P&T Committee Meeting Minutes
Commercial/Marketplace/GHP Kids
March 15, 2022

Present (via Teams):	**Absent:**
Megan Ammon, Pharm.D.	Bret Yarczower, MD, MBA – Chair
Emily Antosh, Pharm.D.	Holly Bones, Pharm.D.
Kristen Bender, Pharm.D.	Kim Castelnovo
Jeremy Bennett, MD	Dean Christian, MD
Briana Blaisure, Pharm.D.	Michael Evans, RPh
Alyssa Cilia, RPh	Nichole Hossler, MD
Kimberly Clark, Pharm.D.	Jason Howay, Pharm.D.
Rajneel Farley, Pharm.D.	Jonas Pearson, RPh
Kelly Faust Pharm.D.	Angela Scarantino
Tricia Heitzman, Pharm.D.	William Seavey, Pharm.D.
Emily Hughes, Pharm.D.	Jill Stone, Pharm.D.
Keith Hunsicker, Pharm.D.	
Kelli Hunsicker, Pharm.D.	
Derek Hunt, Pharm.D.	
Philip Krebs, R.EEG T	
Ted Marines, Pharm.D.	
Lisa Mazonkey, RPh	
Tyreese McCrea, Pharm.D.	
Perry Meadows, MD	
Jamie Miller, RPh	
Mark Mowery, Pharm.D.	
Austin Paisley, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Renn, Pharm.D.	
Kristen Scheib, Pharm.D.	
Michael Shepherd, MD	
Leslie Shumlas, Pharm.D.	
Richard Silbert, MD	
Aubrielle Smith Pharm.D.	
Michael Spishock, RPh	
Todd Sponenberg, Pharm.D.	
Robert Strony, MD MBA	
Kevin Szczecina, RPh	
Amanda Taylor, MD	
Brandon Whiteash, Pharm.D.	
Travis Baughn (non-voting participant)	
MeiLing Montross, Pharm.D. (Pharmacy Resident)	
Jessica Kisenwether, PhD (non-voting participant)	

Call to Order:
Kimberly Clark called the meeting to order at 1:03 p.m., Tuesday, March 15, 2022.

Review and Approval of Minutes:
Kimberly Clark asked for a motion or approval to accept the January 18, 2022 and February 28, 2022 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

TAVNEOS (avacopan)

Review: Tavneos is a complement 5a receptor (C5aR) antagonist indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. Tavneos does not eliminate glucocorticoid use. Tavneos is the first orally administered complement inhibitor and the first drug approved in over 10 years for the GPA and MPA variants of ANCA-associated vasculitis. It is not approved for EPGA at this time. Treatment guidelines have not been updated since the approval of Tavneos, but it is likely that Tavneos will be used during induction therapy with rituximab or cyclophosphamide and glucocorticoids to mitigate the use of high-dose glucocorticoids typically used to induce remission. Although Tavneos was designed as a potential alternative to steroids, the FDA approved labeling specifically states that it does not eliminate glucocorticoid use.

The efficacy of Tavneos was evaluated in the ADVOCATE trial, a double-blind active-controlled phase 3 clinical trial in 330 adult patients with newly diagnosed or relapsed ANCA-associated vasculitis. Patients were randomized 1:1 to receive treatment with Tavneos (n=166)30 mg twice daily for 52 weeks plus prednisone-matching placebo for 20 weeks or avacopan-matched placebo twice daily for 52 weeks plus prednisone (tapered from 60 mg/day to 0 over 20 weeks). Patients in both groups received treatment with a standard immunosuppressive regimen,

The primary endpoints were disease remission at Week 26 and sustained disease remission at Week 52. Disease remission was defined as a BVAS of 0 and no use of glucocorticoids for treatment of ANCA-associated vasculitis from Week 22 to Week 26. Sustained remission was remission at Week 26 sustained through Week 52 without relapse (BVAS score of 0 and no use of glucocorticoids for treatment of ANCA-associated vasculitis from Week 48 to Week 52). Relapse was occurrence of one BVAS major item, at least 3 BVAS non-major items, or 1 or 2 BVAS non-major items for at least 2 consecutive visits after remission was achieved. Remission was achieved by 72.3% of patients in the Tavneos group compared to 70.1% of patients in the prednisone group by Week 26 (treatment difference: 3.4%, 95% CI [-6.0%, 12.8%]). At Week 52, a significantly higher percentage of patients had sustained remission in the Tavneos group (65.7%) compared to prednisone (54.9%) (Table 2).

There are no black box warnings for Tavneos. Warnings and precautions include risk of hepatotoxicity, hypersensitivity reactions, hepatitis B virus reactivation, and risk of serious infections. Tavneos is contraindicated in patients with serious hypersensitivity reaction to avacopan. During clinical trials of Tavneos, the most frequent serious adverse reactions that were reported were pneumonia, GPA, acute kidney injury, and urinary tract infection. The most common adverse reactions occurring in at least 5% of patients and were higher for Tavneos compared to prednisone were headache, nausea, diarrhea, vomiting, hypertension, rash, fatigue, upper abdominal pain, dizziness, increased blood creatinine, and paresthesia. During the ADVOCATE trial, 19 patients (11.6%) in the prednisone group and 22 patients (13.3%) in the Tavneos group had hepatic-related adverse reactions, including hepatobiliary adverse reactions and liver enzyme abnormalities. Study medication was paused or permanently discontinued by 9 patients in the Tavneos group and serious hepatic-related adverse reactions were reported in 9 patients in the Tavneos group. During the ADVOCATE trial, 2 patients developed angioedema and one event was serious adverse reaction requiring hospitalization.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.
Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: Keith asked if it is only given for a short period of time or is there no standard duration? There is no standard duration, and the guidelines don't provide any guidance. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Tavneos is a pharmacy benefit and will not be added to the formulary. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**

- Medical record documentation of severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis classified as one of the following variants:
    - granulomatosis with polyangiitis (GPA) **OR**
    - microscopic polyangiitis (MPA)

AND

- Medical record documentation of both of the following:
    - Medical record documentation of a positive test for anti-proteinase 3 (PR3) or anti-myeloperoxidase (MPO) **AND**
    - Medical record documentation of at least 1 major item, 3 non-major items, or 2 renal items of proteinuria and hematuria on the Birmingham Vasculitis Activity Score (BVAS)

AND

- Medical record documentation that Tavneos will be administered in combination with standard therapy that will include, but is not limited to rituximab or cyclophosphamide, and glucocorticoids

QUANTITY LIMIT: 6 capsules per day, 30 day supply per fill

AUTHORIZATION DURATION: Initial approval will be given for six months. Subsequent approvals will be for an additional twelve months and will require:

- Medical record documentation of continued disease improvement or lack of disease progression **AND**
- Medical record documentation that the member is responding positively to therapy as evidenced by a reduction in the Birmingham Vasculitis Activity Score (BVAS)

The medication will no longer be covered if patient experiences toxicity or worsening of disease.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

LIVMARLI (maralixibat)

Review: Livmarli is an IBAT inhibitor indicated for the treatment of cholestatic pruritus in patients with ALGS 1 year of age and older. Livmarli is the first FDA-approved therapy for the treatment of ALGS. It is currently in phase 3 trials for the treatment of PFIC and in phase 2 trials for treatment of biliary atresia. Bylvay, another ileal bile acid transporter, is currently in phase III trials for the treatment of ALGS. Bylvay is approved for PFIC. Livmarli and Bylvay will compete, however the long-term use will be contingent upon their success in preventing liver-related outcomes.

Diagnosis ALGS can be suspected in patients who have a reduced number of bile ducts upon liver biopsy. Symptoms of liver disease or cholestasis, heart defect, bone abnormality, eye abnormality, and distinctive facial features can be used to further support diagnosis. Diagnosis can be confirmed through molecular genetic testing; however, while some patients present with mutations in the JAG1 or NOTCH2 gene, in rare cases, patients do not present with these mutations and a diagnosis is made upon clinical presentation alone.

Patients with ALGS require comprehensive care, given that multiple organ systems are affected. For patients with cholestatic liver disease, patients can trial ursodiol, cholestyramine, rifampin, naltrexone, diphenhydramine, and sertraline. However, pruritus is often resistant to treatment. In severe cases of cirrhosis or where other therapies are unsuccessful, patrial external biliary diversion (PEBD) surgery or liver transplant may be required. Vitamin and specialty nutrition supplementation to support growth and development is usually provided for patients with Alagille syndrome.

Livmarli is supplied as 9.5 mg of maralixibat per mL in a 30 mL bottle. The recommended dose is 380 mcg/kg once daily, taken 30 minutes before the first meal of the day. The starting dose is 190 mcg/kg administered orally

once daily; after one week, increase to 380 mcg/kg once daily, as tolerated. The maximum daily dose volume for patients above 70 kg is 3 mL or 28.5 mg per day.

Livmarli was studied in an 18-week open label treatment period; a 4-week randomized, double-blind, placebo-controlled drug withdrawal period; a subsequent 26-week open-label treatment period; and a long-term open-label extension period. The trial included 31 pediatric ALGS patients with cholestasis and pruritus. Approximately 90.3% of patients received at least one medication to treat pruritus at study entry. All patients had JAGGED1 mutation. Randomized patients had a median age of 5 years (range 1 to 15 years). Patents were included in the trial if their average pruritus score was greater than 2.0 (moderate) in the 2 weeks prior to baseline. A single-item observer-reported outcome was used to measure patients' pruritus symptoms as observed by their caregiver twice daily on the Itch Reported Outcome Instrument. For randomized patients, the mean (SD) at baseline (pre-treatment) was 3.1 (0.5) and the mean (SD) at Week 18 (pre-randomized withdrawal period) was 1.4 (0.9). On average, patients administered Livmarli for 22 weeks maintained pruritus reduction whereas those in the placebo group who were withdrawn from Livmarli after Week 18 returned to baseline pruritus scores by Week 22. After re-entering the open-label treatment phase, both randomized treatment groups had similar mean pruritus scores by Week 28, the first week placebo patients received the full dosage of Livmarli after withdrawal.

There are no contraindications to Livmarli use. Livmarli has warnings for liver test abnormalities, gastrointestinal adverse reactions, and fat-soluble vitamin deficiency. The most common adverse reactions (≥ 5%) are diarrhea, abdominal pain, vomiting, fat-soluble vitamin deficiency, liver test abnormalities, gastrointestinal bleeding, and bone fractures. The safety and effectiveness of Livmarli have been established in pediatric patients 1 to 15 years of age.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Livmarli is a pharmacy benefit and will be added to the formulary on the specialty tier or the brand non-preferred tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- Prescription written by or in consultation with a hepatologist or gastroenterologist **AND**
- Medical record documentation of diagnosis of Alagille Syndrome (ALGS) **AND**
- Medical record documentation of the presence of moderate to severe pruritus **AND**
- Medical record documentation of age greater than or equal to 1 year **AND**
- Medical record documentation that the member is receiving an appropriate dose* based on the patient's weight **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ursodiol and one of the following: cholestyramine, rifampin, naltrexone, sertraline

NOTE: The recommended dose of Livmarli is shown in the table below.

Patient Weight (kg)	Days 1-7 (190 mcg/kg once daily)		Beginning Day 8 (380 mcg/kg once daily)	
	Volume QD (mL)	Dosing dispenser size (mL)	Volume QD (mL)	Dosing dispenser size (mL)
5 to 6	0.1	0.5	0.2	0.5
7 to 9	0.15		0.3	
10 to 12	0.2		0.45	
13 to 15	0.3		0.6	1
16 to 19	0.35		0.7	
20 to 24	0.45		0.9	
25 to 29	0.5		1	
30 to 34	0.6	1	1.25	3
35 to 39	0.7		1.5	
40 to 49	0.9		1.75	
50 to 59	1		2.25	
60 to 69	1.25	3	2.5	
70 or higher	1.5		3	

QUANTITY LIMIT: 3 mL per day, 30 day supply per fill

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require the following:

- Medical record documentation of improvement in pruritus from baseline AND
- Medical record documentation that the member is receiving an appropriate dose* based on the patient's weight

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

KIMMTRAK (tebentafusp-tebn)

Review: Kimmtrak is a bispecific gp100 peptide-HLA-directed CD3 T cell engager indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable/metastatic uveal melanoma. Uveal melanoma is the most common primary ocular cancer. There are approximately 1,275 – 1,700 uveal melanomas diagnosed in the U.S. annually. Up to 50% of patients with uveal melanoma will have recurrence of distant metastases, most often developing in the liver. The prognosis is often poor. Patients with metastatic disease have a mean OS of approximately 1 year.

