concerns: - Hepatic impairment - Renal impairment Special populations: - Elderly: Uncontrolled studies and post marketing reports suggest an increased incidence of blood dyscrasias (i.e., agranulocytosis, neutropenia, pancytopenia) in patients >65 years of age
Hydrocortisone (Cortifoam®, Cortenema®)	Concerns related to adverse effects: - Adrenal suppression - Anaphylactic reactions - Contact dermatitis - Immunosuppression - Kaposi sarcoma - Myopathy - Psychiatric disturbances - Sensitization

Medication	Warnings/Precautions
	- Systemic effects: Absorption of corticosteroids may cause manifestations of Cushing syndrome, hyperglycemia, or glycosuria Disease-related concerns: - Cardiovascular disease - Diabetes - GI disease - Hepatic impairment - Myasthenia gravis - Myocardial infarction: Corticosteroids have been associated with myocardial rupture - Ocular disease: Increased intraocular pressure, glaucoma, and cataracts have occurred with prolonged use - Osteoporosis - Renal impairment: Fluid retention may occur - Thyroid disease: Metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid ones - Ulcerative colitis: With severe ulcerative colitis, it may be hazardous to delay surgery while waiting for response to treatment Special populations: - Elderly - Pediatric: Children may absorb larger amounts and may be more prone to systemic effects; prolonged use may affect growth velocity Dosage form specific issues: - Benzyl alcohol: Some dosage forms may contain benzyl alcohol and/or sodium benzoate/benzoic acid; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates - Rectal enema (Cortenema®): Damage to the rectal wall may occur from improper or careless insertion of the enema tip - Rectal foam (Cortifoam®): Contents of foam are under pressure
Budesonide (Entocort® EC, Uceris®, Ortikos®)	Concerns related to adverse effects: - Adrenal suppression: May cause hypercortisolism or suppression of hypothalamic-pituitary-adrenal (HPA) axis, particularly in patients receiving high doses for prolonged periods. HPA axis suppression may lead to adrenal crisis - Anaphylactoid reactions - Immunosuppression: Prolonged use of corticosteroids may also increase the incidence of secondary infection, mask acute infection (including fungal infections), prolong or exacerbate viral infections, or limit response to vaccines - Kaposi sarcoma - Myopathy - Psychiatric disturbances Disease-related concerns: - Cardiovascular disease: Use has been associated with fluid retention, electrolyte disturbances, and hypertension - Diabetes: May alter glucose production/regulation leading to hyperglycemia - GI disease - Hepatic impairment - Myasthenia gravis - Ocular disease: Increased intraocular pressure, open-angle glaucoma, and cataracts have occurred with prolonged glucocorticoid use - Osteoporosis - Renal impairment: Fluid retention may occur - Seizure disorders: Seizures have been reported with adrenal crisis - Systemic sclerosis: Increase in scleroderma renal crisis incidence has been observed with corticosteroid use

Medication	Warnings/Precautions
	- Thyroid disease: Metabolic clearance of corticosteroids increases in hyperthyroid patients and decreases in hypothyroid patients Special populations: - Elderly Dosage form specific issues: - Flammable contents: Rectal foam contains flammable propellants

PRACTICE GUIDELINES

Ulcerative Colitis

Feuerstein JD, Isaacs KL, Schneider Y, et al. American Gastroenterological Association (AGA) Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461.

- In adult outpatients with moderate to severe UC, the AGA suggests early use of biologic agents with or without immunomodulatory therapy, rather than gradual step up after failure of 5-ASA (Conditional recommendation, very low quality of evidence).
    - Patients, particularly those with less severe disease, who place higher value on the safety of 5-ASA therapy, and lower value on the efficacy of biologic agents, may reasonably choose gradual step therapy with 5-ASA therapy.
- In adult outpatients with moderate to severe UC who have achieved remission with biologic agents and/or immunomodulators, or tofacitinib, the AGA suggests against continuing 5-ASA for induction and maintenance of remission (Conditional recommendation, very low quality of evidence).

Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology. 2019;156(3):748-764.

- In patients with extensive mild–moderate UC, the AGA recommends using either standard-dose mesalamine (2–3 g/d) or diazo-bonded 5-ASA rather than low-dose mesalamine, sulfasalazine, or no treatment (Strong recommendation, moderate quality of evidence).
    - Patients already on sulfasalazine in remission or patients with prominent arthritic symptoms may reasonably choose sulfasalazine 2–4 g/d if alternatives are cost-prohibitive, albeit with higher rate of intolerance.
- In patients with extensive or left-sided mild–moderate UC, the AGA suggests adding rectal mesalamine to oral 5-ASA (Conditional recommendation, moderate quality of evidence).
- In patients with mild–moderate UC with suboptimal response to standard-dose mesalamine or diazo-bonded 5-ASA or with moderate disease activity, the AGA suggests using high-dose mesalamine (>3 g/d) with rectal mesalamine (Conditional recommendation, moderate quality evidence [induction of remission], low quality of evidence [maintenance of remission]).
- In patients with mild–moderate UC being treated with oral mesalamine, the AGA suggests using once-daily dosing rather than multiple times per day dosing (Conditional recommendation, moderate quality of evidence).
- In patients with mild–moderate UC, the AGA suggests using standard-dose oral mesalamine or diazo-bonded 5-ASA, rather than budesonide multi matrix (MMX) or controlled ileal release budesonide for induction of remission (Conditional recommendation, low quality of evidence).
- In patients with left-sided mild–moderate ulcerative proctosigmoiditis or proctitis, the AGA suggests using mesalamine enemas (or suppositories) rather than oral mesalamine (Conditional recommendation, very low quality of evidence).
    - Patients who place a higher value on convenience of oral medication administration and a lower value on effectiveness could reasonably choose oral mesalamine.
- In patients with mild–moderate ulcerative proctosigmoiditis who choose rectal therapy over oral therapy, the AGA suggests using mesalamine enemas rather than rectal corticosteroids (Conditional recommendation, moderate quality of evidence).
    - Patients who place a higher value on avoiding difficulties associated with mesalamine enemas and a lower value on effectiveness may reasonably select rectal corticosteroid foam preparations.
- In patients with mild–moderate ulcerative proctitis who choose rectal therapy over oral therapy, the AGA recommends using mesalamine suppositories (Strong recommendation, moderate quality of evidence).
- In patients with mild–moderate ulcerative proctosigmoiditis or proctitis being treated with rectal therapy who are intolerant of or refractory to mesalamine suppositories, the AGA suggests using rectal corticosteroid therapy rather than no therapy for induction of remission (Conditional recommendation, low quality of evidence).

- In patients with mild–moderate UC refractory to optimized oral and rectal 5-ASA, regardless of disease extent, the AGA suggests adding either oral prednisone or budesonide MMX (Conditional recommendation, low quality of evidence).

Recommendation Definitions

AGA Strength of Recommendation	Wording in the Guideline	Definition
Strong	"The AGA recommends…"	Most individuals should receive the recommended course of action. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.
Conditional	"The AGA suggests…"	Different choices would be appropriate for different patients. Decision aids may be useful in helping individuals in making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a decision.
No Recommendation	"The AGA makes no recommendation…"	The confidence in the effect estimate is so low that any effect estimate is speculative at this time.

AGA Quality Grade	Definition
High	We are very confident that the true effect lies close to the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different.
Low	Our confidence in the estimate is limited. The true effect may be substantially different from the estimate of effect.
Very Low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.
Knowledge Gap	Available evidence is insufficient to determine true effect.

Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. American College of Gastroenterology (ACG) Clinical Guideline: Ulcerative Colitis (UC) in Adults. Am J Gastroenterol. 2019;114(3):384-413.

Induction of remission in mildly active ulcerative colitis

- In patients with mildly active ulcerative proctitis, we recommend rectal 5-ASA therapies at a dose of 1 g/d for induction of remission (Strong recommendation, high quality of evidence).
- In patients with mildly active left-sided colitis, we recommend rectal 5-ASA enemas at a dose of at least 1 g/d preferred over rectal steroids for induction of remission (Strong recommendation, moderate quality of evidence).
- In patients with mildly active left-sided UC, we suggest rectal 5-ASA enemas at a dose of at least 1 g/d combined with oral 5-ASA at a dose of at least 2 g/d compared with oral 5-ASA therapy alone for induction of remission (Conditional recommendation, low quality of evidence).
- In patients with mildly active left-sided UC who are intolerant or nonresponsive to oral and rectal 5-ASA at appropriate doses (oral at least 2 g/d and rectal at least 1 g/d), we recommend oral budesonide MMX 9 mg/d for induction of remission (Strong recommendation, moderate quality of evidence).
- In patients with mildly active extensive colitis, oral 5-ASA at a dose of at least 2 g/d is recommended to induce remission (Strong recommendation, moderate quality of evidence).
- In patients with UC of any extent who fail to respond to 5-ASA therapy, we recommend oral systemic corticosteroids to induce remission (Strong recommendation, low quality of evidence).
- In patients with mildly active UC who fail to reach remission with appropriately dosed 5-ASA (at least 2 g/d oral 5-ASA and/or at least 1 g/d rectal 5-ASA), we suggest against changing to an alternate 5-ASA formulation to induce remission. Alternative therapeutic classes should be considered (Conditional recommendation, low quality of evidence).
- In patients with mildly active UC of any extent, we suggest using a low dose (2–2.4 g/d) of 5-ASA compared with a higher dose (4.8 g/d), as there is no difference in the remission rate (Conditional recommendation, very low quality of evidence).

- In patients with mildly to moderately active UC not responding to oral 5-ASA, we recommend the addition of budesonide MMX 9 mg/d to induce remission (Strong recommendation, moderate quality of evidence).
- In patients with mildly to moderately active UC of any extent using 5-ASA to induce remission, we recommend either once-daily or more frequently dosed oral 5-ASA based on patient preference to optimize adherence, as efficacy and safety are no different (Strong recommendation, moderate quality of evidence).

Maintenance of remission in patients with previously mildly active ulcerative colitis

- In patients with mildly active ulcerative proctitis, we recommend rectal 5-ASA at a dose of 1 g/d to maintain remission (Strong recommendation, moderate quality of evidence).
- In patients with mildly active left-sided or extensive UC, we recommend oral 5-ASA therapy (at least 2 g/d) for maintenance of remission (Strong recommendation, moderate quality of evidence).
- We recommend against systemic corticosteroids for maintenance of remission in patients with UC (Strong recommendation, moderate quality of evidence).

Induction of remission in moderately to severely active ulcerative colitis

- In patients with moderately active UC, we recommend oral budesonide MMX for induction of remission (Strong recommendation, moderate quality of evidence).
- In patients with moderately to severely active UC of any extent, we recommend oral systemic corticosteroids to induce remission (Strong recommendation, moderate quality of evidence).
- In patients with moderately to severely active UC who have failed 5-ASA therapy and in whom anti-TNF therapy is used for induction of remission, we suggest against using 5-ASA for added clinical efficacy (Conditional recommendation, low quality of evidence).

Maintenance of remission in patients with previously moderately to severely active ulcerative colitis

- In patients with previously moderately to severely active UC who have achieved remission but previously failed 5-ASA therapy and are now on anti-TNF therapy, we recommend against using concomitant 5-ASA for efficacy of maintenance of remission (Conditional recommendation, low quality of evidence).
- We recommend against systemic corticosteroids for maintenance of remission in patients with UC (Strong recommendation, moderate quality of evidence).
- For patients with previously moderately to severely active UC now in remission due to corticosteroid induction, we suggest thiopurines for maintenance of remission compared with no treatment or corticosteroids (Conditional recommendation, low quality of evidence).

Recommendation Definitions

ACG Strength of Recommendation	Definition
Strong	Benefits clearly outweigh the negatives and/or the result of no action.
Conditional	Some uncertainty remains about the balance of benefits and potential harm.

ACG Quality Grade	Definition
High	Further research is unlikely to change the authors' confidence in the estimate of effect and that we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	Moderate confidence in the effect estimate, although further research would be likely to have an impact on the confidence of the estimate.
Low	Further study would likely have an important impact on the confidence in the estimate of the effect and would likely change the estimate.
Very Low	Very little confidence in the effect estimate and that the true effect is likely to be substantially different than the estimate of effect.

Crohn's Disease

Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018;113(4):481-517.

Mild-to-moderately severe disease/low-risk disease

- Sulfasalazine is effective for treating symptoms of colonic CD that is mild to moderately active and can be used as treatment for this patient population (Conditional recommendation, low level of evidence).
- Oral mesalamine has not consistently been demonstrated to be effective compared with placebo for induction of remission and achieving mucosal healing in patients with active CD and should not be used to treat patients with active CD (Strong recommendation, moderate level of evidence).
- Controlled ileal release budesonide at a dose of 9 mg once daily is effective and should be used for induction of symptomatic remission for patients with mild-to-moderate ileocecal CD (strong recommendation, low level of evidence).
- Ciprofloxacin has shown similar efficacy to mesalamine in active luminal CD but has not been shown to be more effective than placebo to induce remission in CD and should not be used as therapy for luminal inflammatory CD (Conditional recommendation, very low level of evidence).

Moderate-to-severe disease/moderate-to-high-risk disease

- Oral corticosteroids are effective and can be used for short-term use in alleviating signs and symptoms of moderate to severely active CD (Strong recommendation, moderate level of evidence).
- Conventional corticosteroids do not consistently achieve mucosal healing and should be used sparingly (Weak recommendation, low level of evidence).

Severe/fulminant disease

- Intravenous corticosteroids should be used to treat severe or fulminant CD (Conditional recommendation, moderate level of evidence)

Maintenance Therapy of Luminal Crohn's Disease

- Oral 5-aminosalicylic acid has not been demonstrated to be effective for maintenance of medically induced remission in patients with CD, and is not recommended for long-term treatment (Strong recommendation, moderate level of evidence).
- Corticosteroids are not effective for maintenance of medically induced remission in CD and should not be used for long-term treatment (Strong recommendation, moderate level of evidence).
- Budesonide should not be used to maintain remission of CD beyond 4 months (Strong recommendation, moderate level of evidence).

Postoperative Crohn's Disease

- Mesalamine is of limited benefit in preventing postoperative CD, but in addition to no treatment is an option for patients with an isolated ileal resection and no risk factors for recurrence (Conditional recommendation, moderate level of evidence).

Recommendation Definitions

ACG Strength of Recommendation	Definition
Strong	Benefits clearly outweigh the negatives and/or the result of no action.
Conditional	Some uncertainty remains about the balance of benefits and potential harm.

ACG Quality Grade	Definition
High	Further research is unlikely to change the authors' confidence in the estimate of effect and that we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	Moderate confidence in the effect estimate, although further research would be likely to have an impact on the confidence of the estimate.
Low	Further study would likely have an important impact on the confidence in the estimate of the effect and would likely change the estimate.
Very Low	Very little confidence in the effect estimate and that the true effect is likely to be substantially different than the estimate of effect.

Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160(7):2496-2508.

- In adult outpatients with moderate to severe CD, the AGA suggests early introduction with a biologic with or without an immunomodulator rather than delaying their use until after failure of 5-ASA and/or corticosteroids (Conditional recommendation, low quality of evidence).
- In adult outpatients with moderate to severe CD, the AGA suggests the use of corticosteroids over no treatment for induction of remission (Conditional recommendation, moderate quality of evidence).
- In adult outpatients with moderate to severe CD, the AGA recommends against the use of corticosteroids over no treatment for maintenance of remission (Strong recommendation, moderate quality of evidence).
- In adult outpatients with moderate to severe CD, the AGA recommends against the use of 5-ASA or sulfasalazine over no treatment for the induction or maintenance of remission (Strong recommendation, moderate quality of evidence).

Nguyen GC, Loftus EV, Hirano I, et al. AGA Institute Guideline on the Management of Crohn's Disease After Surgical Resection. Gastroenterology. 2017;152(1):271-275.

- In patients with surgically induced remission of CD, the AGA suggests early pharmacological prophylaxis over endoscopy-guided pharmacological treatment (Conditional recommendation, very low quality of evidence).
    - Patients, particularly those at lower risk of recurrence, who place a higher value on avoiding the small risks of adverse events from pharmacological prophylaxis and a lower value on the potential risk of early disease recurrence may reasonably select endoscopy-guided pharmacological treatment over prophylaxis.
- In patients with surgically induced remission of CD, the AGA suggests using anti-TNF therapy and/or thiopurines over other agents (Conditional recommendation, moderate quality of evidence).
    - Patients at lower risk of disease recurrence or who place a higher value on avoiding the small risk of adverse events of thiopurines or anti-TNF treatment and a lower value on a modestly increased risk of disease recurrence may reasonably choose nitroimidazole antibiotics (for 3–12 months).
- In patients with surgically induced remission of CD, the AGA suggests against using mesalamine (or other 5-ASA), budesonide, or probiotics (Conditional recommendation, low quality of evidence and very low quality of evidence).

Recommendation Definitions

AGA Strength of Recommendation	Wording in the Guideline	Definition
Strong	"The AGA recommends…"	Most individuals should receive the recommended course of action. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.
Conditional	"The AGA suggests…"	Different choices would be appropriate for different patients. Decision aids may be useful in helping individuals in making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a decision.
No Recommendation	"The AGA makes no recommendation…"	The confidence in the effect estimate is so low that any effect estimate is speculative at this time.

AGA Quality Grade	Definition
High	We are very confident that the true effect lies close to the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different.
Low	Our confidence in the estimate is limited. The true effect may be substantially different from the estimate of effect.
Very Low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.
Knowledge Gap	Available evidence is insufficient to determine true effect.

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Barberio B, Segal JP, Quraishi MN, Black CJ, Savarino EV, Ford AC. Efficacy of oral, topical, or combined oral and topical 5-aminosalicylates, in ulcerative colitis: systematic review and network meta-analysis. J Crohns Colitis. 2021;15(7):1184-1196.	Systematic review conducted by searching MEDLINE, EMBASE, EMBASE Classic, and the Cochrane Central Register of Controlled Trials for studies up to December 2020. Randomized controlled trials (RCTs) comparing oral, topical, or combined oral and topical 5-ASAs, with each other or placebo for induction of remission or prevention of relapse of UC were included. A total of 63 RCTs were included, involving 11,733 patients.	• Primary efficacy endpoints: failure to achieve remission in active UC and occurrence of relapse of disease activity in quiescent UC
Results: Topical mesalamine, or oral and topical mesalamine combined ranked first and second for clinical and endoscopic remission combined. Combined therapy ranked first in trials where ≥50% of patients had left-sided/extensive disease, and topical mesalamine first in trials where ≥50% of patients had proctitis/proctosigmoiditis. High-dose (≥3.3 g/day) oral mesalamine ranked third in most analyses, with the most trials and most patients. For relapse of disease activity, combined therapy and high-dose oral mesalamine ranked first and second, with topical mesalamine third. 5-ASAs were safe and well tolerated, regardless of regimen. **Conclusion**: The results of this review support previous evidence; however, higher doses of oral mesalamine had more evidence for induction of remission than combined therapy and were significantly more efficacious than lower doses. Future RCTs should better establish the role of combined therapy for induction of remission, as well as optimal doses of oral 5-ASAs to prevent relapse.		
Citation	**Design**	**Endpoints**
Wang Y, Parker CE, Bhanji T, Feagan BG, Macdonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2016;4:CD000543.	Systematic review conducted by searching MEDLINE, EMBASE and the Cochrane Library up to July 2015. Prospective RCTs of oral 5-ASA therapy for treatment of patients with active UC compared with placebo, sulfasalazine or other formulations of 5-ASA were included. Studies that compared once daily 5-ASA treatment with conventional dosing of 5-ASA (two or three times daily) and 5-ASA dose ranging studies were also included. A total of 53 RCTs were included, involving 8,548 patients.	• Primary efficacy endpoints: failure to induce global/clinical remission, global/clinical improvement, endoscopic remission, and endoscopic improvement.
Results: 5-ASA was significantly superior to placebo with regard to all measured outcome variables. Seventy-one percent of 5-ASA patients failed to enter clinical remission compared to 83% of placebo patients (risk ratio [RR], 0.86; 95% confidence interval [CI], 0.82 to 0.89). No statistically significant differences in efficacy were found between 5-ASA and sulfasalazine. Fifty-four percent of 5-ASA patients failed to enter remission compared to 58% of sulfasalazine patients (RR, 0.90; 95% CI, 0.77 to 1.04). No statistically significant differences in efficacy or adherence were found between once daily and conventionally dosed 5-ASA. Forty-five percent of once daily patients failed to enter clinical remission compared to 48% of conventionally dosed patients (RR, 0.94; 95% CI, 0.83 to 1.07). There does not appear to be any difference in efficacy among the various 5-ASA formulations. Sulfasalazine was not as well tolerated as 5-ASA. Twenty-nine percent of sulfasalazine patients experienced an adverse event compared to 15% of 5-ASA patients (RR, 0.48; 95% CI, 0.37 to 0.63). **Conclusion**: 5-ASA was superior to placebo and no more effective than sulfasalazine. Considering their relative costs, a clinical advantage to using oral 5-ASA in place of sulfasalazine appears unlikely. 5-ASA dosed once daily appears to be as efficacious and safe as conventionally dosed 5-ASA.There do not appear to be any differences in efficacy or safety among the various 5-ASA formulations. A daily dosage of 2.4 g appears to be a safe and effective induction therapy for patients with mild to moderately active ulcerative colitis. Patients with moderate disease may benefit from an initial dose of 4.8 g/day.		
Citation	**Design**	**Endpoints**

Bonovas S, Nikolopoulos GK, Piovani D, et al. Comparative assessment of budesonide-MMX and mesalamine in active, mild-to-moderate ulcerative colitis: A systematic review and network meta-analysis. Br J Clin Pharmacol. 2019	Systematic review/network meta-analysis conducted by searching PUBMED, SCOPUS, EMBASE, the Cochrane Library, clinical trial registries, regulatory agencies' websites and international conference up to July 2018. RCTs of adult patients with active, mild-to-moderate UC, comparing budesonide-MMX or mesalamine against placebo, or against each other, or different dosing strategies, for induction of remission were included. A total of 15 RCTs were included, involving 4,083 patients.	• Primary efficacy endpoint: induction of clinical and endoscopic remission at the last time of assessment.
Results: Budesonide-MMX 9 mg/day and mesalamine >2.4 g/day had similar efficacy for induction of clinical and endoscopic remission (odds ratio [OR], 0.97; 95% CI, 0.59 to 1.60), both showing superiority over placebo (OR, 2.68; 95% CI, 1.75 to 4.10, and OR, 2.75; 95% CI, 1.94 to 3.90, respectively). Mesalamine >2.4 g/day was more efficacious than mesalamine 1.6 to 2.4 g/day (OR, 1.27; 95% CI, 1.03 to 1.56). Secondary analyses showed that mesalamine >2.4 g/day ranks at the top among comparator treatments regarding safety and tolerability. **Conclusion**: Budesonide-MMX and mesalamine >2.4 g/day had similar efficacy for induction of clinical and endoscopic remission in active, mild-to-moderate UC; however, mesalamine >2.4 g/day showed better tolerability. Further high-quality research is warranted.		
Citation	**Design**	**Endpoints**
Zhao X, Zhou C, Ma J, et al. Efficacy and safety of rectal 5-aminosalicylic acid versus corticosteroids in active distal ulcerative colitis: a systematic review and network meta-analysis. Sci Rep. 2017;7:46693.	Systematic review/network meta-analysis conducted by searching PUBMED, MEDLINE, EMBASE and the Cochrane Library, up to May 2016. RCTs comparing different doses of topical 5-ASA and corticosteroids with placebo or against each other, or different dosing strategies, for induction of clinical or endoscopic remission were included. Studies in which topical drug utilization was just treated as adjuvant treatment and patients who presented with indeterminate colitis (IC), idiopathic proctitis or CD were excluded. A total of 34 RCTs were included, involving 4,973 patients.	• Primary efficacy endpoint: clinical and endoscopic remission rates in active distal UC patients at 4 weeks.
Results: Rectal 5-ASA 1 g/day, or higher dosage (1.5 to 2.0 and 4 g/day) had significant superiority over placebo in inducing endoscopic remission (OR, 6.45; 95% CI, 4.23 to 9.82; OR, 4.49; 95% CI, 2.61 to 7.73; and OR, 6.86; 95% CI, 3.53 to 13.34, respectively). Additionally, budesonide ≥4 mg/day (OR, 2.88; 95% CI, 1.99 to 4.26) and budesonide 2 to 3 mg/day (OR, 2.30; 95% CI, 1.50 to 3.47) were shown to be superior to placebo. **Conclusion**: Rectal 5-ASA at different doses (1–4 g/day) showed significant advantages over placebo in inducing clinical and endoscopic remission, and also did not increase the rate of adverse events.		
Citation	**Design**	**Endpoints**
Zeng J, Lv L, Mei ZC. Budesonide foam for mild to moderate distal ulcerative colitis: A systematic review and meta-analysis. J Gastroenterol Hepatol. 2017;32(3):558-566.	Systematic review/meta-analysis conducted by searching the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE databases for studies up to July 2016. Studies that were included were randomized placebo-controlled trials that assessed the efficacy and safety of budesonide foam in mild-to-moderate distal UC. A total 3 RCTs were included, involving 711 patients.	• Primary efficacy endpoints: clinical remission, endoscopic improvement, and elimination of rectal bleeding
Results: Pooled analyses showed that budesonide foam was significantly superior to placebo for induction of clinical remission (RR, 1.83; 95%CI 1.41 to 2.37; P < 0.001) and endoscopic improvement (RR, 1.44; 95% CI, 1.23 to 1.68; P < 0.001), and eliminating rectal bleeding at week 6 (RR, 1.76; 95% CI, 1.45 to 2.14; P < 0.001). No statistically significant difference was observed in the incidence of adverse events and therapeutic discontinuation because of adverse events between budesonide foam and placebo.		

Conclusion: Budesonide foam is well tolerated and superior to placebo in inducing clinical remission and endoscopic improvement, and eliminating rectal bleeding for mild-to-moderate distal UC.		
Citation	**Design**	**Endpoints**
Coward S, Kuenzig ME, Hazlewood G, et al. Comparative Effectiveness of Mesalamine, Sulfasalazine, Corticosteroids, and Budesonide for the Induction of Remission in Crohn's Disease: A Bayesian Network Meta-analysis. Inflamm Bowel Dis. 2017;23(3):461-472.	Network meta-analysis conducted by searching MEDLINE and EMBASE and Cochrane CENTRAL Registry of Controlled Trials up to November 2015. RCTs that compared mesalamine, sulfasalazine, budesonide, and corticosteroids with placebo or each other in adults (≥18 years old) with CD were included. Studies of combination therapy (e.g., mesalamine versus mesalamine + corticosteroids) and those that evaluated postoperative remission were excluded. A total of 22 RCTs were included, involving 2,968 patients.	• Primary efficacy endpoint: induction of remission (defined by a CDAI < 150) by week 8 to 17 of treatment
Results: Corticosteroids (OR, 3.80; 95% credible interval [CrI], 2.48 to 5.66), high-dose budesonide (OR, 2.96; 95% CrI, 2.06 to 4.30), and high-dose mesalamine (OR, 2.29; 95% CrI, 1.58 to 3.33) were superior to placebo at inducing remission. Corticosteroids were similar to high-dose budesonide (OR, 1.21; 95% CrI, 0.84 to 1.76), but more effective than high-dose mesalamine (OR, 1.83; 95% CrI, 1.16 to 2.88). Sulfasalazine was not significantly superior to any therapy including placebo. **Conclusion**: Corticosteroids and high-dose budesonide were effective treatments for inducing remission in mild-to-moderate Crohn's disease. High-dose mesalamine is an option among patients preferring to avoid steroids.		
Citation	**Design**	**Endpoints**
Kuenzig ME, Rezaie A, Kaplan GG, et al. Budesonide for the induction and maintenance of remission in crohn's disease: systematic review and meta-analysis for the cochrane collaboration. J Can Assoc Gastroenterol. 2018;1(4):159-173.	Systematic review conducted by searching MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and PubMed for studies up to November 2017. RCTs comparing budesonide to placebo or another active agent were considered for inclusion. Studies comparing different doses of budesonide RCTs comparing budesonide to a placebo or active comparator were also considered for inclusion. Studies comparing different doses of budesonide were excluded if they did not also include a non-budesonide comparison arm. A total of 23 RCTs were included, involving 2,777 patients.	• Primary efficacy endpoints: induction and maintenance of remission at eight weeks and one year
Results: Thirteen induction and 10 maintenance trials were included. Budesonide 9 mg was more effective than placebo (RR, 1.93; 95% CI, 1.37 to 2.73) but less effective than conventional steroids (RR, 0.85; 95% CI, 0.75 to 0.97) to induce remission. Corticosteroid-related adverse events occurred less often with induction doses of budesonide than steroids (RR, 0.64; 95% CI, 0.54 to 0.76); budesonide did not increase adverse events relative to placebo (RR, 0.97; 95% CI, 0.76 to 1.23). Budesonide 6 mg was not different from placebo for maintaining remission (RR, 1.13; 95% CI, 0.94 to 1.35). Both induction and maintenance budesonide treatment increased the risk of an abnormal adrenocorticotropic hormone (ACTH) test compared with placebo, but less than conventional steroids. **Conclusion**: For induction of clinical remission, budesonide was more effective than placebo, but less effective than conventional steroids. Budesonide was not effective for the maintenance of remission. Budesonide was safer than conventional steroids, but the long-term effects on the adrenal axis and bone health remain unknown.		

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (4/1/2023 to 6/30/2023)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	**Rx**	**Mbrs**	**Total**	**Avg/Rx**	**Total**	**Approved (%)**	**Current**	**Recommend**
Oral 5-Aminosalicylate Agents								
Mesalamine ER (Apriso®) 0.375 g oral capsules	0	0	$0.00	$0.00	0	0 (0%)	F-ST (t/f sulfasalazine, sulfasalazine DR, or balsalazide)	No change
Mesalamine DR (Asacol® HD) 800 mg oral tablets	3	1	$1,895.97	$631.99	1	0 (0%)	F-PA	No change
Mesalamine DR (Lialda®) 1.2 g oral tablets	0	0	$0.00	$0.00	0	0 (0%)	F-ST (t/f sulfasalazine, sulfasalazine DR, or balsalazide)	No change
Mesalamine DR (Delzicol®) 400 mg oral capsules	3	1	$768.48	$256.16	0	0 (0%)	F-ST (t/f sulfasalazine, sulfasalazine DR, or balsalazide)	No change
Mesalamine ER (Pentasa®) 500 mg oral capsules	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Pentasa® (mesalamine ER) 250 mg oral capsules	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Dipentum® (olsalazine) 250 mg oral capsules	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sulfasalazine (Azulfidine®) 500 mg oral tablets	3	3	$143.03	$47.68	0	0 (0%)	F	No change
Sulfasalazine DR (Azulfidine EN®) 500 mg oral tablets	2	2	$58.94	$29.47	0	0 (0%)	F	No change
Balsalazide (Colazal®) 750 mg oral capsules	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Rectal 5-Aminosalicylate Agents								
Mesalamine (Canasa®) 1,000 mg rectal suppository	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Mesalamine (Rowasa®) 4 g/60 ml rectal enema	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Mesalamine (SFRowasa®) 4 g/60 mL rectal enema	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Oral Glucocorticoids								
Budesonide DR (Entocort® EC) 3 mg oral capsules	5	3	$912.05	$182.41	0	0 (0%)	F-QL (540/365)	No change
Budesonide ER (Uceris®) 9 mg oral tablets	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Ortikos™ (budesonide ER) 6 mg, 9 mg oral capsules	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Rectal Glucocorticoids								
Cortifoam® (hydrocortisone acetate) 10% rectal foam	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
Hydrocortisone (Cortenema®) 100 mg/60 ml rectal enema	0	0	$0.00	$0.00	0	0 (0%)	F	No change
Budesonide (Uceris®) 2mg rectal foam	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
TOTAL	**16**	**10**	**$3,778.47**	**$236.15**	**1**	**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 Chron's disease as an indication, these formulations are only indicated for ulcerative colitis.