Treatment for uveal melanoma depends on tumor size and symptoms. Before the approval of Kimmtrak, there were no FDA-approved systemic therapies for unresectable/metastatic uveal melanoma. Clinical trials were recommended as the preferred option for systemic therapy. If a clinical trial was not appropriate, other systemic therapies were then considered. The most comparable systemic therapy option available in terms of efficacy is Opdivo (nivolumab) + Yervoy (ipilimumab). These agents are not FDA approved to treat unresectable/metastatic uveal melanoma but are rated category 2A by NCCN.

The recommended dose of Kimmtrak is 20 mcg intravenously on Day 1, 30 mcg intravenously on Day 8, 68 mcg intravenously on Day 15, and 68 mcg intravenously once every week thereafter. Kimmtrak is an intravenous infusion that must diluted prior to administration and must be initially administered in a health care setting. The first three infusions should be administered over 15 to 20 minutes and patients must be monitored during the infusion and for at least 16 hours after the infusion. If the patient does not experience Grade 2 or worse hypotension after the third infusion, subsequent doses may be administered in an ambulatory care setting, where patients should be monitored at least 30 minutes after each infusion.

Kimmtrak was studied in a randomized, open-label, multicenter trial. 378 adult patients with HLA-A*0201–positive (identified by a central assay), previously untreated, advanced uveal melanoma were randomized (2:1) to receive Kimmtrak (N=252) or Investigator's choice (N=126) of Keytruda (pembrolizumab), Yervoy

(ipilimumab), or dacarbazine. The major efficacy endpoint was overall survival (OS). The median OS of patients treated with Kimmtrak was 21.7 months (95% CI 18.6, 28.6), while the OS for patients in the investigator's choice arm was 16 months (hazard ratio [HR] = 0.51; 95% CI: 0.37, 0.71; P <0.0001).

Kimmtrak carries a black box warning for Cytokine Release Syndrome (CRS), which may be serious or life threatening if not appropriately managed. It is important to monitor patients during and for 16 hours following the first three infusions for signs or symptoms of CRS. Kimmtrak also has warnings/precautions for potential skin reactions, elevated liver enzymes, and embryo-fetal toxicity. Patients should be monitored for and aware of the potential for such reactions. Among the patients treated with Kimmtrak, the most common Grade 3 or higher adverse reactions were rash (18%), pyrexia (4%), and pruritus (5%). In the 245 patients who received Kimmtrak, Grade 3 CRS occurred in <1% of patients and was generally well-managed. There were no Grade 4 or fatal CRS events observed in the Phase 3 trial. Dose modifications do exist to address adverse reactions depending on severity.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Kimmtrak is a medical benefit. Kimmtrak will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Kimmtrak will process at the Specialty tier or the Brand Non-Preferred tier for members with a three-tier benefit. The following prior authorization criteria should apply:

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is greater than or equal to 18 years of age **AND**
- Medical record documentation of a diagnosis of unresectable or metastatic uveal melanoma **AND**
- Medical record documentation of HLA-A*02:01–positive disease **AND**
- Medical record documentation that Kimmtrak is not being used in combination with any other agents for the treatment of unresectable or metastatic uveal melanoma

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

OPZELURA (ruxolitinib)

Review: Opzelura is the first, and only, topical JAK inhibitor currently approved in the United States. It is currently approved for topical short-term and noncontinuous chronic treatment of mild to moderate atopic dermatitis in immunocompetent patients 12 years of age or older who do not have adequate control of their AD with topical prescription therapies. Opzelura is supplied as a 1.5% cream that is available in 5g and 60g tubes. It is to be applied twice daily to affected areas. Application areas should not exceed 20% BSA, and the max dose if 60g/week. If signs/symptoms have not resolved in 8 weeks, therapy should be reassessed. Therapy is to be discontinued upon resolution of signs/symptoms. Opzelura is not for ophthalmic, oral, or intravaginal use.

There are several black box warnings for Opzelura. They include risk of serious infections, mortality, malignancies, major adverse cardiovascular events, and thrombosis. Many of these risks arise from observations in treatment with oral JAK inhibitors. There are no contraindications listed in the manufacturer's labeling, however warning and precautions are listed in relation to adverse effects of hematological toxicity, lipid abnormalities, and nonmelanoma skin cancers. Disease related concerns include avoiding use in immunocompromised patients.

The use of Opzelura is not recommended in combination with other therapeutic biologic agents, JAK inhibitors, or potent immunosuppressants. Ruxolitinib is a major substrate of CYP3A4. Because of this several major drug interacts exist, as well as many others. Prescribing information contains a complete list that should be referenced.

Currently, AD is managed in a stepwise approach by the use of nonpharmacological agents, topical corticosteroids, topical calcineurin inhibitors, crisabole, dupilumab, cyclosporine, or azathioprine. Systemic steroids are not recommended, however are to be reserved for acute use. Many of these have undesirable long-term effects. Opzelura is thought to eliminate the need for these by providing another therapeutic option. Results from Phase 3 clinical trials showed that when compared with a vehicle placebo, ruxolitinib showed significant success in Investigator's Global Assessment scores. In addition, significant itch reductions were reported within the first 12 hours of application when compared to placebo and application site reactions were lower with ruxolitinib versus placebo. No reactions were would to be clinically significant. Guidelines have not yet been updated at this time to include Opzelura.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.
Outcome: Opzelura is a pharmacy benefit and will be added to the formulary on the brand non-preferred tier. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of mild to moderate atopic dermatitis **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation that member is immunocompetent **AND**
- Medical record documentation that Opzelura is being prescribed by or in consultation with a dermatologist, allergist, or immunologist **AND**
- Medical record documentation of Body Surface Area (BSA) less than or equal to 20% **AND**
- Medical record documentation that Opzelura is NOT being used in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ALL of the following:
    - One formulary topical calcineurin inhibitor
    - One formulary topical corticosteroid unless deemed inadvisable due to potential risks such as (a) use on sensitive skin areas (face, axillae, or groin) **OR** (b) member is less than 15 years of age
    - Eucrisa

QUANTITY LIMIT: 240 g per 28 days

AUTHORIZATION DURATION: 3 months

REAUTHORIZATION CRITERIA: The medication will no longer be covered if patient experiences resolution of symptoms of atopic dermatitis. Subsequent approvals will be for an additional 6 months and will require:

- Medical record documentation of tolerability and positive clinical response to Opzelura **AND**
- Medical record documentation of symptomatic atopic dermatitis that requires additional treatment with Opzelura **AND**
- Medical record documentation that Opzelura is NOT being used in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

QULIPTA (atogepant)

Review: Qulipta is a calcitonin gene-related peptide receptor (CGRP) antagonist indicated for the preventive treatment of episodic migraine in adult patients. Qulipta is the third approved oral gepant, which is a class of CGRP-targeted small molecules. It will directly compete with Nurtec ODT. Qulipta will also compete with the CGRP-targeted monoclonal antibodies (mABs) all of which are indicated for migraine prevention (Aimovig, Ajovy, Emgality, and Vyepti). Qulipta is currently under investigation for chronic migraine prevention and Nurtec ODT is not. However, neither are currently approved for 15 or more headache days per month and in those cases, an injectable CGRP inhibitor should be considered.

Qulipta is supplied as 10mg, 30mg, and 60 mg tablets. The recommended dose is 10 mg, 30 mg, or 60 mg taken orally once daily with or without food. The dose of Qulipta is modified for interactions with strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, OATP inhibitors, and severe renal impairment and end-stage renal disease (Clcr <30 mL/min).

Qulipta was studied in two randomized, multicenter, double-blind, placebo-controlled studies. Patients included in the trials had a 1 year history of migraine. Patients had 4-14 migraine days per month in the 3 months prior to the first study visit. The mean migraine frequency at baseline was approximately 8 migraine days per month and was similar across treatment groups. The study excluded patients with myocardial infarction, stroke, or transient ischemic attacks within 6 months prior to screening. Patients were randomized to receive Qulipta 10 mg, 30 mg, 60 mg, or placebo once daily for 12 weeks in both studies. Qulipta demonstrated statistically significant reductions in mean monthly migraine and headache days compared to placebo across all dosages.

There are no contraindications to Qulipta use. There are no warnings and precautions for Qulipta use either. The most common adverse reactions (at least 4% and greater than placebo) are nausea, constipation, and fatigue. There were cases with transaminase elevations over 3 times the upper limit of normal that were temporally associated with Qulipta treatment and they resolved within 8 weeks of discontinuation. There were no cases of severe liver injury or jaundice. The safety and effectiveness in pediatric patients have not been established.

It is unclear if Ubrelvy and Qulipta can be used together for prevention and acute treatment. A phase 1B trial is evaluating this and has an estimated primary completion date of June 2021, but the results have not been shared. Although since both Ubrelvy and Qulipta are significantly metabolized through the CYP3A4 pathway and have known interactions involving this pathway, coadministration is not advisable.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Qulipta is a pharmacy benefit and will be added to the formulary on the brand non-preferred tier. The following prior authorization criteria will apply:

- Medical record documentation that Qulipta is prescribed by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura, based on the International Classification of Headache Disorders (ICHD)-III diagnostic criteria **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**
- Medical record documentation of diagnosis of episodic migraine (no more than 14 headache days per month) **AND**
- Medical record documentation that Qulipta will not be used concomitantly with another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the preventive treatment of migraine (e.g., Aimovig, Ajovy, Emgality, Vyepti, Nurtec ODT) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least three (3) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/sodium valproate
    - Amitriptyline
    - Venlafaxine AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Aimovig **AND** Emgality **AND**
- Medical record documentation that Qulipta will not be used in combination with botulinum toxin for the preventive treatment **OR**
    - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

QUANTITY LIMIT: 1 tablet per day (for all strengths)

AUTHORIZATION DURATION: Initial approval will be for six (6) months and subsequent approvals will be for twelve (12) months. Requests for continuation of coverage will be approved for members who meet the following criteria:

- Medical record documentation of continued or sustained reduction in migraine or headache frequency or has experienced a decrease in severity or duration of migraine **AND**
- Medical record documentation that Qulipta will not be used concomitantly with another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the preventive treatment of migraine (e.g., Aimovig, Ajovy, Emgality, Vyepti, Nurtec ODT) **AND**
- Medical record documentation that Qulipta will not be used in combination with botulinum toxin for preventive treatment **OR**
    - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

TYRVAYA (varenicline)

Review: Tyrvaya nasal spray is a cholinergic agonist indicated for the treatment of the signs and symptoms of dry eye disease. Intranasal varenicline (Tyrvaya) adds novel therapy; a multi-dose nasal spray without being administered on the already irritated surfaces of the eyes. It is a nicotinic acetylcholine receptor agonist. Its mechanism of action is not known but is suspected to activate the trigeminal parasympathetic pathway, therefore stimulating natural tear production.

The most common adverse event was sneezing, which was reported in 82% of the participants (in ONSET trials). 5 to 16% of patients reported cough, throat irritation and nose irritation. Currently, there are no contraindications to Tyrvaya.

Tyrvaya is a new option for patients with dry eye disease. It also appears to have a faster onset of action than traditional agents used for DED.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.
Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Tyrvaya is a pharmacy benefit and will not be added to the formulary. The following prior authorization will apply:

- Medical record documentation of a diagnosis of dry eye disease **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Xiidra **AND** cyclosporine (Restasis)

QUANTITY LIMIT: 8.4ml per 30 days (max dose)

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VUITY (pilocarpine hydrochloride)

Review: Vuity is the first and only FDA-approved eye drop specifically indicated for the treatment of presbyopia in adults. Prior to approval the only treatments of presbyopia have included corrective lenses, such as eyeglasses or contact lenses, or laser vision refractive surgery. Newer treatments have included corneal inlays, which are tiny devices implanted into the cornea of the eye. Vuity is supplied as a 1.25% ophthalmic solution given 1 drop in both eyes daily.

The efficacy of Vuity was evaluated in two 30-Day Phase 3, randomized, double-masked, vehicle-controlled studies, which showed that Vuity can improve DCNVA starting as soon as 15 minutes after administration and lasting up to 6 hours. The most common side effects in studies were headache, conjunctival hyperemia, blurred vision, eye pain, visual impairment, eye irritation and increased lacrimation.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Vuity is a pharmacy benefit and will be added to the formulary on the brand non-preferred tier. The following prior authorization criteria will apply:

- Prescription written by or in consultation with an optometrist or ophthalmologist **AND**
- Medical record documentation of a diagnosis of Presbyopia **AND**
- Medical record documentation of age greater than or equal to 40 years **AND**
- Medical record documentation of intolerance to, or contraindication to corrective lenses

QUANTITY LIMIT: 2.5 mL per 30 days

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

SKYTROFA (lonapegsomatropin-tcgd)

Review: Skytrofa is a human growth hormone indicated for the treatment of pediatric patients 1 year of age and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH). Skytrofa is the first-FDA approved sustained-release somatropin (growth hormone) product. It is administered as a once-weekly subcutaneous injection. The manufacturer is currently conducting other phase 3 trials, such as extended safety trial in pediatrics and efficacy and safety trial in adults with growth hormone deficiency.

Skytrofa is available as 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg and 13.3 mg prefilled cartridge. The recommended dose for treatment-naïve patients and patients switching from daily somatropin therapy is 0.24 mg/kg body weight, given once weekly. The dose may be titrated based on response. Skytrofa should be discontinued once epiphyseal fusion as occurred.

Skytrofa was studied in a randomized, open-label, active-controlled, parallel-group phase 3 study with 161 treatment naïve, prepubertal pediatric subjects with growth hormone deficiency. Patients were randomized to Skytrofa (n=105) or daily somatropin (n=56). The dose in both arms was 0.24 mg/kg/week. The primary efficacy endpoint was annualized height velocity at Week 52. Treatment with one-weekly Skytrofa for 52 weeks resulted in an annualized height velocity of 11.2 cm/year. Subjects treated with daily somatropin achieved an annualized height velocity of 10.3 cm/year after 52 weeks of treatment, which was statistically significant. Height SDS change from baseline was 1.1 in the Skytrofa arm and 0.96 in the daily somatropin arm at Week 52.

Skytrofa is contraindicated in the following patients: those with acute critical illness after open heart or abdominal surgery or trauma, or those with acute respiratory failure; those with hypersensitivity to somatropin or any of the excipients; patients with closed epiphyses; patients with active malignancy; patients with active proliferative or severe non-proliferative diabetic retinopathy; and those with Prader-Willi syndrome who are severely obese, have a history of upper airway obstruction or sleep apnea or have severe respiratory impairment. There are warnings for increased mortality in patients with acute critical illness or those with acute respiratory failure; systemic hypersensitivity reactions; increased risk of neoplasms. The most common adverse reactions (≥5%) in pediatric patients include viral infection, pyrexia, cough, nausea and vomiting, hemorrhage, diarrhea, abdominal pain, and arthralgia and arthritis. The safety and effectiveness in children less than 1 year of age have not been established.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Skytrofa will be a pharmacy benefit and will be added to the formulary to the Growth Hormone bucket for commercial, Specialty tier or Brand Non-Preferred tier for members with a three tier benefit. Skytrofa will be added to policy 29.0 and require a prior authorization with the following criteria:

- Medical record documentation of use for a Food and Drug Administration (FDA) approved indication **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Norditropin* (if applicable)

MEDISPAN LEVEL: GPI-12

AUTHORIZATION DURATION: Authorization for Growth Hormone will be for a time period of one year. Continuation of coverage will be provided based on medical record documentation to determine if there is appropriate follow up care with the physician, if any endpoint criteria are met, or if any major change in clinical status has occurred.

FDA Approved Indications:
Pediatric Growth Hormone Deficiency: Norditropin, Genotropin, Humatrope, Nutropin AQ, Omnitrope, Saizen, Zomacton, Skytrofa

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

TRUDHESA (dihydroergotamine mesylate intranasal)

Review: Trudhesa is indicated for the acute treatment of moderate to severe migraine headaches with or without aura in adults. Trudhesa is not indicated for the preventative treatment of migraine OR for the management of hemiplegic or basilar migraine.

Similar to Migranal, Trudhesa is a nasal spray composed of dihydroergotamine mesylate. However, the main differentiating factor from Migranal is the way in which Trudhesa is delivered. Trudhesa utilizes propellant enabled Precision Olfactory Delivery (POD) technology which works to deliver the dihydroergotamine mesylate to the upper nasal space versus the lower nasal space as seen with Migranal. The upper nasal space is considered to be more vascular rich versus the lower nasal cavity where most nasal sprays deliver to. The typical dosage of Migranal is 2 mg (0.5 mg in each nostril and then repeated 15 minutes later) while the dose of Trudhesa is 1.45 mg (0.725 mg in each nostril) with a potential for an additional dose 1 hour later if needed.

In regard to place in therapy, it is perceived that we will initially see the use of Trudhesa in patients who have failed or have a contraindication to Triptans and abortive CGRPs. Triptan medications are the mainstay of therapy for acute migraines but they do show that the response to treatment decreases over time. CGRPs are well tolerated and have shown little evidence to suggest medication overuse headache or vasoconstriction.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.
Outcome: Trudhesa is a pharmacy benefit and will not be added to the formulary. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Trudhesa will be used for the acute treatment of moderate to severe migraine headaches with or without aura **AND**
- Medical record documentation of therapeutic failure on, in tolerance to, or contraindication to three (3) formulary alternatives, one of which must be dihydroergotamine nasal spray

QUANTITY LIMIT: 12 mL per 28 days

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

APRETUDE (cabotegravir extended release)

Review: Apretude is indicated at-risk adults and adolescents for PrEP to reduce the risk of sexually acquired HIV-1 infection. PrEP is used by people without HIV infection who are at risk of being exposed to HIV through sexual contact or injection drug use. Cabotegravir may be right for people who had problems taking oral PrEP as prescribed, who prefer getting a shot every 2 months instead of taking oral PrEP, or who have serious kidney disease that prevents the use of other PrEP medications. Prior to initiating Apretude, an oral lead-in dose may be used for approximately 1 month with the recommended dosage to assess the tolerability of Apretude. The patient may proceed directly to injection of Apretude without an oral lead-in. Apretude is for gluteal intramuscular (IM) injection only and must be administered by a healthcare provider.

Apretude has a black box warning for the risk of drug resistance with use for PrEP in undiagnosed HIV-1 infection and is contraindicated in patients with unknown or positive HIV-1 status.

Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Apretude is a medical benefit. and will not be added to the formulary. If Apretude is processed at a specialty pharmacy, it will process as a $0 preventative. The following quantity limit will apply, if able to be implemented via the claims editing process:

QUANTITY LIMIT: 3 mL (1 injection) per claim, 7 claims per year

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CLASS REVIEWS

FDA Approved Indications:

Trade Name/ Manufacturer/ Benefit Type	Generic Name	Mechanism of Action	FDA Approved Indication
Evkeeza *Regeneron Pharmaceuticals, Inc.* Medical Benefit (Commercial/Medicaid) Medical or Pharmacy Benefit (Medicare)	evinacumab-dgnb	Angiopoietin-like 3 (ANGPTL3) inhibitor	• An adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH). <u>Limitations:</u> - The safety and effectiveness of Evkeeza have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH). - The effects of Evkeeza on cardiovascular morbidity and mortality have not been determined.
Juxtapid *Amryt Pharmaceuticals, Inc.* Pharmacy Benefit	lomitapide	Microsomal triglyceride transfer protein (MTP) inhibitor	• An adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). <u>Limitations:</u> - The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH). - The effect of JUXTAPID on cardiovascular morbidity and mortality has not been determined.
Praluent *Regeneron Pharmaceuticals, Inc.* Pharmacy Benefit	alirocumab	Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor	• To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease. • As adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia,

			including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C. • As an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.
Nexletol/Nexlizet *Esperion Therapeutics, Inc.* Pharmacy Benefit	bempedoic acid bempedoic acid/ezetimibe	Adenosine triphosphate-citrate lyase (ACL) inhibitor Adenosine triphosphate-citrate lyase (ACL) inhibitor/cholesterol absorption inhibitor	• As an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C. Limitations: - The effect of Nexletol/Nexlizet on cardiovascular morbidity and mortality has not been determined.
Updated Indication			
Repatha *Amgen, Inc.* Pharmacy Benefit	evolocumab	Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor	• In adults with established cardiovascular disease (CVD) to reduce the risk of myocardial infarction, stroke, and coronary revascularization • As an adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C • As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 10 years and older* with HeFH, to reduce LDL-C • As an adjunct to other LDL-C-lowering therapies in adults and pediatric patients aged 10 years and older* with homozygous familial hypercholesterolemia (HoFH), to reduce LDL-C *Previous age for HeFH was ≥ 18 years, Previous age for HoFH was ≥ 13 years
New FDA Approved Drug			
Leqvio *Novartis Pharmaceuticals Corporation*	inclisiran	Small interfering RNA (siRNA) directed to PCSK9 (proprotein convertase	• An adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering

Medical Benefit (Commercial/Medicaid) Medical or Pharmacy Benefit (Medicare)		subtilisin/kexin type 9) mRNA	of low-density lipoprotein cholesterol (LDL-C). Limitations: - The effect of Leqvio on cardiovascular morbidity and mortalilty has not been determined

Background of Familial Hypercholesterolemia: Familial Hypercholesterolemia is a genetic disorder characterized by high levels of circulating low density lipoproteins (LDL) cholesterol due to mutations in the genes encoding proteins involved in the metabolism of LDL. HeHF is estimated to occur in approximately 1 in 200-300 individuals while HoFH is a rarer condition origianlly estimated to occur in 1 to 1,000,000 in the 1970s but more recent genetic analysis surveys suggest it occures more frequently, closer to 1 in 170,000 to 300,000.

Patients with heterozygous familial hypercholesterolemia (HeFH) carry the mutated gene in a single allele (one parent with HeFH), can have plasma LDL-cholesterol levels twice the normal levels or higher, and often experience their first cardiovascular event in their thirties. A diagnosis of homozygous familial hypercholesterolemia (HoFH) encompasses homozygous patients with identical mutations in both alleles (both parents with HeFH), compound heterozygotes who inherited different mutations in both alleles, and double heterozygotes who have mutations in 2 different genes. In HoFH, the activity of the LDL receptor is completely or almost completely absent and severity depends on residual LDL receptor activity (receptor-negative [<2% residual acitvity] or receptor defective [2-25% residual activity]).

Plasma LDL-C levels in patients with HoFH are typically at least twice as high as patients with HeFH and four times higher than normal levels, although there is some overlap between HoFH and severe HeFH. Mean LDL-C level and severity depend on several factors including the specific genetic defect(s) and residual LDL receptor activity. In general, patients with HoFH have a poorer prognosis, may be refractory to many lipid-lowering drugs, and can develop cardiovascular complications as early as the first decade of their life. Angina and mycoardial infarction in infancy, and aortic supravalvular and valvular stenosis are often noted in HoFH. Systemic atherosclerosis can develop with aging and can lead to aortic aneurysms, peripheral artery disease, and cerebrovascular disease. If left untreated, most patients will die of ASCVD prior to age 30 so aggressive LDL-C lowering should be initiated as early as possible.

In addition to elevated LDL-C levels, tendon or skin xanthomas (cholesterol deposits under the skin) are important in the diagnosis of FH and are more prominent in patients with HoFH compared to HeFH. Corneal arcus, a white or grey ring around the cornea, can also be indicative of FH, occuring in about 30% of FH patients under the age of 50.

There is no universally agreed-upon criteria for the diagnosis of FH, but several diagnostic tools have been developed, including the US Make Early Diagnosis to Prevent Early Death (MEDPED) criteria, the UK Simon Broome system, the Dutch Lipid Clinic Network criteria, and the National Lipid Association expert panel recommendations. The American Heart Association has also proposed a simple set of criteria, but these have not been widely accepted or implemented. Table 1 shows some of the differences in diagnostic criteria. Although these diagnositic tools do not differentiate between HeFH and HoFH, in clinical practices HoFH is commonly diagnosed using criteria based on clinical manifestations (cutaneous or tendon xanthoma), personal and familial history of premature cardiovasccular disease, and high LDL-C levels with or without genetic testing.

Genetic testing can provide a definitive diagnosis of familial hypercholesterolemia, however the genes commonly associated with FH are only identified in about 60 to 80% of patients and genetic testing dose not exclude the possibility of HoFH due to unknown gene mutations. Most commonly identified mutations occur in the low-density lipoprotein (LDL) receptor (LDLr) gene, but mutations in the apolipoprotein B (ApoB) gene, proprotein convertase subtilisin/kexin type 9 (PCSK9) gene, or LDL protein receptor adaptor 1 (LDLRAP1) gene (milder phenotype that only appears to be implicated in HoFH) can also lead to FH.