Mesalamine	
Therapeutic Classes (AHFS)	Anti-Inflammatory Agents (GI Drugs)
Medications	Formulary Mesalamine (Canasa) suppository Mesalamine (Rowasa) rectal enema Mesalamine (SFRowasa) rectal enema Formulary, Step Therapy Mesalamine DR (Delzicol DR) capsule Mesalamine ER (Apriso) capsule Mesalamine DR (Lialda) tablet Formulary, PA Required Mesalamine ER (Pentasa) 500mg capsule Pentasa (mesalamine) 250mg capsule Mesalamine DR (Asacol HD) tablet Any other mesalamine 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), and the Drug Package Insert.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If criteria are not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for Authorization Mesalamine DR (Delzicol DR), mesalamine ER (Apriso), or mesalamine DR (Lialda) are approved when all of the following criteria are met: • Documentation of a diagnosis of ulcerative colitis ~~or Crohn's disease~~ • Documentation of a trial and failure or contraindication to sulfasalazine or balsalazide Mesalamine ER (Pentasa), Pentasa (mesalamine) or mesalamine DR (Asacol HD) are approved when all of the following criteria are met: • Documentation of a diagnosis of ulcerative colitis ~~or Crohn's disease~~ • Documentation of a trial and failure or contraindication to sulfasalazine or balsalazide AND mesalamine DR (Lialda) or mesalamine DR (Delzicol DR) or mesalamine ER (Apriso)
Criteria Statement	Mesalamine DR (Lialda) tablet, mesalamine DR (Delzicol) or mesalamine ER (Apriso) are reserved for members who have ulcerative colitis ~~or Crohn's disease~~ and have used (or cannot/should not use) sulfasalazine or balsalazide. Mesalamine ER (Pentasa), Pentasa (mesalamine) or mesalamine DR (Asacol HD) are reserved for members with ulcerative colitis ~~or Crohn's~~ who have used (or cannot/should not use) sulfasalazine or balsalazide AND mesalamine DR (Lialda) tablet, mesalamine DR (Delzicol), or mesalamine ER (Apriso).
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Change brand/generic status of Uceris foam
- Add new medication Ortikos and criteria for use

Corticosteroids for Ulcerative Colitis and Crohn's disease	
Therapeutic Classes (AHFS)	Corticosteroids, Adrenals
Medications	Formulary budesonide (Entocort EC) capsule (QL 540/365) Hydrocortisone (Cortenema) rectal enema Formulary, Prior Authorization Required budesonide (Uceris) tablet Cortifoam (hydrocortisone acetate) foam ~~Uceris (b~~Budesonide (Uceris)~~)~~ 2mg foam Ortikos (budesonide) capsule Any other corticosteroid for ulcerative colitis or Crohn's disease
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), and the Drug Package Insert.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** — **Budesonide (Uceris) foam, Cortifoam, or Budesonide tablet (Uceris)** If the criteria are met, the request will be approved for up to a 2 month duration **Approval to Exceed QL:** — 3 months If criteria are not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for Authorization Budesonide (Uceris) tablet is approved when all of the following criteria are met: • Documentation of a diagnosis of mild to moderate ulcerative colitis and failed remission • Documentation of trial and failure, contraindication, intolerance, or inability to use maximum tolerated and therapeutic dose of oral aminosalicylates (i.e. sulfasalazine or balsalazide) for 8 weeks AND rectal mesalamine for up to 6 weeks Budesonide (Uceris) foam and Cortifoam are approved when all of the following criteria are met: • Documentation of a diagnosis of ulcerative colitis. • Documentation of a trial and failure, intolerance, contraindication, or inability to formulary rectal mesalamine and formulary rectal corticosteroids. Ortikos is approved when all of the following criteria are met: • Documentation of a diagnosis of mild to moderate Crohn's disease involving the ileum and/or the ascending colon • Documentation of trial and failure, contraindication, intolerance, or inability to use budesonide (Entocort EC) capsule Requests for exceeding quantity limit of 540 capsules per 365 days for budesonide (Entocort EC) capsule

	• 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	Budesonide (Uceris) tablet is reserved for members who have mild to moderate ulcerative colitis and have used (or cannot/should not use) the maximum tolerated and therapeutic dose of oral aminosalicylates (sulfasalazine or balsalazide) for 8 weeks AND rectal mesalamine for up to 6 weeks Budesonide (Uceris) foam or Cortifoam are reserved for members who have ulcerative colitis and have used (or cannot/should not use) formulary rectal mesalamine and formulary rectal corticosteroids. Ortikos is reserved for members who have mild to moderate Crohn's disease involving the ileum and have used (or cannot/should not use) budesonide (Entocort EC) capsule. Requests for budesonide (Entocort EC) capsule above the quantity limit are reserved for members who have used (or cannot/should not use) this medication in doses under the quantity limit and whose prescriber has a reason why the quantity limit is inadequate.
Last P&T Review Date	~~9/2022~~9/2023

REFERENCES

1. Lexicomp Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on May 31, 2023.
2. ClinicalTrials.gov. U.S. National Institutes of Health. Available at: https://clinicaltrials.gov/. Accessed on May 31, 2023.
3. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on May 31, 2023.
4. Pubmed.gov. U.S. National Library of Medicine, National Institutes of Health. Available at: https://www.ncbi.nlm.nih.gov/pubmed. Accessed on May 31, 2023.
5. Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; Accessed on May 31, 2023.
6. U.S. Food and Drug Administration. U.S. Department of Health and Human Services. Available at: http://www.fda.gov/. Accessed on May 31, 2023.
7. IPD Analytics. Bay Harbor Islands, Florida: IPD Analytics, LLC. http://www.ipdanalytics.com. Accessed on May 31, 2023.
8. Feuerstein JD, Isaacs KL, Schneider Y, et al. AGA Clinical Practice Guidelines on the Management of Moderate to Severe Ulcerative Colitis. Gastroenterology. 2020;158(5):1450-1461.
9. Ko CW, Singh S, Feuerstein JD, et al. AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology. 2019;156(3):748-764.
10. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019;114(3):384-413.
11. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018;113(4):481-517.
12. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160(7):2496-2508.
13. Nguyen GC, Loftus EV, Hirano I, et al. AGA Institute Guideline on the Management of Crohn's Disease After Surgical Resection. Gastroenterology. 2017;152(1):271-275.
14. Barberio B, Segal JP, Quraishi MN, Black CJ, Savarino EV, Ford AC. Efficacy of oral, topical, or combined oral and topical 5-aminosalicylates, in ulcerative colitis: systematic review and network meta-analysis. J Crohns Colitis. 2021;15(7):1184-1196.
15. Wang Y, Parker CE, Bhanji T, Feagan BG, Macdonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. Cochrane Database Syst Rev. 2016;4:CD000543.
16. Bonovas S, Nikolopoulos GK, Piovani D, et al. Comparative assessment of budesonide-MMX and mesalamine in active, mild-to-moderate ulcerative colitis: A systematic review and network meta-analysis. Br J Clin Pharmacol. 2019
17. Zhao X, Zhou C, Ma J, et al. Efficacy and safety of rectal 5-aminosalicylic acid versus corticosteroids in active distal ulcerative colitis: a systematic review and network meta-analysis. Sci Rep. 2017;7:46693.
18. Zeng J, Lv L, Mei ZC. Budesonide foam for mild to moderate distal ulcerative colitis: A systematic review and meta-analysis. J Gastroenterol Hepatol. 2017;32(3):558-566.
19. Coward S, Kuenzig ME, Hazlewood G, et al. Comparative Effectiveness of Mesalamine, Sulfasalazine, Corticosteroids, and Budesonide for the Induction of Remission in Crohn's Disease: A Bayesian Network Meta-analysis. Inflamm Bowel Dis. 2017;23(3):461-472.
20. Kuenzig ME, Rezaie A, Kaplan GG, et al. Budesonide for the induction and maintenance of remission in crohn's disease: systematic review and meta-analysis for the cochrane collaboration. J Can Assoc Gastroenterol. 2018;1(4):159-173.

Chelators

Executive Summary

CLASS OVERVIEW

Chelating agents are medications that form chelates within the body to help remove excess metals including copper (Cu), iron (Fe), and lead (Pb). A chelate is a chemical compound formed between a metal ion and the chelating agent. Chelators can form several bonds to a single metal ion. The resulting chelates can be excreted from the body, making these medications useful in treating Wilson disease, iron overload, and lead poisoning. Wilson disease is a rare genetic disorder that prevents the liver from properly eliminating copper resulting in its accumulation in the liver, brain and eyes. Although liver transplantation is the only curative measure for this disease, chelating medications such as trientine (Syprine®), penicillamine (Depen®, Cuprimine®), and Galzin® (zinc acetate) are mainstays of therapy to reduce copper levels and improve patient quality of life. Deferasirox (Exjade®, Jadenu®), Ferriprox™ (deferiprone), and deferoxamine (Desferal®) all have FDA indications for the treatment of iron overload. Iron overload is caused by increased iron intake (e.g., from blood transfusions) or increased iron absorption (e.g., hereditary hemochromatosis [HH], ineffective erythropoiesis that occurs in certain inherited anemias, and liver disease). Excessive iron stores must be treated to prevent end organ damage. Important in the treatment of severe, symptomatic lead toxicity are Chemet® (succimer), BAL in Oil (dimercaprol), and Calcium Disodium Versenate (edetate calcium disodium). Asymptomatic cases of lead toxicity are treated with remediation and removal of the source of lead exposure. BAL in Oil (dimercaprol) can also be used in the treatment of arsenic, gold, and mercury poisoning. This scope of this class review will only be on chelating agents for the treatment of Wilson disease, thalassemia, HH, and lead poisoning.

UTILIZATION FINDINGS

There was 1 claim for 1 member, for a total cost of $80 for deferasirox (Exjade®) dispersible tablet. There were 2 prior authorization requests with 1 approval (50%).

RECOMMENDATIONS

- No changes

PRODUCT TABLE (4/1/2023 to 6/30/2023)

Medication	Rx	Current Status	Recommendation
Copper Chelators			
trientine (Syprine®) 250 mg capsule	0	F-PA-SP	No change
Cuvrior® (trientine tetrahydrochloride) 300mg tablet	0	NF	No change
penicillamine (Cuprimine®) 250 mg capsule	0	F-PA-SP	No change
penicillamine (Depen® Titratabs) 250 mg tablet	0	F-PA	No change
D-penamine® (penicillamine) 125 mg oral tablet	0	NF	No change
Galzin® (zinc acetate) 25, 50 mg capsule	0	NF	No change
Iron Chelators			
deferoxamine (Desferal®) 500 mg, 2 g solution for injection	0	F-SP	No change
deferasirox (Exjade®) 125 mg, 250 mg, 500 mg dispersible tablet	0	F-PA-AL (min 21 years)	No change
deferasirox (Jadenu®) 90 mg tablet	1	F-PA	No change
deferasirox (Jadenu® Sprinkle) 90 mg oral granules in packet	0	F-PA	No change
deferiprone (Ferriprox™) 500, 1000 mg tablet	0	NF	No change
Ferriprox™ (deferiprone) 100 mg/mL oral solution	0	NF	No change
Lead (and Other) Chelators			
Chemet® (succimer) 100 mg capsule	0	NF	No change
Bal in Oil (dimercaprol) 100 mg/mL intramuscular solution	0	NF	No change
Calcium Disodium Versenate 200 mg/mL injection solution	0	NF	No change

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

CLINICAL SUMMARY

Chelating agents are medications that form chelates within the body to help remove excess metals including copper (Cu), iron (Fe), and lead (Pb). A chelate is a chemical compound formed between a metal ion and the chelating agent. Chelators can form several bonds to a single metal ion. The resulting chelates can be excreted from the body, making these medications useful in treating Wilson disease, iron overload, and lead poisoning.

Wilson disease is an inherited autosomal recessive disorder occurring in 1 in 30,000 live births and leads to impaired function of the intracellular copper transporter, ATP7B. Copper build-up occurs primarily in the liver, brain, and cornea and over time, the liver becomes cirrhotic. Neurologic manifestations may also occur including dysarthria, gait abnormalities, dystonia, drooling, and tremor. Some patients may also experience psychiatric manifestations including depression, personality changes, impulsiveness, and in severe cases, psychosis. Although liver transplantation is the only curative measure for this disease, chelating medications such as trientine (Syprine®), penicillamine (Depen®, Cuprimine®), and Galzin® (zinc acetate) are mainstays of therapy to reduce copper levels and improve patient quality of life. Penicillamine or trientine should be used as initial treatment for acute, symptomatic patients with Wilson disease. Presymptomatic patients should be treated with zinc acetate, penicillamine, or trientine. Cuvrior™ (trientine tetrahydrochloride), an alternative salt version comparable to the existing hydrochloride salt version, was approved in April 2022 for the treatment of adult patients with stable Wilson's disease who are de-coppered and tolerant to penicillamine. It was marketed in the first half of 2023.

Iron overload is caused by increased iron intake (e.g., from blood transfusions) or increased iron absorption (e.g., HH, ineffective erythropoiesis that occurs in certain inherited anemias, and liver disease). Excessive iron stores must be treated to prevent end organ damage. Chelation therapy is recommended in iron-overloaded, transfusion-dependent patients (e.g., beta thalassemia major [TM], severe beta thalassemia intermedia, sickle cell anemia, myelodysplasia, aplastic anemia, Diamond-Blackfan anemia) and patients with hemochromatosis and unstable hemodynamic status because phlebotomy cannot be used in these patient populations. In patients with hemochromatosis eligible for phlebotomy, this is preferred due to high efficacy, avoidance of side effects, and paucity of clinical data for chelators in this setting. Chelation therapy is also recommended in non-transfusion dependent thalassemia (NTDT) as well as other iron-overloaded conditions. Deferasirox (Exjade®, Jadenu®), Ferriprox™ (deferiprone), and deferoxamine (Desferal®) all have FDA indications for the treatment of iron overload. Deferoxamine must be given by continuous infusion, either subcutaneously (SQ) or intravenously (IV), while deferiprone and deferasirox are orally active. Each has its own benefits, toxicities, and requirements for monitoring of side effects.

Acute lead poisoning can occur due to occupational or environmental exposure. Chemet® (succimer) is labeled for use in pediatric patients with lead poisoning and retains an off-label use for adults. Dimercaprol and calcium disodium versenate are indicated to treat lead poisoning in pediatric patients as well as adults. Dimercaprol is additionally indicated to treat arsenic, gold, and mercury poisoning. Lead chelation therapy is only ever used for symptomatic patients or those with severely high blood lead levels. Rather, asymptomatic lead-exposed patients with low to moderate blood lead levels are treated by removing the source of lead exposure.

There are currently no drugs in phase III or later development for the treatment of Wilson disease. iron overload, or lead poisoning. No existing agents are under investigation for a label expansion and no new agents are up for approval within the upcoming year

INDICATIONS, DOSING and ADMINISTRATION

Medication	Indications	Dosing/Administration
Copper Chelators		
Trientine hydrochloride (Syprine®) 250 mg oral capsule	Wilson disease in patients who are intolerant of penicillamine	• Adult: 750 mg to 1250 mg/day orally given in divided doses 2 to 4 times daily (max: 2g/day) • Pediatric: 20 mg/kg/day orally in 2 to 3 divided doses (max: 1500 mg/day)
Cuvrior™ (trientine tetrahydrochloride) 300 mg oral tablet	Wilson disease in patients who are de-coppered and tolerant to penicillamine	300 to 3000 mg/day orally in 2 equally divided doses based on penicillamine total daily dose
Penicillamine (Cuprimine®) 250 mg oral capsule Penicillamine (Depen® Titratabs) 250 mg oral tablet	Cystinuria	• Adult: 1 to 4 g/day orally in 4 divided doses • Pediatric: 20 to 40 mg/kg/day orally in 4 divided doses (max: 40 mg/kg/day)
	Wilson disease	• Adult: 750 mg to 1500 mg/day orally in divided doses (max: 2g/day) • Pediatric: 20 mg/kg/day orally in 2 to 3 divided doses (max: 1500 mg/day)
Galzin® (zinc acetate) 25 mg, 50 mg oral capsule	Wilson disease, maintenance treatment following chelation therapy	• Adult: 50 mg orally 3 times daily • Pediatric (≥ 10 years): 25 mg to 50 mg orally 3 times daily
Iron Chelators		
Deferoxamine (Desferal®) 500 mg, 2 g solution for injection	Acute iron toxicity	1g, either IM or IV, may be followed by 500 mg every 4 hours for 2 doses (max: 6 g/day)
	Chronic iron overload	• IM: 500 mg to 1 g/day (max: 1 g/day) • IV: 40 to 50 mg/kg/day (max: 60 mg/kg/day) over 8 to 12 hours for 5 to 7 days per week • SQ: 1 g to 2 g/day or 20 to 40 mg/kg/day (max: 60 mg/kg/day) over 8 to 12 hours for 5 to 7 days per week
Deferasirox (Exjade®) 125 mg, 250 mg, 500 mg oral dispersible tablet	• Chronic iron overload due to transfusions • Chronic iron overload in non-transfusion-dependent thalassemia syndromes	• Chronic iron overload due to transfusions: 20 to 40 mg/kg orally once daily • Chronic iron overload in non-transfusion-dependent thalassemia syndromes: 10 to 20 mg/kg orally once daily
Deferasirox (Jadenu®) 90 mg oral tablet Deferasirox (Jadenu® Sprinkle) 90 mg oral granules in packet		• Chronic iron overload due to transfusions: 14 to 28 mg/kg once daily • Chronic iron overload in non-transfusion-dependent thalassemia syndromes: 7 to 14 mg/kg orally once daily
Deferiprone (Ferriprox™) 500, 1,000 mg tablet Ferriprox™ (deferiprone) 100 mg/mL oral solution	Transfusional iron overload	75 mg/kg/day orally in 2 divided doses (using 1000 mg twice-a-day tablet formulation only) or 3 divided doses (using oral solution, 500 mg tablet, or 1,000 mg 3-times-a-day tablet formulation) (max: 99 mg/kg/day)
Lead (and Other) Chelators		
Chemet® (succimer) 100 mg oral capsule	Arsenic poisoning (off-label) Lead poisoning (off-label) Mercury poisoning (off-label)	10 mg/kg orally 3 times daily for 5 days followed by 10 mg/kg orally twice daily for 14 days

Medication	Indications	Dosing/Administration
BAL in Oil (dimercaprol) 100 mg/mL intramuscular solution	Treatment of arsenic, gold, and mercury poisoning	• Acute mercury poisoning: 5 mg/kg IM initially, followed by 2.5 mg/kg 1 to 2 times daily for 10 days • Arsenic or gold poisoning ○ Mild: 2.5 mg/kg IM every 6 hours for 2 days, then every 12 hours on the 3rd day, followed by once daily for 10 days ○ Severe: 3 mg/kg IM every 4 hours for 2 days, then every 6 hours on the 3rd day, followed by every 12 hours for 10 days
	Treatment of acute lead poisoning when used concomitantly with edetate calcium disodium injection	• 4 mg/kg IM alone the first dose, thereafter at 4-hour intervals in combination with edetate calcium disodium injection • For less severe poisoning, reduce the dose to 3 mg/kg after the first dose • Maintain treatment for 3 to 5 days
Calcium Disodium Versenate 200 mg/mL injection solution	Lead poisoning (acute and chronic), lead encephalopathy, lead nephropathy	• Symptomatic patients, patients with lead encephalopathy, or patients whose blood lead level (BLL) is > 100 mcg/dL: ○ 1500 mg/m^2/day or 50 to 75 mg/kg/day IM or IV for 5 days in conjunction with dimercaprol • Lead nephropathy: ○ SCr 2 to 3 mg/dL: 500 mg/m^2 IM or IV every 24 hours for 5 days ○ SCr 3 to 4 mg/dL: 500 mg/m^2 IM or IV every 48 hours for 3 doses ○ SCr >4 mg/dL: 500 mg/m^2 IM or IV once weekly

BOXED WARNINGS and CONTRAINDICATIONS

Medication	Boxed Warnings	Contraindications
Copper Chelators		
Trientine (Syprine®, Cuvrior™)	None	Hypersensitivity
Penicillamine (Cuprimine®, Depen® Titratabs)	• **Experienced physician**: Should be administered under close supervision of a physician familiar with dosage and toxicity considerations • **Toxicity symptoms**: Warn patients to promptly report any symptoms suggesting toxicity (fever, sore throat, chills, bruising, bleeding)	• Renal insufficiency (in rheumatoid arthritis [RA] patients) • Breast-feeding • Pregnancy (in RA patients) • Previous penicillamine-related aplastic anemia or agranulocytosis
Galzin® (zinc acetate)	None	Hypersensitivity
Iron Chelators		
Deferoxamine (Desferal®)	None	• Hypersensitivity • Severe renal disease • Anuria
Deferasirox (Exjade®, Jadenu®)	• **Gastrointestinal (GI) hemorrhage**: GI hemorrhages, which may be fatal, can occur and more likely in elderly patients with advanced hematologic malignancies or low platelet counts • **Hepatic failure**: Hepatic injury and failure may occur. Avoid use in patients with severe hepatic impairment and reduce dose with moderate hepatic impairment • **Renal failure**: Acute renal failure and death can occur, particularly in patients with comorbidities and those who are in the advanced stages of their hematologic disorders. Consider dose reductions or interruptions in therapy if increases occur or in patients with preexisting renal disease	• CrCl <40 mL/min • Poor performance status • High-risk myelodysplastic syndromes • Advanced malignancies • Platelet counts less than 50,000/mm^3 • Hypersensitivity
Deferiprone (Ferriprox™)	**Agranulocytosis/Neutropenia**: Can cause agranulocytosis that can lead to serious infections and death. Monitor absolute neutrophil count (ANC) prior to treatment and weekly during therapy. Interrupt treatment if neutropenia or infection develops	Hypersensitivity
Lead (and Other) Chelators		
Chemet® (succimer)	None	Hypersensitivity
BAL in Oil (dimercaprol)		• Hepatic insufficiency • In the setting of iron, cadmium, or selenium poisoning
Calcium Disodium Versenate	**Fatal Toxicity/Cerebral edema**: Capable of producing toxic effects that can be fatal. Patients with lead encephalopathy and cerebral edema may experience a lethal increase in intracranial pressure following IV infusion; the IM route is preferred for these patients	• Anuria • Active renal disease • Hepatitis

WARNINGS/PRECAUTIONS

Medication	Warnings/Precautions
Copper Chelators	
Trientine (Syprine®, Cuvrior™)	• **Concerns related to adverse effects:** Anemia, copper deficiency, neurologic worsening, hypersensitivity
Penicillamine (Cuprimine®, Depen®, Titratabs)	• **Concerns related to adverse effects:** Allergic reactions, anti-glomerular basement membrane (GBM) disease (Goodpasture syndrome) bronchiolitis obliterans, dermatologic concerns, drug fever, taste alteration, agranulocytosis, aplastic anemia, thrombocytopenia, hepatotoxicity, lupus-like syndrome, proteinuria, pemphigus, hematuria, myasthenic syndrome, penicillin cross-sensitivity, toxicity symptoms • **Disease-related concerns:** Cystinuria, lead poisoning, Wilson disease • **Concurrent drug therapy issues:** Hematopoietic-depressant drugs • **Special populations:** Elderly patients may be more susceptible to skin rash and/or taste alterations • **Other:** Should be administered under the close supervision of a physician familiar with the toxicity and dosage considerations
Galzin® (zinc acetate)	• **Concerns related to adverse effects:** Neurological deterioration, gastric irritation/upset • **Other**: Not recommended in symptomatic patients
Iron Chelators	
Deferoxamine (Desferal®)	• **Concerns related to adverse effects:** Acute respiratory distress syndrome (ARDS), auditory effects, growth retardation, infection, infusion reactions, mucormycosis, ocular effects, renal effects, urine discoloration • **Disease-related concerns:** Aluminum toxicity, hemochromatosis, myasthenia gravis • **Concurrent drug therapy issues:** Combination treatment with ascorbic acid (>500 mg/day in adults) may impair cardiac function
Deferasirox (Exjade®, Jadenu®)	• **Concerns related to adverse effects:** Auditory disturbances, bone marrow suppression, dermatologic toxicity, GI reactions, hepatic failure, hypersensitivity, ocular disturbances, renal failure • **Special population:** Elderly patients have higher risk of toxicity and fatal events; associated with serious and fatal adverse events in pediatric population, usually associated with volume depletion or continued doses of 20 to 40 mg/kg/day (Exjade®) or 14 to 28 mg/kg/day (Jadenu®) • **Dosage form specific issues**: Some formulations may contain lactose • **Other:** Overchelation of iron may increase development of renal toxicity with doses >25 mg/kg/day (Exjade®) or >17.5 mg/kg/day (Jadenu®) while serum ferritin values <1,000 mcg/L; may cause variable decreases in the serum concentration of zinc and copper
Deferiprone (Ferriprox™)	• **Concerns related to adverse effects:** Agranulocytosis/neutropenia, hepatotoxicity, hypersensitivity, zinc deficiency • **Dosage form specific issues:** Available in 2 different 1000 mg oral tablet formulations (twice-a-day and 3-times-a-day formulation)
Lead (and Other) Chelators	
Chemet® (succimer)	• **Concerns related to adverse effects:** Mild to moderate neutropenia, hepatic effects, hypersensitivity reactions • **Disease-related concerns:** Encephalopathy, lead poisoning, renal impairment • **Other**: Adequate hydration should be maintained during therapy
BAL in Oil (dimercaprol)	• **Concerns related to adverse effects**: Nephrotoxicity • **Special populations**: Caution in patients with glucose 6-phosphate dehydrogenase deficiency due to increased risk of hemolytic anemia; fever may occur and persist in pediatric patients • **Disease-related concerns**: Investigate, identify, and remove sources of lead exposure; consultation with a clinical toxicologist or an expert in the treatment of heavy metal poisoning is highly recommended before use

Medication	Warnings/Precautions
	• **Dosage form specific issues**: Some dosage forms may contain large amounts of benzoic acid a metabolite of benzyl alcohol large amounts of which have been associated with potentially fatal neonatal "gasping syndrome"; contains peanut oil
Calcium Disodium Versenate	• **Concerns related to adverse effects**: Arrhythmia, ECG changes during IV therapy, nephrotoxicity • **Disease related concerns**: Investigate, identify, and remove sources of lead exposure; consultation with a clinical toxicologist or an expert in the treatment of heavy metal poisoning is highly recommended before use; caution in renal impairment • **Other**: Name confusion with edetate disodium (not commercially available in the U.S.) which should never be used to treat lead poisoning

PRACTICE GUIDELINES

Wilson Disease

Socha P, Janczyk W, Dhawan A, et al. Wilson's Disease in Children: A Position Paper by the Hepatology Committee of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 2018 Feb;66(2):334-344. doi: 10.1097/MPG.0000000000001787.

- Given its safety profile, zinc salts, preferably zinc acetate, could be used in presymptomatic children identified through family screening, or as maintenance therapy after de-coppering with chelators as long as serum transaminase levels remain normal. Grade 2C
- Children with signs of significant liver disease, such as cirrhosis or abnormal INR, should be preferably treated with copper chelating agents. Grade 2B
- Children with decompensated liver cirrhosis should be treated with a chelating agent or a combination of zinc salts and a chelating agent that may preclude the need for a liver transplantation. The King's Wilson index should be monitored for prognostic assessment and timely decision for LT. Grade 2B
- Because liver transplantation corrects the enzymatic defect, chelating agents or zinc treatment is no longer required after transplantation. Grade 1A
- Evidence for non-adherence to zinc can be assessed by measuring serum zinc levels and/or urinary zinc/copper 24-hour excretion. Grade 2B
- If increased transaminases remain or relapse despite treatment, poor compliance should be suspected. Grade 2B
- The occurrence of penicillamine-related adverse events should prompt discontinuation and switching to trientine or zinc salts according to the severity of liver disease. Grade 2B

Recommendation Definitions

Strength of Recommendation	Description
Strong (1)	Factors influencing the strength of the recommendation included the quality of the evidence, presumed patient-important outcomes, and cost
Weak (2)	Variability in preferences and values, or more uncertainty. Recommendation is made with less certainty, or higher cost or resource consumption

Quality of Evidence	Description
High (A)	Further research is unlikely to change confidence in the estimate of the effect
Moderate (B)	Further research is likely to have impact on confidence in the estimate of effect and may change the estimate
Low (C)	Any estimate of effect is very uncertain

Roberts EA, Schilsky ML; American Association for Study of Liver Diseases (AASLD). Diagnosis and treatment of Wilson disease: an update. Hepatology. 2008 Jun; 47(6): 2089-111.

- Initial treatment for symptomatic patients should include a chelating agent (D-penicillamine or trientine). Trientine may be better tolerated (Class I, Level B).
- Treatment of presymptomatic patients or those on maintenance therapy can be accomplished with a chelating agent or with zinc. Trientine may be better tolerated (Class I, Level B).
- Patients with acute liver failure due to Wilson disease should be referred for and treated with liver transplantation immediately (Class I, Level B).
- Treatment for Wilson disease should be continued during pregnancy, but dosage reduction is advisable for D-penicillamine and trientine (Class I, Level C).
- Treatment is lifelong and should not be discontinued, unless a liver transplant has been performed (Class I, Level B).
- For routine monitoring, serum copper and ceruloplasmin, liver biochemistries and international normalized ratio, complete blood count and urinalysis (especially for those on chelation therapy), and physical examination should be performed regularly, at least twice annually. Patients receiving chelation therapy require a complete blood count and urinalysis regularly, no matter how long they have been on treatment (Class I, Level C).

Recommendation Definitions

Classification	Description
Class I	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa	Weight of evidence/opinion is in favor of usefulness/ efficacy.
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.
Class III	Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/ effective and in some cases may be harmful.

Level of Evidence	Description
Level A	Data derived from multiple randomized clinical trials or meta-analyses.
Level B	Data derived from a single randomized trial, or nonrandomized studies.
Level C	Only consensus opinion of experts, case studies, or standard-of-care.

Hereditary Hemochromatosis

Kowdley KV, Brown KE, Ahn J, Sundaram V. American College of Gastroenterology Clinical Guideline: Hereditary Hemochromatosis. Am J Gastroenterol. 2019 Aug;114(8):1202-1218.

- We recommend that phlebotomy be used as the first-line treatment in patients diagnosed with HH as determined by C282Y homozygosity or C282Y/H63D compound heterozygosity (Strong recommendation, moderate quality of evidence).
- We recommend against chelation as the first-line therapy for HH, given the effectiveness of phlebotomy, the associated side effects of chelation including hepatic and renal toxicity, and the relatively small sample size of clinical trials supporting chelation (Strong recommendation, low quality of evidence).
- We recommend the use of iron chelation for the treatment of HH in the patient who is intolerant or refractory to phlebotomy or when phlebotomy has the potential for harm such as in patients with severe anemia or congestive heart failure (Strong recommendation, low quality of evidence).
- We recommend against the routine use of proton pump inhibitors (PPIs) as the primary treatment of HH (Strong recommendation, low quality of evidence).

Recommendation Definitions

Strength of Recommendation	Description
Strong	Factors influencing the strength of the recommendation included the quality of the evidence, presumed patient-important outcomes, and cost.
Weak	Variability in preferences and values, or more uncertainty. Recommendation is made with less certainty, or higher cost or resource consumption.

Quality of Evidence	Description
High	Further research is unlikely to change confidence in the estimate of the clinical effect.
Moderate	Further research may change confidence in the estimate of the clinical effect.
Low	Further research is very likely to affect the confidence on the estimate of clinical effect.
Very low	Any estimate of the effect is very certain.

Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS; American Association for the Study of Liver Diseases. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology. 2011 Jul; 54(1): 328-43

- Patients with hemochromatosis and iron overload should undergo therapeutic phlebotomy weekly (as tolerated). (1A) Target levels of phlebotomy should be a ferritin level of 50-100 µg/L. (1B)
- In the absence of indicators suggestive of significant liver disease (ALT, AST elevation), C282Y homozygotes who have an elevated ferritin (but <1000 µg/L) should proceed to phlebotomy without a liver biopsy (1B)

- Patients with end-organ damage due to iron overload should undergo regular phlebotomy to the same endpoints as indicated above (1A)
- We recommend treatment by phlebotomy of patients with non-*HFE* iron overload who have an elevated hepatic iron concentration (HIC). (1B)
- Iron chelation with either deferoxamine mesylate or deferasirox is recommended in iron overloaded patients with dyserythropoietic syndromes or chronic hemolytic anemia. (1A)

Recommendation Definitions

Strength of Recommendation	Description
Strong (1)	Factors influencing the strength of the recommendation included the quality of the evidence, presumed patient-important outcomes, and cost.
Weak (2)	Variability in preferences and values, or more uncertainty. Recommendation is made with less certainty, or higher cost or resource consumption.