Current treatment guidelines recommend LDL-C goals of less than 130 mg/dL in pediatric patients and less than 100 mg/dL in adult patients for primary prevention. Although not stated in the pediatric guidelines, most sources suggest that pediatric goals should be the same as adult HoFH in secondary prevention (less than 70 mg/dL).

Most patients with FH cannot achieve LDL goals with lifestyle interventions and drug therapy will be required, starting with statins as first line treatment (Figures 2, 3, and 4). When statins alone are not sufficient, other lipid lowering therapies such as ezetimibe can be added. The ENHANCE study showed that the addition of ezetimibe to statin therapy resulted in a further reduction of LDL-C levels in patients with FH. PCSK9 inhibitors have also been showed to be effective in the reduction of LDL-C levels in patients with FH, depending on the residual LDL receptor activity. Many patients with HoFH may be refractory to these treatments, but if any are effective they should be continued together with additional treatments such as Juxtapid, Evkeeza, or lipoprotein apheresis.

Although LDL apheresis, the physical removal of lipoproteins from the blood, is an effective treatment for FH, particularly in those who hare no responsive to statins or who are statin-intolerant, guidelines vary from country to country on when LDL apheresis should be initiated in patients with HoFH and all guidelines recommend that it be used in combination with other lipid-lowering therapies. Although apheresis can result in a 50-70% reduction in LDL-C levels, levels may gradually return to baseline during the period to the next apheresis treatment. Access to apheresis treatments, substantial annual costs, and impact on quality of life due to the invasive nature of the procedure are some other limitations to apheresis treatment for HoFH.

Figure 2. Treatment for Patients 15 Years and Older with Heterozygous FH[7]

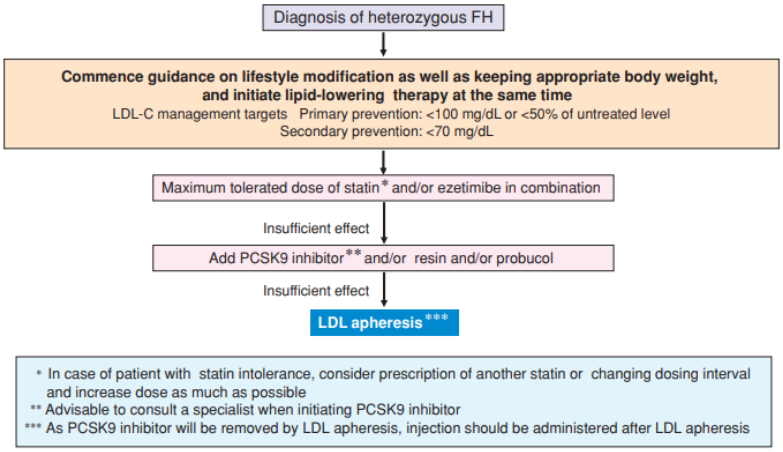


Figure 3. Treatment for Patients 15 Years and Older with Homozygous FH[7]

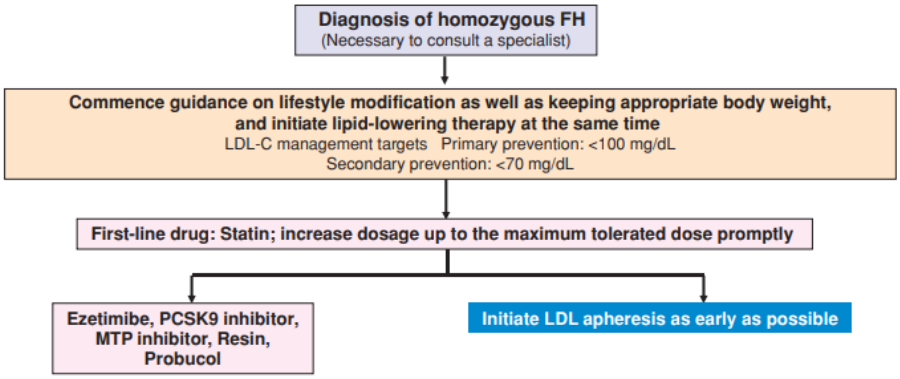
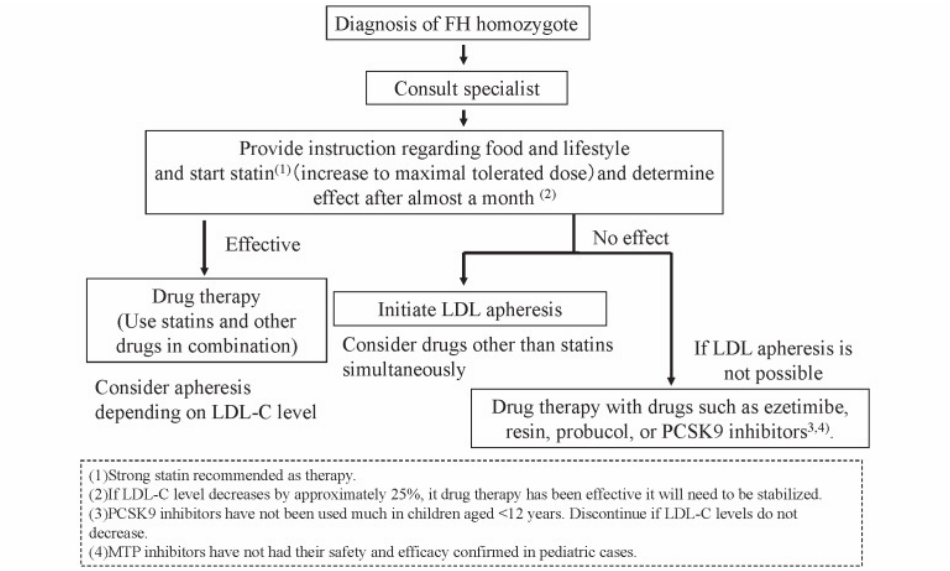


Figure 4. Treatment for Pediatric Patients with Homozygous FH[6]



Evkeeza Update

No changes should be made to Evkeeza for formulary placement or authorization duration. The following changes are recommended to MBP 242.0 and Part D Policy 876.0D for Evkeeza to expand the indication to include additional genes commonly associated with HoFH, include failure of treatment with ezetimibe to achieve LDL-C goals, and removal of LDL apheresis from criteria.

Medical Benefit Policy 242.0 Evkeeza

- Medical record documentation of a diagnosis of homozygous familial hypercholesterolemia (HoFH) ~~that is caused by mutations of the low-density lipoprotein (LDL) receptor (LDLr) gene~~ **AND** either
  - Genetic testing to confirm diagnosis showing a mutation in the low-density lipoprotein (LDL) receptor (LDLr) gene, apolipoprotein B (ApoB) gene, proprotein convertase subtilisin/kexin type 9 (PCSK9) gene, or LDL protein receptor adaptor 1 (LDLRAP1) gene **OR**
  - Diagnosis made based on history of an untreated low-density lipoprotein cholesterol (LDL-C) greater than 500 mg/dL **AND** either xanthoma before 10 years of age **OR** evidence of heterozygous familial hypercholesterolemia (HeFH in both parents)

AND

- Medical record documentation that Evkeeza is prescribed by a lipidologist or cardiologist **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation of failure to adequately control low-density lipoprotein (LDL) levels with combination of maximum tolerated statin dose and ezetimibe ~~low-density lipoprotein (LDL) apheresis treatment~~ defined as:
  - Greater than or equal to 130 mg/dL in pediatric patients greater than or equal to 12 years of age and less than 18 years of age OR
  - Greater than or equal to 100 mg/dL in adult patients without cardiovascular disease OR
  - Greater than or equal to 70 mg/dL in ~~adult~~ patients with established cardiovascular disease

AND

- Medical record documentation of Evkeeza to be used in adjunct with maximum tolerated statin dose AND other low-density lipoprotein-cholesterol (LDL-C) lowering therapies ~~AND low-density lipoprotein (LDL) apheresis~~ **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to one formulary proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor **AND**
- If the request is for use in combination with Juxtapid:

- Medical record documentation of failure to adequately control low-density lipoprotein (LDL) levels with a minimum 6-month trial of maximum tolerated Juxtapid dose without the concomitant use of Evkeeza

AUTHORIZATION DURATION: Initial authorization will be for a period of six (6) months. After the initial six (6) month approval, subsequent approvals for coverage will be for a duration of one (1) year. Reevaluation of coverage will be every one (1) year, requiring medical record documentation that current medical necessity criteria are met and that therapy has been effective.

Juxtapid Update

No changes should be made to Juxtapid for formulary placement, authorization duration, or quantity limit. The following changes are recommended to Commercial Policy 293.0 and Part D Policy 301.0D for Juxtapid to expand the indication to include additional genes commonly associated with HoFH, include failure of treatment with ezetimibe to achieve LDL-C goals, and removal of LDL apheresis from criteria.

Commerical Policy 293.0 Juxtapid

- Medical record documentation of a diagnosis of homozygous familial hypercholesterolemia (HoFH) ~~that is caused by mutations of the low-density lipoprotein (LDL) receptor (LDLr) gene~~ **AND** either
  - Genetic testing to confirm diagnosis showing a mutation in the low-density lipoprotein (LDL) receptor (LDLr) gene, apolipoprotein B (ApoB) gene, proprotein convertase subtilisin/kexin type 9 (PCSK9) gene, or LDL protein receptor adaptor 1 (LDLRAP1) gene **OR**
  - Diagnosis made based on history of an untreated low-density lipoprotein cholesterol (LDL-C) greater than 500 mg/dL **AND** either xanthoma before 10 years of age **OR** evidence of heterozygous familial hypercholesterolemia (HeFH in both parents)

  AND
- Medical record documentation that Juxtapid is prescribed by a hepatologist, lipidologist, or cardiologist registered with the Juxtapid risk evaluation and mitigation strategies (REMS) program **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of failure to adequately control low-density lipoprotein (LDL) levels with combination of maximum tolerated statin dose and ezetimibe ~~low-density lipoprotein (LDL) apheresis treatment~~ defined as:
  - Greater than or equal to 100 mg/dL in patients without cardiovascular disease
  - Greater than or equal to 70 mg/dL in patients with established cardiovascular disease

AND

- Medical record documentation of Juxtapid to be used in adjunct with maximum tolerated statin dose **AND** other low-density lipoprotein-cholesterol (LDL-C) lowering therapies ~~low-density lipoprotein (LDL) apheresis~~ **AND**
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Repatha* AND~~
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to one formulary proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor **AND**
- If the request is for use in combination with Evkeeza: Medical record documentation of failure to adequately control low-density lipoprotein (LDL) levels with a minimum 3-month trial of Evkeeza without the concomitant use of Juxtapid

Praluent Update:

No changes should be made to Praluent for formulary placement, authorization duration, or quantity limit. The following changes are recommended to Commercial Policy 392.0 and Part D Policy 482.0D for Praluent to change the diagnostic criteria tool for the commercial policy for HeFH, expand the indication to include additional genes commonly associated with HoFH, and remove the critiera that say Praluent will not be used in combination with Juxtapid.