Quality of Evidence	Description
High (A)	Further research is unlikely to change confidence in the estimate of the clinical effect.
Moderate (B)	Further research may change confidence in the estimate of the clinical effect.
Low (C)	Further research is very likely to impact confidence on the estimate of clinical effect.

Thalassemia

Cappellini M, Cohen A, Porter J, Taher A, Vprakasit V, eds. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT) [Internet]. 4th edition. Thalassaemia International Federation; 2021. Available at: https://www.thalassemia.org/boduw/wp-content/uploads/2021/06/TIF-2021-Guidelines-for-Mgmt-of-TDT.pdf

Iron Overload and Chelation

- Chelation therapy is an effective treatment modality in improving survival, decreasing the risk of heart failure and decreasing morbidities from transfusion-induced iron overload (A).
- Chelation therapy at the correct doses and frequency can balance iron excretion with iron accumulation from transfusion (A).
- Absolute change in total body iron in response to chelation can be calculated from change in LIC (B).
- Direction of change in body iron in response to transfusion and chelation can usually but not always be estimated from the trend in serum ferritin (B).
- Prevention of iron accumulation using chelation therapy is preferable to rescue treatment because iron-mediated damage is often irreversible, and removal of storage iron by chelation is slow - particularly after it has escaped the liver (B).
- Response to chelation is dependent on the dose applied and the duration of exposure (A).
- Response to chelation is affected by the rate of blood transfusion (B).
- Chelation can reverse iron-mediated cardiac dysfunction rapidly (within weeks) by rapid chelation of labile iron, if 24 h chelation cover is achieved (A).
- Chelation therapy removes myocardial storage iron slowly (months or years) (A).
- Over-chelation increases side effects from chelation therapy, and doses should therefore be decreased as serum ferritin or liver iron levels fall (demonstrated most clearly with DFO) (B).
- The optimal chelation regime must be tailored for the individual and will vary with their current clinical situation. (*not a graded recommendation*)
- Chelation therapy will not be effective if it is not taken regularly – a key aspect of chelation management is to work with patients to optimise adherence (B).

Cardiac Complications in Thalassemia Major

- Combined therapy with deferoxamine and deferiprone represent the best available intensive chelation for thalassaemia major patients with severe cardiac iron overload, with or without overt cardiac dysfunction or heart failure (B).

Liver Disease

- Deferoxamine, deferiprone and deferasirox are effective in decreasing total body iron burden as well as LIC (A).

Infections

- As a measure, temporary discontinuation of deferoxamine during a febrile illness until establishing whether the episode is caused by a pathogen that can use deferoxamine as siderophore or taken under control is strongly advised (B).
- Deferasirox or deferiprone can be continued during febrile episodes (C).

Endocrine Disease

- Short Stature and Retarded Growth
  - Prevention and Treatment of growth abnormalities in patients with TM should include:
    - Use of new iron-chelators with lower toxicity on the skeleton and with better patient compliance. (*not a graded recommendation*)
- Hypothyroidism
  - If subclinical hypothyroidism is detected, chelation should be intensified and the patient carefully monitored

- Impaired Glucose Tolerance (IGT) and Diabetes Mellitus (DM)
- Intensive chelation therapy is effective to normalize β-cell function and may improve insulin secretion and glucose tolerance and reduce liver iron deposition (*not a graded recommendation*).
- Summary
  - Endocrine complications, growth and pubertal delay are common manifestations of iron overloading in TM and carry significant morbidity. As such, patients with TM need regular monitoring for signs and symptoms of endocrine complications. Prevention remains the priority, and there are limited data to support a role for chelation therapy in this. Once endocrine complications have developed, management should focus on halting the progression of such complications and treating associated symptoms. (*not a graded recommendation*)
  - Normalization of total body iron load with very intensive combined chelation (deferoxamine plus deferiprone) reverses cardiac and endocrine complications of TM (B).

Osteoporosis

- Adequate iron chelation may prevent iron toxicity in the bone and sufficient blood transfusions may help prevent and treat early bone loss (*not a graded recommendation*).

Psychological Support

- Patient-reported health outcome shows that oral chelation therapy has a beneficial impact, relative to parenteral chelation (B).
- Benefits of psychological support have been suggested using a variety of approaches (C) which include:
  - targeting changes in institutional organization practices
  - patient group sessions
  - family therapy
  - patient chelation camps

Quality of Evidence	Description
A	Data derived from multiple randomized clinical trials or meta-analyses.
B	Data derived from a single randomized clinical trial or large non-randomized studies.
C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

Taher A, Musallam K, Domenica Cappellini M, eds. Guidelines for the Management of Non Transfusion Dependent Thalassemia (NTDT) [Internet]. 2nd edition. Nicosia (CY): Thalassaemia International Federation; 2018. Available at: https://thalassaemia.org.cy/wp-content/uploads/2017/10/NTDT-final-combined-1.pdf.

Iron Overload and Chelation Therapy

Phlebotomy is not an option in NTDT considering that the disease is already complicated with anemia. Some simple measures may be of benefit, like tea consumption, which decreases iron absorption and has antioxidant properties. However, iron chelation therapy is an inevitable option in iron overloaded patients with NTDT. As iron overload has been an 'overlook' condition in NTDT in the past, only few, mostly small, studies determined the efficacy and safety of iron chelation therapy in NTDT patients.

- Iron chelation therapy with deferasirox should be initiated in NTDT patients ≥ 10 years of age if:
  - Liver iron concentration ≥ 5 mg Fe/g dry weight
  - Serum ferritin level ≥ 800 ng/mL
  - Serum ferritin level > 300 to < 800 ng/mL (if liver iron concentration measurement is not possible) and other clinical or laboratory measures indicative of iron overload
- Deferasirox therapy should be discontinued when patients reach a liver iron concentration value of 3 mg Fe/g dry weight or serum ferritin level 300 ng/mL and patients should continue to be monitored for iron overload as indicated earlier
- The use of other iron chelators cannot be recommended until larger, randomized studies are available

Thrombotic Disease

- There is no sufficient evidence to recommend iron chelation or hydroxyurea therapy for the primary or secondary prevention of thrombotic or cerebrovascular disease, although when used for different indications a beneficial effect may be observed

Leg Ulcers

- There is no sufficient evidence to recommend blood transfusion, iron chelation or hydroxyurea therapy for the prevention of leg ulcers in NTDT patients, although when used for different indications a beneficial effect may be observed

Lead poisoning

WHO Guideline for Clinical Management of Exposure to Lead. World Health Organization; 2021. Available at: https://www.who.int/publications/i/item/9789240037045.

Chelation therapy in individuals exposed to lead

- Children ≤ 10 years of age
  - For a child (≤ 10 years) with a blood lead concentration ≥ 45 µg/dL, oral or parenteral chelation therapy is recommended (Strong recommendation, very low-certainty evidence).
  - For a child (≤ 10 years) with a blood lead concentration of 40 to 44 µg/dL, when there is doubt about the accuracy of the measurement, a persistently elevated blood lead concentration in spite of measures to stop exposure or significant clinical features of lead poisoning, oral chelation therapy should be considered (Conditional recommendation, very low-certainty evidence).
  - For a child (≤ 10 years) with lead encephalopathy, urgent hospital admission and parenteral chelation therapy are recommended (Strong recommendation, very low-certainty evidence).
- Non-pregnant adolescents (11–18 years) and adults (≥ 19 years) with blood lead concentration 45 to 70 µg/dL
  - For a non-pregnant adolescent girl or woman of child-bearing age who has a blood lead concentration of 45 to 70 µg/dL but who does not show clinical features of lead poisoning, oral chelation therapy should be considered (Conditional recommendation, very low-certainty evidence).
  - For a male patient aged ≥ 11 years or a woman who is no longer of child-bearing age who has a blood lead concentration of 45 to 70 µg/dL but who does not show clinical features of lead poisoning, chelation therapy is not indicated. The patient should, however, be re-evaluated within 2–4 weeks to ensure that the blood lead concentration is decreasing and the patient remains well (Conditional recommendation, very low-certainty evidence).
  - For a non-pregnant adolescent or adult with a blood lead concentration of 45 to 70 µg/dL and who has mild–moderate clinical features of lead poisoning (such as abdominal pain, constipation, arthralgia, headache, lethargy), chelation therapy is suggested (Conditional recommendation, very low-certainty evidence).
- Non-pregnant adolescents (11–18 years) and adults (≥ 19 years) with blood lead concentrations of >70 to 100 µg/dL
  - For a non-pregnant adolescent or an adult with a blood lead concentration >70 to 100 µg/dL but who does not show significant neurological features of toxicity, chelation therapy is suggested (Conditional recommendation, very low-certainty evidence).
  - For a non-pregnant adolescent or adult with a blood lead concentration >70 to 100 µg/dL and with significant neurological features of lead toxicity (e.g., irritability, drowsiness, ataxia, convulsions, coma) or lead encephalopathy, urgent parenteral chelation therapy is recommended (Strong recommendation, very low-certainty evidence).
- Pregnant women
  - For a pregnant woman with lead encephalopathy, regardless of trimester, urgent chelation therapy is recommended. The preferred chelating agent depends on the stage of the pregnancy and available data on safety of use in pregnancy (Strong recommendation, very low-certainty evidence).
  - For a pregnant woman with a blood lead concentration ≥ 45 µg/dL, with or without clinical features of lead poisoning, but without lead encephalopathy:

- In the first trimester: the guideline development group could not make a recommendation because of an uncertain balance of risks and benefits (No recommendation).
- In the second or third trimester: chelation therapy is recommended (Strong recommendation, very low-certainty evidence).

Recommendation Definitions

Strength of Recommendation	Description
Strong	The group is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.
Weak	The group concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects but is not confident of this interpretation.

Certainty of Evidence	Description
High	Further research is unlikely to change confidence in the estimate of the clinical effect.
Moderate	Further research may change confidence in the estimate of the clinical effect.
Low	Further research is very likely to affect the confidence on the estimate of clinical effect.
Very low	Any estimate of the effect is very certain.

Medical Management Guidelines for Lead. Agency for Toxic Substances and Disease Registry. Last reviewed October 2014. Available at: https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=1203&toxid=22.

- Chelation therapy should be considered for treatment of severe symptoms or markedly elevated blood lead levels. Chelation therapy is controversial in cases of asymptomatic and mildly symptomatic intoxication and should never be given prophylactically or during ongoing lead exposure. Once initiated, chelation therapy should be continued until symptoms improve and acceptable blood lead levels are achieved (Dart et al. 2004).
- Adults: In the presence of severe encephalopathy or when blood lead levels exceed 100 µg/dL, chelation should start with dimercaprol (BAL) followed in 4 hours by another dose of BAL and either succimer (if oral administration is tolerated) or CaNa2-EDTA (if intravenous infusion is required). BAL treatment is phased out while treatment with one of the other chelating agents is continued (typically for 5 days), followed by decreased or interrupted dosing because continued chelator usage is associated with decreasing amounts of urinary lead excretion (Dart et al. 2004).
- Children: Use of chelators is not recommended for blood lead levels less than 25 µg/dL. At blood lead levels between 25 and 45 µg/dL, oral chelators may be of benefit if elevated blood levels persist following environmental intervention. Children with blood lead levels between 45 and 70 µg/dL should undergo chelation, usually with oral succimer; those with encephalopathy or with blood lead levels in excess of 70 µg/dL should be admitted to the hospital for parenteral therapy with BAL and EDTA. Therapy begins with BAL intramuscularly every 4 hours, establishment of adequate urinary output (hydration as needed), followed by CaNa2-EDTA continuous infusion. CaNa2-EDTA may be administered intramuscularly in divided doses every 4 hours. This combined therapy is continued for 5 days while liver and renal functions and blood lead levels are monitored. If blood lead levels rebound after 2 days without chelation therapy, a second course of therapy may be necessary (Dart et al. 2004).

Medical Management Guidelines for Lead-exposed Adults. Association of Occupational and Environmental Clinics. April 24, 2007.

- Chelation therapy is recommended for adults with BLLs 100 µg/dL (4.83 µmol/L) or greater, can be strongly considered for BLLs 80 to 99 µg/dL (3.86-4.78 µmol/L), and possibly considered for BLLs between 50 and 79 µg/dL (2.41-3.81 µmol/L) in the presence of lead-related symptoms.

CLINICAL TRIALS/SYSTEMATIC REVIEWS/META-ANALYSES

Citation	Design	Endpoints
Schilsky ML, Czlonkowska A, Zuin M, et al. Trientine tetrahydrochloride versus penicillamine for maintenance therapy in Wilson disease (Chelate): a randomized, open-label, non-inferiority, phase 3 trial. Lancet Gastroenterol Hepatol. 2022;7(12):1092-1102.	Randomized, open-label, non-inferiority, phase 3 trial comparing penicillamine with trientine tetrahydrochloride for maintenance therapy in patients with Wilson disease. N=53 Arms: Patients were randomly assigned (1:1) to continue receiving oral penicillamine or switched to oral trientine tetrahydrochloride Inclusion criteria: Patients aged 18-75 years with stable Wilson disease who were treated for at least 1 year with penicillamine Exclusion criteria: None listed	**Primary:** Serum non-caeruloplasmin-bound copper (NCC) levels at 24 weeks **Secondary:** Urinary copper excretion at 24 weeks, side effects
Results: After 24 weeks, the mean difference in serum NCC between the penicillamine group and trientine tetrahydrochloride group was -9.1 µg/L (95% confidence interval [CI], -24.2 to 6.1), with the lower limit of the 95% CI within the defined non-inferiority margin. At 24 weeks, urinary copper excretion was lower with trientine tetrahydrochloride than with penicillamine (mean difference, 238 µg/24 h [99% CI, 116 to 360]). At 48 weeks, trientine tetrahydrochloride remained non-inferior to penicillamine in terms of NCC (mean difference NCC, -15.5 µg/L [95% CI, -34.5 to 3.6]). Urinary copper excretion at 48 weeks remained in the expected range for well treated patients in both study groups, and the mean difference (125 µg/24 h [99% CI, -37.6 to 287]) was not significantly different. The most common treatment-emergent adverse events were headache for penicillamine (19% vs. 8%) and abdominal pain for trientine tetrahydrochloride (4% vs. 15%); all treatment-emergent adverse events resolved and were mild to moderate. **Conclusion**: The efficacy of trientine tetrahydrochloride as oral maintenance therapy was non-inferior to penicillamine and well tolerated in adults with Wilson disease.		
Citation	**Design**	**Endpoints**
Bollig C, et al. Deferasirox for managing iron overload in people with thalassaemia. Cochrane Database Syst Rev. 2017 Aug 15;8:CD007476.	Systematic review and meta-analysis of randomized controlled trials (RCTs) of trials through August 2016 of deferasirox versus no therapy, placebo or another iron-chelating treatment in patients with transfusion-dependent thalassemia or NTDT. N=16 studies; 1,807 participants	**Primary:** Overall mortality measured at any point in time **Secondary:** Reduced end-organ damage, measures of iron overload, measures of iron excretion **Safety:** Any adverse events (i.e., increased SCr, kidney failure, rash, GI disturbance)
Results: Deferasirox was effective at removing iron in patients with transfusion-dependent thalassaemia when compared to placebo. Nine studies compared deferasirox with standard treatment of deferoxamine – similar effectiveness for overall mortality, reduced end-organ damage, measures of iron overload, and measures of iron excretion was considered achievable depending on the doses of the two drugs being compared. Although rates of discontinuation were similar for both drugs, patients had a higher satisfaction rate with deferasirox over deferoxamine due to fewer adverse events. **Conclusion**: Although deferasirox does not seem to be superior to deferoxamine, similar efficacy is likely achievable. Deferasirox could be offered as a reasonable, first-line option to individuals with thalassaemia and secondary iron overload who show a strong preference to deferasirox.		
Citation	**Design**	**Endpoints**
Appenenzeller-Herzog C, Mathes T, Heeres MLS, Heinz Weiss K, Houwen RHJ, Ewald H.	Systematic review and meta-analysis of prospective and retrospective, randomized and non-randomized, controlled studies and comparative observational trials through	**Primary:** Mortality and asymptomatic/improved

Comparative effectiveness of common therapies for Wilson disease: A systematic review and meta-analysis of controlled studies. Liver Int. 2019 Nov;39(11):2136-2152.	January 2019 of patients with Wilson disease (any age or stage) mostly comparing D-penicillamine to no treatment, zinc, trientine or succimer. N=23 studies; 2,055 participants	**Secondary:** Side effects, early neurological deterioration, treatment discontinuation and orthotopic liver transplantation (OLT).

Results:

D-penicillamine vs. no treatment

- Mortality – Odds ratio (OR), 0.013 (95% CI, 0.0010 to 0.17; I^2 = 31%)
- Remaining or becoming asymptomatic – OR, 22.3 (95% CI, 0.40 to 1.2 x 10^3; I^2 = 86%)
- Other outcomes were not reported for this comparison

D-penicillamine vs. zinc salts

- Mortality – OR, 0.73 (95% CI, 0.16 to 3.40; I^2 = 37%)
- Asymptomatic/improved – OR, 0.84 (95% CI, 0.48 to 1.48; I^2 = 0%)
- Side effects – OR, 3.28 (95% CI, 0.542 to 19.9; I^2 = 24%)
- Neurological deterioration – OR, 3.71 (95% CI, 0.42 to 32.7; I^2 = 10%)
- Treatment discontinuation – OR, 2.96 (95% CI, 1.14 to 7.66; I^2 = 48%)
- OLT – OR, 1.74 (95% CI, 0.066 to 46.0; I^2 = 37%)

Other comparisons

- Not enough studies comparing other drug combinations to perform meta-analysis.

Conclusion: There are some indications that zinc is safer than D-penicillamine therapy while being similarly effective in preventing or reducing hepatic or neurological Wilson Disease symptoms. Study quality was low warranting cautious interpretation of our findings.

Citation	Design	Endpoints
Cao Y, Chen A, Bottai M, Caldwell KL, Rogan WJ. The impact of succimer chelation on blood cadmium in children with background exposures: a randomized trial. J Pediatr. 2013 Aug; 163(2):598-600.	Randomized, double-blind, placebo-controlled trial utilizing cadmium, a toxic metal with known detrimental effects including renal toxicity, hypertension, and skeletal disorders, to investigate the use of the drug in lead poisoning. N=780 Arms: Children received up to three 26-day courses of succimer or placebo Inclusion criteria: Children between 12 and 33 months of age, who had a confirmed blood lead concentration between 20 and 44 µg/dL, and who lived in a residence suitable for lead dust reduction Exclusion criteria: None listed	**Primary:** Blood cadmium levels after 1-week of treatment

Results: There was almost no difference in blood cadmium levels when measured after one week. The 90th percentile group receiving succimer actually saw a slight increase in blood cadmium levels when measured after one week.

Between Group Difference of Blood Cadmium Level (µ/L) After Treatment

	Median		**75th Percentile**		**90th Percentile**	
	Difference (95% CI)	**P-value**	**Difference (95%CI)**	**P value**	**Difference (95%CI)**	**P value**

Adjusted	0.00 (-0.01 to 0.01)	0.98	0.00 (-0.01 to 0.01)	0.69	0.01 (-0.01 to 0.02)	0.42

Conclusion: Succimer has shown efficacy in animals diminishing GI absorption and cadmium tissue retention, however there is no evidence for therapeutic efficacy following chronic cadmium exposure. This trial specifically finds that succimer has no effect on background blood cadmium concentrations resulting from background exposure in U.S. children. Succimer may not reduce cadmium because succimer is mainly distributed in extracellular space while cadmium is mostly bound intracellularly to metallothionein. However it is approved for the treatment of pediatric lead poisoning as of 1991.

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (4/1/2023 to 6/30/2023)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Copper Chelators								
trientine (Syprine®) 250 mg capsule	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
Cuvrior® (trientine tetrahydrochloride) 300mg tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
penicillamine (Cuprimine®) 250 mg capsule	0	0	$0.00	$0.00	0	0 (0%)	F-PA-SP	No change
penicillamine (Depen® Titratabs) 250 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
D-Penamine (penicillamine) 125 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Galzin®(zinc acetate) 25, 50 mg capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Iron Chelators								
deferoxamine (Desferal®) 500 mg, 2 g solution for injection	0	0	$0.00	$0.00	0	0 (0%)	F-SP	No change
deferasirox (Exjade®) 125 mg, 250 mg, 500 mg dispersible tablet	0	0	$0.00	$0.00	0	0 (0%)	F-PA-AL (min 21 years)	No change
deferasirox (Jadenu®) 90 mgtablet	1	1	$80.06	$80.06	2	1 (50%)	F-PA	No change
deferasirox (Jadenu® Sprinkle) 90 mg oral granules in packet	0	0	$0.00	$0.00	0	0 (0%)	F-PA	No change
deferiprone (Ferriprox™) 500, 1000 mg tablet	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Ferriprox™ (deferiprone) 100 mg/mL oral solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Lead (and Other) Chelators								
Chemet® (succimer) 100 mg capsule	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Bal in Oil (dimercaprol) 100 mg/mL intramuscular solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Calcium Disodium Versenate 200 mg/mL injection solution	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
TOTAL	**1**	**1**	**$80.06**	**$80.06**	**2**	**1 (50%)**		

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

PRIOR AUTHORIZATION CRITERIA

Recommendation:

- For Ferriprox, also require a trial and failure of deferasirox (Exjade, Jadenu) as deferiprone is more expensive.

Iron-chelating Agents	
Therapeutic Classes (AHFS)	Heavy Metal Antagonists
Medications	Formulary, PA required Deferasirox (Jadenu) tablet -PREFERRED Deferasirox (Jadenu) granules Deferasirox (Exjade) tablet Non-Formulary Ferriprox (deferiprone) tablet Ferriprox (2 times a day) (deferiprone) 1,000 mg tablet Ferriprox (deferiprone) solution
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Physician must be a hematologist.
Coverage Duration	**Initial/Re-Approval** If all conditions are met, the request will be approved for up to 6 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.

PA Review Criteria	**INITIAL CRITERIA FOR CHRONIC IRON OVERLOAD DUE TO BLOOD TRANSFUSIONS FOR DEFERASIROX**
	• Patient must be ≥ 2 years old. (check AAH active CCS cases for members < 21 years of age)
	• Diagnosis of chronic iron overload due to blood transfusions
	• Patient receiving blood transfusions on a regular basis/participating in blood transfusion program
	• Serum ferritin concentration consistently greater than 1000mcg/L.
	  ○ If serum ferritin falls to <1,000 mcg/L at 2 consecutive visits, consider dose reduction (especially if dose is >17.5 mg/kg/day)
	  ○ (If the serum ferritin levels fall below 500 mcg/L on any one monitoring visit, deferasirox therapy discontinued).
	• Documented treatment failure, contraindication, or significant intolerance to deferoxamine (Desferal) treatment.
	• If the request is for deferasirox (Exjade) tablet, member must have tried and failed deferoxamine (Desferal) AND deferasirox (Jadenu) tablet OR a medical reason why member is unable to use (e.g. intolerance, contraindication, etc.) deferoxamine (Desferal) AND deferasirox (Jadenu) tablet must be provided.
	• If the request is for deferasirox (Jadenu) granules, member must meet the criteria above and have tried and failed deferoxamine (Desferal) AND deferasirox (Exjade) tablet AND (Jadenu) tablet OR a medical reason why member is unable to use (e.g. intolerance, contraindication, etc.) deferoxamine (Desferal) AND deferasirox (Exjade) tablet AND deferasirox (Jadenu) tablet must be provided
	
	REAUTHORIZATION CRITERIA FOR CHRONIC IRON OVERLOAD DUE TO BLOOD TRANSFUSIONS FOR DEFERASIROX

- If the request is for deferasirox (Exjade) tablet, member must have tried and failed deferoxamine (Desferal) AND deferasirox (Jadenu) tablet OR a medical reason why member is unable to use (e.g. intolerance, contraindication, etc.) deferoxamine (Desferal) AND deferasirox (Jadenu) tablet must be provided.
- Serum ferritin concentration consistently greater than 1000 mcg/L.
    - If serum ferritin falls to <1,000 mcg/L at 2 consecutive visits, consider dose reduction (especially if dose is >17.5 mg/kg/day)
    - If the serum ferritin levels fall consistently below 500 mcg/L on any one monitoring visit, deferasirox therapy must be discontinued

INITIAL CRITERIA FOR CHRONIC IRON OVERLOAD IN NON-TRANSFUSION DEPENDENT THALASSEMIA SYNDROMES FOR DEFERASIROX

- Patient must be ≥ 10 years old (check AAH active CCS cases for members < 21 years of age)
- Diagnosis of thalassemia syndrome
- Liver iron content (LIC) by liver biopsy of ≥ 5 mg Fe/g dry weight
- Serum ferritin level on ≥ 2 measurements at least one month apart of >300 mcg/L
- If the request is for deferasirox (Exjade) tablet, member must have tried and failed deferasirox (Jadenu) tablet OR a medical reason why member is unable to use (e.g. intolerance, contraindication, etc.) deferasirox (Jadenu) tablet must be provided.
- If the request is for deferasirox (Jadenu) granules, member must meet the criteria above and have tried and failed deferasirox (Exjade) tablet AND deferasirox (Jadenu) tablet OR a medical reason why member is unable to use (e.g. intolerance, contraindication, etc.) deferasirox (Exjade) tablet AND deferasirox (Jadenu) tablet must be provided

REAUTHORIZATION CRITERIA FOR CHRONIC IRON OVERLOAD IN NON-TRANSFUSION DEPENDENT THALASSEMIA SYNDROMES FOR DEFERASIROX

- If the request is for deferasirox (Exjade) tablet, member must have tried and failed deferasirox (Jadenu) tablet OR a medical reason why member is unable to use (e.g. intolerance, contraindication, etc.) deferasirox (Jadenu) tablet must be provided.
- Serum ferritin consistently > 300 mcg/L.
- If serum ferritin < 300 mcg/L, LIC must be obtained. If LIC < 3 mg Fe/g, treatment should be discontinued.

INITIAL CRITERIA FOR TRANSFUSIONAL IRON OVERLOAD DUE TO THALASSEMIA SYNDROMES OR SICKLE CELL DISEASE AND OTHER ANEMIAS FOR FERRIPROX (DEFERIPRONE)

- Patient must be ≥ 3 years old for oral solution OR ≥ 8 years old for tablets (check AAH active CCS cases for members < 21 years of age)
- Diagnosis of thalassemia syndrome ~~OR~~, or sickle cell disease, or other anemia
- Patient receiving blood transfusions on a regular basis/participating in blood transfusion program
- Serum ferritin concentration is consistently > 1000 mcg/L. If the serum ferritin levels fall consistently below 500 mcg/L, Ferriprox must be discontinued
- Documentation that the patient is unable to use deferoxamine (Desferal) parenterally
- Documented trial and failure of deferasirox (Exjade, Jadenu) or medical reason why deferasirox cannot be used
- Brand Ferriprox (2 times a day) 1000mg tablets and Ferriprox liquid will be approved with documentation of trial and failure, contraindication, or intolerance to generic deferiprone tablets

	REAUTHORIZATION CRITERIA FOR TRANSFUSIONAL IRON OVERLOAD DUE TO THALASSEMIA SYNDROMES OR SICKLE CELL DISEASE AND OTHER ANEMIAS FOR FERRIPROX (DEFERIPRONE) • Patient continues to receive blood transfusions on a regular basis/ or participates in a blood transfusion program • Serum ferritin concentration is consistently > 1000 mcg/L. If the serum ferritin levels fall consistently below 500 mcg/L, Ferriprox must be discontinued • If the request is for brand Ferriprox (2 times a day) 1000mg tablets or Ferriprox liquid, documentation of trial and failure, contraindication, or intolerance to generic deferiprone tablets
Criteria Statement	For chronic iron overload due to blood transfusions deferasirox (Jadenu) tablet is reserved for members who have used (or cannot/should not use) deferoxamine. Deferasirox (Exjade) tablet is reserved for members who have used (or cannot/should not use) deferoxamine AND (Jadenu) tablet. Deferasirox (Jadenu) granules are reserved for members who have used (or cannot/should not use) deferoxamine AND deferasirox (Jadenu) tablet AND deferasirox (Exjade) tablet. For chronic iron overload in non-transfusion dependent thalassemia syndromes deferasirox (Exjade) tablet is reserved for members who have used (or cannot/should not use) deferasirox (Jadenu) tablet. Deferasirox (Jadenu) granules are reserved for members who have used (or cannot/should not use) deferasirox (Jadenu) tablet AND deferasirox (Exjade) tablet. For transfusional iron overload due to thalassemia syndromes or sickle cell disease and other anemias, deferiprone (Ferriprox) tablet is reserved for members who are receiving blood transfusions who have used (or cannot/should not use) deferoxamine (Desferal) and deferasirox (Exjade, Jadenu). Brand Ferriprox (2 times a day) 1000mg tablets and Ferriprox liquid are reserved for members who have used (or cannot/should not use) generic deferiprone tablets.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Add the new medication Cuvrior to the policy along with criteria for review.
  - The monthly cost at the maximum dose is $57,300 per month (or $20,055/ month based on 15mg/kg dose for 70kg patient), compared to trientine at $1,745.

Penicillamine (Depen, Cuprimine), Trientine HCl (Syprine) for Wilson's disease	
Therapeutic Classes (AHFS)	Heavy Metal Antagonists
Medications	Formulary, PA required Penicillamine (Depen Titratabs) tablet Trientine (Syprine) Penicillamine (Cuprimine) capsule Non-Formulary Cuvrior (trientine tetrahydrochloride)
Covered Uses	Medically accepted indications 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** — If all criteria are met, approve for up to a 6 month duration; if all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review. **Reauthorization** — If all criteria are met, approve for up to a 12 month duration; if all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for initial approval: • Documented confirmed diagnosis of Wilson's disease • For penicillamine (Depen, Cuprimine), documented adequate trial (at least 3 months) and failure of, or intolerance to, due to significant side effects/toxicity, or a contraindication to therapy with trientine (Syprine) • For Cuvrior (trientine tetrahydrochloride), documented adequate trial (at least 3 months) and failure of, or intolerance to, due to significant side effects/toxicity, or a contraindication to therapy with BOTH trientine (Syprine) and penicillamine Criteria for re-authorization: • Documentation of positive clinical response.
Criteria Statement	Penicillamine (Depen, Cuprimine) are reserved for members who have used (or cannot/should not use) trientine (Syprine). Cuvrior (trientine tetrahydrochloride) is reserved for members who have used (or cannot/should not use) both trientine (Syprine) and penicillamine.
Last P&T Review Date	~~9/2022~~9/2023

REFERENCES

1. Lexicomp Online, Lexi-Drugs, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; June 16, 2023.
2. Facts & Comparisons, Facts & Comparisons eAnswers, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; 2013; June 16, 2023.
3. Drugs@FDA: FDA-Approved Drugs. U.S. Food and Drug Administration. www.fda.gov. Accessed on June 16, 2023.
4. Biomedtracker. Informa. Available at: www.biomedtracker.com. Accessed on June 16, 2023.
5. Bacon BR, Kwiatkowski JL. Approach to the Patient with Iron Overload. Mentzer WC, Mahoney DH, Tirnauer JS, Kunins L, eds. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on June 16, 2023.
6. Bacon BR. Iron chelators: Choice of agent, dosing, and adverse effects. Mentzer WC, Tirnauer JS, eds. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on June 16, 2023.
7. Aaseth J, Skaug MA, Cao Y, Anderson O. Chelation in metal intoxication—Principles and paradigms. J Trace Elem Med Biol. 2015; 31:260-6.
8. Socha P, Janczyk W, Dhawan A, et al. Wilson's Disease in Children: A Position Paper by the Hepatology Committee of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr. 2018 Feb;66(2):334-344. doi: 10.1097/MPG.0000000000001787.
9. Roberts EA, Schilsky ML; American Association for Study of Liver Diseases (AASLD). Diagnosis and treatment of Wilson disease: an update. Hepatology. 2008 Jun; 47(6): 2089-111.
10. Kowdley KV, Brown KE, Ahn J, Sundaram V. American College of Gastroenterology Clinical Guideline: Hereditary Hemochromatosis. Am J Gastroenterol. 2019 Aug;114(8):1202-1218. doi: 10.14309/ajg.0000000000000315.
11. Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS; American Association for the Study of Liver Diseases. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver Diseases. Hepatology. 2011 Jul; 54(1): 328-43.
12. Cappellini M, Cohen A, Porter J, Taher A, Vprakasit V, eds. Guidelines for the Management of Transfusion Dependent Thalassaemia (TDT) [Internet]. 4th edition. Thalassaemia International Federation; 2021. Available at: https://www.thalassemia.org/boduw/wp-content/uploads/2021/06/TIF-2021-Guidelines-for-Mgmt-of-TDT.pdf.
13. Taher A, Musallam K, Domenica Cappellini M, eds. Guidelines for the Management of Non Transfusion Dependent Thalassemia (NTDT) [Internet]. 2nd edition. Nicosia (CY): Thalassaemia International Federation; 2018. Available at: https://thalassaemia.org.cy/wp-content/uploads/2017/10/NTDT-final-combined-1.pdf.
14. WHO Guideline for Clinical Management of Exposure to Lead. World Health Organization; 2021. Available at: https://www.who.int/publications/i/item/9789240037045.
15. Medical Management Guidelines for Lead. Agency for Toxic Substances and Disease Registry. Last reviewed October 2014. Available at: https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=1203&toxid=22.
16. Medical Management Guidelines for Lead-exposed Adults. Association of Occupational and Environmental Clinics. April 24, 2007. Available at: http://www.aoec.org/documents/positions/MMG_FINAL.pdf.
17. Schilsky ML, Czlonkowska A, Zuin M, et al. Trientine tetrahydrochloride versus penicillamine for maintenance therapy in Wilson disease (Chelate): a randomized, open-label, non-inferiority, phase 3 trial. Lancet Gastroenterol Hepatol. 2022;7(12):1092-1102.
18. Bollig C, et al. Deferasirox for managing iron overload in people with thalassaemia. Cochrane Database Syst Rev. 2017 Aug 15;8:CD007476.
19. Appenenzeller-Herzog C, Mathes T, Heeres MLS, Heinz Weiss K, Houwen RHJ, Ewald H. Comparative effectiveness of common therapies for Wilson disease: A systematic review and meta-analysis of controlled studies. Liver Int. 2019 Nov;39(11):2136-2152.
20. Cao Y, Chen A, Bottai M, Caldwell KL, Rogan WJ. The impact of succimer chelation on blood cadmium in children with background exposures: a randomized trial. J Pediatr. 2013 Aug; 163(2):598-600.

PERFORMRx℠

Respiratory Aids, Devices and Equipment

Executive Summary

CLASS OVERVIEW

The following review includes a variety of devices and equipment used for the treatment of respiratory conditions such as Chronic Obstructive Pulmonary Disease (COPD) and asthma. Commonly, patients can experience difficulty with proper inhaler technique for a variety of reasons, leading to deposition of the inhaled medication to the oral mucosa or upper airways rather than the lungs. This can result in sub-optimal therapeutic results and in some cases (such as with inhaled corticosteroids) adverse drug reactions such as fungal infections of the mouth.

Devices such as spacers and nebulizers are designed to assist in delivery of the respective medication more efficiently to the lungs. Spacers and valved-holding chambers are devices which are attached to the mouthpiece of the inhaler and reduce the particle size of the plume released, and can allow more time for a slower inhale or alleviate some of the coordination issues some patients may have with actuation and inhalation. Nebulizers, while there are several different types of devices, all function to atomize liquid medication into a mist, which is then inhaled by the patient through a mouthpiece or mask over several minutes time. There is no need to coordinate actuation and breath with a nebulizer, and they can be used in special circumstances such as mechanically ventilated patients or in patients with a tracheostomy.

Peak flow meters are devices used to measure the maximum expiratory rate of a patient over a short and forceful exhale. This measurement reasonably correlates to a patient's percent predicted value for the forced expiratory volume in one second (FEV_1), which indicates the degree of airflow limitation being experienced by the patient and is helpful in monitoring asthma symptoms and severity.

There are a wide variety of products available in this category, and device selection is driven by multiple variables such as patient preferences, condition and severity, choice of pharmacotherapy, provider experience, availability, and cost. Many of these products require prescription, but over the counter (OTC) options also exist.

UTILIZATION FINDINGS

There were 4 claims for 4 members, for a total cost of $97, and an average cost per claim of $24. There were no prior authorization requests.

RECOMMENDATIONS

- Align formulary all peak flow meters and nebulizers to have a QL of 1 per 365 days
- Align formulary spacers to have a QL of 2 per 365 days

FORMULARY PLACEMENT, UTILIZATION AND COST EXPERIENCE (4/1/2023 to 6/30/2023)

UTILIZATION HISTORY			COST		PRIOR AUTH HISTORY		FORMULARY PLACEMENT	
Medication	Rx	Mbrs	Total	Avg/Rx	Total	Approved (%)	Current	Recommend
Nebulizers and Supplies-OTC								
Easy Neb Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
EasyAir Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Compact Ultrasonic Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Compact Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Intelligent Mesh Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
PureAir Mini Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
nebulizers	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Peak Flow Meters-OTC								
Airzone Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	F	→ **F-QL (1/365)**
Asthma Check Meter	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Clever Choice Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
In-Check Oral Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Microlife Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Peak Air Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
Pocket Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
PureComfort Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Spacers and Accessories-OTC								
Mouthpiece device	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
One Way Valved Mouthpiece device	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Panda Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Pediatric Medium Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Pediatric Panda Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Pediatric Small Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Personal Best Full Range device	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
Personal Best Low Range device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Piko 1 device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pro Comfort Spacer-Adult Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Pro Comfort Spacer-Child Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Pro Comfort Spacer-Infant Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Pure Comfort Spacer-Adult Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Sidestream Pediatric Face Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change

Silicone Mask - Pediatric	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Vortex Adult Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
WINDMILL TRAINER device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
In-Check Dial Training Device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
In-Check Nasal With Mask	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Nasal Strips, Vaporizers, Humidifiers-OTC								
Breathe Right strips	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Breathe Right Vapor topical strips	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Nasal Strips Large	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Nasal Strips Medium-Large	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Nasal Strips Small-Medium	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
humidifiers	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Cool Mist Humidifier	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Procare Humidifier	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pure Comfort Humidifier	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Warm Steam Vaporizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
vaporizers	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Vicks Warm Steam Vaporizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Nebulizers and Supplies-Rx								
AeroEclipse II Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	F	**→ F-QL (1/365)**
Aeroneb Go Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Airs Disposable Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
Altera Nebulizer Handset	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Altera Nebulizer System	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Aura Portaneb misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Clever Choice Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Clever Choice Whisper Aire Pediatric device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Comp-Air Nebulizer Compressor	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Devilbiss Disposable Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
DeVilbiss Pulmo-Aide Compressor	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Devilbiss PulmoMate Compressor	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
DeVilbiss PulmoNeb LT Compressor-Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Devilbiss Traveler Compressor	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
eBase Controller device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
FLYP Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Home Nebulizer Plus Sidestream	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
InnoSpire Deluxe device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
InnoSpire Elegance device	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
InnoSpire Essence device	1	1	$26.29	$26.29	0	0 (0%)	F-QL (1/365)	No change

Innospire Go Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
InnoSpire Mini device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
MicroAir Mesh Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Mini Plus Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
nebulizer and compressor	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Ombra Compressor System	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pari LC Plus Nebulizer Set	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
Pari LC Sprint Sinus misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pari Sinus Aerosol System device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pari Trek S Combo Pack device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pari Trek S Compact Compressor	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pediatric Bear Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pediatric Comp-Air Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pediatric Dinosaur Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pediatric Dog Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pediatric Frog Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
PFLEX Inspiratory Trainer device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Portable Nebulizer System	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Procare Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Procare Pediatric Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Prodigy Mini-Mist Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Proneb Max Compressor-LC Plus	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Proneb Max Compressr-LC Sprint device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Provent nasal device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Provent Starter nasal device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Pulmo-Aide Compressor	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
PulmoNeb LT Compressor Nebul	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Quake Vibratory PEP device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sami The Seal device	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
Sidestream misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sidestream Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sidestream Plus misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sinustar Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
SmartNeb Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
SootheNeb Compressor Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
SootheNeb Mesh Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Sunrise Compressor-Nebulizer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Threshold IMT Trainer device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Threshold PEP Device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

TruNeb Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Vios Aerosol Delivery System	0	0	$0.00	$0.00	0	0 (0%)	F-QL (1/365)	No change
VixOne Nebulizer misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Willis The Whale Compressor Nebulizer System	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Peak Flow Meters-Rx								
Mini Wright Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	F	→ **F-QL (1/365)**
Truzone Peak Flow Meter	0	0	$0.00	$0.00	0	0 (0%)	F	→ **F-QL (1/365)**
Spacers and Accessories-Rx								
Ace Aerosol Cloud Enhancer spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerobika Oscillating PEP System device	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Aerochamber Mini	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerochamber MV spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerochamber Plus Flow-Vu	1	1	$36.36	$36.36	0	0 (0%)	F-QL (2/365)	No change
Aerochamber Plus Flow-Vu,Large Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerochamber Plus Flow-Vu,Medium Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerochamber Plus Flow-Vu,Small Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerochamber Plus Z Stat Large Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
AeroChamber Plus Z Stat Medium Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
AeroChamber Plus Z Stat Small Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerochamber Plus Z Stat spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
AeroChamber Z-Stat Plus-Flow Signal	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerogear Action Asthma Kit	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
AeroTrach Plus spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Aerovent Plus spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Asthmapack Children's kit	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
BreatheRite MDI Spacer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
BreatheRite Spacer and Mask, Adult	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
BreatheRite Spacer and Mask, Child	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
BreatheRite Spacer and Mask, Infant	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
BreatheRite Spacer and Mask, Neonate	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
BreatheRite Spacer and Mask, Small Child	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
BreatheRite Valved MDI Chamber spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
BreatheRite Valved MDI Spacer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Clever Choice Holding Chamber-Large Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Clever Choice Holding Chamber-Medium Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Clever Choice Holding Chamber-Small Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Compact Space Chamber	1	1	$17.58	$17.58	0	0 (0%)	F-QL (2/365)	No change
Compact Space Chamber-Lrg Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Compact Space Chamber-Med Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change

Compact Space Chamber-Sm Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
EasiVent Holding Chamber	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
EasiVent Mask Large	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
EasiVent Mask Medium	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
EasiVent Mask Small	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Flexichamber spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Flexichamber-Large Child Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Flexichamber-Small Adult Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Flexichamber-Small Child Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
InspiraChamber spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
InspiraChamber with Mask-Large	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
InspiraChamber with Mask-Med	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
InspiraChamber with Mask-Small	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
LC Plus misc	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
LC Plus Nebulizer-Pediatric Mask	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
LiteAire MDI Chamber	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Lite Touch-Medium Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
LiteTouch-Large Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
LiteTouch-Small Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Microchamber spacer	0	0	$0.00	$0.00	0	0 (0%)	F	**→ F-QL (2/365)**
Microspacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Optichamber Adult Mask-Large	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
OptiChamber Diamond VHC spacer	1	1	$17.31	$17.31	0	0 (0%)	F-QL (2/365)	No change
OptiChamber Diamond VHC with Large Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
OptiChamber Diamond VHC with Medium Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
OptiChamber Diamond VHC with Small Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
POCKET CHAMBER spacer	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
PrimeAire spacer	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
Procare Spacer With Adult Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Procare Spacer With Child Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
ProChamber	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
RiteFlo Aerochamber	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Silicone Mask - Infant	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Space Chamber	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Space Chamber with Large Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Space Chamber with Medium Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Space Chamber with Small Mask	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
VixOne Nebulizer-Adult Mask	0	0	$0.00	$0.00	0	0 (0%)	NF	No change
VixOne Nebulizer-Pediatric Mask	0	0	$0.00	$0.00	0	0 (0%)	NF	No change

Vortex Holding Chamber	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Vortex VHC Frog Mask-Child	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Vortex VHC Ladybug Mask-Toddler	0	0	$0.00	$0.00	0	0 (0%)	F-QL (2/365)	No change
Total	**4**	**4**	**$97.54**	**$24.39**	**0**	**0 (0%)**		

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

PRIOR AUTHORIZATION CRITERIA

Recommendation:

- Retire. There are various formulary spacers. All non-formulary items can be reviewed via the general non-formulary policy.

Inhaler Assistant Devices	
Therapeutic Classes (AHFS)	Devices
Medications	Preferred formulary spacers with quantity limit of #2 per 365 days: Vortex (Rx) Aerochamber (Rx)
Covered Uses	Medically accepted indications 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 #2 spacers per 365 days. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	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. Non-formulary spacers are approved when the following criteria is met: • Documentation of adequate justification for using a non-formulary spacer instead of a formulary product
Criteria Statement	Non-formulary spacers are reserved for members who have used (or cannot/should not use) a formulary spacer
Last P&T Review Date	~~9/2022~~9/2023

REFERENCES

1. Hess D, Dhand R. The use of inhaler devices in adults. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on February 6, 2023.
2. Hess D, Dhand R. Delivery of inhaled medication in adults. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed February 6, 2023.
3. Gerald L, Carr T. Peak expiratory flow monitoring in asthma. UpToDate. Waltham, MA: UpToDate Inc. http://www.uptodate.com. Accessed on February 6, 2023.

Alameda Medication Request Guidelines (MRGs) For Review Q3 2023 P&T: Changes

Recommendation:

- Change indication- this medication's labeled indication now is for PBA and is no longer is limited to PBA secondary to ALS or MS.

Nuedexta (dextromethorphan/quinidine)	
Therapeutic Classes (AHFS)	Central nervous system agents, miscellaneous
Medications	Formulary, PA required Nuedexta (dextromethorphan/quinidine)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be a neurologist 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	Criteria for initial authorization: • For a diagnosis of Pseudobulbar Affect (PBA) ~~secondary ALS or MS,~~ approve • For all other diagnoses, use off label criteria Criteria for re-authorization: • Patient is stable and continuing the medication AND • Medication is used for appropriate indication and at appropriate dose
Criteria Statement	Nuedexta is reserved for members who have a diagnosis of pseudobulbar affect.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Remove sodium hyaluronate from list, as it is off the market

Cartilaginous Repair Agents	
Therapeutic Classes (AHFS)	Anti-inflammatory/antiarthritic agents, misc; devices
Medications	Formulary, PA required Euflexxa (hyaluronate sodium) – preferred agent Non-formulary (non-preferred agents) Hyalgan (hyaluronate sodium) Durolane Genvisc 850 Trivisc ~~Sodium hyaluronate~~ Synvisc Synvisc-One Orthovisc Monovisc Gel-One Visco-3 Hymovis Triluron Gelsyn-3 Supartz FX Any other hyaluronic acid/cartilaginous repair agent 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 Approval** One complete course of treatment (based on the FDA labeled dose of the drug requested). **Later approvals** One complete course of treatment (based on the FDA labeled dose of the drug requested).
PA Review Criteria	****ALL requests are to be forwarded to AAH for review**** Initial authorization: • Diagnosis of osteoarthritis (OA)/degenerative joint disease (DJD) of the knee • Documentation (in claim history or provider statement) the patient recently (over the past 4 months) has had adequate trials on simple analgesics (acetaminophen containing products) AND NSAIDs (including 2 different prescription strength NSAIDS) on a continuous basis for 3 months without success or has a medical reason (intolerance, hypersensitivity, contraindication, etc.) for not being able to utilize simple analgesic products and NSAIDs. • Documentation patient has recently (within past 12 months) tried at least ONE steroid injection without success, per affected knee or has a medical reason for not being able to utilize steroid injections.

	• Documentation of at least one course of physical therapy for knee osteoarthritis • Attestation confirming that the patient has no contraindications to the injections (active joint infection, bleeding disorder) • If the medication request is for hyaluronic acid derivative (HAD) product other than Euflexxa, the patient has a documented medical reason (intolerance, hypersensitivity, contraindication, etc.) for not taking Euflexxa to treat their medical condition. Re-authorization • Documentation was submitted that the patient had an objective response to the treated knee(s) (e.g. decreased joint pain or stiffness, improved knee range of motion, etc) that lasted for ≥ 6 months to previous HAD therapy. • Documentation was submitted that the member has a return of symptoms of osteoarthritis that has not responded to analgesics or NSAIDs, or has a medical reason (intolerance, hypersensitivity, contraindication, etc) for not being able to utilize these therapies. • If the medication request is for hyaluronic acid derivative (HAD) product other than Euflexxa, the patient has a documented medical reason (intolerance, hypersensitivity, contraindication, etc) for not taking Euflexxa to treat their medical condition.
Criteria Statement	For osteoarthritis (OA)/degenerative joint disease (DJD) of the knee, Euflexxa is reserved for members who have used (or cannot/should not use) acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) and steroids, and have had physical therapy for knee osteoarthritis. For osteoarthritis (OA)/degenerative joint disease (DJD) of the knee, other hyaluronic acid derivative products are reserved for members who have used (or cannot/should not use) Euflexxa.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Add new medication Miebo to policy and F-PA status (DDID 223267)
  - Price for 3ml container = $ 771.00
- Update diagnoses to be all inclusive of all listed agents in policy
- Remove bullet point regarding approvals for ocular graft vs host disease and transplant rejection. These are off label and should be reviewed via the off label policy
- Spelling correction

Ophthalmic Anti-inflammatory Immunomodulators	
Therapeutic Classes (AHFS)	EENT anti-inflammatory agents, miscellaneous.
Medications	**Formulary, step therapy required** Cyclosporine (Restasis) 0.05% ~~droperette~~dropperette **Formulary PA (prior authorization required)** Restasis multidose (cyclosporine) 0.05% drops Xiidra (lifitegrast) 5% ~~droperette~~dropperette Cequa (cyclosporine) 0.09% ophthalmic ~~droperette~~dropperette Tyrvaya (varenicline) 0.03mg nasal spray Miebo (perfluorohexyloctane) 100% drops (1.338 gm/ml) Any other newly approved agents
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **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 cyclosporine (Restasis) 0.05% ~~droperette~~dropperette: • Diagnosis of dry eye syndrome (decreased tear production) whose lack of tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca, dry eye, or treatment of the signs and symptoms of dry eye disease. AND • Documented trial and failure or intolerance to at least 30-day trials each of two different artificial tear products, one of which must be high viscosity artificial tears (e.g. methylcellulose, polyvinyl alcohol, polyethylene glycol, or oil containing) ~~OR~~ ~~• Diagnosis of ocular graft vs. host disease or corneal transplant rejection prophylaxis~~ The following criteria must be met for formulary prior authorization required medications~~Restasis Multidose, Xiidra, Cequa, or Tyrvaya~~: • Diagnosis of dry eye syndrome (decreased tear production) whose lack of tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca, dry eye, or treatment of the signs and symptoms of dry eye disease.. AND

	• Documented trial and failure or intolerance to at least 30-day trials each of two different artificial tear products, one of which must be high viscosity artificial tears (e.g. methylcellulose, polyvinyl alcohol, polyethylene glycol, or oil containing) AND • Documented trial and failure, intolerance, contraindication, or inability (i.e., drug interaction, allergy, adverse reaction, etc.) to use cyclosporine (Restasis) 0.05% ~~droperette~~dropperette
Criteria Statement	For dry eye syndrome, cyclosporine (Restasis) 0.05% ~~droperette~~dropperette is reserved for members who have previously used (or cannot/should not use) artificial tears~~. OR members who have a diagnosis of ocular graft vs. host disease or corneal transplant rejection prophylaxis~~. Restasis Multidose, Xiidra, Cequa, Miebo, or Tyrvaya are reserved for members who have previously used (or cannot/should not use) artificial tears and cyclosporine (Restasis) 0.05% ~~droperette~~dropperette.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Retire policy.
- This medication is available generically for less than $0.60 per tablet.
- A psychiatrist specialist requirement represents an operational barrier.
- Defer to the general Non-Formulary and PA Required Medications without Drug-Specific Criteria policy which requires trial and failure of 2 preferred formulary medications.

Desvenlafaxine succinate (Pristiq)	
Therapeutic Classes (AHFS)	Antidepressants
Medications	Formulary, PA required desvenlafaxine succinate (Pristiq)
Covered Uses	Medically accepted indications 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	Prescribing physician is a psychiatrist
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 • Prescribing physician is a psychiatrist OR • Diagnosis of depression AND documented previous trial and failure of two formulary antidepressant alternatives (i.e. venlafaxine, venlafaxine ER capsules, fluoxetine, citalopram, paroxetine, or sertraline).
Criteria Statement	Desvenlafaxine succinate (Pristiq) is reserved for members who have a diagnosis of depression and have used (or cannot/should not use) two formulary alternatives, for example, venlafaxine, venlafaxine ER capsules, fluoxetine, citalopram, paroxetine, or sertraline.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Add new products Stimufend (pegfilgrastim-fpgk), Fylnetra (pegfilgrastim-pbbk), and Rolvedon (eflapegrastim-xnst) to policy and rearrange order of listings.

White Blood Cell Stimulators	
Therapeutic Classes (AHFS)	Hematopoietic agents
Medications	Formulary, PA required Mozobil (plerixafor) Leukine (sargramostim) Ziextenzo (pegfilgrastim-bmez) – PREFERRED AGENT Fulphila (pegfilgrastim-jmdb) Udenyca (pegfilgrastim-cbqv) ~~Ziextenzo (pegfilgrastim-bmez) – PREFERRED AGENT~~ Stimufend (pegfilgrastim-fpgk) Fylnetra (pegfilgrastim-pbbk) Nivestym (filgrastim-aafi) – PREFERRED AGENT Zarxio (filgrastim-sndz) Releuko (filgrastim-ayow) Non-formulary Nyvepria (pegfilgrastim-apgf) Neulasta (pegfilgrastim) Neulasta (pegfilgrastim) Onpro Neupogen (filgrastim) Granix (filgrastim-aafi) ~~Nyvepria (pegfilgrastim-apgf)~~ Rolvedon (eflapegrastim-xnst) Any other newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber must be a hematologist/oncologist.
Coverage Duration	**Initial Approval** 12 weeks or as recommended per FDA approved indications and/or as defined by the medical compendium as defined above and/or per the NCCN or ASCO standard of care guidelines If conditions are not met, the request will be sent to a clinical reviewer. **Later Approval** For all indications except chronic neutropenia: 12 weeks. For chronic neutropenia: 24 weeks. If all of the criteria are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	For approval: • Drug is being used for an FDA-approved indication at an FDA approved dose. AND

	• If the request is for Leukine: Documentation is submitted of the patient's current diagnosis, current bodyweight, body surface area and absolute neutrophil count (within 30 days of the request). • If the request is for a pegfilgrastim formulation or Rolvedon: ○ The patient has a documented treatment failure (i.e. failure to reach and/or maintain target ANC, prolonged febrile neutropenia or infection requiring prolonged anti-infection use) with the use of the preferred agent: Ziextenzo and/or has another documented medical reason (intolerance, hypersensitivity, etc.) for not using Ziextenzo to treat their medical condition. ○ If the request is for acute hematopoietic radiation injury syndrome, Neulasta can be approved without prior use of Ziextenzo or medical reason for not using Ziextenzo. • If the request is for a filgrastim formulation:~~.~~ ○ The patient has a documented treatment failure (i.e. failure to reach and/or maintain target ANC, prolonged febrile neutropenia or infection requiring prolonged anti-infection use) with the use of the preferred agent: Nivestym and/or has another documented medical reason (intolerance, hypersensitivity, etc.) for not using Nivestym. ○ If the request is for acute hematopoietic radiation injury syndrome, Neupogen can be approved without prior use of Nivestym or medical reason for not using Nivestym. • If the request is for Mozobil: Documentation is submitted of the patient's current diagnosis, current body weight, and that the patient is using Mozobil in combination with a granulocyte-colony stimulating factor (G-CSF) agent (i.e. Zarxio or Fulphila)
Criteria Statement	Neupogen, Zarxio, Releuko, and Granix are reserved for members who have used (or cannot/should not use) Nivestym. Neulasta, Fulphila, Nyvepria, Stimufend, Fylnetra, Rolvedon, and Udenyca are reserved for members who have used (or cannot/should not use) Ziextenzo. Mozobil is reserved for members who are using Mozobil in combination with a granulocyte-colony stimulating factor (G-CSF) agent (i.e. Zarxio or Fulphila)
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Remove the age limit from the estradiol patch products (restricted to members aged 40 and above).

DDID	Drug name
64319	Estradiol Transdermal Patch Twice Weekly 0.025 MG/24HR
64322	Estradiol Transdermal Patch Twice Weekly 0.05 MG/24HR
64323	Estradiol Transdermal Patch Twice Weekly 0.075 MG/24HR
64325	Estradiol Transdermal Patch Twice Weekly 0.1 MG/24HR
64326	Estradiol Transdermal Patch Weekly 0.025 MG/24HR
82730	Estradiol Transdermal Patch Weekly 0.0375 MG/24HR
66199	Estradiol Transdermal Patch Weekly 0.05 MG/24HR
82731	Estradiol Transdermal Patch Weekly 0.06 MG/24HR
64328	Estradiol Transdermal Patch Weekly 0.075 MG/24HR
66200	Estradiol Transdermal Patch Weekly 0.1 MG/24HR

- Remove Vantas from criteria as it was discontinued and is no longer available.
- Update covered uses section to most current resources

Drugs for Gender Dysphoria For Less Than 21 Years Old	
Therapeutic Classes (AHFS)	Androgens; Antineoplastic Agents; Estrogens; Gonadotropins; Mineralocorticoid (Aldosterone) Antagonists; 5-Alpha-Reductase Inhibitors; Progestins
Medications	**Anti-androgens and progestins (Adjunct)** Formulary • Spironolactone (Aldactone) 25, 50, 100mg tablet • Finasteride (Proscar) 5mg tablet • Dutasteride (Avodart) 0.5mg capsule • Progesterone (Prometrium) 100, 200mg capsule • Medroxyprogesterone 2.5, 5mg tablet • Medroxyprogesterone acetate intramuscular (Depo-Provera) 150mg/mL Non-formulary: • Depo-Provera 400mg/mL injectable suspension • Progesterone 50mg/mL oil solution **Estrogen Agents for Male-to-Female (MTF)** Formulary • Estradiol (Estrace) 0.5, 1, 2mg tablet • Premarin 0.3, 0.45, 0.625, 0.9, 1.25mg tablet • Estradiol-*once*-weekly 0.025, 0.0375, 0.05, 0.06, 0.075, 0.1mg patch: ~~restricted to members ≥40 years old and~~QL of #12 per 84 days • Estradiol-*twice*-weekly 0.025, 0.05, 0.075, 0.1mg patch: ~~restricted to members ≥40 years old and~~QL of #24 per 84 days • Estradiol valerate 20mg/mL, 40mg/mL vial: 1 vial per 30 days Non-formulary • Depo-Estradiol (estradiol cypionate) 5mg/mL **Testosterone Agents for Female-to-Male (FTM)** Formulary (first-line) • Testosterone cypionate 100mg/mL (QL #10 ml/30 days), 200mg/mL intramuscular oil (QL #5 ml/30 days)

Drugs for Gender Dysphoria For Less Than 21 Years Old	
	• Testosterone (Vogelxo) 1% gel pump (QL #300gm/30 days) • Testosterone (Androgel) 1.62% gel pump (QL #300gm/30 days) Formulary, PA required (second-line) • 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) Non-formulary • 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 **Gonadotropin-Releasing Hormone Receptor Agonists (GnRHa)** Formulary, PA required • Lupron Depot-Ped 1-Month (leuprolide) 7.5, 11.25, 15, 30 mg syringe kit (for less than 18 years) • Lupron Depot (leuprolide) 3.75, 7.5, 11.25, 22.5, 30, 45mg syringe kit • Leuprolide acetate 1mg/0.2mL solution kit Non-formulary • Trelstar (triptorelin) 3.75, 11.25, 22.5 mg Mixject suspension • Eligard (leuprolide acetate) 7.5, 22.5, 30, 45mg subQ • Zoladex (goserelin acetate) 3.6, 10.8mg subQ implant • ~~Vantas (histrelin) 50mg subQ implant kit~~ • Supprelin LA (histrelin) 50mg subQ implant kit • Triptodur 6-month (triptorelin) 22.5mg • Fensolvi (leuprolide acetate) syringe kit Any other newly marketed agent to treat gender dysphoria *Requests for greater than indicated quantity or age limits will be reviewed on a case by case basis
Covered Uses	Medically accepted indications are defined using the following disease specific guidelines:Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline ~~the Endocrine Society clinical practice guidelines for transsexual persons~~; ~~the~~ World Professional Association for Transgender Health (WPATH) Standards of care for the health of transgender and gender diverse people; American College of Obstetrician and Gynecologists (ACOG): Committee opinion on health care for transgender and gender diverse individuals: the TransActive Education and Advocacy Group; the World Health Organization (WHO)
Exclusion Criteria	Contraindications to any of the medications listed above

Drugs for Gender Dysphoria For Less Than 21 Years Old	
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	See "**PA Review Criteria**" below
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 24 months **Exception Approval** 3 months if requested labs are outside of recommended range or not provided; further approval requires requested labs and/or action plan submitted
PA Review Criteria	****Cosmetic medications used to treat gender dysphoria, mental health, or substance use disorder ARE approved as appropriately indicated (e.g. FDA approval, compendia supported, etc.).**** ****ALL requests are to be forwarded to AAH for review**** **INITIAL CRITERIA to start treatment for non-preferred drugs and preferred drugs that require PA, the following must be met:** • Clinic notes or consult detailing the diagnosis of gender dysphoria / gender identity disorder (GID) per DSM-V diagnostic criteria made by a qualified mental health professional • Documentation of patient readiness to start GnRHa and/or cross-sex hormone therapy • Must meet the class specific criteria outlined below • Dosage prescribed based on recommendations from medical compendia and/or the Food And Drug Administration (FDA) as appropriate • For formulary agents with prior authorization, approve for 12 months if meet ALL of the initial criteria to start treatment; for non-formulary agents, must have documentation showing trial and failure, contraindication, intolerance and/or side effects to formulary agents, as outlined in the individual sections below **Estrogen Agents (for Male-to-Female):** INITIAL CRITERIA to start treatment: • Documentation member is at least 16 years of age AND at least in Tanner stage 2 • Documentation member does NOT have: history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months; known or suspected breast cancer • If requesting estradiol cypionate injection, documentation trial and failure, contraindication, intolerance and/or side effects to one formulary oral estrogen agent and estradiol valerate injection • If requesting transdermal estrogen patch, ~~and under the age limit,~~ documentation of trial and failure, contraindication, intolerance and/or side effects to formulary oral **and** injectable estrogen agents • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") RENEWAL CRITERIA: • Documentation of estradiol levels (less than 200 pg/ml) and testosterone levels (less than 55 ng/dL) • Documentation member does NOT have: history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months; known or suspected breast cancer • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration" for approval limit)