Commercial Policy 392.0 Praluent

- Medical record documentation of a diagnosis of:
  - Clinical atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes (a history of myocardial infarction or unstable angina), coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin **OR**
  - Primary hyperlipidemia **OR**
  - Heterozygous familial hypercholesterolemia **AND** either:
    - Genetic testing to confirm a mutation in the low-density lipoprotein (LDL) receptor, PCSK9, or ApoB gene **OR**
    - Medical record documentation of definite heterozygous familial hypercholesterolemia (HeFH) (score greater than 8) on the diagnostic criteria scoring system (Table 1) ~~as defined by the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines and the World Health Organization~~ as defined by the Dutch Lipid Clinic Network diagnostic criteria **OR**
  - Homozygous familial hypercholesterolemia (HoFH) AND either:
    - Genetic testing to confirm diagnosis showing a mutation in the low-density lipoprotein (LDL) receptor (LDLr) gene, apolipoprotein B (ApoB) gene, proprotein convertase subtilisin/kexin type 9 (PCSK9) gene, or LDL protein receptor adaptor 1 (LDLRAP1) gene ~~at least one LDL receptor defective mutation~~ **OR**
    - Diagnosis made based on a history of an untreated low-density lipoprotein cholesterol (LDL-C) greater than 500 mg/dL AND either xanthoma before 10 years of age **OR** evidence of heterozygous familial hypercholesterolemia (HeFH) in both parents **AND**
- Medical record documentation of a baseline low-density lipoprotein (LDL) drawn within 3 months of the start of PCSK9 therapy showing:
  - Low-density lipoprotein (LDL) greater than 100 if the member is using Praluent for primary prevention **OR**
  - Low-density lipoprotein (LDL) greater than 70 if the member is using Praluent for secondary prevention **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that patient is currently on and is adherent to (taking at least 90% of prescribed doses over the past three months) maximally tolerated dose of atorvastatin or rosuvastatin or has documented therapeutic failure on, intolerance to, or contraindication to atorvastatin and rosuvastatin **AND**
- Medical record documentation that non-pharmacologic therapies are in place including cholesterol lowering diet, exercise, and weight management strategies **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to ezetimibe **AND**
- Medical record documentation that Praluent is not being used in combination with another PCSK9 inhibitor ~~or Juxtapid~~

AUTHORIZATION DURATION: Initial authorizations for Praluent will be approved for a period of 12 months. Reauthorizations will be for a period of 12 months each provided the following criteria are met:

- Medical record documentation of an up to date low density lipoprotein (LDL) cholesterol level since the date of the previous review showing the patient has had a clinically significant response to treatment with a PCSK9 inhibitor **AND**
- Medical record documentation that the patient is not experiencing any significant adverse events related to therapy **AND**
- Claims history and attestation from the provider showing the patient is adherent to PCSK9 therapy **AND**
- Claims history or attestation from the provider that the patient is staying adherent to (filling at least 90% of doses) statin therapy (if statin tolerant) **AND**

- Medical record documentation that Praluent continues to not be used in combination with another PCSK9 inhibitor ~~or Juxtapid~~

*Diagnostic criteria for the clinical diagnosis of HeFH (Dutch Lipid Network diagnostic criteria)

Dutch Lipid Clinic Network diagnostic criteria for familial hypercholesterolaemia

Criteria	Points
1) Family history	
▪ First-degree relative with known premature (men: <55 years; women: <60 years) coronary or vascular disease, or ▪ First-degree relative with known LDL-C above the 95th percentile	1
▪ First-degree relative with tendinous xanthomata and/or arcus cornealis, or ▪ Children <18 years of age with LDL-C above the 95th percentile	2
2) Clinical history	
▪ Patient with premature (men: <55 years; women: <60 years) coronary artery disease	2
▪ Patient with premature (men: <55 years; women: <60 years) cerebral or peripheral vascular disease	1
3) Physical examination	
▪ Tendinous xanthomata	6
▪ Arcus cornealis before age 45 years	4
4) LDL-C levels	
▪ LDL-C ≥8.5 mmol/L (325 mg/dL)	8
▪ LDL-C 6.5 to 8.4 mmol/L (251-325 mg/dL)	5
▪ LDL-C 5 to 6.4 mmol/L (191-250 mg/dL)	3
▪ LDL-C 4 to 4.9 mmol/L (155-190 mg/dL)	1
5) DNA analysis	
▪ Functional mutation in the LDLR, apoB, or PCSK9 gene	8
Choose only one score per group, the highest applicable diagnosis (diagnosis is based on the total number of points obtained) ▪ A "definite" FH diagnosis requires >8 points ▪ A "probable" FH diagnosis requires 6 to 8 points ▪ A "possible" FH diagnosis requires 3 to 5 points	

FH: familial hypercholesterolaemia; LDL-C: low-density lipoprotein-cholesterol.
* Exclusive of each other (ie, maximum six points if both are present).

Reprinted from: Familial hypercholesterolaemia (FH) : report of a second WHO consultation, Geneva, 4 September 1998. World Health Organization, p. 13, Copyright © 1998. Available at: http://apps.who.int/iris/handle/10665/66346 (Accessed on April 9, 2013).

UpToDate®

Nexletol/Nexlizet Update:

No changes should be made to Nexletol or Nexlizet for formulary placement, authorization duration, or quantity limit. The following changes are recommended to Commercial Policy 640.0, Commercial Policy 641.0 and Part D Policy 824.0 D for Nexletol and Nexlizet to change the diagnostic criteria tool for HeFH.

Commercial Policy 640.0 Nexletol

- Medical record documentation of a diagnosis of:
  - Clinical atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes (a history of myocardial infarction or unstable angina), coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin **OR**

    - Heterozygous familial hypercholesterolemia (HeFH) **AND** either:
        - Genetic testing to confirm a mutation in the low-density lipoprotein (LDL) receptor, PCSK9, or ApoB gene **OR**
        - Medical record documentation of definite heterozygous familial hypercholesterolemia (HeFH) (score greater than 8) on the diagnostic criteria scoring system (Table 1) ~~as defined by the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines and the World Health Organization~~ as defined by the Dutch Lipid Clinic Network diagnostic criteria **AND**
- Medical record documentation that Nexletol is prescribed by a cardiologist or lipidologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a baseline low-density lipoprotein (LDL) drawn within 3 months of the start of Nexletol therapy with one of the following:
    - Low-density lipoprotein (LDL) greater than 100 if the patient has a diagnosis of heterozygous familial hypercholesterolemia (HeFH) and is using Nexletol for primary prevention **OR**
    - Low-density lipoprotein (LDL) greater than 70 if the patient has a diagnosis of atherosclerotic cardiovascular disease (ASCVD) or either heterozygous familial hypercholesterolemia (HeFH) and is using Nexletol for secondary prevention **AND**
- Medical record documentation that patient is currently on and is adherent to (taking at least 90% of prescribed doses over the past three months) maximally tolerated dose of atorvastatin or rosuvastatin or has documented therapeutic failure on, intolerance to, or contraindication to atorvastatin and rosuvastatin **AND**
- Medical record documentation that non-pharmacologic therapies are in place including cholesterol lowering diet, exercise, and weight management strategies AND
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to ezetimibe

Commercial Policy 640.0 Nexlizet

- Medical record documentation of a diagnosis of:
    - Clinical atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes (a history of myocardial infarction or unstable angina), coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin **OR**
    - Heterozygous familial hypercholesterolemia (HeFH) AND either:
        - Genetic testing to confirm a mutation in the low-density lipoprotein (LDL) receptor, PCSK9, or ApoB gene **OR**
        - Medical record documentation of definite heterozygous familial hypercholesterolemia (HeFH) (score greater than 8) on the diagnostic criteria scoring system (Table 1) ~~as defined by the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines and the World Health Organization~~ as defined by the Dutch Lipid Clinic Network diagnostic criteria **AND**
- Medical record documentation that Nexlizet is prescribed by a cardiologist or lipidologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a baseline low-density lipoprotein (LDL) drawn within 3 months of the start of Nexlizet therapy with one of the following:
    - Low-density lipoprotein (LDL) greater than 100 if the patient has a diagnosis of heterozygous familial hypercholesterolemia (HeFH) and is using Nexlizet for primary prevention **OR**
    - Low-density lipoprotein (LDL) greater than 70 if the patient has a diagnosis of atherosclerotic cardiovascular disease (ASCVD) or either heterozygous familial hypercholesterolemia (HeFH) and is using Nexlizet for secondary prevention **AND**
- Medical record documentation that patient is currently on and is adherent to (taking at least 90% of prescribed doses over the past three months) maximally tolerated dose of atorvastatin or rosuvastatin or has documented therapeutic failure on, intolerance to, or contraindication to atorvastatin and rosuvastatin **AND**

- Medical record documentation that non-pharmacologic therapies are in place including cholesterol lowering diet, exercise, and weight management strategies **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to ezetimibe alone

Repatha New Indication/Update

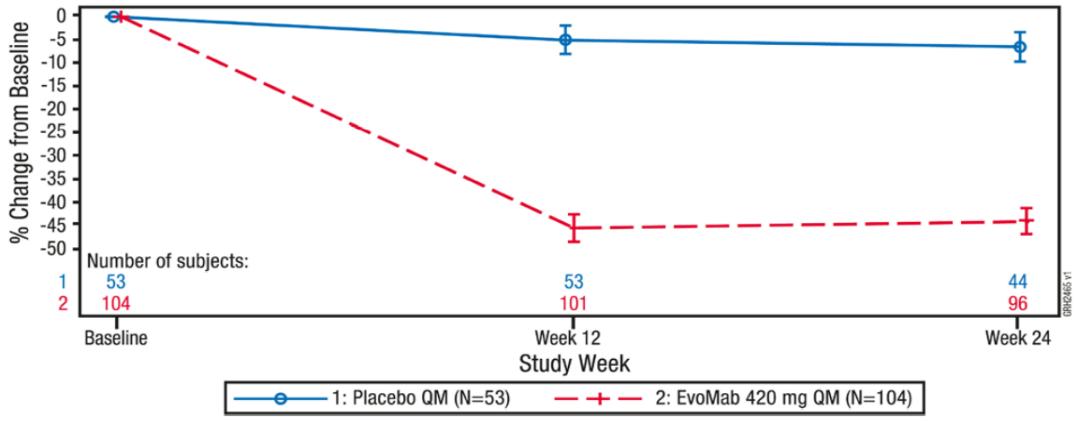
Updated Indication[3]: Repatha is now indicated for patients 10 and over with HeFH or HoFH. Previously Repatha was indicated for treatment of adult patients with primary hyperlipidemia, including HeFH and for adults and pediatric patients 13 years and older for HoFH. For patients with established cardiovascular disease or primary hyperlipidemia Repatha remains indicated only for adult patients.

Updated Dosing for New Indication[3]: There are no changes to the recommended dosage for HeFH or HoFH for the new pediatric population.

Summary of Updated Clinical Studies[3]:

Pediatric Patients with HeFH: Changes to the indication are supported by previous clinical trials in adult patients with HeFH and Study 6, a randomized, double-blind, placebo-controlled 24-week trial comparing Repatha to placebo in 157 pediatric patients (age 10 to 17 years) with HeFH. Patients were randomized 2:1 to receive once monthly 420 mg Repatha (n=104) or placebo (n=53). The difference between Repatha and placebo for mean percent change in LDL-C from baseline to Week 24 was -38% (Figure 5) and Table 2 shows the effect of Repatha on the lipid parameters.

Figure 5. Effect of Repatha on LDL-C in Pediatric Patients with HeFH (Mean % change from baseline)[3]



EvoMab = evolocumab; LDL-C = low density lipoprotein cholesterol; QM = monthly (subcutaneous)
N = number of patients randomized and dosed in the full analysis set.
Vertical lines represent the standard error around the mean. Plot is based on observed data and no imputation is used for missing values.

Table 2. Effect of Repatha on Lipid Parameters in Pediatric Patients with HeFH (Mean % Change from baseline to week 24)[3]

Treatment Group	LDL-C	Non-HDL-C	Apo B	Total Cholesterol
Placebo once monthly (n = 53)	-6	-6	-2	-5
REPATHA 420 mg once monthly (n = 104)	-44	-41	-35	-32
Mean difference from placebo (95% CI)	-38 (-45, -31)	-35 (-42, -28)	-32 (-39, -26)	-27 (-32, -21)

All adjusted p-values < 0.0001.
n = number of patients randomized and dosed in the full analysis set.

Pediatric Patients with HoFH: Changes to the HoFH indication are supported by previous clinical trials in adults and pediatric patients 13 years and older and Study 9, an open-label, single-arm, 80-week study evaluating safety,

tolerability, and effiacy of Repatha for LDL-C reduction in pediatric patients aged 10 to 17 years with HoFH. Twelve patients with HoFH received 420 mg Repatha subcutaneously once monthly. The mean age was 12 years (range 11 to 17 years). Mean LDL-C at baseline was 398 mg/dL and all patients were on statins (atorvastatin or rosuvastatin) and ezetimibe. No patients were receiving lipid apheresis. The median percent change in LDL-C from baseline to week 80 was -14%. Two of the three subjects with <5% LDLR activity responded to evolucumab treatment.