Drugs for Gender Dysphoria For Less Than 21 Years Old	
	Testosterone Agents (for Female-to-Male): INITIAL CRITERIA to start treatment: • Documentation member is at least 16 years of age **and** at least in Tanner stage 2 • No evidence of known or suspected breast cancer and/or pregnancy • If requesting formulary-prior authorization required testosterone agents, documentation trial and failure, contraindication, intolerance and/or side effects to one first-line formulary injectable testosterone agent AND one first-line formulary topical testosterone agent • If requesting non-formulary testosterone agents, documentation trial and failure, contraindication, intolerance and/or side effects to one first-line formulary injectable testosterone agent AND one first-line formulary topical testosterone agent AND at least one formulary PA-required, (second-line) testosterone agent • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") RENEWAL CRITERIA: • Documentation of hematocrit less than 50% • Documentation of testosterone levels; discontinue or reduce dose if greater than 1000 ng/dL • No evidence of known or suspected breast cancer and/or pregnancy • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") **Antiandrogens and Progesterone Agents (Adjunct):** INITIAL CRITERIA for non-formulary agents: • Documentation member is at least 18 years of age • Require documentation of trial and failure, intolerance, contraindication, or inability to use spironolactone, dutasteride, finasteride, medroxyprogesterone acetate tablet and medroxyprogesterone acetate IM. • Documentation member does NOT have known or suspected pregnancy • For medroxyprogesterone: documentation member does NOT have history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months and/or severe liver disease • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") RENEWAL CRITERIA for non-formulary agents: • No evidence that member is currently pregnant • For medroxyprogesterone: documentation member does NOT have history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months and/or severe liver disease • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") **GnRHa:** INITIAL CRITERIA to start treatment: • Documentation of baseline labs for LH, FSH, estradiol and testosterone levels at pubertal levels AND at least in Tanner stage 2 • Documentation of weight • Members less than 18 years old: Lupron Depot-Ped 1-Month and leuprolide acetate solution are preferred agents • Members greater than or equal to 18 years old: Lupron Depot (1-, 3-, 4-, and 6)-Month and leuprolide acetate solution are preferred agents

Drugs for Gender Dysphoria For Less Than 21 Years Old	
	• If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") RENEWAL CRITERIA: • Members less than 16 years of age: Documentation of bone age on x-ray of left hand AND bone density on x-ray absorptiometry • Documentation there is a continual need to delay puberty until at least 21 years of age (i.e. extreme short stature) **For requests over the quantity limit:** • The member must have a documented treatment failure with the drug prescribed at the health plan's quantity limit **OR** the member requires a dose within prescribing guidelines that exceeds the plan's quantity limit~~.~~ **AND** • The provider has submitted a medical reason why the plan's quantity limit will be inadequate based on the member's condition and treatment history~~.~~ **AND** • The dose requested is supported by the Medical Compendia or current treatment guidelines. **Continuation of therapy for NEW members from another health plan:** • If criteria are met for initial authorization, coverage duration is 12 months • If criteria are not met for initial authorization and/or requested labs are outside of recommended range **or** not provided, allow one-time coverage duration of 3 months until all of requested labs and clinic notes are received
Criteria Statement	**Estradiol cypionate injection:** For use in gender dysphoria, estradiol cypionate injection is reserved for members who have previously used (or cannot/should not take) formulary oral estradiol or Premarin tablet and estradiol valerate injection **Estrogen patch ~~for members less than 40 years old~~:** For use in gender dysphoria, ~~E~~estradiol patches are reserved for members who have previously used (or cannot/should not take) oral estradiol or Premarin tablet and estradiol injection or members who have had a history of cardiovascular events. **Testosterone 1% packet or tube, testosterone 30mg/1.5ml solution pump or testosterone enanthate 200mg/mL intramuscular oil** For use in gender dysphoria, [Formulary, PA required (second-line) medications] <INSERT: testosterone packets/tube/solution pump or testosterone enanthate 200mg/mL intramuscular oil> are reserved for members who have previously used (or cannot/should not take) testosterone cypionate injection AND testosterone 1% gel pump or testosterone (Androgel) 1.62% gel pump. For use in gender dysphoria, 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. **Quantity Limits:** 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. **Exception approval:** The criteria for approval has not been met. The Alliance cannot cover xxDRUGxx as requested because insufficient information was received from your doctor to approve this medication as requested. The Alliance uses the Gender Dysphoria Drug Coverage Guidelines to determine what information is needed. Specifically, information required that has not yet been received includes: [1] Clinic notes that

Drugs for Gender Dysphoria For Less Than 21 Years Old	
	describe the diagnosis and treatment plan; and [2] Lab results showing [enter required labs]. We recommend that you talk with your provider about the needed information before we can approve for the full duration as requested. We will instead approve a 3-month supply of xxDRUGxx from [enter dates of approval].
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Remove the age limit from the estradiol patch products (restricted to members aged 40 and above).
- Remove Vantas from criteria as it was discontinued and is no longer available.
- Update covered uses section to most current resources

Drugs for Gender Dysphoria For At Least 21 Years Old	
Therapeutic Classes (AHFS)	Androgens; Antineoplastic Agents; Estrogens; Gonadotropins; Mineralocorticoid (Aldosterone) Antagonists; 5-Alpha-Reductase Inhibitors; Progestins
Medications	**Anti-androgens and progestins (Adjunct)** Formulary • Spironolactone (Aldactone) 25, 50, 100mg tablet • Finasteride (Proscar) 5mg tablet • Dutasteride (Avodart) 0.5mg capsule • Progesterone (Prometrium) 100, 200mg capsule • Medroxyprogesterone 2.5, 5mg tablet • Medroxyprogesterone acetate intramuscular (Depo-Provera) 150mg/mL Non-formulary: • Depo-Provera 400mg/mL injectable suspension • Progesterone 50mg/mL oil solution **Estrogen Agents for Male-to-Female (MTF)** Formulary: • Estradiol (Estrace) 0.5, 1, 2mg tablet • Premarin 0.3, 0.45, 0.625, 0.9, 1.25mg tablet • Estradiol-*once*-weekly 0.025, 0.0375, 0.05, 0.06, 0.075, 0.1mg patch: ~~restricted to members ≥40 years old and~~QL of #12 per 84 days • Estradiol-twice-weekly 0.025, 0.05, 0.075, 0.1mg patch: ~~restricted to members ≥40 years old and~~ QL of #24 per 84 days • Estradiol valerate 20mg/mL, 40mg/mL vial: 1 vial per 30 days Non-formulary • Depo-Estradiol (Estradiol cypionate) 5mg/mL **Testosterone Agents for Female-to-Male (FTM)** Formulary (first-line) • 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) Formulary, PA required (second-line) • 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 (quantity limit #5 ml/30 days) Non-formulary • Testosterone (Fortesta) 2% gel pump • Testosterone (Androgel) 1.62% gel packets • Androderm (testosterone transdermal patch) 2mg/24 hours, 4mg/24 hours

Drugs for Gender Dysphoria For At Least 21 Years Old	
	• 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 **Gonadotropin-Releasing Hormone Receptor Agonists (GnRHa)** Formulary, PA required • Lupron Depot-Ped 1-Month (leuprolide) 7.5, 11.25, 15, 30 mg syringe kit (for less than 18 years) • Lupron Depot (leuprolide) 3.75, 7.5, 11.25, 22.5, 30, 45mg syringe kit • Leuprolide acetate 1mg/0.2mL solution kit Non-formulary • Trelstar (triptorelin) 3.75, 11.25, 22.5 mg Mixject suspension • Eligard (leuprolide acetate) 7.5, 22.5, 30, 45mg subQ • Zoladex (goserelin acetate) 3.6, 10.8mg subQ implant • ~~Vantas (histrelin) 50mg subQ implant kit~~ • Supprelin LA (histrelin) 50mg subQ implant kit • Triptodur 6-month (triptorelin) 22.5mg • Fensolvi (leuprolide acetate) syringe kit Any other newly marketed agent to treat gender dysphoria *Requests for greater than indicated quantity or age limits will be reviewed on a case by case basis
Covered Uses	Medically accepted indications are defined using the following disease specific guidelines: Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline~~the Endocrine Society clinical practice guidelines for transsexual persons~~; World Professional Association for Transgender Health (WPATH): Standards of care for the health of transgender and gender diverse people~~the World Professional Association for Transgender Health (WPATH~~); American College of Obstetrician and Gynecologists (ACOG): Committee opinion on health care for transgender and gender diverse individuals; the TransActive Education and Advocacy Group; the World Health Organization (WHO)
Exclusion Criteria	Contraindications to any of the medications listed above
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	See "**PA Review Criteria**" below
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 24 months **Exception Approval** 3 months if requested labs are outside of recommended range or not provided; further approval requires requested labs and/or physician attestation they have educated the member and explained the risks
PA Review Criteria	****Cosmetic medications used to treat gender dysphoria, mental health, or substance use disorder ARE approved as appropriately indicated (e.g. FDA approval, compendia supported, etc.).**** ****ALL requests are to be forwarded to AAH for review****

Drugs for Gender Dysphoria For At Least 21 Years Old	
	INITIAL CRITERIA to start treatment for non-preferred drugs and preferred drugs that require PA, the following must be met: • Clinic notes or consult detailing the diagnosis of gender dysphoria / gender identity disorder (GID) per DSM-V diagnostic criteria made by a qualified mental health professional • Documentation of patient readiness to start GnRHa and/or cross-sex hormone therapy • Must also meet the class specific criteria outlined below • Dosage prescribed based on recommendations from medical compendia and/or the Food And Drug Administration (FDA) as appropriate • For formulary agents with prior authorization, approve for 12 months if meet ALL of the initial criteria to start treatment; for non-formulary agents, must have documentation showing trial and failure, contraindication, intolerance and/or side effects to formulary agents, as outlined in the individual sections below **Estrogen Agents (for Male-to-Female):** INITIAL CRITERIA to start treatment: • Documentation member does NOT have: history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months; known or suspected breast cancer • If requesting estradiol cypionate injection, documentation trial and failure, contraindication, intolerance and/or side effects to one formulary oral estrogen agent [or estradiol patches ~~(for members over 40)~~] and estradiol valerate injection • If requesting transdermal estrogen patch, ~~and under the age limit,~~ documentation trial and failure, contraindication, intolerance and/or side effects to formulary oral **and** injectable estrogen agents • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") RENEWAL CRITERIA: • Documentation of estradiol levels (less than 200 pg/ml) and testosterone levels (less than 55 ng/dL) • Documentation member does NOT have: history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months; known or suspected breast cancer • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") **Testosterone Agents (for Female-to-Male):** INITIAL CRITERIA to start treatment: • No evidence of known or suspected breast cancer and/or pregnancy • If requesting formulary-prior authorization required testosterone agents, documentation trial and failure, contraindication, intolerance and/or side effects to one first-line formulary injectable testosterone agent AND one first-line formulary topical testosterone agent • If requesting non-formulary testosterone agents, documentation trial and failure, contraindication, intolerance and/or side effects to one first-line formulary injectable testosterone agent AND one first-line formulary topical testosterone agent AND at least one formulary PA-required, (second-line) testosterone agent • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration")

Drugs for Gender Dysphoria For At Least 21 Years Old	
	RENEWAL CRITERIA: • Documentation of hematocrit less than 50% • Documentation of testosterone levels; discontinue or reduce dose if greater than 1000 ng/dL • No evidence of known or suspected breast cancer and/or pregnancy **Antiandrogens and Progesterone Agents (Adjunct use):** INITIAL CRITERIA for non-formulary agents: • Require documentation of trial and failure, intolerance, contraindication, or inability to use spironolactone, dutasteride, finasteride, medroxyprogesterone acetate tablet and medroxyprogesterone acetate IM • No evidence of known or suspected pregnancy • For medroxyprogesterone: documentation member does NOT have history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months and/or severe liver disease • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") RENEWAL CRITERIA for non-formulary agents: • Documentation member does NOT have known or suspected pregnancy • For medroxyprogesterone: documentation member does NOT have history of DVT/PE, thromboembolic disease, stroke and/or MI within the last 12 months and/or severe liver disease • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") **GnRHa (Adjunct use):** INITIAL CRITERIA to start treatment: • Require documentation of trial and failure, intolerance, contraindication, or inability to use spironolactone, dutasteride, finasteride, medroxyprogesterone acetate tablet and medroxyprogesterone acetate IM • Documentation of baseline labs for LH, FSH, estradiol and testosterone levels • Documentation member is on CONCOMITANT hormone replacement therapy (as verified by claims history) • No evidence of known or suspected pregnancy (if Female-to-Male transition) • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") RENEWAL CRITERIA: • Documentation of estradiol and testosterone levels • If any labs are out of recommended range or not provided, follow Exception Approval process (see "Coverage Duration") **For requests over the quantity limit:** • The member must have a documented treatment failure with the drug prescribed at the health plan's quantity limit **OR** the member requires a dose within prescribing guidelines that exceeds the plan's quantity limit **AND** • The provider has submitted a medical reason why the plan's quantity limit will be inadequate based on the member's condition and treatment history **AND** • The dose requested is supported by the Medical Compendia or current treatment guidelines. **Continuation of therapy for NEW members from another health plan:** • If criteria are met for initial authorization, coverage duration is 12 months

Drugs for Gender Dysphoria For At Least 21 Years Old	
	• If criteria are not met for initial authorization and/or requested labs are outside of recommended range **or** not provided, allow one-time coverage duration of 3 months until all of requested labs and clinic notes are received
Criteria Statement	**Estradiol cypionate injection:** For use in gender dysphoria, estradiol cypionate injection is reserved for members who have previously used (or cannot/should not take) formulary oral estradiol or Premarin tablets or estradiol patches ~~(for members over 40)~~ and estradiol valerate injection. **Estrogen patch ~~for members less than 40 years old~~:** For use in gender dysphoria, estradiol patch is reserved for members who have previously used (or cannot/should not take) oral estradiol or Premarin tablets and estradiol valerate injection or have a history of cardiovascular disease. **Testosterone 1% packet or tube, testosterone 30mg/1.5ml solution pump or testosterone enanthate 200mg/mL intramuscular oil** For use in gender dysphoria, [Formulary, PA required (second-line) medications] <INSERT: testosterone packets/tube/solution pump or testosterone enanthate 200mg/mL intramuscular oil> are reserved for members who have previously used (or cannot/should not take) testosterone cypionate injection AND testosterone 1% gel pump or testosterone (Androgel) 1.62% gel pump. For use in gender dysphoria, 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. **Quantity Limits:** 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. **Any GnRHa:** For use in gender dysphoria, GnRHa products are reserved for members with ALL of the following: 1) have previously used (or cannot/should not take) ALL of the following: spironolactone, dutasteride, finasteride, medroxyprogesterone; AND 2) records showing you are currently using hormone therapy. **Exception approval:** The criteria for approval has not been met. The Alliance cannot cover xxDRUGxx as requested because insufficient information was received from your doctor to approve this medication as requested. The Alliance uses the Gender Dysphoria Drug Coverage Guidelines to determine what information is needed. Specifically, information required that has not yet been received includes: [1] Clinic notes that describe the diagnosis and treatment plan; and [2] Lab results showing [enter required labs]. We recommend that you talk with your provider about the needed information before we can approve for the full duration as requested. We will instead approve a 3-month supply of xxDRUGxx from [enter dates of approval].
Last P&T Review Date	~~9/20229~~/2023

Recommendation:

- Add Flonase Sensimist (DDID 196615) to formulary along with other first line agents and also step therapy coding for flunisolide and mometasone.
- Generic Rhinocort allergy is already a first line formulary medication, add to step therapy coding for flunisolide and mometasone. (DDIDs 198579, 201361, 201590, 205811)
- Pricing
    - Fluticasone (Flonase) Nasal Suspension: 50mcg $23.35/18.2 mL bottle
    - Flonase Sensimist (fluticasone) Nasal Suspension $26.86/9.1 mL bottle
    - Budesonide (Rhinocort Allergy) Nasal Suspension: 32mcg $15.99/8.43 mL bottle
    - Triamcinolone (Nasacort Allergy) Nasal Solution: 55mcg $30.33/16.6 mL bottle
    - Flunisolide Nasal Solution: 25mcg $46/25 mL bottle
    - Nasonex (mometasone) Nasal Suspension: 50mcg $119/17 gm

Intranasal Steroids	
Therapeutic Classes (AHFS)	Corticosteroids, nasal
Medications	Formulary, step therapy required Flunisolide 0.025% spray Mometasone 50 mcg actuation nasal suspension spray (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 Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	Flunisolide or mometasone nasal spray are approved when the following criteria are met: • Documentation of a trial and failure, contraindication, or inability to use (nasal burning, headache, etc.) fluticasone nasal spray OR Flonase Sensimist OR triamcinolone nasal spray OR budesonide (Rhinocort Allergy) 32mcg nasal suspension Non-formulary intranasal steroids are approved when the following criteria are met: • Documentation of a trial and failure, contraindication, or inability to use (nasal burning, headache, etc.) fluticasone nasal spray OR Flonase Sensimist OR triamcinolone nasal spray OR budesonide (Rhinocort Allergy) 32mcg nasal suspension AND • Documentation of a trial and failure, contraindication, or inability to use (nasal burning, headache, etc.) flunisolide 0.025% spray OR mometasone 50 mcg nasal spray For requests above the quantity limit • The member must have a documented treatment failure with the drug prescribed at the health plan's quantity limit OR the member requires a dose within prescribing guidelines that exceeds the plan's quantity limit. AND

Intranasal Steroids	
	• 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	Flunisolide nasal spray or mometasone nasal spray are reserved for members who have used (or cannot/should not use) fluticasone nasal spray OR Flonase Sensimist OR triamcinolone nasal spray OR budesonide (Rhinocort Allergy) 32mcg nasal suspension. Non-formulary steroidal nasal sprays are reserved for members who have used (or cannot/should not use) fluticasone nasal spray or Flonase Sensimist or triamcinolone nasal spray or budesonide (Rhinocort Allergy) 32mcg nasal suspension AND flunisolide nasal spray or mometasone nasal spray.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Remove prescriber restrictions as the DATA 2000 waiver has been discontinued
- Add new medication Brixadi to policy with criteria for review
- Rearrange sections for clarity

Opioid Use Disorder (OUD) Agents	
Therapeutic Classes (AHFS)	Opiate Partial Agonists
Medications	Formulary (with quantity limit) Buprenorphine (Subutex) sublingual tablet Buprenorphine/naloxone (Suboxone) sublingual tablet Formulary, PA required: Buprenorphine/naloxone (Suboxone) film Zubsolv (buprenorphine/naloxone) sublingual tablet Non-formulary, PA required: Sublocade (buprenorphine) subcutaneous injection Brixadi (buprenorphine) Weekly or Monthly subcutaneous injection Any other newly marketed agent for opioid use disorder
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A ~~Prescriber meets all qualifications to prescribe buprenorphine/naloxone (Federal, State, and Local)~~ ~~It is assumed that since the prescribing practitioner has the appropriate DEA designation to prescribe this medication, the prescribing practitioner has had the full training in its proper use.~~
Coverage duration	**Initial/Re-Approval:** If all conditions are met, the request will be approved for up to 12 months. If all criteria are not met, the request is referred to Clinical Reviewer for medical necessity review.
PA Review Criteria	**INTIAL CRITERIA** **Buprenorphine/naloxone (Suboxone) film or Zubsolv (buprenorphine/naloxone) sublingual tablet** • Patient has a diagnosis of opioid use disorder ~~(requests for pain will be denied)~~ • Dosing maximum of 24mg/day of buprenorphine or equivalent is requested (Dosing above 24mg/day may be approved on a case by case basis • Documented trial and failure, contraindication, or intolerance to one of the following medications: buprenorphine (Subutex) tablet OR buprenorphine/naloxone (Suboxone) tablet is required ~~for approval of formulary prior authorization required and non-formulary medications~~ ~~For~~ **Sublocade**~~:~~ ~~requests, all of the following must be met~~ • Patient has a diagnosis of moderate to severe opioid use disorder

	• Documented trial and failure, contraindication, or intolerance to one of the following medications: buprenorphine (Subutex) tablet OR buprenorphine/naloxone (Suboxone) tablet is required • Patient has initiated treatment with an oral or transmucosal buprenorphine containing product at a daily dose of 8-24 mg buprenorphine for at least 7 days prior to initiating treatment • Patient will not be receiving supplemental oral, sublingual, or transmucosal buprenorphine. **Brixadi:** • Patient has a diagnosis of moderate to severe opioid use disorder • Documented trial and failure, contraindication, or intolerance to one of the following medications: buprenorphine (Subutex) tablet OR buprenorphine/naloxone (Suboxone) tablet is required • Patient has initiated treatment with a single dose of at least 4mg of a transmucosal buprenorphine product or are already being treated with buprenorphine **RENEWAL CRITERIA** • Patient has a diagnosis of opioid use disorder ~~(requests for pain will be denied)~~ • For buprenorphine/naloxone (Suboxone) film or Zubsolv (buprenorphine/naloxone) sublingual tablet, ~~D~~documentation must be provided for renewals after the first year that indicated prescriber has reevaluated the patient on an annual basis for a dosage lower than 24mg/day For requests above the quantity limit The provider has submitted a medical reason why the plan's quantity limit will be inadequate based on the member's condition and treatment history.
Criteria Statement	Sublocade (buprenorphine) subcutaneous injection, Brixadi (buprenorphine) Weekly or Monthly subcutaneous injection, Zubsolv, and buprenorphine/naloxone (Suboxone) film are reserved for members who have used (or cannot use) buprenorphine (Subutex) tablets or buprenorphine/naloxone (Suboxone) tablets.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Remove soluble fiber requirement. According to the 2021 ACG guidelines, there are strong recommendations for use of fiber to treat global IBS symptoms, however, there is more evidence to support its use in IBS-C. The 2022 AGA update on role of diet in IBS also supports use of fiber in treating global IBS, but not IBS-D specifically.
- Minor format changes
- Remove gender restrictions

Alosetron (Lotronex)	
Therapeutic Classes (AHFS)	Anti-Inflammatory Agents (GI Drugs)
Medications	Alosetron (Lotronex)
Covered Uses	Medically accepted indications 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	~~Patient is Male~~N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	None
Prescriber Restrictions	None
Coverage Duration	**Initial Approval** If the criteria are met, approve up to #2 tablets/day for 3 months initially. **Later Approvals** If patient is tolerating and responding to treatment after 3 months, subsequent requests may be approved for #2 tablets/day for 12 months. If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for Approval • Patient has diagnosis of severe chronic diarrhea-predominant irritable bowel syndrome (IBS-D) and has had anatomic or biochemical GI abnormalities excluded and has symptoms that have lasted 6 months or longer (includes one or more of the following: frequent and severe abdominal pain/discomfort; frequent bowel urgency or fecal incontinence; disability or restriction of daily activities due to IBS) ~~AND~~ ~~• Patient is female. AND~~ • ~~Documented trial and failure, contraindication, or intolerance to soluble fiber (e.g. psyllium) AND~~ • Documented trial and failure, contraindication, or intolerance to a tricyclic antidepressant (TCA) (~~e.g.~~e.g., amitriptyline)
Criteria Statement	Alosetron is reserved for women who have severe chronic diarrhea-predominant irritable bowel syndrome (IBS-D) ~~IBS-diarrhea predominant~~ who have used (or cannot/should not use) ~~soluble fiber (e.g. psyllium) AND~~ a tricyclic antidepressant (TCA) (~~e.g.~~e.g., amitriptyline).
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Adding requirement for members to have a gallbladder and also to not drink more than 3 alcoholic beverages per day, as these are both contraindications. The most recent AGA guidelines also emphasize this point.
- Remove soluble fiber requirement. According to the 2021 ACG guidelines, there are strong recommendations for use of fiber to treat global IBS symptoms, however, there is more evidence to support its use in IBS-C. The 2022 AGA update on role of diet in IBS also supports use of fiber in treating global IBS, but not IBS-D specifically.

Viberzi (eluxadoline)	
Therapeutic Classes (AHFS)	GI Drugs, Miscellaneous
Medications	Viberzi (eluxadoline)
Covered Uses	Medically accepted indications 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	Viberzi is contraindicated in patients with sphincter of Oddi spasms.
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial Approval** If the criteria are met, approve up to #2 tablets/day for 3 months initially. **Later Approvals** If patient is tolerating and responding to treatment after 3 months, subsequent requests may be approved for #2 tablets/day for 12 months. If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for Approval • ~~Patient has~~ ~~d~~Diagnosis of irritable bowel syndrome with diarrhea (IBS-D) ~~AND~~ • Provider attestation that the member has a gallbladder and does not drink more than 3 alcoholic beverages per day. • ~~Documented trial and failure, contraindication, or intolerance to soluble fiber (e.g. psyllium) AND~~ • Documented trial and failure, contraindication, or intolerance to a tricyclic antidepressant (TCA) (e.g., amitriptyline).
Criteria Statement	Viberzi (eluxadoline) is reserved for members who have diagnosis of irritable bowel syndrome with diarrhea (IBS-D) who have a gallbladder, and do not drink more than 3 alcoholic beverages per day and have used (or cannot/should not use) ~~soluble fiber (e.g. psyllium) AND~~ a tricyclic antidepressant (TCA) (e.g. amitriptyline).
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Remove soluble fiber requirement for Xifaxan. According to the 2021 ACG guidelines, there are strong recommendations for use of fiber to treat global IBS symptoms, however, there is more evidence to support its use in IBS-C. The 2022 AGA update on role of diet in IBS also supports use of fiber in treating global IBS, but not IBS-D specifically.

Rifamycin Antibiotics	
Therapeutic Classes (AHFS)	Rifamycin Antibiotics
Medications	Formulary Prior Authorization Required Xifaxan (rifaximin) Aemcolo DR (rifamycin)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), and the Drug Package Insert.
Exclusion Criteria	N/A
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	N/A
Coverage Duration	**Initial/Re-Approval** **Traveler's diarrhea (Xifaxan and Aemcolo):** If all of the criteria are met, approve up 1 fill up to FDA approved maximum dosing. **IBS-D (Xifaxan):** If all of the criteria are met, the request will be approved for up to #42/14 days for 3 fills for 1 year. **Hepatic encephalopathy (Xifaxan):** If all of the criteria are met, the initial request will be approved for up to 6 months. For re-approvals if all criteria are met, the request will be approved for up to 12 months. If criteria is not met, request will be sent to a Medical Director/clinical reviewer for medical necessity review.
PA Review Criteria	Criteria for Authorization For all diagnoses **(Xifaxan and Aemcolo):** • Drug is being prescribed at FDA approved dose (including patient age) For diagnosis of traveler's diarrhea **(Xifaxan and Aemcolo):** • Documented trial and failure, contraindication, or intolerance to a fluoroquinolone (e.g. ciprofloxacin) OR azithromycin For reduction of overt hepatic encephalopathy recurrence or treatment of hepatic encephalopathy **(Xifaxan):** • Documented trial and failure, contraindication, or intolerance to lactulose in previous 30 days **OR** • Patient will be using lactulose concurrently For treatment of irritable bowel syndrome – diarrhea predominant (IBS-D) **(Xifaxan):**

	• Patient has diagnosis of moderate to severe disease (includes one or more of the following: frequent and severe abdominal pain/discomfort; frequent bowel urgency or fecal incontinence; disability or restriction of daily activities due to IBS) **AND** ~~• Documented trial and failure, contraindication, or intolerance to soluble fiber (e.g. psyllium) **AND**~~ • Documented trial and failure, contraindication, or intolerance to a tricyclic antidepressant (TCA) (e.g. amitriptyline)
Criteria Statement	For traveler's diarrhea, Xifaxan and Aemcolo DR are reserved for members who have used (or cannot/should not use) a fluoroquinolone (e.g. ciprofloxacin) or azithromycin. For hepatic encephalopathy, Xifaxan is reserved for members who have used (or cannot/should not use) lactulose in the prior 30 days or are concurrently using lactulose. For irritable bowel syndrome –diarrhea predominant, Xifaxan is reserved for members who have used (or cannot/should not use) ~~a soluble fiber (e.g. psyllium) AND~~ a tricyclic antidepressant (TCA) (e.g. amitriptyline.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Remove requirement for documentation of evaluation of baseline renal function. As these patients are being management by oncologists or endocrinologists, it's safe to assume that their renal function is being monitored.

Injectable/Infusible Bone-Modifying Agents for Oncology Indications	
Therapeutic Classes (AHFS)	Bone resorption inhibitors
Medications	**Preferred Agent, prior authorization required** Pamidronate disodium (Aredia): 3mg/ml, 6 mg/ml, 9 mg/ml liquid in10 ml vials, 30 mg, 90 mg vials Zoledronic Acid (Zometa) 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:** ~~• Documentation was provided that baseline renal function has been evaluated~~ • 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 generic pamidronate (Aredia) OR zoledronic acid (Zometa) 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 generic pamidronate (Aredia) OR zoledronic acid (Zometa) 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	~~9/2022~~9/2023

Recommendation:

- Remove Paser from policy – obsolete.
- Adjust Sirturo and Pretomanid initial approval durations per most updated guidance.
- Remove duplicative statement under Sirturo section.

Medications for the treatment of Multi-Drug Resistant Tuberculosis	
Therapeutic Classes (AHFS)	Antitubercular agents
Medications	Formulary, Step Therapy required Cycloserine (Seromycin) 250 mg capsule Trecator (ethionamide) 250 mg tablet ~~Paser (aminosalicylic acid) 4 g granules~~ Moxifloxacin (Avelox) 400 mg tablet Linezolid (Zyvox) 600 mg tablet and 100 mg/5 ml suspension Formulary PA required Sirturo (bedaquiline fumarate) tablet Pretomanid tablet
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Diagnosis of latent tuberculosis or drug-susceptible tuberculosis
Required Clinical Information	See "**PA Review Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber is an infectious disease specialist or working in consultation with infectious disease specialist
Coverage Duration	**Initial Approval** Trecator, Cycloserine, ~~Paser,~~ Moxifloxacin, Linezolid: Up to 20 months Sirturo: 24~~12~~ months Pretomanid: ~~24~~ 9 months
PA Review Criteria	Formulary, Step Therapy required medications criteria for approval: • Documentation member has intolerance, contraindication, or inability to use at least one first-line treatment: isoniazid, ethambutol, rifampin, OR pyrazinamide Formulary PA required medications criteria for approval: Sirturo (bedaquiline) One of the following: • Diagnosis is laboratory confirmed pulmonary multidrug-resistant tuberculosis (MDR-TB) or rifampicin-resistant tuberculosis (RR-TB) with an isolate showing genotypic or phenotypic resistance to rifampin (RIF) AND one of the following: ○ Short-course (generally 9-12 months) ▪ ~~Disease is limited to pulmonary~~ ▪ Resistance to fluoroquinolones (FQ) has been ruled out ▪ Is being prescribed in combination with other TB medications ○ Long-course (generally 15-24 months) ▪ Is being prescribed in combination with other TB medications • Is being used in combination with Pretomanid as below Pretomanid • Diagnosis is laboratory confirmed pulmonary extensively drug resistant (XDR)-TB or treatment-intolerant or non-responsive MDR-TB or RR-TB with an isolate showing genotypic or phenotypic resistance to RIF. • Documented FQ resistance • Is being used in combination with Sirturo (bedaquiline) and linezolid

	• Medical reason why other guideline-recommended regimens cannot be used For requests for therapy to continue beyond the coverage duration initial approval time period, approve if medical justification provided (e.g. extensively drug resistant [XDR]-TB) for continuation of therapy ****For moxifloxacin and linezolid requests for diagnoses other than MDRTB, see the drug-specific criteria for each.**
Criteria Statement	For multi-drug resistant tuberculosis, Trecator, Cycloserine, ~~Paser,~~ moxifloxacin, or linezolid are reserved for members who have used (or cannot/should not use) isoniazid, ethambutol, rifampin, or pyrazinamide Pretomanid tablet is reserved for members with a diagnosis of multi-drug resistant or rifampin resistant tuberculosis, with documented fluoroquinolone resistance, when used as part of a 3-drug or regimen. Sirturo tablet is reserved for members with a diagnosis of multi-drug resistant or rifampin resistant tuberculosis, when used in combination with Pretomanid and other medications to treat tuberculosis.
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Add in patients with clinically significant CHD diagnosed by invasive or non-invasive testing as they are in trial protocols, not all patients in studies had to have actually experienced an event.
- Minor formatting update

Adenosine Triphosphate-Citrate Lyase (ACL) inhibitors	
Therapeutic Classes (AHFS)	Anticonvulsants, Miscellaneous
Medications	Formulary, PA required Nexletol (bempedoic acid) Nexlizet (bempedoic acid/ezetimibe) Any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), and the Drug Package Insert.
Exclusion Criteria	None
Required Clinical Information	See "PA Review Criteria" below
Age Restrictions	18 years or older
Prescriber Restrictions	Prescriber must be a cardiologist or specialist in the treatment of lipid disorders
Coverage Duration	**Initial Approval** 3 months **Later Approval** 12 months If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	**Initial Authorization:** • Member must have documentation of baseline low density lipoprotein cholesterol (LDL-C) • Member has a diagnosis of heterozygous familial hypercholesterolemia (FH) OR • Member has a diagnosis of hyperlipidemia and atherosclerotic cardiovascular disease (ASCVD) as evidenced by a history of least one of the following: o Myocardial infarction or acute coronary syndrome, o Stroke or transient ischemic attack, o Coronary artery disease with stable angina, o Coronary or other arterial revascularization, o Peripheral vascular disease, or o Aortic aneurysm o Clinically significant CHD diagnosed by invasive or non-invasive testing (such as coronary angiography, stress test using treadmill, stress echocardiography, or nuclear imaging) AND o Member must have a fasting LDL-C ≥ 70 mg/dL • Member has tried and failed a high-intensity statin (i.e. atorvastatin 40-80 mg, rosuvastatin 20-40 mg) at maximum tolerated dose for 3 months via claim history or chart notes OR documentation has been provided that the member is not able to tolerate a statin. • Member has tried and failed ezetimibe at a maximum tolerated dose or documentation has been provided that the member is not able to tolerate ezetimibe. • Member will continue on maximum tolerated statin dose while receiving Nexletol/Nexlizet or documentation has been provided that the member is not able to tolerate a statin.