Summary of Updated Safety Considerations[3]: The most common adverse reactions reported with Repatha during Study 6 for HeFH were nasopharyngitis, headache, oropharyngeal pain, influenza, and upper respiratory tract infection. No new safety concerns were reported in Study 9 with Repatha for HoFH

Recommendations:
No changes should be made to Repatha for formulary placement, authorization duration, or quantity limit. The following changes are recommended to Commercial Policy 393.0 and Part D Policy 497.0D for Repatha to change the diagnostic criteria tool for the commercial policy for HeFH, expand the indication to include additional genes commonly associated with HoFH, change the required age to 10 years and include appropriate LDL levels for pediatric patients, and remove the critiera that say Repatha will not be used in combination with Juxtapid.

Commercial Policy 393.0 Repatha

- Medical record documentation of a diagnosis of:
  - Clinical atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes (a history of myocardial infarction or unstable angina), coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin **OR**
  - Primary hyperlipidemia **OR**
  - Heterozygous familial hypercholesterolemia (HeFH) AND either:
    - Genetic testing to confirm a mutation in the low-density lipoprotein (LDL) receptor, PCSK9, or ApoB gene **OR**
    - Medical record documentation of definite heterozygous familial hypercholesterolemia (HeFH) (score greater than 8) on the diagnostic criteria scoring system (Table 1) ~~as defined by the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines and the World Health Organization~~ as defined by the Dutch Lipid Clinic Network diagnostic criteria **OR**
  - Homozygous familial hypercholesterolemia (HoFH) **AND** either:
    - Genetic testing to confirm diagnosis showing a mutation in the low-density lipoprotein (LDL) receptor (LDLr) gene, apolipoprotein B (APOB) gene, proprotein convertase subtilisin/kexin type 9 (PCSK9) gene, or LDL protein receptor adaptor 1 (LDLRAP1) gene ~~at least one low-density lipoprotein (LDL) receptor-defective mutation~~ **OR**
    - Diagnosis made based on a history of an untreated low-density lipoprotein cholesterol (LDL-C) greater than 500 mg/dL AND either xanthoma before 10 years of age **OR** evidence of heterozygous familial hypercholesterolemia (HeFH) in both parents **AND**
- Medical record documentation of a baseline low-density lipoprotein (LDL) drawn within 3 months of the start of PCSK9 therapy
  - Low-density lipoprotein (LDL) greater than 130 mg/dL if the member is greater than or equal to 10 years of age and less than 18 years of age **OR**
  - Low-density lipoprotein (LDL) greater than 100 mg/dL if the member is greater than or equal to 18 years of age and using Repatha for primary prevention **OR**
  - Low-density lipoprotein (LDL) greater than 70 mg/dL if the member is using Repatha for secondary prevention **AND**
- Medical record documentation of age greater than or equal to 18 years if the diagnosis is clinical atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH)

or primary hyperlipidemia **OR** medical record documentation of age greater than or equal to ~~13~~ 10 years if the diagnosis is homozygous familial hypercholesterolemia (HoFH) **AND**

- Medical record documentation that patient is currently on and is adherent to (taking at least 90% of prescribed doses over the past three months) maximally tolerated dose of atorvastatin or rosuvastatin or has documented therapeutic failure on, intolerance to, or contraindication to atorvastatin and rosuvastatin **AND**
- Medical record documentation that non-pharmacologic therapies are in place including cholesterol lowering diet, exercise, and weight management strategies **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to ezetimibe **AND**
- Medical record documentation that Repatha is not being used in combination with another PCSK9 inhibitor ~~or Juxtapid~~ **AND**
- If requesting Repatha Syringe or Repatha Sureclick 420 mg dose (3 mL), medical record documentation of therapeutic failure on, intolerance to, or contraindication to Repatha Pushtronex **OR**
- If requesting 420 mg every 2 weeks:
    - Medical record documentation of a diagnosis of Homozygous Familial Hypercholesterolemia (HoFH) **AND**
    - One of the following:
        - Medical record documentation that the member has been on 420 mg once monthly for 12 weeks and a clinically meaningful response has not been achieved **OR**
        - Medical record documentation that the member is on lipid apheresis every 2 weeks

AUTHORIZATION DURATION: Initial authorizations for Repatha will be approved for a period of 12 months. Reauthorizations will be for a period of 12 months each provided the following criteria are met:

- Medical record documentation of an up to date low density lipoprotein (LDL) cholesterol level since the date of the previous review showing the patient has had a clinically significant response to treatment with a PCSK9 inhibitor **AND**
- Medical record documentation that the patient is not experiencing any significant adverse events related to therapy **AND**
- Claims history and attestation from the provider showing the patient is adherent to PCSK9 therapy **AND**
- Claims history or attestation from the provider that the patient is staying adherent to (filling at least 90% of doses) statin therapy (if statin tolerant) **AND**
- Medical record documentation that Repatha continues to not be used in combination with another PCSK9 inhibitor ~~or Juxtapid~~ **AND**
- If requesting Repatha Syringe or Repatha Sureclick 420 mg dose (3 mL), medical record documentation of therapeutic failure on, intolerance to, or contraindication to Repatha Pushtronex **OR**
- If requesting 420 mg every 2 weeks:
    - Medical record documentation of a diagnosis of Homozygous Familial Hypercholesterolemia (HoFH) **AND**
    - One of the following:
        - Medical record documentation that the member has been on 420 mg once monthly for 12 weeks and a clinically meaningful response has not been achieved **OR**
        - Medical record documentation that the member is on lipid apheresis every 2 weeks

Leqvio Clinical Review

Pharmacology/Place in Therapy[5,14]: Leqvio is a double-stranded small interfering ribonucleic acid (siRNA) conjugated on the sense strand with triantennary N-Acetylgalactosamine (GalNAc) to facilitate uptake by hepatocytes where it directs catalytic breakdown of mRNA for PCSK9 through the RNA interference mechanism. PCSK9 is responsible for the degradation of hepatocellular LDL receptors. By targeting PCSK9, Leqvio

increases LDL-C receptor recycling and expression on hepatocyte cell surface leading to increased LDL-C uptake and lower LDL-C circulation.
Leqvio is a first-in-class siRNA and has a novel mechanism of action for lowering LDL-C compared to other PCSK-9 inhibitors. While Praluent and Repatha inhibit PCSK9, Leqvio inhibits the synthesis of PCSK9. There are no clinical trials directly comparing these agents, but it appears that all PCSK9 therapies are highly effective in LDL-C reduction.

Leqvio is indicated as an adjunct to diet and exercise for LDL-C lowering in adult patients with HeFH and ASCVD. It is not indicated in HoFH or in children at this time. The effect of Leqvio on cardiovascular morbidity and mortality has not been established but clinical trials are underway and expected to be completed in 2026. Currently Leqvio will be covered as a medical benefit, but as a subcutaneous injection it could potentially be available for self-administration in the future.

Clinical Discussion: Keith asked what the definition of interruption in therapy is (for needing repeat loading dose) – 3 months. Would like to consider adding a quantity limit if it can be implemented. Will table the quantity limit until more investigation can be done on what is capable in the medical claims system. No other comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed

Recommendations: Leqvio will be a medical benefit. Leqvio will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Leqvio will process at the Specialty tier or Brand Non-Preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of:
    - Clinical atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes (a history of myocardial infarction or unstable angina), coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin **OR**
    - Heterozygous familial hypercholesterolemia **AND** either:
        - Genetic testing to confirm a mutation in the low-density lipoprotein (LDL) receptor, PCSK9, or ApoB gene OR
        - Medical record documentation of definite heterozygous familial hypercholesterolemia (HeFH) (score greater than 8) on the diagnostic criteria scoring system (Table 1) as defined by the Dutch Lipid Clinic Network diagnostic criteria

AND

- Medical record documentation of a baseline low-density lipoprotein (LDL) drawn within 3 months of the start of PCSK9 therapy showing:
    - Low-density lipoprotein (LDL) greater than 100 if the member is using Leqvio for primary prevention **OR**
    - Low-density lipoprotein (LDL) greater than 70 if the member is using Leqvio for secondary prevention **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that patient is currently on and is adherent to (taking at least 90% of prescribed doses over the past three months) maximally tolerated dose of atorvastatin or rosuvastatin or has documented therapeutic failure on, intolerance to, or contraindication to atorvastatin and rosuvastatin **AND**
- Medical record documentation that non-pharmacologic therapies are in place including cholesterol lowering diet, exercise, and weight management strategies **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to ezetimibe **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Repatha* **OR** Praluent* **AND**
- Medical record documentation that Leqvio is not being used in combination with another PCSK9 inhibitor

AUTHORIZATION DURATION: Initial authorizations for Leqvio will be approved for a period of 12 months. Reauthorizations will be for a period of 12 months each provided the following criteria are met:

- Medical record documentation of an up to date low density lipoprotein (LDL) cholesterol level since the date of the previous review showing the patient has had a clinically significant response to treatment with a PCSK9 inhibitor AND
- Medical record documentation that the patient is not experiencing any significant adverse events related to therapy AND
- Claims history and attestation from the provider showing the patient is adherent to PCSK9 therapy AND
- Claims history or attestation from the provider that the patient is staying adherent to (filling at least 90% of doses) statin therapy (if statin tolerant) AND
- Medical record documentation that Leqvio continues to not be used in combination with another PCSK9 inhibitor

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CLASS REVIEW – INTRAVITREAL VEGF INHIBITORS

Susvimo (ranibizumab) is a VEGF inhibitor that binds to the receptor sites of multiple biologically active forms of VEGF-A. When ranibizumab prevents VEGF-A to bind on the surface of endothelial cells, it reduces endothelial cell proliferation, vascular leakage and new blood vessel formation.

Vabysmo (faricimab) is a humanized bispecific antibody that acts through inhibition of two pathways: binding to VEGF-A and Ang-2. When faricimab inhibits VEGF-A it suppresses endothelial cell proliferation, neovascularization and vascular permeability. When faricimab inhibits Ang-2, it is thought to promote vascular stability and desensitize blood vessels to the effects of VEGF-A. The contribution of Ang-2 inhibition to the treatment effect and clinical response for nAMD and DME has yet to be established.

Susvimo is the fifth VEGF inhibitor and Vabysmo is the first VEGF and Ang-2 inhibitor approved for use in neovascular (wet) age-related macular degeneration (nAMD). Susvimo contains the same active ingredient as the intravitreal injection Lucentis (ranibizumab). The other approved VEGF inhibitors are Eylea (aflibercept), Beovu (brolucizumab) and the off-label used product Avastin (bevacizumab). Macugen (pegaptanib) was discontinued in the United States on September 17th, 2020. Susvimo is unique in that it consists of a small surgically implanted "port" that releases a customized formulation of ranibizumab continually for up to 6 months, at which time the port gets refilled. All other available VEGF inhibitors are intravitreal injections. Vabysmo is unique in that the labeling allows for extended dose intervals up to 16 weeks in both nAMD and DME. IPD Analytics states 1 of 3 treatment schedules are followed by most doctors when using anti-VEGF therapy. Option one includes injecting the first three monthly doses, then following with treatment on an as needed basis ("treat and observe"). Option two includes injecting the first three monthly doses, then gradually increasing time between treatments until wet AMD is stabilized ("treat and extend"). Option three includes injecting monthly or bimonthly.

The prescribing information for Vabysmo for nAMD recommends three maintenance regimens. 1) injections on weeks 28 and 44; 2) injections on weeks 24, 36 and 48; or 3) injections on weeks 20, 28, 36 and 44. Some patients may need every 4 week dosing after the loading dose, although not demonstrated to be additionally effective. The prescribing information for Vabysmo for DME recommends two maintenance regimens. 1) interval extensions of up to 4 week intervals and interval reductions of up to 8 week intervals; or 2) intervals of once every 8 weeks. Some patients may need every 4 week dosing after the loading dose, although not demonstrated to be additionally effective.

The prescribing information for Lucentis for nAMD recommends a maintenance dose of once every month, and states less frequent dosing may be used, although not as effective. In addition, one dose every 3 months may be used, although not as effective. The prescribing information for Lucentis for DME recommends injections once a month.

The prescribing information for Eylea for nAMD recommends a maintenance dose of once every 8 weeks, however states that some patients may need every 4 week dosing after the loading dose and some patients may also be treated with one dose every 12 weeks after one year of effective therapy, although not as effective as every 8 week dosing. The prescribing information for Eylea for DME recommends a maintenance dose of once every 8 weeks. Some patients may need every 4 week dosing after the loading dose, although not demonstrated to be additionally effective.