	• Documentation was provided indicating provider has counseled member on smoking cessation and following a “heart healthy diet”. • Dose is appropriate per label or supported by compendia/standard of care guidelines **Reauthorization:** • Documentation was provided that the member has obtained clinical benefit from medication (e.g. LDL-C lowering from baseline) • Dose continues to be appropriate per label or supported by compendia/standard of care guidelines • Member will continue on: o maximum tolerated statin dose while receiving Nexlizet or documentation has been provided that the member is not able to tolerate a statin, OR o maximum tolerated statin and ezetimibe dose while receiving Nexletol ORor o documentation has been provided that the member is not able to tolerate a statin and/or ezetimibe.
Criteria Statement	Nexletol and Nexlizet are reserved for members who have a diagnosis of heterozygous familial hypercholesterolemia (FH) OR a diagnosis of hyperlipidemia and atherosclerotic cardiovascular disease (ASCVD) who have used (or cannot/should not use) a high-intensity statin and ezetimibe, and who have received counseling on smoking cessation and are following a “heart healthy diet”.
Last P&T Review Date	9/20229/2023

Recommendation:

- Minor update in the preterm labor section, as the new guidance from ACOG on use of vaginal progesterone states those patients without a short cervix have not derived a benefit.

Vaginal Progesterone	
Therapeutic Classes (AHFS)	Progestins
Medications	Non-formulary, prior authorization required: Crinone (micronized progesterone) gel Endometrin (micronized progesterone) vaginal insert
Covered Uses	Medically accepted indications 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 OB-GYN specialist
Coverage Duration	Prevention of spontaneous preterm delivery: • Crinone and Endometrin will be approved for 30 single use applicators/inserts per 30 days until the end of pregnancy Secondary Amenorrhea: • Crinone will be approved for up to 6 single use applicators Assisted Reproductive Technology (ART): • Crinone and Endometrin will be approved for: 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**Prevention of Spontaneous Preterm Delivery:** • Current singleton pregnancy and prior preterm birth ~~or~~ and short cervix • Patient has tried and failed, or has a contraindication or intolerance to micronized progesterone (Prometrium) capsules • If the request is for Crinone, the patient has tried and failed, has a contraindication or intolerance to, or other medical justification for not using Endometrin **Secondary Amenorrhea:** • Member has a diagnosis of secondary amenorrhea • Member has tried and failed, or has contraindication or intolerance to, oral progestin therapy (e.g. medroxyprogesterone acetate, norethindrone acetate tablets, micronized progesterone) • If the request is for Crinone 8% gel the patient has tried and failed, or has a contraindication or intolerance to, Crinone 4% gel. **Assisted Reproductive Technology (ART):** • The request is for iatrogenic infertility (infertility caused directly or indirectly by surgery, chemotherapy, radiation, or other medical treatment) ○ Requests for other causes of infertility will be denied • Member requires intravaginal progesterone as part of an ART treatment plan
Criteria Statement	**Prevention of Spontaneous Preterm Delivery:**

	Endometrin is reserved for members who are currently pregnant with one child, who also have history of preterm birth ~~or~~ and short cervix and have used (or cannot/ should not use) micronized progesterone (Prometrium) capsules. Crinone is reserved for members who are currently pregnant with one child, who also have history of preterm birth ~~or~~ and short cervix, who have used (or cannot/ should not use) micronized progesterone (Prometrium) capsules AND Endometrin. **Secondary Amenorrhea:** Crinone is reserved for members who a diagnosis of secondary amenorrhea and have used (or cannot/ should not use) oral progestin therapy (e.g. medroxyprogesterone acetate, norethindrone acetate tablets, micronized progesterone). Crinone 8% gel is reserved for members who have used (or cannot/ should not use) Crinone 4% gel. **Assisted Reproductive Technology (ART):** Crinone and Endometrin are reserved for members who require assisted reproductive technology (ART), as a result of iatrogenic infertility (infertility caused directly or indirectly by surgery, chemotherapy, radiation, or other medical treatment).
Last P&T Review Date	~~9/2022~~9/2023

Recommendation:

- Update requirements to glucocorticoid-induced osteoporosis.
  - The newest guideline updates have added a very high-risk category.
  - Additionally, there are no recommendations for patients with moderate risk to use injectable osteoporosis treatments – remove section with FRAX between 1-3 percent and 10-19 percent.

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) Forteo (teriparatide) Teriparatide Tymlos (abaloparatide) 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:** • 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. ○ 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: o A bone mineral density (BMD) value consistent with osteoporosis (i.e., T-scores equal to or less than –2.5) o Has had an osteoporotic fracture o 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: o 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 o 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 Teriparatide, a medical reason why the member is unable to use Tymlos or Evenity, if appropriate, based on the diagnosis. o 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:** • Documentation that the member is currently utilizing glucocorticoid therapy for a minimum of 3 months • Documentation that the dosage of the glucocorticoid therapy is greater than 2.5 mg of prednisone daily or its equivalent • Member is 40 years of age or older • Member has a ~~moderate to~~ high to very high risk of fracture based on ONE of the following: o History of osteoporotic fracture o BMD less than or equal to -2.5 at the hip or spine o FRAX 10-year probability of hip or combined major osteoporotic fracture of ≥3 and 20 percent, respectively o ~~FRAX 10-year probability of hip or combined major osteoporotic fracture between 1 to 3 percent and 10 to 19 percent, respectively~~ • 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: o 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 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, have a ~~moderate to~~ high 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	~~9/2022~~9/2023

Recommendation:

- Retire. There is no AAH IHSS membership under 12 years old. The new monoclonal antibody Beyfortus, indicated for the prevention of RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season and children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season, would now be used in place of Synagis.

Synagis	
Therapeutic Classes (AHFS)	Monoclonal antibodies
Medications	Non-formulary Synagis (palivizumab) 50mg/0.5ml, 100 mg/ml vial
Covered Uses	Medically accepted indications 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** Up to a quantity sufficient to provide coverage for RSV season, which typically starts in November, but can vary according to geographic area, with October, November, or December starts, with a maximum quantity of 5 doses. ****MAXIMUM APPROVABLE DOSES**** ALL PATIENTS will receive Synagis treatment for a **maximum of 5 doses**. There are no valid clinical reasons for a 6th dose of Synagis and, therefore, all requests for a 6th dose will be denied. If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**NOTE: **For Synagis, please send to plan for review**** All requests require documentation of the following: • Child's gestational age at birth, chronological age, and current weight • Pertinent medical risk factors Approval requires that Synagis is ordered for the FDA approved indication of Respiratory Syncytial Virus (RSV) infection prophylaxis in high risk patients and that it is requested at the FDA approved dose of 15mg/kg/dose every 30 days. **PLEASE NOTE: Synagis prophylaxis is NOT recommended for otherwise healthy infants born after 29 weeks, 0 days gestation, OR for patients greater than 24 months old.** If an infant or child who is receiving Synagis immunoprophylaxis experiences a breakthrough RSV infection, monthly prophylaxis should be discontinued. **Synagis requests are approvable if the patient meets one of the following**: If child has a chronological age of < 12 months old: 1. The child was born prematurely with a gestational age of 28 weeks & 6 days or less, and the child's current chronological age is less than or equal to 1 year at the beginning of RSV season (which typically begins November 1st, but can vary).

Synagis

2. The child was born with a Gestational Age (GA) of <32 weeks, 0 days and required continuous oxygen for at least 28 days after birth, **AND** has confirmed diagnosis of chronic lung disease of prematurity (CLD) a.k.a. bronchopulmonary dysplasia (BPD), (ICD10: P27.1)
3. The child was born with significant heart disease requiring medication to control CHF, moderate to severe pulmonary hypertension, or cyanotic heart disease (**see Table 1 & 2**) that could be complicated by pulmonary disease.
4. The child will be profoundly immunocompromised during the RSV season (**see Table 3**).
5. The child has a congenital abnormality of the airway or a neuromuscular disease that compromise handling of respiratory secretions during the first year of life.
6. The child has diagnosis of cystic fibrosis with evidence of CLD and/or nutritional compromise the first year of life

<u>If child has a chronological age of 12 to 24 months old:</u>

1. The child was born with a Gestational Age (GA) of <32 weeks, 0 days and required continuous oxygen for at least 28 days after birth, **AND** has confirmed diagnosis of chronic lung disease of prematurity (CLD) a.k.a. bronchopulmonary dysplasia (BPD), (ICD10: P27.1), **AND** continues to require medical treatment with either supplemental oxygen, chronic corticosteroids, bronchodilator or diuretic treatment within 6 months of the start of or during the current RSV season.
2. The child will be profoundly immunocompromised during the RSV season (**see Table 3**).
3. The child will be undergoing cardiac transplantation during the RSV season.
4. Cystic fibrosis with manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in first year of life) or weight for length less than 10th percentile.

<u>Table 1</u>

EXAMPLES OF SIGNIFICANT AND APPROVABLE CARDIAC CONDITIONS
Examples of significant hemodynamic cyanotic congenital heart disease:
Tetralogy of Fallot, Transposition of the great vessels, Ebstein's anomaly, Tricuspid atresia, Total anomalous pulmonary venous return, Truncus arteriosus, Hypoplastic left heart syndrome.

<u>Table 2</u>

NON-APPROVABLE CONDITIONS	
Insignificant hemodynamic heart disease (and therefore are NOT approvable indications):	**Indications in which patients are NOT at an increased risk for RSV (and therefore are NOT approvable indications)**
Secundum atrial septal defect, small ventricular septal defect, pulmonic stenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, patent ductus arteriosus	Lesions adequately corrected by surgery (unless the patient continues to require medications for CHF) Mild cardiomyopathy who are not receiving medical therapy.

<u>Table 3</u>

EXAMPLES OF SEVERE IMMUNODEFICIENCES/IMMUNOSUPPRESSION:
Advanced Acquired Immunodeficiency Syndrome (AIDS), Transplant, Chemotherapy, Severe Combined Immunodeficiency (SCID)

Synagis	
Criteria Statement	If the child has a chronological age of less than 12 months, Synagis is reserved for premature children with a gestational age of 28 weeks & 6 days or less, born with a Gestational Age (GA) of <32 weeks, 0 days and required continuous oxygen for at least 28 days after birth and has chronic lung disease of prematurity, has significant heart disease, has a congenital abnormality or the airway or neuromuscular disease, or cystic fibrosis If the child has chronological age of 12 to 14 months, Synagis is reserved for children born with a Gestational Age (GA) of <32 weeks, 0 days and required continuous oxygen for at least 28 days after birth, AND has confirmed diagnosis of chronic lung disease of prematurity AND requires medical treatment within 6 months of RSV season, the child will be immunocompromised during RSV season, undergoing heart transplant during RSV season, or has cystic fibrosis with manifestations of severe lung disease, or weight for length less than 10th percentile.
Last P&T Review Date	~~3/20239~~/2023

Recommendation:

- Retire

Specialty Biological Agents Preferred Products	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	***Two preferred biological agents must be tried and failed, prior to approval of non-preferred biological agents, unless not FDA indicated*** **Please refer to each indication-based policy below for FDA-indicated biological agents** **STATUS: Preferred Biological Agents- Require Prior Authorization** HUMIRA (adalimumab) ACTEMRA (tocilizumab) TALTZ (Ixekizumab) XELJANZ (tofacitinib) XELJANZ XR (tofacitinib) SKYRIZI (risankizumab-rzaa) RINVOQ (upadacitinib) AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only) **STATUS: Non-Preferred Biological Agents- Require Prior Authorization (Second Line)** COSENTYX (secukinumab) CIMZIA (certolizumab) ENBREL (etanercept) KEVZARA (sarilumab) KINERET (anakinra) ORENCIA (abatacept) SIMPONI (golimumab) SIMPONI (golimumab) Aria SILIQ (brodalimumab) TREMFYA (guselkumab) STELARA (ustekinumab) ENTYVIO (vedolizumab) OTEZLA (apremilast) REMICADE (infliximab) INFLECTRA (infliximab-dyyb) RENFLEXIS (infliximab-abda) AVSOLA (infliximab-axxq) Infliximab ILARIS (canakinumab) TYSABRI (natalizumab) ILUMYA (tildrakizumab-asmn) OLUMIANT (baricitinib) SOTYKTU (deucravacitinib) **Or any newly marketed agent**

Recommendation:

- Retire

Specialty Biological Agents for Crohn's Disease	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agents- Require Prior Authorization **HUMIRA (adalimumab)** **SKYRIZI (risankizumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **REMICADE (infliximab)** **INFLIXIMAB** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **AVSOLA (infliximab-axxq)** **CIMZIA (certolizumab)** **ENTYVIO (vedolizumab)** **STELARA (ustekinumab)** **TYSABRI (natalizumab)** **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	Prescriber is a gastroenterologist
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	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **PA CRITERIA FOR APPROVAL FOR CROHN'S DISEASE:** • The medication is being prescribed at an appropriate FDA approved dose (for age and weight) • The member has a diagnosis of severe/fulminant or perianal/fistulizing Crohn's disease **OR** • The member has a diagnosis of moderate-to-severe/moderate-to-high risk Crohn's disease AND has had an adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using, one of the following: azathioprine, 6-mercaptupurine, corticosteroids, or methotrexate consistent with pharmacy claims/medical record data/chart notes/physician attestation **OR** • The member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using conventional oral therapy to manage their condition

Specialty Biological Agents for Crohn's Disease	
	• If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not using at least TWO of the preferred biological agents • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **PA CRITERIA FOR RE-AUTHORIZATION FOR CROHN'S DISEASE:** • The medication is being prescribed at a Food and Drug Administration (FDA) approved dosage. • The member has been receiving the medication and documentation was provided that the provider has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.

Recommendation:

- Retire

Specialty Biological Agents for Ulcerative Colitis	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agents- Require Prior Authorization **HUMIRA (adalimumab)** **XELJANZ (tofacitinib)** **XELJANZ XR (tofacitinib)** **RINVOQ (upadacitinib)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **REMICADE (infliximab)** **INFLIXIMAB** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **AVSOLA (infliximab-axxq)** **SIMPONI (golimumab)** **ENTYVIO (vedolizumab)** **STELARA (ustekinumab)** **ZEPOSIA (ozanimod)** **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	Prescriber is a gastroenterologist
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	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **PA CRITERIA FOR APPROVAL FOR ULCERATIVE COLITIS:** • The member has moderate to severe active ulcerative colitis. • The patient has a documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation failure after receiving an adequate trial of at least 4-8 weeks of: ○ Sulfasalazine or mesalamine or azathioprine or 6-mercaptopurine or oral corticosteroids or has a documented medical reason (gastrointestinal (GI) intolerance such as nausea, vomiting, bloating, and diarrhea, hypersensitivity, etc.) for not taking any of these medications to treat their medical condition. • The medication requested is being prescribed at an FDA-approved dosage for age and weight.

Specialty Biological Agents for Ulcerative Colitis	
	• If the request is for Rinvoq or Xeljanz, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of a preferred Tumor Necrosis Factor (TNF) inhibitor agent • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using at least TWO of the preferred biological agents • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used • For requests for Zeposia (ozanimod): Documentation of results of varicella zoster virus (VZV) antibody testing indication previous infection or vaccination. ○ If negative, documentation of VZV vaccination must be provided with the request **PA CRITERIA FOR RE-AUTHORIZATION FOR ULCERATIVE COLITIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.
Criteria Statement	Humira, Amjevita, Rinvoq, Xeljanz, and Xeljanz XR are reserved for members who have moderate to severe ulcerative colitis and have used (or cannot/should not use) sulfasalazine, mesalamine, azathioprine, 6-mercaptopurine, or oral corticosteroids. Non-preferred medications are reserved for members who have used (or cannot/should not use) two of the following: Humira, Amjevita, Rinvoq, or Xeljanz/Xeljanz XR.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Rheumatoid Arthritis	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agents- Require Prior Authorization **HUMIRA (adalimumab)** **ACTEMRA (tocilizumab)** **XELJANZ (tofacitinib)** **XELJANZ XR (tofacitinib)** **RINVOQ (upadacitinib)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **ENBREL (etanercept)** **REMICADE (infliximab)** **INFLIXIMAB** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **AVSOLA (infliximab-axxq)** **CIMZIA (certolizumab)** **KEVZARA (sarilumab)** **KINERET (anakinra)** **ORENCIA (abatacept)** **SIMPONI (golimumab)** **SIMPONI ARIA (golimumab)** **OLUMIANT (baricitinib)** **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	Prescriber is a rheumatologist
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	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **PA CRITERIA FOR APPROVAL FOR RHEUMATOID ARTHRITIS:** • The member has a diagnosis of rheumatoid arthritis. • Member has a documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking one disease modifying anti-rheumatic drug (DMARD) (e.g. methotrexate, leflunomide, sulfasalazine or hydroxychloroquine) to manage their condition. • The medication requested is being prescribed at an FDA-approved dosage for age and weight.

Specialty Biological Agents for Rheumatoid Arthritis	
	• If the request is for Xeljanz, Xeljanz XR, or Rinvoq, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of a preferred Tumor Necrosis Factor (TNF) inhibitor agent • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using at least TWO of the preferred biological agents • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **PA CRITERIA FOR RE-AUTHORIZATION FOR RHEUMATOID ARTHRITIS:** • The member has been receiving the medication and documentation was provided that a rheumatologist has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. • For members who require dose increases to Humira 40 mg weekly or 80mg every other week, documentation must be submitted indicating that the member is not on concomitant methotrexate and has a medical reason (e.g. intolerance, hypersensitivity, contraindication) for not receiving concomitant methotrexate. • The medication is being prescribed at an FDA-approved dosage.
Criteria Statement	Humira, Amjevita, Actemra, Xeljanz/Xeljanz XR, or Rinvoq are reserved for members who have rheumatoid arthritis and who have used (or cannot/should not use) at least one other alternative disease-modifying antirheumatic drug (DMARD) such as methotrexate, leflunomide, sulfasalazine, or hydroxychloroquine. Xeljanz, Xeljanz XR, or Rinvoq are reserved for members who have used (or cannot/should not use) a preferred Tumor Necrosis Factor (TNF) inhibitor agent. Non-preferred medications are reserved for members who have used (or cannot/should not use) at least two of the following: Humira, Amjevita, Actemra, Xeljanz/Xeljanz XR, or Rinvoq.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Adult Psoriatic Arthritis (PsA)	
Therapeutic Classes (AHFS)	Disease Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agents- Require Prior Authorization **HUMIRA (adalimumab)** **TALTZ (ixekizumab)** **SKYRIZI (risankizumab-rzaa)** **XELJANZ (tofacitinib)** **XELJANZ XR (tofacitinib)** **RINVOQ (upadacitinib)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **ENBREL (etanercept)** **CIMZIA (certolizumab)** **SIMPONI (golimumab)** **SIMPONI (golimumab) Aria** **COSENTYX (secukinumab)** **REMICADE (infliximab)** **INFLIXIMAB** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **AVSOLA (infliximab-axxq)** **OTEZLA (apremilast)** **STELARA (ustekinumab)** **ORENCIA (abatacept)** **TREMFYA (guselkumab)** **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	Prescriber is a rheumatologist
Coverage Duration	**Initial** 12 months **Reauthorization** 12 months If all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** ****For requests for Juvenile Psoriatic Arthritis, please see the Specialty Biologic Agents for Juvenile Idiopathic Arthritis policy**** **PA CRITERIA FOR ADULT PSORIATIC ARTHRITIS (PsA):** • The member has a diagnosis of psoriatic arthritis.

	• If there is documentation of severe erosive disease with functional limitation, a preferred biologic agent may be approved • For all other members there is a documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking at least one conventional DMARD such as methotrexate, leflunomide, or sulfasalazine OR one formulary non-steroidal anti-inflammatory drug (NSAID) or cyclooxygenase-2 (COX-2) inhibitor to manage their medical condition. **OR** • Member has axial disease (i.e. involving the sacroiliac joints and spine) or enthesitis (i.e. involving the plantar fascia and Achilles tendon insertion) and has documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking NSAID or COX-2 inhibitor to manage the condition. • The medication requested is being prescribed at an FDA-approved dosage for age and weight. • If the request is for Rinvoq, Xeljanz or Xeljanz XR documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of a preferred Tumor Necrosis Factor (TNF) inhibitor agent • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using at least TWO of the preferred biological agents • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **PA CRITERIA FOR RE-AUTHORIZATION FOR ADULT PSORIATIC ARTHRITIS (PsA):** • The medication is being prescribed at an FDA approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.
Criteria Statement	Humira, Amjevita, Taltz, Skyrizi, Rinvoq, and Xeljanz/Xeljanz XR are reserved for members who have a documentation of severe erosive disease with functional limitation OR a diagnosis of adult psoriatic arthritis and have used (or cannot/should not use) conventional DMARDs OR NSAIDs or COX-2 inhibitors. For members with axial disease (i.e. involving the sacroiliac joints and spine) or enthesitis (i.e. involving the plantar fascia and Achilles tendon insertion), Humira, Amjevita, Taltz, Skyrizi, Rinvoq, and Xeljanz/Xeljanz XR are reserved for members who have used (or cannot/should not use) NSAIDs or COX-2 inhibitor therapy. Rinvoq, Xeljanz and Xeljanz XR are reserved for members who have used (or cannot/should not use) a preferred Tumor Necrosis Factor (TNF) inhibitor agent. Non-preferred biologics are reserved for members who have used (or cannot/should not use) at least two of the following: Humira, Amjevita, Taltz, Skyrizi, Rinvoq, or Xeljanz/Xeljanz XR.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Psoriasis	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agents- Require Prior Authorization **HUMIRA (adalimumab)** **TALTZ (ixekizumab)** **SKYRIZI (risankizumab-rzaa)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **ENBREL (etanercept)** **REMICADE (infliximab)** **INFLIXIMAB** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **AVSOLA (infliximab-axxq)** **OTEZLA (apremilast)** **COSENTYX (secukinumab)** **STELARA (ustekinumab)** **SILIQ (brodalimumab)** **TREMFYA (guselkumab)** **ILUMYA (tildrakizumab-asmn)** **CIMZIA (certolizumab)** **SOTYKTU (deucravacitinib)** **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	Prescriber is a 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	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **PA CRITERIA FOR APPROVAL FOR PSORIASIS:** • The member has a diagnosis of plaque psoriasis. • Documentation that the patient has had (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not using 3 of the treatment bullet points listed below, at least one of which must be either systemic therapy or phototherapy: ○ topical steroids ○ calcipotriene, tazarotene ○ Topical anthralin, salicylic acid or a coal tar preparation

Specialty Biological Agents for Psoriasis	
	○ Oral methotrexate or cyclosporine ○ Oral acitretin ○ Topical tacrolimus or pimecrolimus ○ UVB phototherapy or PUVA (psoralen – oral or topical methoxsalen plus UVA therapy) • The medication requested is being prescribed at an FDA-approved dosage for age and weight. • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using at least TWO of the preferred biological agents • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used • If the request is for Stelara, the initial dose must start at 45mg at 0 and 4 weeks before 90mg dose can be considered. This also applies to those weighing over 100kg. Subsequent doses every 12 weeks thereafter may be increased to 90mg for those over 100kg with dermatologist attestation for clinical need of increase in dose/lack of efficacy on 45mg **PA CRITERIA FOR RE-AUTHORIZATION FOR PSORIASIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.
Criteria Statement	Humira, Amjevita, Skyrizi and Taltz are reserved for members who have plaque psoriasis and have used (or cannot/should not use) 3 different treatment options, at least one of which must be either systemic therapy or phototherapy. Non-preferred medications are reserved for members who have used (or cannot/should not use) at least two of the following: Humira, Amjevita, Skyrizi or Taltz
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Juvenile Idiopathic Arthritis	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**See section for each disease-state indication subtype below in "PA Review Criteria" for disease-state specific indicated medications** **HUMIRA (adalimumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **XELJANZ (tofacitinib)** **ACTEMRA (tocilizumab)** **ORENCIA (abatacept)** **ENBREL (etanercept)** **ILARIS (canakinumab)** **COSENTYX (secukinumab)** **SIMPONI Aria (golimumab)** **REMICADE (infliximab)** **AVSOLA (infliximab-axxq)** **RENFLEXIS (infliximab-abda)** **INFLECTRA (infliximab-dyyb)** **INFLIXIMAB** **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	Prescriber is 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	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **PA CRITERIA FOR APPROVAL FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS:** Preferred Pharmacy Benefit Agents: Humira (adalimumab) Amjevita (adalimumab-atto) 40mg/0.8mL auto injector Xeljanz (tofacitinib) Actemra (tocilizumab) Non-Preferred Pharmacy Benefit Agents Orencia (abatacept) Enbrel (etanercept)

Specialty Biological Agents for Juvenile Idiopathic Arthritis	

	Stelara (ustekinumab)
	
	• The member has diagnosis of **polyarticular** juvenile idiopathic arthritis.
	• The medication requested is being prescribed at an FDA-approved dosage for age and weight.
	• The member has an adequate trial (consistent with pharmacy claims/medical record data/physician attestation) with one disease modifying anti-rheumatic drug (DMARD) (e.g. methotrexate or leflunomide or sulfasalazine), or one of the following is true:
	  ○ Member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using conventional therapy to manage their condition.
	  ○ Member has one or more of the following: Risk factors (ex. positive rheumatoid factor, positive anti-cyclic citrullinated peptide antibodies, joint damage) and have involvement of high-risk joints, high disease activity, and/or those judged to be at high-risk of disabling joint damage
	• If the request is for Xeljanz (tofacitinib), there is documented (consistent with pharmacy claims/medical record data/physician attestation), adequate trial of a preferred tumor necrosis factor (TNF) inhibitor.
	• If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes, physician attestation) adequate trial of two preferred biological agents.
	• For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used
	
	PA CRITERIA FOR APPROVAL FOR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS:
	
	Pharmacy Benefit Agents:
	Humira (adalimumab)
	Amjevita (adalimumab-atto) 40mg/0.8mL auto injector
	Actemra (tocilizumab)
	Orencia (abatacept)
	Ilaris (canakinumab)
	Kineret (anakinra)
	
	• The member has diagnosis of **systemic** juvenile idiopathic arthritis.
	• The medication requested is being prescribed at an FDA-approved dosage for age and weight
	• If there is documentation of sJIA with macrophage activation syndrome (MAS), a preferred biologic agent may be approved
	OR
	• One of the following is true:
	  ○ The member has an adequate trial (consistent with pharmacy claims/medical record data/physician attestation) with one of the following:
	  ▪ Non-steroidal anti-inflammatory drug (NSAID)
	  ▪ Systemic glucocorticoids
	  ▪ Methotrexate
	  ▪ Leflunomide
	  ▪ Cyclosporine or tacrolimus

Specialty Biological Agents for Juvenile Idiopathic Arthritis	
	○ The member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using conventional therapy to manage their condition. ○ For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **PA CRITERIA FOR APPROVAL FOR JUVENILE PSORIATIC ARTHRITIS:** Pharmacy Benefit Agents: Cosentyx (secukinumab) Stelara (ustekinumab) • The member has diagnosis of juvenile psoriatic arthritis. • The medication is being prescribed at an appropriate FDA approved dose (for age and weight). • One of the following is true: ○ The member has an adequate trial (consistent with pharmacy claims/medical record data/physician attestation) with nonsteroidal anti-inflammatory drugs (NSAIDs) or a cyclooxygenase-2 (COX-2) inhibitor and then a conventional DMARD (e.g. leflunomide, methotrexate or sulfasalazine) ○ Member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using NSAIDs or COX-2 inhibitors, then a DMARD to manage their condition. ○ There is documentation of severe erosive disease with functional limitation. ○ Member has axial disease (i.e., involving the sacroiliac joints and spine) or enthesitis (i.e involving the plantar fascia and Achilles tendon insertion) and has tried and failed NSAIDs or COX-2 inhibitor therapy. **PA CRITERIA FOR APPROVAL FOR ENTHESITIS-RELATED ARTHRITIS:** Pharmacy Benefit Agents: Cosentyx (secukinumab) Humira (adalimumab) Amjevita (adalimumab-atto) 40mg/0.8mL auto injector Enbrel (etanercept) • The member has diagnosis of enthesitis-related arthritis. • The medication is being prescribed at an appropriate FDA approved, or compendia supported, dose (for age and weight). • The member has an adequate trial with a nonsteroidal anti-inflammatory drug (NSAID) or a cyclooxygenase-2 (COX-2) inhibitor, or member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using one of these agents. • If the request is for a TNF inhibitor other than Humira or Amjevita, one of the following: ○ Documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation), adequate trial of Humira or Amjevita. ○ Member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using Humira or Amjevita to manage their condition.

Specialty Biological Agents for Juvenile Idiopathic Arthritis	
	• For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **PA CRITERIA FOR RE-AUTHORIZATION** • The medication is being prescribed at an appropriate FDA approved, or compendia supported, dose (for age and weight) • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit).
Criteria Statement	Humira, Amjevita, Xeljanz, and Actemra are reserved for members who have polyarticular juvenile idiopathic arthritis and have used (or cannot/should not use) at least one disease-modifying anti-rheumatic drug (DMARD) (e.g. methotrexate, leflunomide or sulfasalazine) OR those with high disease activity and high risk of disabling joint damage. Medications for systemic juvenile idiopathic arthritis are reserved for members who have macrophage activation syndrome (MAS) OR who have used (or cannot/should not use) one of the following: a non-steroidal anti-inflammatory drug (NSAID), systemic glucocorticoids, methotrexate, leflunomide, or cyclosporine/tacrolimus. Medications for juvenile psoriatic arthritis are reserved for members who have used (or cannot/should not use) a nonsteroidal anti-inflammatory drug (NSAID) or a cyclooxygenase-2 (COX-2) inhibitor and then a conventional DMARD (e.g. leflunomide, methotrexate or sulfasalazine) OR those with axial disease or enthesitis who have used (or cannot/should not use) a nonsteroidal anti-inflammatory drug (NSAID) or a cyclooxygenase-2 (COX-2) inhibitor OR those with severe erosive disease with functional limitation. Medications for enthesitis-related arthritis are reserved for members who have used (or cannot/should not use) a nonsteroidal anti-inflammatory drug (NSAID) or a cyclooxygenase-2 (COX-2) inhibitor.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Ankylosing Spondylitis	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agents- Require Prior Authorization **HUMIRA (adalimumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **TALTZ (ixekizumab)** **XELJANZ (tofacitinib)** **XELJANZ XR (tofacitinib)** **RINVOQ (upadacitinib)** **STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **CIMZIA (certolizumab)** **ENBREL (etanercept)** **COSENTYX (secukinumab)** **SIMPONI (golimumab)** **SIMPONI ARIA (golimumab)** **REMICADE (infliximab)** **INFLIXIMAB** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **AVSOLA (infliximab-axxq)** **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	Prescriber is a rheumatologist
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	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **PA CRITERIA FOR ANKYLOSING SPONDYLITIS** • The member has a diagnosis of ankylosing spondylitis. • The member has a documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking at least two different nonsteroidal anti-inflammatory drugs (NSAIDs), one of which must be a COX-2 selective inhibitor if member reports recent history of GI upset or intolerance, at max tolerated doses for at least one month. • The medication requested is being prescribed at an FDA approved dosage for age and weight.

Specialty Biological Agents for Ankylosing Spondylitis	
	• If the request is for Rinvoq, Xeljanz or Xeljanz XR documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of a preferred Tumor Necrosis Factor (TNF) inhibitor agent • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using at least TWO of the preferred biological agents • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **PA CRITERIA FOR RE-AUTHORIZATION FOR ANKYLOSING SPONDYLITIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.
Criteria Statement	Rinvoq, Humira, Amjevita, Xeljanz/Xeljanz XR, and Taltz, are reserved for members who have ankylosing spondylitis who have used (or cannot/should not use) at least two different nonsteroidal anti-inflammatory drugs (NSAIDs). Rinvoq, Xeljanz and Xeljanz XR are reserved for members who have used (or cannot/should not use) a preferred Tumor Necrosis Factor (TNF) inhibitor agent. Non-preferred agents are reserved for members who have used (or cannot/should not use) Rinvoq, Humira, Amjevita, Xeljanz/Xeljanz XR, or Taltz.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Nonradiographic Axial Spondyloarthritis (nr-axSpA)	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agents- Require Prior Authorization **TALTZ (ixekizumab)** **RINVOQ (upadacitinib)** **STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **CIMZIA (certolizumab)** **COSENTYX (secukinumab)** **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	Prescriber is a rheumatologist
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**PA CRITERIA FOR NONRADIOGRAPHIC AXIAL SPONDYLOARTHRITIS (nr-axSpA)** • The member has a diagnosis of nonradiographic axial spondyloarthritis (nr-axSpA) • The member has a documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking at least two different nonsteroidal anti-inflammatory drugs (NSAIDs), one of which must be a COX-2 selective inhibitor if member reports recent history of GI upset or intolerance, at max tolerated doses for at least one month. • The medication requested is being prescribed at an FDA approved dosage for age and weight. • If the request is for Rinvoq, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of or an inadequate response to or intolerance to a Tumor Necrosis Factor inhibitor (TNFi) agent • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking BOTH of the preferred biological agents o If the request is for Cimzia, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of both preferred products or documentation that a TNFi is medically necessary and no other TNFi agent is indicated **PA CRITERIA FOR RE-AUTHORIZATION FOR NONRADIOGRAPHIC AXIALSPONDYLOARTHRITIS:**

Specialty Biological Agents for Nonradiographic Axial Spondyloarthritis (nr-axSpA)	
	• The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.
Criteria Statement	Taltz and Rinvoq are reserved for members who have nonradiographic axial spondyloarthritis (nr-axSpA). Non-preferred agents are reserved for members who have used (or cannot/should not use) Taltz and Rinvoq. Rinvoq is reserved for members who have used (or cannot/should not use) a Tumor Necrosis Factor (TNF) inhibitor agent.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Hidradenitis Suppurativa	
Therapeutic Classes (AHFS)	Disease Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agent- Requires Prior Authorization **HUMIRA (adalimumab)** **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	Prescriber is a dermatologist
Coverage Duration	**Initial** — If all criteria are met, approve for up to a 12 month duration; if all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review. **Reauthorization** — If all criteria are met, approve for up to a 12 month duration; if all of the criteria are not met, the request is referred to a clinical reviewer for medical necessity review.
PA Review Criteria	**PA CRITERIA FOR APPROVAL FOR HIDRADENITIS SUPPURATIVA:** • Diagnosis of moderate to severe hidradenitis suppurativa classified as Hurley stage II or III • The medication requested is being prescribed at an FDA-approved dosage for age and weight • The member has a documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not taking an adequate trial (of at least 10 weeks) with oral antibiotics (e.g. doxycycline, tetracycline, or minocycline) • If the request is for a non-preferred biological agent, documented medical reason as to why patient is unable to utilize the preferred product. **PA CRITERIA FOR RE-AUTHORIZATION FOR HIDRADENITIS SUPPURATIVA:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication
Criteria Statement	Humira is reserved for members with moderate to severe hidradenitis suppurativa classified as Hurley stage II or III who have tried and failed, or have a reason not to use oral antibiotics.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Giant Cell Arteritis	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agent- Requires Prior Authorization ACTEMRA (tocilizumab) 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	Prescriber is a rheumatologist, neurologist, or ophthalmologist
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**PA CRITERIA FOR APPROVAL FOR GIANT CELL ARTERITIS (GCA):** • The member has a diagnosis of giant cell arteritis. • Documentation that the patient has had an adequate trial of (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking corticosteroids (e.g. prednisone) and methotrexate • If the request is for a non-preferred biological agent, documented medical reason as to why patient is unable to utilize the preferred agent **PA CRITERIA FOR RE-AUTHORIZATION FOR GIANT CELL ARTERITIS (GCA)::** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.
Criteria Statement	Actemra is reserved for members who have used (or cannot/should not use) corticosteroids and methotrexate.
Last P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire

Specialty Biological Agents for Uveitis	
Therapeutic Classes (AHFS)	Disease-Modifying Antirheumatic Agents
Medications	**STATUS:** Preferred Biological Agent- Requires Prior Authorization HUMIRA (adalimumab) 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	Prescriber is a rheumatologist, ocular immunologist or ophthalmologist
Coverage Duration	**Initial Approval** 12 months **Later Approvals** 12 months If conditions are not met, the request will be sent to a clinical reviewer.
PA Review Criteria	**PA CRITERIA FOR APPROVAL FOR UVEITIS:** • The member has a diagnosis of non-infectious intermediate, posterior panuveitis. • Chronic, recurrent, treatment-refractory OR vision-threatening disease • Documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using conventional therapy (e.g. corticosteroids or immunosuppressive drugs, for example, azathioprine, cyclosporine, methotrexate). • If the request is for a non-preferred biological agent, documented medical reason as to why patient is unable to utilize the preferred agent **PA CRITERIA FOR RE-AUTHORIZATION FOR UVEITIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication.
Criteria Statement	Humira is reserved for members who have used (or cannot/should not use) corticosteroids or immunosuppressive drugs, for example, azathioprine, cyclosporine, or methotrexate.
Last P&T Review Date	~~3/2023~~9/2023

Alameda Medical PAD Policies for Review Q3 2023 P&T: Changes

Recommendation:

- Rearrange bullet points and requirements to standardize the language and format between this policy and the new Leqembi policy
- Require only one evidence score for diagnosis vs all. In practice multiple cognitive tests to determine AD staging is not necessary.
- Update documentation requirement confirmation of beta amyloid to align with package insert and trial
- For reauthorization, in place of outlining all safety parameters listed in package insert, require provider attestation that safety monitoring and management of amyloid related imaging abnormalities (ARIA) and intracerebral hemorrhage is being done

Aduhelm (aducanumab)	
Medications	Aduhelm (aducanumab)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	Patients with moderate to severe Alzheimer's Disease (AD) Patients with neurodegenerative disease caused by other than AD
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	N/A
Prescriber Restrictions	Prescriber must be a neurologist
Maximum Billable Units	variable
Coverage Duration	**Initial Authorization** The request will be approved in accordance with the FDA-indicated titration schedule for up to 6 months **Reauthorization** If all of the conditions are met, the request will be approved for 6 months.

Other Criteria	**Initial Authorization**
	• Diagnosis of mild cognitive impairment (MCI) caused by AD or mild AD as evidenced by at least one of the following:
	  ○ Clinical Dementia Rating Global (CDR-G) score of 0.5 (very mild dementia)
	  ○ Repeatable Battery for Assessment of Neuropsychological Status (RBANS) delayed memory index (DMI) score ≤ 85 (low average)
	  ○ Mini-Mental State Examination (MMSE) score ≥ 24 (questionably significant impairment)
	• The request is for an FDA approved dose
	• Documentation of BOTH of the following:
	  ○ Recent, within past year, positive results for the presence of beta-amyloid plaques on a positron emission tomography (PET) scan or cerebrospinal fluid testing
	  ○ Recent, within past year, baseline Magnetic Resonance Imaging (MRI) scan
	~~• Clinical Dementia Rating Global (CDR-G) score of 0.5 (very mild dementia)~~
	~~• Repeatable Battery for Assessment of Neuropsychological Status (RBANS) delayed memory index (DMI) score ≤ 85 (low average)~~

	~~• Mini-Mental State Examination (MMSE) score ≥ 24 (questionably significant impairment)~~ ~~• Patient is not taking any chronic medications that can substantially contribute to cognitive impairment (i.e. strong anticholinergics such as first-generation antihistamines, tricyclic antidepressants; benzodiazepines; antipsychotics; barbiturates; skeletal muscle relaxants; see Beer's List)~~ • Not currently using blood thinners (except aspirin) • No recent (past 1 year) history of stroke or transient ischemic attack (TIA) **Reauthorization** • The request is for an FDA approved dose • Provider attestation of safety monitoring and management of amyloid related imaging abnormalities (ARIA) and intracerebral hemorrhage, as recommended per the manufacturer's prescribing information. ~~• Before the 7th and 13th doses, documentation (i.e. chart notes, test results) of repeat MRI scan to monitor for amyloid related imaging abnormalities (ARIA) including the following:~~ ~~○ Type of ARIA (-edema [E] or hemosiderin deposition [H]), if any~~ ~~○ Severity of ARIA (mild, moderate, severe), if any~~ ~~○ If severe ARIA-H, approval of continued therapy is contingent upon repeat MRI demonstrating radiographic stabilization~~ • Patient continues to have a diagnosis of mild cognitive impairment (MCI) caused by AD or mild AD consistent with Stage 3 or Stage 4 Alzheimer's disease as evidenced by at least one of the following: ○ CDR-G score of 0.5 (very mild dementia) ○ RBANS DMI score ≤ 85 (low average) ○ MMSE score of 24-30 ~~• Patient is not taking any medications that can substantially contribute to cognitive impairment (i.e. strong anticholinergics such as first-generation antihistamines, tricyclic antidepressants; benzodiazepines; antipsychotics; barbiturates; skeletal muscle relaxants; see Beer's List)~~ • Not currently using blood thinners (except aspirin) • No recent (past 1 year) history of stroke or TIA • Recent, within past year, positive results for the presence of beta-amyloid plaques on a positron emission tomography (PET) scan If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~9/2022~~9/2023

Recommendation:

- Add new medication Vowst to policy and change name. It is given orally but could potentially be administered inpatient during CDI treatment.

Fecal microbiotaRebyota	
Medications	Rebyota (fecal microbiota, live-jslm) Vowst (fecal microbiota spores, live-brpk)
Covered Uses	Medically accepted indications 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	Treatment of Clostridioides difficile infection (CDI)
Required Clinical Information	See "other criteria"
Age Restrictions	According to package insert
Prescriber Restrictions	N/A
Coverage Duration	If all the criteria are met, the request will be approved for 1 treatment course
Maximum Billable Units	Variable
Other Criteria	**Initial Authorization:** • Medication is prescribed at an FDA approved dose • Diagnosis of at least 1 recurrent episode of CDI (≥2 total CDI episodes) • Current episode of CDI must be controlled (<3 unformed/loose stools/day for 2 consecutive days) • Positive stool test for C. difficile within 30 days before prior authorization request • Administration will occur 24–72 hours following completion of antibiotic course for CDI treatment • For Vowst only: confirmation patient will bowel cleanse using magnesium citrate or polyethylene glycol electrolyte solution the day before the first dose of Vowst *Rebyota and Vowst areis limited to 1 treatment course* If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	3/20239/20239/2023

Recommendation:

- Update requirements to glucocorticoid-induced osteoporosis.
  - The newest guideline updates have added a very high-risk category.
  - Additionally, there are no recommendations for patients with moderate risk to use injectable osteoporosis treatments – remove section with FRAX between 1-3 percent and 10-19 percent.
- Remove duplicative diagnosis requirement in reauthorization criteria

Injectable/Infusible Agents for Osteoporosis and Paget's Disease	
Medications	ibandronate (Boniva) injection zoledronic acid (Reclast) Prolia (denosumab) Forteo (teriparatide) Teriparatide Tymlos (abaloparatide) Evenity (romosozumab-aqqg) Pamidronate Or any newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	N/A
Coverage Duration	If all conditions are met, the request will be approved for up to 12 months. ***FORTEO/TERIPARATIDE/TYMLOS REQUESTS WILL ONLY BE APPROVED FOR A TOTAL DURATION OF 24 MONTHS*** *** EVENITY WILL ONLY BE APPROVED FOR A TOTAL OF 12 MONTHS*** reauthorization requests will be approved for up to 12 months.
Maximum Billable Units	Variable

Other Criteria	**CRITERIA FOR APPROVAL FOR ALL REQUESTS:**
	• Dose is appropriate per label or supported by compendia/standard of care guidelines
	• The member is taking adequate calcium and vitamin D supplementation
	• The member has a documented (consistent with pharmacy claims) adequate trial of an oral bisphosphonate or has a medical reason (e.g. intolerance, hypersensitivity, contraindication, etc.) for not using an oral bisphosphonate
	
	POSTMENOPAUSAL OR MALE OSTEOPOROSIS:
	• If the request is for very high risk postmenopausal osteoporosis or postmenopausal osteoporosis, with prior fractures, a documented trial and failure of an oral bisphosphonate will not be required.
	  ○ Very high risk is defined as having one or more of the following:
	  ▪ History of fracture in the past 12 months
	  ▪ Multiple fractures
	  ▪ Fractures while on drugs causing skeletal harm (e.g. long-term glucocorticoids)
	  ▪ Very low T scores (< -3.0)
	  ▪ High risk for falls
	  ▪ History of injurious falls

	▪ Very high fracture probability as determined by fracture risk assessment tool (FRAX) (e.g. major osteoporosis fracture >30%, hip fracture > 4.5%) • Documentation was submitted indicating the member is a postmenopausal woman or a male over 50 years of age and one of the following: o A bone mineral density (BMD) value consistent with osteoporosis (i.e., T-scores equal to or less than –2.5) o Has had an osteoporotic fracture o 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: o 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 o 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 Teriparatide, a medical reason why member is unable to use Tymlos or Evenity, if appropriate, based on the diagnosis. o Requests for brand Forteo (teriparatide) also require a medical reason why the member is unable to use Teriparatide • If the request is for Evenity, the member does not have a history of a heart attack or stroke within the preceding year **GLUCOCORTICOID-INDUCED OSTEOPOROSIS THERAPY:** • Documentation that the member is currently utilizing glucocorticoid therapy for a minimum of 3 months • Documentation that the dosage of the glucocorticoid therapy is greater than 2.5 mg of prednisone daily or its equivalent • Member is 40 years of age or older • Member has a ~~moderate to~~ high to very high risk of fracture based on ONE of the following: o History of osteoporotic fracture o BMD less than or equal to -2.5 at the hip or spine o FRAX 10-year probability of hip or combined major osteoporotic fracture of ≥3 and 20 percent, respectively o ~~FRAX 10-year probability of hip or combined major osteoporotic fracture between 1 to 3 percent and 10 to 19 percent, respectively~~ • 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: o 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 patient is at risk for complication from Paget's disease

	CRITERIA FOR REAPPROVAL: • The member has documentation of clinical benefit from the medication • ~~Documentation of a confirmed diagnosis of Paget's disease~~.
Last Review Date	~~9/2022~~9/2023

Recommendation:

- Add new products Stimufend (pegfilgrastim-fpgk), Fylnetra (pegfilgrastim-pbbk), and Rolvedon (eflapegrastim-xnst) to policy.

White Blood Cell Stimulators	
Medications	Mozobil (plerixafor) Leukine (sargramostim) **Long acting-CSF** Neulasta (pegfilgrastim) Neulasta (pegfilgrastim) Onpro Fulphila (pegfilgrastim-jmdb) - biosimilar Udenyca (pegfilgrastim-cbqv) - biosimilar Ziextenzo (pegfilgrastim-bmez) - biosimilar Nyvepria (pegfilgrastim-apgf) – biosimilar Fylnetra (pegfilgrastim-pbbk) – biosimilar Stimufend (pegfilgrastim-fpgk) – biosimilar Rolvedon (eflapegrastim-xnst) **Short acting-CSF** Neupogen (filgrastim) Zarxio (filgrastim-sndz) - biosimilar Nivestym (filgrastim-aafi) - biosimilar Granix (tbo-filgrastim) – biosimilar Releuko (filgrastim-ayow) - biosimilar Any other newly marketed agent
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "**Other Criteria**" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber must be a hematologist/oncologist.
Maximum Billable Units	variable
Coverage Duration	**Initial Approval** 12 weeks or as recommended per FDA approved indications and/or as defined by the medical compendium as defined above and/or per the NCCN or ASCO standard of care guidelines **Later Approval** For all indications except chronic neutropenia: 12 weeks. For chronic neutropenia: 24 weeks.
Other Criteria	**** When this biosimilar is indicated, the member must have documented dates of trial and failure, intolerance, inability to use, or contraindication to the biosimilar medication prior to the brand medication approval, 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.** For approval: • If the request is for Leukine:

	○ Documentation is submitted of the patient's current diagnosis, current bodyweight, body surface area and absolute neutrophil count (within 30 days of the request) • If the request is for Mozobil: ○ Documentation is submitted of the patient's current diagnosis, current bodyweight, and that the patient is using Mozobil in combination with a granulocyte-colony stimulating factor (G-CSF) agent (i.e. Zarxio or Fulphila) • If the request is for a pegfilgrastim formulation or Rolvedon: ○ The patient has a documented treatment failure (i.e. failure to reach and/or maintain target ANC, prolonged febrile neutropenia or infection requiring prolonged anti-infection use) with the use of a biosimilar and/or has another documented medical reason (intolerance, hypersensitivity, etc.) for not using a biosimilar. ○ If the request is for acute hematopoietic radiation injury syndrome, Neulasta can be approved without prior use of a biosimilar or medical reason for not using a biosimilar. • If the request is for a filgrastim formulation: ○ The patient has a documented treatment failure (i.e. failure to reach and/or maintain target ANC, prolonged febrile neutropenia or infection requiring prolonged anti-infection use) with the use of a biosimilar and/or has another documented medical reason (intolerance, hypersensitivity, etc.) for not using a biosimilar. ○ If the request is for acute hematopoietic radiation injury syndrome, Neupogen can be approved without prior use of a biosimilar or medical reason for not using a biosimilar. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~9/2022~~9/2023

Recommendation:

- Update policy for Injectafer's new indication as of 5/2023: for treatment of iron deficiency in adult patients with heart failure and New York Heart Association Class II/III to improve exercise capacity
    - Allow approval for Injectafer with diagnosis of NYHA class II/III only
- Update coverage duration to be inclusive of both possible dosing schedules for iron deficiency anemia for Injectafer

Iron-containing Products	
Medications	Injectafer (ferric carboxymaltose) injection, solution Ferumoxytol (Feraheme) Monoferric (ferric derisomaltose)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "other criteria"
Age Restrictions	Check AAH active CCS cases for members < 21 years of age ~~for MCAL~~
Prescriber Restrictions	N/A
Coverage Duration	If all of the criteria are met, request may be approved for: • Injectafer: two (2) doses of up to 750mg maximum at least seven (7) days apart, or 1 dose of up to 1000mg maximum once. May reapprove for recurrent anemia • Ferumoxytol (Feraheme): 2 doses of 510mg maximum at least 3-8 days apart. May re-approve for persistent or recurrent anemia • Monoferric (ferric derisomaltose): 1 dose of up to 1000mg maximum once. May re-approve for recurrent anemia
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	• Diagnosis of iron deficiency anemia
	  ○ Members who have intolerance to oral iron or have tried and failed oral iron, or
	  ○ Members for whom initiation of oral iron would be medically contraindicated (such as malabsorption syndromes, severe blood loss, etc.) or
	  ○ Members is a dialysis patient
	• Medication is being prescribed at an age appropriate FDA approved dose or is supported by compendia or standard of care guidelines
	• The member has tried and failed, has an intolerance, or inability to use one of the following: iron dextran (Infed), iron sucrose (Venofer), or sodium ferric gluconate complex (Ferrlecit)
	OR
	• Diagnosis of iron deficiency in adult patients with heart failure and New York Heart Association class II/III (Injectafer only)
	
	Re-authorization:
	• Medication is being prescribed at an FDA approved dose or is supported by compendia or standard of care guidelines
	• Documentation provided that member had a positive response to therapy (as evidenced by improved lab values such as hemoglobin, ferritin, transferrin saturation) but continues to have iron deficiency or iron deficiency anemia

	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.
Last Review Date	~~9/2022~~9/2023

Recommendation:

- Criteria updates to reflect Tepezza's newly gained, expanded indication (active and **inactive** thyroid eye disease) based off a study showing improvement in proptosis at 24 weeks even in patients without clinically active disease.
- Remove CAS requirement: CAS is a measure used to determine disease activity. With inactive TED patients now approved for treatment, this should be removed.
- Differentiate prerequisite therapies based on disease activity: Steroids are not appropriate in inactive TED, these patients may undergo corrective surgery.

Tepezza	
Medications	Tepezza (teprotumumab-trbw)
Covered Uses	Medically accepted indications 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	Member must be 18 years age or older
Prescriber Restrictions	Prescriber must be an ophthalmologist or endocrinologist
Coverage Duration	If all of the criteria are met, the request will be approved for up to 24 weeks of treatment (8 total infusions). Retreatment requests will not be allowed beyond the 8 dose limit.
Maximum Billable Units	Variable

Other Criteria	**Initial Authorization:**
	Tepezza is approved when all of the following are met:
	• Dosing does not exceed dosing guidelines as outlined in the package insert
	• Member has a confirmed diagnosis of Graves' disease
	• Documentation of ~~active~~ moderate-severe thyroid eye disease as evidenced by one or more of the following:
	  ○ Lid retraction of >2mm
	  ○ Moderate or severe soft-tissue involvement
	  ○ Proptosis ≥3mm above normal values for race and sex
	  ○ Periodic or constant diplopia
	~~• Members Clinical Activity Score must be ≥4 (must be submitted with request)~~
	• Member must be euthyroid or thyroxine and free triiodothyronine levels are less than 50% above or below normal limits (submit laboratory results with request)
	• Members of reproductive potential: attestation the member is not pregnant, and appropriate contraception methods will be used before, during, and 6 months after the last infusion
	~~•~~ Member has had a trial and therapy failure of, or contraindication to~~, oral or IV glucocorticoids to treat their condition~~
	  ○ For active disease: oral or IV glucocorticoids
	  ○ For chronic/inactive disease: rehabilitative surgery
	Re-authorization:
	• Retreatment or renewal requests beyond a total of 24 weeks of treatment (8 total infusions) will not be allowed.
	
	If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review.

Last Review Date	~~12/2022~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Crohn's Disease	
Medications	**<u>PREFERRED STATUS:</u>** Preferred Biological Agents **HUMIRA (adalimumab)** **SKYRIZI (risankizumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **<u>PREFERRED STATUS:</u>** Non-Preferred Biological Agents (Second Line) **REMICADE (infliximab)** **INFLIXIMAB** **AVSOLA (infliximab-axxq)** - biosimilar **INFLECTRA (infliximab-dyyb)** - biosimilar **RENFLEXIS (infliximab-abda)** - biosimilar **CIMZIA (certolizumab)** **ENTYVIO (vedolizumab)** **STELARA (ustekinumab)** **TYSABRI (natalizumab)** **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 "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a gastroenterologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **<u>CRITERIA FOR APPROVAL FOR CROHN'S DISEASE:</u>** • The medication is being prescribed at an appropriate FDA approved dose (for age and weight) • The member has a diagnosis of severe/fulminant or perianal/fistulizing Crohn's disease **OR** • The member has a diagnosis of moderate-to-severe/moderate-to-high risk Crohn's disease AND has had an adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using, one of the following: azathioprine, 6-mercaptupurine, corticosteroids, or methotrexate consistent with pharmacy claims/medical record data/chart notes/physician attestation **OR** • The member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using conventional oral therapy to manage their condition • If the request is for a non-preferred agent, documented (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of, or has a documented

Specialty Biological Agents for Crohn's Disease	
	medical reason (e.g. allergy, intolerance, contraindication), for not using at least TWO of the preferred biological agents • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **CRITERIA FOR RE-AUTHORIZATION FOR CROHN'S DISEASE:** • The medication is being prescribed at a Food and Drug Administration (FDA) approved dosage. • The member has been receiving the medication and documentation was provided that the provider has evaluated the member and recommends continuation of therapy • Documentation submitted indicates that the member has obtained clinical benefit from the medication If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Ulcerative Colitis	
Medications	**PREFERRED STATUS:** Preferred Biological Agents **HUMIRA (adalimumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **PREFERRED STATUS:** Non-Preferred Biological Agents (Second Line) **REMICADE (infliximab)** **INFLIXIMAB** **AVSOLA (infliximab-axxq)** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **SIMPONI (golimumab)** **ENTYVIO (vedolizumab)** **STELARA (ustekinumab)** **ZEPOSIA (ozanimod)** 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 “Other Criteria” below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a gastroenterologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.**** **CRITERIA FOR APPROVAL FOR ULCERATIVE COLITIS:** • The member has moderate to severe active ulcerative colitis. • The patient has a documented (consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history) treatment failure after receiving an adequate trial of at least 4-8 weeks of: ○ Sulfasalazine or mesalamine or azathioprine or 6-mercaptopurine or oral corticosteroids or has a documented medical reason (gastrointestinal (GI) intolerance such as nausea, vomiting, bloating, and diarrhea, hypersensitivity, etc.) for not taking any of these medications to treat their medical condition. • The medication requested is being prescribed at an FDA-approved dosage for age and weight. • If the request is for a non-preferred agent, documented (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using BOTH of the preferred biological agents. • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used

Specialty Biological Agents for Ulcerative Colitis	
	• For requests for Zeposia (ozanimod): Documentation of results of varicella zoster virus (VZV) antibody testing indication previous infection or vaccination. • If negative, documentation of VZV vaccination must be provided with the request **CRITERIA FOR RE-AUTHORIZATION FOR ULCERATIVE COLITIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Rheumatoid Arthritis	
Medications	**PREFERRED STATUS:** Preferred Biological Agents **HUMIRA (adalimumab)** **ACTEMRA (tocilizumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **PREFERRED STATUS:** Non-Preferred Biological Agents (Second Line) **ENBREL (etanercept)** **Ruxience (rituximab-pvvr) -** biosimilar **Truxima (rituximab-abbs)** - biosimilar **RITUXAN (rituximab)** **INFLECTRA (infliximab-dyyb)** - biosimilar **RENFLEXIS (infliximab-abda)** - biosimilar **REMICADE (infliximab)** **INFLIXIMAB** **AVSOLA (infliximab-axxq)** - biosimilar **CIMZIA (certolizumab)** **KEVZARA (sarilumab)** **KINERET (anakinra)** **ORENCIA (abatacept)** **SIMPONI (golimumab)** **SIMPONI ARIA (golimumab)** **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 “Other Criteria” below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a rheumatologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.**** **CRITERIA FOR INITIAL APPROVAL FOR RHEUMATOID ARTHRITIS:** • The member has a diagnosis of rheumatoid arthritis. • The member has a documented adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using one disease modifying anti-rheumatic drug (DMARD) (e.g. methotrexate, leflunomide, sulfasalazine or hydroxychloroquine) to manage their condition • The medication requested is being prescribed at an FDA-approved dosage for age and weight. • If the request is for a non-preferred agent, documented (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of at least TWO of preferred biological agents or medical reason as to why the patient is unable to utilize the preferred products.