The prescribing information for Beovu recommends a maintenance dose of once every 8-12 weeks. Off-label bevacizumab has a maintenance dose of once every month or on an as needed basis. Each intravitreal injection (i.e. Eylea, Lucentis, Beovu and off-label bevacizumab) has a loading dose of once a month injections for the first 3 doses, Lucentis also allows a dosing regimen of once a month injections for the first 4 doses, and Vabysmo has a loading dose of once a month for the first 4 doses and allows for a dosing regimen for DME for once a month injections for the first 6 doses. Novartis updated Beovu's label to include additional safety information regarding retinal vasculitis and retinal vascular occlusion, and in June 2021, Phase 3 clinical trials for the use of Beovu

every 4 weeks were discontinued. Novartis recommends physicians not to use Beovu at intervals less than 2 months for maintenance dosing.

Susvimo phase three trials are currently underway for diabetic macular edema and diabetic retinopathy, with results expected in 2022 and 2023. Byooviz, a biosimilar for Lucentis, was approved on September 17th, 2021 and is expected to have freedom to market starting June 2022. An FDA decision for Cimerli, a biosimilar for Lucentis, is expected by August 2nd, 2022 and at least 2 other Lucentis biosimilars are in Phase III development. Lytenava, a biosimilar for bevacizumab for use specifically in retinal indications, has a potential FDA approval date of early 2023. Several manufacturers currently have Eylea biosimilars in Phase III development however, all are unlikely to launch until 2024 due to patent protections.

Vabysmo is a vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2) inhibitor indicated for the treatment of patients with Neovascular (Wet) Age-Related Macular Degeneration (nAMD) and Diabetic Macular Edema (DME). Vabysmo is the 6th VEGF inhibitor approved for the use in nAMD and the 3rd VEGF inhibitor approved for use in DME. Other VEGF inhibitors approved for nAMD are Lucentis (ranibizumab), Susvimo (ranibizumab), Eylea (aflibercept), Beovu (brolucizumab) and the off-label used product Avastin (bevacizumab). Macugen (pegaptanib) was discontinued in the United States on September 17th, 2020. Other VEGF inhibitors approved for DME are Eylea, Lucentis and the off-label used product Avastin. Vabysmo is unique in that the labeling allows for extended dose intervals up to 16 weeks in both nAMD and DME.

The prescribing information for Vabysmo for nAMD recommends three maintenance regimens. 1) injections on weeks 28 and 44; 2) injections on weeks 24, 36 and 48; or 3) injections on weeks 20, 28, 36 and 44. Some patients may need every 4 week dosing after the loading dose, although not demonstrated to be additionally effective. The prescribing information for Vabysmo for DME recommends two maintenance regimens. 1) interval extensions of up to 4 week intervals and interval reductions of up to 8 week intervals; or 2) intervals of once every 8 weeks. Some patients may need every 4 week dosing after the loading dose, although not demonstrated to be additionally effective.

TENAYA and LUCERNE were two identically designed, randomized, multi-center, double masked, active comparator-controlled, 2 year studies to evaluate the efficacy of Vabysmo compared to Eylea in patients with nAMD who were newly diagnosed and treatment naïve. Patients were randomized 1: 1 to receive either Eylea fixed dosing or Vabysmo variable dosing. In both studies, Vabysmo treated patients had a non-inferior mean change from baseline in Best Corrected Visual Acuity (BCVA) compared to Eylea treated patients.

YOSEMITE and RHINE were two identically designed, randomized, multi-center, double masked, active comparator-controlled studies to evaluate the efficacy of Vabysmo compared to Eylea in patients with DME who were either anti-VEGF naïve or had been previously treated with a VEGF inhibitor. Patients were randomized 1:1:1 to receive either Eylea fixed dosing, Vabysmo fixed dosing, or Vabysmo variable dosing. In both studies, Vabysmo fixed every 8 weeks and Vabysmo variable treated patients had a mean change in baseline in BCVA that was non-inferior to the patients treated with Eylea fixed every 8 weeks.

Contraindications for Vabysmo include ocular or periocular infections, active intraocular inflammation and hypersensitivity to faricimab or any of the excipients in Vabysmo. Warnings and precautions for Vabysmo include endophthalmitis and retinal detachments, increase in intraocular pressure seen within 60 minutes of injection and thromboembolic events including nonfatal stroke, nonfatal myocardial infarction or vascular death (including deaths of unknown cause). Common adverse reactions observed in greater than 1% of 1,926 patients across four Phase 3 studies included conjunctival hemorrhage, vitreous floaters, retinal pigment epithelial tear, intraocular pressure increase, eye pain, intraocular inflammation, eye irritation, ocular discomfort, and vitreous hemorrhage.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Recommendations from National Agencies or Organizations[7,8,9]:

American Academy of Ophthalmology

The American Academy of Ophthalmology (AAO) Age-Related Macular Degeneration Preferred Practice Pattern guidelines state anti-vascular endothelial growth factor (VEGF) agents (eg. aflibercept, bevacizumab, and ranibizumab) are the most effective way to manage AMD and is first line treatment. Additionally, symptoms suggestive of post injection endophthalmitis or retinal detachment require prompt evaluation. The Comparison of AMD Treatment Trials (CATT) compared safety and effectiveness of bevacizumab with ranibizumab and found comparable VA improvements for monthly dosing of each product.

The Diabetic Retinopathy Preferred Practice Pattern guidelines state anti-VEGF agents are effective in the treatment of center-involved diabetic macular edema with vision loss. At the time of publication (2019) laser photocoagulation surgery is the preferred treatment for non-center involved diabetic macular edema and pan-retinal photocoagulation (PRP) surgery remains the mainstay treatment for proliferative diabetic retinopathy (PDR). Additionally, DRCR Protocol T study was a head to head trial comparing bevacizumab, ranibizumab and aflibercept which demonstrated effectiveness similar in all three agents for eyes with visual acuity of 20/40 or better. For visual acuity of 20/50 or worse, a statistically significant difference was found between aflibercept and bevacizumab only.

The Retinal Vein Occlusions Preferred Practice Pattern guidelines state the first line treatment for associated macular edema in central retinal vein occlusions (CRVOs) and branch vein retinal occlusions (BRVOs) is anti-VEGFs. In addition, intravitreal corticosteroids, with the associated risk of glaucoma and cataract formation, have demonstrated efficacy and laser photocoagulation surgery in BRVO has a potential role in treatment. The SCORE2 study compared aflibercept to bevacizumab for macular edema from CRVO. The guidelines state that caution is advised before concluding that the two regimens yield similar visual outcomes and that aflibercept was used for eyes with marginal response to bevacizumab.

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome:

1. Susvimo and Vabysmo will be medical benefits. Susvimo and Vabysmo will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Susvimo and Vabysmo will process at the Specialty tier or the Brand Non-preferred tier for members with a three tier benefit. The following prior authorization criteria apply.
2. Beovu is a medical benefit currently not requiring prior authorization. Beovu is currently on the medical benefit cost share list. If processed at a specialty pharmacy, Beovu will process at the Specialty tier or the Brand Non-preferred tier for members with a three tier benefit. The following prior authorization criteria will now apply to Beovu.

Susvimo

- Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND**
- Medical record documentation patient has previously responded to at least two (2) intravitreal doses of a Vascular Endothelial Growth Factor (VEGF) inhibitor medication **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) additional intravitreal VEGF inhibitors (e.g. Eylea, Beovu, or Lucentis)

AND

- Medical record documentation that Susvimo (ranibizumab) will not be given in combination with an intravitreal Vascular Endothelial Growth Factor (VGEF) inhibitor administration to the same eye **OR**

- If the request is for use in combination with an intravitreal VEGF inhibitor administration to the same eye, all of the following must be met:
    - Medical record documentation Susvimo (ranibizumab) will be given in combination with intravitreal ranibizumab injection (Lucentis) **AND**
    - Medical record documentation intravitreal ranibizumab injection will be administered on an as needed basis, as determined by the prescriber

NOTE: Indicators of intravitreal bevacizumab (Avastin) failure may include:

- Worse or unchanged intraretinal or subretinal fluid.
- Persistent subretinal or intraretinal fluid.
- Recurrent intraretinal or subretinal fluid at current interval or extended interval.
- New subretinal hemorrhage
- In the absence of subretinal fluid, intraretinal fluid, or subretinal hemorrhage a failure documented as
- evidence of growth of the neovascular membrane on clinical exam or multimodal imaging.
- Any ocular or systemic adverse event thought related to the use of intravitreal bevacizumab.

Authorization duration: Approval will be given for an **initial duration of two (2) years** or less if the reviewing provider feels it is medically appropriate. After the initial two (2) year approval, subsequent approvals will be for a **lifetime duration** or less if the reviewing provider feels it is medically appropriate, and will require:

- Medical record documentation that Susvimo (ranibizumab) will not be given in combination with an intravitreal Vascular Endothelial Growth (VEGF) inhibitor

LIMITATION: Susvimo (ranibizumab) to be given in combination with intravitreal ranibizumab (Lucentis) injections after 92 weeks from the start of Susvimo therapy has not been studied in clinical trials and will require prior authorization.

Vabysmo

- Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) additional intravitreal VEGF inhibitors (e.g. Eylea, Beovu, or Lucentis)

OR

- Medical record documentation of a diagnosis of diabetic macular edema **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) additional intravitreal VEGF inhibitors (e.g. Eylea and Lucentis)

NOTE: Indicators of intravitreal bevacizumab (Avastin) failure may include:

- Worse or unchanged intraretinal or subretinal fluid.
- Persistent subretinal or intraretinal fluid.
- Recurrent intraretinal or subretinal fluid at current interval or extended interval.
- New subretinal hemorrhage
- In the absence of subretinal fluid, intraretinal fluid, or subretinal hemorrhage a failure documented as
- evidence of growth of the neovascular membrane on clinical exam or multimodal imaging.
- Any ocular or systemic adverse event thought related to the use of intravitreal bevacizumab.

Authorization Duration: Approvals will be given for a lifetime duration.

Beovu

- Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin)

NOTE: Indicators of intravitreal bevacizumab (Avastin) failure may include:
- Worse or unchanged intraretinal or subretinal fluid.
- Persistent subretinal or intraretinal fluid.
- Recurrent intraretinal or subretinal fluid at current interval or extended interval.
- New subretinal hemorrhage
- In the absence of subretinal fluid, intraretinal fluid, or subretinal hemorrhage a failure documented as
- evidence of growth of the neovascular membrane on clinical exam or multimodal imaging.
- Any ocular or systemic adverse event thought related to the use of intravitreal bevacizumab.

Authorization Duration: Approvals will be given for a lifetime duration.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

FAST FACTS

CUTAQUIG (immune globulin subcutaneous (human) - hipp)

Updated Indication: Cutaquig is now indicated for the treatment of primary humoral immunodeficiency (PI) in adults and pediatric patients 2 years of age and older.

Cutaquig was previously indicated for treatment of primary humoral immunodeficiency (PI) in adults.

Current formulary status: Cutaquig is a medical benefit requiring prior authorization. If processed at a specialty pharmacy, Cutaquig processes at the Specialty tier or the Brand Non-preferred tier for members with a three tier benefit.

Recommendation: There are no changes recommended to the formulary placement, authorization duration or prior authorization criteria of intravenous immune globulin as outlined by MBP 4.0.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

DESOVY (emtricitabine and tenofovir alafenamide)

Updated Indication: Descovy is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infected adult and pediatric patients at least 2 years of age and weighing at least 14 kilograms (kg).

Previously Descovy was indicated in HIV-1 infected adult and pediatric patients weighing at least 25kg. Descovy is also indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection in at-risk adults and adolescents weighing 35kg or more.

Current formulary status: Descovy 200/25mg tablet Brand preferred tier

Recommendation: No changes are needed to the formulary placement or quantity limits of Descovy 200/25mg. It is recommended to add Descovy 120/15mg to the formularies on the Brand preferred tier with a quantity limit of one (1) tablet per day

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

DESLTRIGO (doravirine, lamivudine and tenofovir disoproxil)

Updated Indication: Delstrigo is now FDA approved as a complete regimen for the treatment of HIV-1 infection in pediatric patients weighing at least 35 Kg.

Previously this was only indicated approved as a complete regimen for the treatment of HIV-1 infection in adults.

Current formulary status: Delstrigo is a pharmacy benefit and is on the Brand Preferred tier that does not require a prior authorization.

Recommendation: No changes to formulary placement or restrictions at this time.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

PIFELTRO (doravirine)

Updated Indication: Pifeltro is now FDA approved for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric patients weighing at least 35 Kg.