Specialty Biological Agents for Rheumatoid Arthritis	
	• For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **RITUXIMAB CRITERIA FOR INITIAL APPROVAL FOR RHEUMATOID ARTHRITIS:** • All of the above criteria are met AND • Documentation indicating that rituximab is being used concurrently with methotrexate. • Documentation indicating that the patient has been screened for HBV (hepatitis B virus) prior to initiation of treatment. **CRITERIA FOR RE-AUTHORIZATION FOR RHEUMATOID ARTHRITIS:** • The member has been receiving the medication and documentation was provided that a rheumatologist has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. • For members who require dose increases to Humira 40 mg weekly or 80mg every other week, documentation must be submitted indicating that the member is not on concomitant methotrexate and has a medical reason (e.g. intolerance, hypersensitivity, contraindication) for not receiving concomitant methotrexate. • The medication is being prescribed at an FDA-approved dosage. **RITUXIMAB CRITERIA FOR RE-AUTHORIZATION FOR RHEUMATOID ARTHRITIS:** • All of the above criteria are met AND • At least 16 weeks (4 months) has elapsed since the previous course of rituximab therapy. • Documentation indicating that rituximab is being used concurrently with methotrexate. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Adult Psoriatic Arthritis (PsA)	
Medications	**PREFERRED STATUS:** Preferred Biological Agents **HUMIRA (adalimumab)** **TALTZ (ixekizumab)** **SKYRIZI (risankizumab-rzaa)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **PREFERRED STATUS:** Non-Preferred Biological Agents (Second Line) **ENBREL (etanercept)** **CIMZIA (certolizumab)** **SIMPONI (golimumab)** **SIMPONI** (golimumab) Aria **COSENTYX (secukinumab)** **REMICADE (infliximab)** **INFLIXIMAB** **AVSOLA (infliximab-axxq)** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **STELARA (ustekinumab)** **ORENCIA (abatacept)** **TREMFYA (guselkumab)** **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 “Other Criteria” below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a rheumatologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.**** ****For requests for Juvenile Psoriatic Arthritis, please see the Specialty Biologic Agents for Juvenile Idiopathic Arthritis policy**** **CRITERIA FOR ADULT PSORIATIC ARTHRITIS (PsA):** • The member has a diagnosis of psoriatic arthritis. • If there is documentation of severe erosive disease with functional limitation, a preferred biologic agent may be approved • For all other members there is a documented adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking at least one conventional DMARD such as methotrexate, leflunomide, or sulfasalazine OR one formulary non-steroidal anti-inflammatory drug (NSAID) or cyclooxygenase-2 (COX-2) inhibitor to manage their medical condition. **OR**

	• Member has axial disease (i.e. involving the sacroiliac joints and spine) or enthesitis (i.e. involving the plantar fascia and Achilles tendon insertion) and has tried and failed, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking, NSAID or COX-2 inhibitor therapy to manage the condition. • The medication requested is being prescribed at an FDA-approved dosage for age and weight. • If the request is for a non-preferred agent, documented (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using, at least two preferred biological agents. • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **CRITERIA FOR RE-AUTHORIZATION FOR ADULT PSORIATIC ARTHRITIS (PsA):** • The medication is being prescribed at an FDA approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Psoriasis	
Medications	**PREFERRED STATUS:** Preferred Biological Agents **HUMIRA (adalimumab)** **TALTZ (ixekizumab)** **SKYRIZI (risankizumab-rzaa)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **PREFERRED STATUS:** Non-Preferred Biological Agents (Second Line) **ENBREL (etanercept)** **REMICADE (infliximab)** **INFLIXIMAB** **AVSOLA (infliximab-axxq)** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **STELARA (ustekinumab)** **SILIQ (brodalimumab)** **TREMFYA (guselkumab)** **ILUMYA (tildrakizumab-asmn)** **CIMZIA (certolizumab)** **COSENTYX (secukinumab)** **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 “Other Criteria” below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a dermatologist
Coverage Duration	12 months
Maximum Billable Units	Variable

Other Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.****
	CRITERIA FOR APPROVAL FOR PSORIASIS:
	• The member has a diagnosis of plaque psoriasis.
	• Documentation that the patient has had (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trials of 3 of the treatment bullet points listed below or a documented medical reason for not using this therapy, at least one of which must be either systemic therapy or phototherapy:
	  ○ topical steroids
	  ○ calcipotriene, tazarotene
	  ○ Topical anthralin, salicylic acid or a coal tar preparation
	  ○ Oral methotrexate or cyclosporine
	  ○ Oral acitretin
	  ○ Topical tacrolimus or pimecrolimus
	  ○ UVB phototherapy or PUVA (psoralen – oral or topical methoxsalen plus UVA therapy)

Specialty Biological Agents for Psoriasis	
	• The medication requested is being prescribed at an FDA-approved dosage for age and weight. • If the request is for a non-preferred agent, documented (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of at least two preferred biological agents or medical reason as to why the patient is unable to utilize the preferred products. • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used • If the request is for Stelara, the initial dose must start at 45mg at 0 and 4 weeks before 90mg dose can be considered. This also applies to those weighing over 100kg. Subsequent doses every 12 weeks thereafter may be increased to 90mg for those over 100kg with dermatologist attestation for clinical need of increase in dose/lack of efficacy on 45mg **CRITERIA FOR RE-AUTHORIZATION FOR PSORIASIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. 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 P&T Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Ankylosing Spondylitis	
Medications	**PREFERRED STATUS:** Preferred Biological Agents **HUMIRA (adalimumab)** **TALTZ (ixekizumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **PREFERRED STATUS:** Non-Preferred Biological Agents (Second Line) **CIMZIA (certolizumab)** **ENBREL (etanercept)** **COSENTYX (secukinumab)** **SIMPONI (golimumab)** **REMICADE (infliximab)** **INFLIXIMAB** **AVSOLA (infliximab-axxq)** **INFLECTRA (infliximab-dyyb)** **RENFLEXIS (infliximab-abda)** **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 “Other Criteria” below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a rheumatologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.**** **CRITERIA FOR ANKYLOSING SPONDYLITIS** • The member has a diagnosis of ankylosing spondylitis. • The member has a documented (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication), for not taking at least two different nonsteroidal anti-inflammatory drugs (NSAIDs), one of which must be a COX-2 selective inhibitor if member reports recent history of GI upset or intolerance, at max tolerated doses for at least one month • The medication requested is being prescribed at an FDA approved dosage for age and weight. • If the request is for a non-preferred agent, documented (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of, or has a documented medical reason (e.g. allergy, intolerance, contraindication) not to use at lease TWO of the preferred biological agents. • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used

Specialty Biological Agents for Ankylosing Spondylitis	
	CRITERIA FOR RE-AUTHORIZATION FOR ANKYLOSING SPONDYLITIS: • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Nonradiographic Axial Spondyloarthritis (nr-axSpA)	
Medications	**PREFERRED STATUS:** Preferred Biological Agents- Require Prior Authorization **TALTZ (ixekizumab)** **PREFERRED STATUS:** Non-Preferred Biological Agents- Require Prior Authorization (Second Line) **CIMZIA (certolizumab)** **COSENTYX (secukinumab)** **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 "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a rheumatologist
Coverage Duration	A 12 month duration for initial approval and 12 months for renewal
Maximum Billable Units	Variable
Other Criteria	**PA CRITERIA FOR NONRADIOGRAPHIC AXIALSPONDYLOARTHRITIS (nr-axSpA)** • The member has a diagnosis of nonradiographic axial spondyloarthritis (nr-axSpA) • The member has a documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of or has a documented medical reason for not taking at least two different nonsteroidal anti-inflammatory drugs (NSAIDs), one of which must be a COX-2 selective inhibitor if member reports recent history of GI upset or intolerance, at max tolerated doses for at least one month. • The medication requested is being prescribed at an FDA approved dosage for age and weight. • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation) adequate trial of the preferred biological agent or medical reason as to why the patient is unable to utilize the preferred product. **PA CRITERIA FOR RE-AUTHORIZATION FOR NONRADIOGRAPHIC AXIALSPONDYLOARTHRITIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. If all of the above criteria are not met, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Juvenile Idiopathic Arthritis	
Medications	**<u>See section for each disease-state indication subtype below in "PA Review Criteria" for disease-state specific indicated medications</u>** **HUMIRA (adalimumab)** **AMJEVITA (adalimumab-atto) 40mg/0.8mL auto injector (preferred NDCs: 72511040001 & 72511040002 only)** **ACTEMRA (tocilizumab)** **ORENCIA (abatacept)** **ENBREL (etanercept)** **ILARIS (canakinumab)** **COSENTYX (secukinumab)** **SIMPONI Aria (golimumab)** **REMICADE (infliximab)** **AVSOLA (infliximab-axxq)** **RENFLEXIS (infliximab-abda)** **INFLECTRA (infliximab-dyyb)** **INFLIXIMAB** **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 "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age
Prescriber Restrictions	Prescriber is a rheumatologist or dermatologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**** Requests for Remicade require documented trial and failure of, intolerance, inability to use, or contraindication to an infliximab biosimilar, in addition to meeting all applicable criteria below.** **<u>CRITERIA FOR APPROVAL FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS:</u>** <u>Preferred Agents:</u> Humira (adalimumab) Amjevita (adalimumab-atto) 40mg/0.8mL auto injector Actemra (tocilizumab) <u>Non-Preferred Agents</u> Orencia (abatacept) Enbrel (etanercept) Simponi Aria (Golimumab) Stelara (ustekinumab) • The member has diagnosis of **polyarticular** juvenile idiopathic arthritis. • The medication requested is being prescribed at an FDA-approved dosage for age and weight. • The member has an adequate trial (consistent with pharmacy claims/medical

Specialty Biological Agents for Juvenile Idiopathic Arthritis	
	record data/physician attestation) with one disease modifying anti-rheumatic drug (DMARD) (e.g. methotrexate or leflunomide or sulfasalazine), or one of the following is true: ○ Member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using conventional therapy to manage their condition. ○ Member has one or more of the following: Risk factors (ex. positive rheumatoid factor, positive anti-cyclic citrullinated peptide antibodies, joint damage) and have involvement of high-risk joints, high disease activity, and/or those judged to be at high-risk of disabling joint damage • If the request is for a non-preferred agent, documented (consistent with pharmacy claims/medical record data/chart notes, physician attestation) adequate trial of two preferred biological agents. • For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **CRITERIA FOR APPROVAL FOR SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS** Humira (adalimumab) Amjevita (adalimumab-atto) 40mg/0.8mL auto injector Actemra (tocilizumab) Orencia (abatacept) Ilaris (canakinumab) Kineret (anakinra) • The medication is being prescribed at an appropriate FDA approved, or compendia supported, dose (for age and weight). • If there is documentation of sJIA with macrophage activation syndrome (MAS), a preferred biologic agent may be approved OR • One of the following is true: ○ The member has an adequate trial (consistent with pharmacy claims/medical record data/physician attestation) with one of the following: ▪ Non-steroidal anti-inflammatory drug (NSAID) ▪ Systemic glucocorticoids ▪ Methotrexate ▪ Leflunomide ▪ Cyclosporine or tacrolimus ○ The member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using conventional therapy to manage their condition. ○ For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used **PA CRITERIA FOR APPROVAL FOR JUVENILE PSORIATIC ARTHRITIS:** Cosentyx (secukinumab Simponi Aria (golimumab) Stelara (ustekinumab) • The medication is being prescribed at an appropriate FDA approved dose (for

Specialty Biological Agents for Juvenile Idiopathic Arthritis	

	age and weight).
	• One of the following is true:
	  ○ The member has an adequate trial (consistent with pharmacy claims/medical record data/physician attestation) with nonsteroidal anti-inflammatory drugs (NSAIDs) or a cyclooxygenase-2 (COX-2) inhibitor and then a conventional DMARD (e.g. leflunomide, methotrexate or sulfasalazine)
	  ○ Member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using NSAIDs or COX-2 inhibitors, then a DMARD to manage their condition.
	  ○ There is documentation of severe erosive disease with functional limitation.
	  ○ Member has axial disease (i.e., involving the sacroiliac joints and spine) or enthesitis (i.e involving the plantar fascia and Achilles tendon insertion) and has tried and failed NSAIDs or COX-2 inhibitor therapy.
	
	PA CRITERIA FOR APPROVAL FOR ENTHESITIS-RELATED ARTHRITIS:
	
	Cosentyx (secukinumab)
	Humira (adalimumab)
	Amjevita (adalimumab-atto) 40mg/0.8mL auto injector
	Enbrel (etanercept)
	Simponi Aria (golimumab)
	Remicade (infliximab)
	Avsola (infliximab-axxq)
	Renflexis (infliximab-abda)
	Inflectra (infliximab-dyyb)
	Inflectra
	
	• The medication is being prescribed at an appropriate FDA approved, or compendia supported, dose (for age and weight).
	• The member has an adequate trial with a nonsteroidal anti-inflammatory drug (NSAID) or a cyclooxygenase-2 (COX-2) inhibitor, or member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using one of these agents.
	• If the request is for a TNF inhibitor other than Humira or Amjevita, one of the following:
	  ○ Documented (consistent with pharmacy claims/medical record data/chart notes/physician attestation), adequate trial of Humira or Amjevita.
	  ○ Member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using Humira or Amjevita to manage their condition.
	• For Amjevita, if the request is for a non-preferred NDC, there is a documented medical reason why a preferred NDC cannot be used
	
	PA CRITERIA FOR RE-AUTHORIZATION:
	• The medication is being prescribed at an appropriate FDA approved, or compendia supported, dose (for age and weight)
	• The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy (clinical benefit).

Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Hidradenitis Suppurativa	
Medications	**PREFERRED STATUS:** Preferred Biological Agent **HUMIRA (adalimumab)**
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a dermatologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**CRITERIA FOR APPROVAL FOR HIDRADENITIS SUPPURATIVA:** • Diagnosis of moderate to severe hidradenitis suppurativa classified as Hurley stage II or III • The medication requested is being prescribed at an FDA-approved dosage for age and weight • The member has an adequate trial (of at least 10 weeks) (consistent with pharmacy claims/medical record data/chart notes) with oral antibiotics (e.g. doxycycline, tetracycline, or minocycline) OR • Member has a documented medical reason (e.g. allergy, intolerance, contraindication) for not using oral antibiotics (e.g. doxycycline, tetracycline, or minocycline) to manage their condition • If the request is for a non-preferred biological agent, documented medical reason as to why patient is unable to utilize the preferred product. **CRITERIA FOR RE-AUTHORIZATION FOR HIDRADENITIS SUPPURATIVA:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Giant Cell Arteritis	
Medications	**PREFERRED STATUS:** Preferred Biological Agent ACTEMRA (tocilizumab)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a rheumatologist, neurologist, or ophthalmologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**CRITERIA FOR APPROVAL FOR GIANT CELL ARTERITIS (GCA):** • The member has a diagnosis of giant cell arteritis. • Documentation that the patient has had (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of or inability to use, intolerance or contraindication to corticosteroids (e.g. prednisone) and methotrexate • If the request is for a non-preferred biological agent, documented medical reason as to why patient is unable to utilize the preferred product. **CRITERIA FOR RE-AUTHORIZATION FOR GIANT CELL ARTERITIS (GCA):** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

Recommendation:

- Retire policy

Specialty Biological Agents for Uveitis	
Medications	**PREFERRED STATUS:** Preferred Biological Agent HUMIRA (adalimumab)
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), and/or per standard of care guidelines.
Exclusion Criteria	N/A
Required Clinical Information	See "Other Criteria" below
Age Restrictions	Check AAH active CCS cases for members < 21 years of age for MCAL
Prescriber Restrictions	Prescriber is a rheumatologist, ocular immunologist or ophthalmologist
Coverage Duration	12 months
Maximum Billable Units	Variable
Other Criteria	**CRITERIA FOR APPROVAL FOR UVEITIS:** • The member has a diagnosis of non-infectious intermediate, posterior panuveitis. • Chronic, recurrent, treatment-refractory OR vision-threatening disease • Documentation that the patient has had (consistent with pharmacy or medical claims data, OR for new members to the health plan consistent with medical chart history) adequate trial of, or inability to use, intolerance or contraindication to conventional therapy (e.g. corticosteroids or immunosuppressive drugs, for example, azathioprine, cyclosporine, methotrexate). If the request is for a non-preferred biological agent, documented medical reason as to why patient is unable to utilize the preferred product. **CRITERIA FOR RE-AUTHORIZATION FOR UVEITIS:** • The medication is being prescribed at an FDA-approved dosage. • The member has been receiving the medication and documentation was provided that the prescriber has evaluated the member and recommends continuation of therapy. • Documentation submitted indicates that the member has obtained clinical benefit from the medication. If all of the above criteria are not met for initial or re-authorization, the request is referred to a Clinical Reviewer for medical necessity review
Last Review Date	~~3/2023~~9/2023

ALAMEDA Q3 2023 NEW PRODUCT REVIEW

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Trikafta	elexacaftor/tezacaftor/ivacaft 80-40-60 mg (d)/59.5 mg (n) granule pack, and 100-50-75 mg (d)/75 mg (n) granule pack	Vertex Pharmaceuticals Incorporated	Indicated for the treatment of cystic fibrosis (CF) in patients aged 2 years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data	$25,067 per package	Kalydeco, Orkambi, Symdeko	F-PA (already added via CRF)
Gralise	Gabapentin 900mg, 750mg, 450mg extended release tablet	Depomed, Inc.	Indicated for the management of Postherpetic Neuralgia (PHN)	$957	Pregabalin	Non-formulary
Qalsody	Tofersen 100 mg/15 mL (6.7 mg/mL) intrathecal solution	Biogen MA Inc.	Indicated for the treatment of amyotrophic lateral sclerosis (ALS) in adults who have a mutation in the superoxide dismutase 1 (SOD1) gene.	$14,230 (based on maintenance dosing)	Relyvrio, edaravone	Non-formulary (see new PAD policy)
Lupron Depot-Ped 45 mg intramuscular syringe kit	leuprolide acetate 45 mg intramuscular syringe kit	AbbVie Inc	Gonadotropin releasing hormone (GnRH) agonist indicated for the treatment of pediatric patients with central precocious puberty	$23,579 every 6 months	Trelstar, Triptodur, Supprelin, Synarel	F-PA (already added via CRF)
Vowst	fecal microbio spore,live-brpk capsule	Seres Therapeutics, Inc.	Indicated to prevent the recurrence of Clostridioides difficile infection (CDI) in individuals 18 years of age and older following antibacterial treatment for recurrent CDI (rCDI)	$17,500 per treatment (4 capsules once daily for 3 consecutive days)	None	Non-formulary (see new PAD & MRG policy)
Abilify Asimtufii	720 mg/2.4 mL suspension, extend.rel. IM syringe, 960 mg/3.2 mL suspension, extend.rel. IM syringe	Otsuka America Pharmaceutical, Inc.	For the treatment of schizophrenia in adults, and as maintenance monotherapy treatment of bipolar I disorder in adults	$4,078 - $5,438 every 2 months	Abilify Maintena and other atypical antipsychotics	F-PA (already added via CRF)
Lumryz	Sodium oxybate 4.5 gram, 6 gram, 7.5 gram, 9 gram granules extended release in packet	Avadel	Indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy	$8,730 - $17,460 per month	Xyrem, Xywav	Non-formulary
Kalydeco	Ivacaftor 13.4 mg oral granules in packet	Vertex	Indicated for the treatment of cystic fibrosis (CF) in patients age 1 month and older who have at least one mutation in the *CFTR* gene that is responsive to ivacaftor potentiation based on clinical and/or *in vitro* assay data	$25,067 per 28 day package	Trikafta, Orkambi, Symdeko	F-PA (already added via CRF)

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Zolpidem	Zolpidem 7.5 mg capsule	Almatica	Indicated for the short-term treatment of transient insomnia characterized by difficulties with sleep initiation in adults younger than age 65 years of age	$250	Zolpidem tablets	Non-formulary
Uzedy	Risperidone 50 mg/ 0.14 mL, 75 mg/ 0.21 mL, 100 mg/ 0.28 mL, 125 mg/ 0.35 mL, 150 mg/ 0.42 mL, 200 mg/ 0.56 mL, 250 mg/ 0.7 mL subcut extended-release suspension syringe	Teva	Indicated for the treatment of schizophrenia in adults.	$1,232-$3,080	Risperdal Consta, Rykindo	Non-formulary
Udenyca	Pegfilgrastim-cbqv 6 mg/ 0.6 mL subcutaneous auto-injector	Coherus	• Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia. • Increase survival in patients acutely exposed to myelosuppressive doses of radiation (Hematopoietic Subsyndrome of Acute Radiation Syndrome).	$4,175 per 6 mg dose	Ziextenzo	F-PA (already added via CRF)
Sogroya	somapacitan-beco 5 mg/1.5 mL (3.3 mg/mL), 10 mg/1.5 mL (6.7 mg/mL), 15 mg/1.5 mL (10 mg/mL) subcutaneous pen injector	Novo Nordisk	• Treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone. • Replacement of endogenous GH in adults with growth hormone deficiency.	$7,907 per month (for a 45 kg child at starting dose of 0.16mg/kg; Dosing is highly variable and based off weight and response) $1,488-$8,435 per month for adults	Humatrope	Non-formulary
Liqrev	sildenafil citrate 10 mg/mL oral suspension	CMP DEV LLC	Treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group I) in adults to improve exercise ability and delay clinical worsening.	$2,796	Sildenafil oral solution (generic Revatio)	F-PA (already added via CRF)

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Veozah	Fezolinetant 45mg tablet	Astellas Pharma US	Treatment of moderate to severe vasomotor symptoms due to menopause.	$550	None	Non-formulary
Amjevita	adalimumab-atto (CF) 10 mg/0.2 mL subcutaneous syringe	Amgen	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$6,576.48/28 days (10 mg every other week dosing)	Humira, Enbrel, Cimzia	Non-formulary
Tafinlar	dabrafenib mesylate 10 mg tablet for oral suspension	Novartis	In combination with trametinib, for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy	$2,093 - $15,696	None	Non-formulary
Mekinist	trametinib dimethyl sulfoxide 0.05 mg/mL oral solution	Novartis	Treatment, in combination with dabrafenib, of pediatric patients 1 year of age and older with low-grade glioma with a BRAF V600E mutation who require systemic therapy.	$3,098 - $20,652	None	Non-formulary
Elfabrio	pegunigalsidase alfa-iwxj 2 mg/mL intravenous solution	Chiesi	Treatment of adults with confirmed Fabry disease.	$28,946/28 days for a 70 kg adult	Fabrazyme	Non-formulary (see new PAD policy)
Omnipod Go	Omnipod Go pods 10 units, 15 units, 20 units, 25 units, 30 units, 35 units, 40 units/day subcutaneous	Insulet	A standalone, wearable, insulin delivery system that provides a fixed rate of continuous rapid-acting insulin for 72 hours. It is cleared for use for people with type 2 diabetes age 18 or older who would typically take daily injections of long-acting insulin.	$300/month	Other insulin pump devices, use of basal insulin injections	Non-formulary
Bigfoot Unity	Bigfoot Unity pen cap-Novolog device, Humalog device, lispro device, Lyumjev device, Admelog device, Apidra device, aspart device, Tresiba device, Lantus device, Fiasp device, Basaglar device, Toujeo device, Toujeo Max device, Bigfoot Unity program kit	Bigfoot Biomed	Smart pen caps that incorporate integrated continuous glucose monitor (iCGM) data and health care provider instructions to provide insulin dose recommendations for people with diabetes who use multiple daily injections of insulin. Indicated for management of diabetes in persons 12 years and older. Integrates with Freestyle Libre 2.	$1,347 for program kit; individual pen caps listed for $0.01	None	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Kalydeco	Ivacaftor 5.8 mg oral granules in packet	Vertex	Indicated for the treatment of cystic fibrosis (CF) in patients age 1 month and older who have at least one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data	$25,067 per month	Orkambi, Orkambi Symdeko, Trikafta	F-PA (already added via CRF)
Epkinly	Epcoritamab-bysp 48 mg/0.8 mL subcutaneous solution, 4 mg/0.8 mL subcutaneous solution (MUST DILUTE)	Genmab	Indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy.	$15,225 per 48mg vial (dosing varies per cycle)	Lunsumio	Non-formulary
Brixadi	Buprenorphine Weekly 8 mg/0.16 mL, 16 mg/0.32 mL, 24 mg/0.48 mL, 32 mg/0.64 extended release subcutaneous syringe Buprenorphine Monthly 64 mg/0.18mL, 96 mg/0.27 mL, 128 mg/0.36 mL extended release subcutaneous syringe	Pharmaceutics International, Inc.	Indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a single dose of a transmucosal buprenorphine product or who are already being treated with buprenorphine.	$415 per package	None	Non-formulary
Zavzpret	zavegepant hcl 10 mg/actuation nasal spray	Pfizer	Indicated for the acute treatment of migraine with or without aura in adults.	$1,100 per package (one package contains 6 doses)	Reyvow, Ubrelvy, Nurtec ODT	Non-formulary
Inpefa	sotagliflozin 200mg tablet	Lexicon Pharmaceuticals	Indicated to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure or type 2 diabetes mellitus, chronic kidney disease, and other cardiovascular risk factors	$598 – 1,196	Steglatro, Segluromet, Steglujan, Farxiga, Xigduo XR, Qtern, Jardiance, Synjardy, Glyxambi, Trijardy, Invokana, Invokamet	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Olpruva	Sodium phenylbutyrate 2 gram, 3 gram, 4 gram, 5 gram, 6 gram, 6.67 gram oral pellets in packet	Acer Therapeutics Inc.	Indicated as adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients weighing 20 kg or greater and with a body surface area (BSA) of 1.2 m2 or greater, with urea cycle disorders (UCDs) involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS)	Ranges from $17,100- 57,028 per package	Buphenyl, Pheburane, Ravicti	Non-formulary
Zeposia	Ozanimod hydrochloride starter Kit (28-day) 0.23 mg-0.46 mg-0.92 mg capsules dosepack	Bristol Myers Squibb	Indicated for the treatment of: Relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Moderately to severely active ulcerative colitis (UC) in adults.	$7,636	MS: Tecfidera, Gilenya, Copaxone, etc. UC: Humira, Amjevita, Infliximab, Rinvoq, etc.	Non-formulary
Vyjuvek	beremagene geperpavec-svdt 5 x 10exp9 PFU/2.5 mL topical gel	Krystal Biotech, Inc	Indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene	$24,250 per package	None	Non-formulary (see new PAD policy)
Miebo 100 % eye drops	perfluorohexyloctane/pf 100 % eye drops	Bausch & Lomb	Indicated for treatment of the signs and symptoms of dry eye disease.	$771 per package	Xiidra	F-PA (see MRG review)
Zejula	niraparib tosylate 100mg, 200mg, 300mg tablets	GSK	Indicated for the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy. Also indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy.	$17,289 (varies based on platelet count and weight)	Lynparza	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Columvi	glofitamab-gxbm 1 mg/mL intravenous solution	Genentech	Indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma, after two or more lines of systemic therapy.	$30,000 (based on cycles 2-12)	Epkinly	Non-formulary
Talzenna	talazoparib tosylate 0.1mg, 0.35mg capsules	Pfizer	Breast Cancer: As a single agent, for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna. HRR Gene-mutated mCRPC: In combination with enzalutamide for the treatment of adult patients with HRR gene-mutated metastatic castration-resistant prostate cancer (mCRPC).	$17,514	Lynparza	Non-formulary
Vyvgart Hytrulo	efgartigimod-hyaluronidas-qvfc 1,008 mg-11,200 unit/5.6 mL subcutaneous solution	Halozyme Therapeutics	Indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive	$15,773 per package	Vyvgart	Non-formulary
Hulio	adalimumab-fkjp 20 mg/0.4 mL, 40 mg/0.8 mL subcutaneous syringe; 40 mg/0.8 mL subcutaneous auto-injector	Mylan/Viatris/ Biocon	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$3,288 per dose	Humira, Amjevita, Idacio, Cyltezo, Hyrimoz, Yusimry, Yuflyma, Hadlima	Non-formulary
Adalimumab-fkjp	adalimumab-fkjp 20 mg/0.4 mL, 40 mg/0.8 mL subcutaneous syringe; 40 mg/0.8 mL subcutaneous auto-injector	Mylan/Viatris/ Biocon	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$498 per dose	Humira, Amjevita, Idacio, Cyltezo, Hyrimoz, Yusimry, Yuflyma, Hadlima	F-QL (see Humira document)

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Idacio	adalimumab-aacf 40 mg/0.8 mL subcutaneous syringe; 40 mg/0.8 mL subcutaneous auto-injector	Fresenius	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis	$3,288 per dose	Humira, Amjevita, Hulio, Cyltezo, Hyrimoz, Yusimry, Yuflyma, Hadlima	Non-formulary
Rezzayo	rezafungin 200 mg intravenous vial	Cidara Therapeutics	Treatment of candidemia and invasive candidiasis (IC) in adults with limited or no alternative treatment options	$9,750	Caspofungin, Micafungin	Non-formulary
Cyltezo	adalimumab-adbm 10 mg/0.2 ml, 20 mg/0.4 ml, 40 mg/0.8 ml, subcutaneous syringe; 40 mg/0.8 mL subcutaneous auto-injector	Boehringer Ingelheim	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$3,288 per dose	Humira, Amjevita, Hulio, Idacio, Hyrimoz, Yusimry, Yuflyma, Hadlima	Non-formulary
Rystiggo	rozanolixizumab-noli 280 mg/2 ml subcutaneous vial	UCB	Treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) or antimuscle-specific tyrosine kinase (MuSK) antibody positive	$72,600 per 6-week treatment cycle for a 70 kg adult	Vyvgart, Soliris, Ultomiris	Non-formulary
Suflave	polyethylene glycol 3350/sodium sulfate/potassium chloride/magnesium sulfate/sodium chloride 178.7 g-7.3 g-1.12 g-0.9 g-0.5 g oral solution	Braintree Labs	For cleansing of the colon in preparation for colonoscopy in adults	$125 per treatment	Polyethylene glycol 3350, Suprep	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Elevidys	delandistrogene moxeparvovec-rokl 1.33 x 10^{13} intravenous suspension	Sarepta Therapeutics	Treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene. This indication is approved under accelerated approval based on expression of Elevidys microdystrophin in skeletal muscle observed in patients treated with Elevidys. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.	$3.2 million per one-time treatment	Prednisone, Emflaza	Non-formulary (see new PAD policy)
Adalimumab-adaz	adalimumab-adaz 40 mg/0.4 ml subcutaneous syringe; 40 mg/0.4 mL subcutaneous auto-injector	Sandoz	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$658 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Yusimry, Yuflyma, Hadlima	Non-formulary
Hyrimoz	adalimumab-adaz 10 mg/0.1 ml, 20 mg/0.2 ml, 40 mg/0.4 ml, 80 mg/0.8 ml subcutaneous syringe; 40 mg/0.4 mL, 80 mg/0.8 ml subcutaneous auto-injector	Sandoz	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$3,288 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Yusimry, Yuflyma, Hadlima	Non-formulary
Yusimry	adalimumab-aqvh 40 mg/0.8 mL subcutaneous pen injector	Coherus BioSciences	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$498 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yuflyma, Hadlima	Non-formulary
Yuflyma	adalimumab-aaty 40 mg/0.4 mL subcutaneous pen injector	Celltrion	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$3,288 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yusimry, Hadlima	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Hadlima	adalimumab-bwwd 40 mg/0.4 ml, 40 mg/0.8 ml subcutaneous syringe; 40 mg/0.4 mL, 40 mg/0.8 ml subcutaneous auto-injector	Samsung Bioepis	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa, Uveitis	$519 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yusimry Yuflyma	F-QL (see Humira document)
Litfulo	ritlecitinib 50 mg oral tablet	Pfizer	Treatment of severe alopecia areata in adults and adolescents 12 years and older	$4,038	Olumiant	Non-formulary
Austedo XR	deutetrabenazine 6 mg-12mg-24mg ER tablet titration pack	Teva	• Treatment of chorea associated with Huntington's disease • Treatment of tardive dyskinesia	$6,609	Ingrezza, tetrabenazine	Non-formulary
Abrysvo	respiratory syncytial virus vaccine	Pfizer	• Prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older	$295 per dose	Arexvy	F-QL (see monograph)
Adstiladrin	nadofaragene firadenovec-vncg	Ferring Pharmaceuticals	• Treatment of adult patients with high-risk Bacillus CalmetteGuérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors	$20,000	Keytruda	Non-formulary
Arexvy	respiratory syncytial virus vaccine, adjuvanted	GlaxoSmithKline	• Prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in individuals 60 years of age and older	$280 per dose	Abrysvo	F-QL (see monograph)
Roctavian	valoctocogene roxaparvovec-rvox	BioMarin Pharmaceutical	• Treatment of adults with severe hemophilia A (congenital factor VIII deficiency with factor VIII activity < 1 IU/dL) without pre-existing antibodies to adeno-associated virus serotype 5 detected by an FDA-approved test	$2.9 million per one-time treatment	Hemlibra, Eloctate, Altuviiio	Non-formulary (see new PAD policy)
Brenzavvy	bexagliflozin 20 mg oral tablet	TheracosBio	• Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	$47	Jardiance, Farxiga, Invokana, Steglatro	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Xenpozyme	olipudase alfa-rpcp 4 mg intravenous vial	Sanofi	• Treatment of non–central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients	$64,278 for a 30 kg child	None	Non-formulary (see new PAD policy)
Vanflyta	quizartinib 17.7 mg, 26.5 mg oral tablets	Daiichi Sankyo	• To be used in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test	$16,380	Rydapt	Non-formulary
Ngenla	somatrogon-ghla 24 mg/1.2 ml, 60 mg/1.2 ml subcutaneous pen injector	Pfizer	• Treatment of pediatric patients aged 3 years and older who have growth failure due to inadequate secretion of endogenous growth hormone	$7,968 for a 30 kg child	Humatrope, Nutropin, Sogroya, Skytrofa	Non-formulary
Cosentyx	Secukinumab 300 mg/2 ml subcutaneous auto-injector	Novartis	Human interleukin-17A antagonist indicated for the treatment of: • Moderate to severe plaque psoriasis in patients 6 years and older who are candidates for systemic therapy or phototherapy • Active psoriatic arthritis (PsA) in patients 2 years of age and older • Adults with active ankylosing spondylitis (AS) • Adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation • Active enthesitis-related arthritis (ERA) in patients 4 years of age and older	$6,924 for maintenance dose	Hadlima, Humira, Infliximab, Taltz, Skyrizi	F-PA (already added via CRF)
Yuflyma	adalimumab-aaty 40 mg/0.4 mL subcutaneous prefilled syringe	Celltrion	Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis, Hidradenitis Suppurativa	$3,288 per dose	Humira, Amjevita, Hulio, Idacio, Cyltezo, Hyrimoz, Yusimry, Hadlima	Non-formulary

BRAND NAME	GENERIC NAME/ DOSAGE FORM	MANUFACTURER	INDICATION	PRICING*	FORMULARY ALTERNATIVES	RECOMMENDATION^
Xdemvy	lotilaner 0.25% ophthalmic solution	Tarsus Pharmaceuticals	• Treatment of Demodex blepharitis	$1,850 per 6-week treatment course	Ivermectin	Non-formulary
Beyfortus	nirsevimab-alip 50 mg/0.5 ml, 100 mg/ml intramuscular syringe	Sanofi/AstraZeneca	Prevention of respiratory syncytial virus (RSV) lower respiratory tract disease in: • Neonates and infants born during or entering their first RSV season • Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season	$495 per dose	Synagis	Non-formulary
Xacduro	sulbactam/durlobactam 1 g-1 g intravenous vial	Entasis Therapeutics	• Treatment of hospital-acquired bacterial pneumonia (HABP) and ventilator-associated bacterial pneumonia (VABP), caused by susceptible isolates of Acinetobacter baumanii-calcoaceticus complex (ABC) in patients 18 years of age and older	$8,866 per 14-day treatment course	Ampicillin/sulbactam, Colistin, Fetroja	Non-formulary
Izervay	avacincaptad pegol 2 mg/0.1 ml intravitreal vial	Iveric Bio	• Treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)	$2,100 per eye	Syfovre	Non-formulary

*	Pricing reflects Wholesale Acquisition Cost (WAC) per month unless otherwise noted.
†	Pricing based on standard twice-monthly dosing for most indications.
‡	Pricing is per each kit on items listed as a kit.