Previously this was only indicated for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults

Current formulary status: Pifeltro is a pharmacy benefit and is on the Brand Preferred tier that does not require a prior authorization.

Recommendation: No changes to formulary placement or restrictions at this time.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

REXULTI (brexiprazole)

Updated Indication: Rexulti is now indicated for the treatment of schizophrenia in pediatric patients ages 13 years and older. Previously, it was indicated for schizophrenia and adjunctive therapy to antidepressants for treatment of major depressive disorder in adults.

Current formulary status: Rexulti is a pharmacy benefit and is non-formulary. Rexulti requires prior authorization.

Recommendation: There are no changes to formulary status or quantity limits at this time. However, it is recommended to update the prior authorization criteria to the following.

Schizophrenia
- Medical record documentation of a diagnosis of schizophrenia **AND**
- Medical record documentation of an age greater than or equal to 13 years **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to three generic, formulary atypical antipsychotics

Major Depressive Disorder

- Medical record documentation of a diagnosis of major depressive disorder (MDD) **AND** medical record documentation that the patient is using Rexulti as adjunctive therapy **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least a 4 week trial of combination therapy with aripiprazole and an antidepressant **AND**
- One of the following:
    - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least a 4 week trial of combination antidepressant therapy (such as a selective serotonin reuptake inhibitor [SSRI] and bupropion or an serotonin and norepinephrine reuptake inhibitor [SNRI] and bupropion) **OR**
    - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least a 4 week trial of an antidepressant with augmentation therapy (including, but not limited to lithium, valproate, carbamazepine and lamotrigine)

Discussion: No comments or questions

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

DEXTENZA (dexamethasone ophthalmic insert)

Updated Indication: Ocular itching associated with allergic conjunctivitis.

Previous indication: Treatment of ocular inflammation and pain following ophthalmic surgery

Current formulary status: Covered as a medical benefit, no prior authorization required for the treatment of ocular inflammation and pain following ophthalmic surgery.

Recommendation: Note: Prior authorization is not required for Dextenza for the diagnosis of ocular inflammation and pain following ophthalmic surgery (diagnosis codes H59.8, H57.10). In the event of a request for Dextenza for a use other than post operative ocular inflammation, including ocular itching associated with allergic conjunctivitis OR in the event a requestor would like a medical necessity review completed, the following prior authorization criteria would apply for the new indication of ocular itching associated with allergic conjunctivitis.

1. Medical record documentation of a diagnosis of ocular itching associated with allergic conjunctivitis **AND**
2. Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to up to 3 formulary alternatives if available.

Discussion: While prior authorization is not required for ocular inflammation and pain following ophthalmic surgery, Keith recommended adding the diagnosis to the policy in the event a provider requests a review. No additional comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as amended. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

ZEPATIER (elbasvir and grazoprevir)

Updated Indication: Zepatier is now indicated for the treatment of chronic Hepatitis C virus (HCV) genotype 1 or 4 infection in adult and pediatric patients 12 years of age and older or weighing at least 30 kg.

Previously Zepatier was indicated for patients 18 years of age and older for the treatment of chronic Hepatitis C virus (HCV) genotype 1 or 4 infection.

Current formulary status: Non formualry

Recommendation: No changes to the current formulary placement recommended. The following changes to the prior authorization criteria and authorization duration are recommended.

- Medical record documentation of age greater than or equal to ~~18 years~~ 12 years of age OR weighing at least 30 kg AND

AUTHORIZATION DURATION:

- ~~Genotype 1a~~
  - ~~Zepatier will be approved for a time period of 12 weeks if NS5A- OR~~
  - ~~Zepatier will be approved for a time period of 16 weeks if NS5A+ OR~~
- ~~Genotype 1b~~
  - ~~Zepatier will be approved for a time period of 12 weeks OR~~
- ~~Genotype 4~~
  - ~~Zepatier will be approved for a time period of 12 weeks OR~~
  - ~~Zepatier will be approved for a time period of 16 weeks if peginterferon and ribavirin treatment experienced~~

Per AASLD/IDSA guidelines

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VOCABRIA (cabotegravir)

Updated Indication: Vocabria is now indicated in at-risk adults and adolescents weighing at least 35kg for short-term pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating Vocabria for HIV-1 PrEP. Vocabria may be used as:

- Oral lead-in to assess the tolerability of cabotegravir prior to administration of Cabenuva (cabotegravir extended-release injectable suspension; rilpirivine extended-release injectable suspension) for HIV-1 treatment or Apretude (cabotegravir extended-release injectable suspension) for HIV-1 PrEP
- Oral therapy for patients who will miss planned injection dosing with Cabenuva for HIV-1 treatment or Apretude for HIV-1 PrEP

Vocabria was previously indicated in combination with Edurant (rilpirivine) for short-term treatment of HIV-1 infection in adults who are virologically suppressed (HIV-1 RNA less than 50 copies/mL) on a stable antiretroviral regimen with no history of treatment failure and with no known or suspected resistance to either cabotegravir or rilpirivine, for use as:

- Oral lead-in to assess the tolerability of cabotegravir prior to administration of Cabenuva
- Oral therapy for patients who will miss planned injection dosing with Cabenuva

Current formulary status: Vocabria is a pharmacy benefit on the Brand Preferred tier for Commercial, Marketplace, and CHIP formularies with no prior authorization required. A quantity limit of 1 tablet per day applies.

Recommendation: It is recommended if Vocabria is being used for PrEP, it will process as a $0 preventative via submission clarification codes at point of service.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

UPDATES

COSENTYX (secukinumab)

Background: Cosentyx is available as 150 mg/mL auto-injector and syringe in single and two-packs. Our current quantity limits for commercial plans are as follows:

- Cosentyx (300 mg dose) 150 mg/mL prefilled syringe and auto-injector: 2 mL per 28 days
- Cosentyx 150 mg/mL prefilled syringe and auto-injector: 2 mL per 28 days
- Cosentyx 75mg/0.5mL prefilled syringe: 1 mL per 28 days

Recommendation: It is recommended to update the quantity limits for the 150 mg/mL single pack prefilled syringe and auto-injector to:

- 1mL per 28 days

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

STELARA (ustekinumab)

Discussion: Stelara is available as 45 mg vial and we currently do not have a quantity limit. For pediatric plaque psoriasis patients weighing less than 60 kg should receive 0.75mg/kg every 12 weeks. The 45 mg/0.5 mL single-dose vials is used for pediatric patients weighing less than 60 kg. A 59 kg patient would get 44.25 mg every 12 weeks, so a maximum of one 45 mg vial.

Also, for Crohn's disease and Ulcerative Colitis, it is recommended to remove the approval language for the initial infusion, since majority of those initial claims are not dispensed by specialty pharmacies and billed on the pharmacy benefit. I will add a note to the policy in the event we need to add an authorization for the vials to Darwin.

Recommendation:

Pediatric Plaque Psoriasis

It is recommended to update the quantity limit for 45 mg vials to <u>1 vial per 12 weeks</u>.

Stelara 45 mg vial (less than 60 kg)

1. In PA Hub: Add PA, DS, OQL, min day supply 28, max day supply 28, and number of claims authorized 1, with a duration of 3 weeks.
2. In Darwin: Add DS, min day supply 84, max day supply 84, with an end date of 12/31/2099. Start date of this authorization is 3 weeks after initial approval date.
    - QL FOR LETTER: Loading dose: 1 vial per 28 days; Maintenance dose: 1 vial per 84 days

Crohn's Disease and Ulcerative Colitis

It is recommended to update the quantity limit to the following:

1. In PA Hub: Add PA, number of claims authorized 1, enter for the remainder of the calendar year
2. In Darwin: Add DS, min day supply 56, max day supply 56, with an end date of 12/31/2099
    - QL FOR LETTER: 1 mL per 56 days

Note: If the initial infusion will be billed through the pharmacy benefit (i.e. specialty pharmacy trying to process the 130 mg/26 mL intravenous solution), in Darwin enter PA, OQL, DS only by GPI 52504070002020, enter 1 in

the max number of claims authorized, max quantity 104, min and max day supply 56) with a duration of 1 month. This will be in addition to the authorization above. Also, you will need to update the QL for the letter to the following:

- QL FOR LETTER: Intravenous loading dose: 104 mL per 56 days; 90 mg Syringe maintenance dose: 1 mL per 56 days

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

TALTZ (ixekizumab)

Background: Taltz is available as 80 mg/mL auto-injector or prefilled syringe. The quantity limit that is coded in the extract is 1 mL per 28 days. For the loading doses, we enter quantity limits into the authorizations. On annual policy review, we noticed the loading dose quantity limits need to be updated for ankylosing spondylitis (AS), psoriatic arthritis (PsA), pediatric plaque psoriasis for patient's weighing ≥ 50 kg.

The dose for PsA, AS, pediatric plaque psoriasis (weighing ≥ 50 kg) is 160 mg once (2 mL), followed by 80 mg every 4 weeks.

Our current quantity limit for the loading dose for these indications is 3 mL per 28 days.

Recommendation: It is recommended to update the loading dose quantity limits for ankylosing spondylitis, psoriatic arthritis, and pediatric plaque psoriasis for patient's weighing ≥ 50 kg.

MEDISPAN AUTHORIZATION LEVEL: GPI-10
QUANTITY LIMIT – *Quantity limit must be entered in the authorization.*

- 160 mg once, followed by 80 mg every 4 weeks
    1. In PA Hub: Add ST, PA, PE, OQL, DS. enter 1 in max number of claims authorized, and 2 mL per 28 days (max quantity 2, min/max day supply 28) with a duration of one month.
        - QL FOR LETTER: Loading dose: 2 mL per 28 days; Maintenance dose: 1 mL per 28 days

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

VENTOLIN HFA (albuterol)

Background: We are not receiving any rebates on Ventolin HFA. It was recommended to remove Ventolin HFA from formulary and to prefer generic, albuterol HFA. Ventolin HFA costs $68.42 per 18 gram inhaler. The cost of albuterol HFA is $32.90 per 18 gram inhaler.

Recommendation: It is recommended to remove Ventolin HFA from formulary. Requests for Ventolin HFA will be reviewed with the brand vs. generic policy 9.0.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

DUPIXENT, NUCALA, & XOLAIR

Background: Dr. Warden Hwan, Geisinger Allergy and Immunology, reached out regarding our Dupixent policy. He requested that we allow allergists to prescribe Dupixent for severe chronic sinusitis and nasal polyps. In his experience ENT providers often ask allergists to prescribe and monitor Dupixent therapy due to their experience with prescribing biologic therapy compared to ENT.

Chronic rhinosinusitis with nasal polyps (CRSwNP) often co-occurs with other type 2 immune-mediated conditions such as asthma, allergies, and/or nonsteroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD). About 26%-48% of patients with CRSwNP have comorbid asthma. Polyps usually develop in the third or fourth decade of life and are characterized by elevated levels of eosinophils.

Recommendation:
Dupixent, Nucala, Xolair
For policy 457.0, 661.0, 592.0, MBP 22.0 and MBP 141.0, it is recommended to update the specialist requirement for chronic rhinosinusitis with nasal polyps to the following:
"Prescribed by or in consultation with an allergist, pulmonologist, immunologist or otolaryngologist (ENT provider)"

Dupixent
At January P&T, we updated the GPI level and enter all authorizations by GPI-10. GPI-10 includes all Dupixent pens and syringes. Therefore, it is recommended to update the age restriction in policy 457.0 for atopic dermatitis and asthma. The age restriction should be updated to the following for those indications:
"Medical record documentation of age greater than or equal to 6 years"

Discussion: Keith questioned the need for including a pulmonologist in the criteria. No additional comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

NEXVIAZYME & LUMIZYME

Background: Dr. Yarczower and I had a call with Dr. Priya Kishnani, pediatric medical genetics specialist at Duke and she offered her expertise regarding Nexviazyme and Lumizyme and the management of Pompe disease.

Dr. Kishnani mentioned that in general, late-onset Pompe disease (LOPD) can be distinguished from infantile onset Pompe disease (IOPD) by the absence of cardiomyopathy in the first year of life. If a patient has cardiomyopathy the first year of life, they would be diagnosed with IOPD. The residual enzyme activity prevents patients with LOPD from developing cardiomyopathy in the first year of life. She noted how Nexviazyme is only FDA approved for LOPD, however it is being studied in patients with IOPD.

She mentioned it would not be appropriate to require failure of Lumizyme for patients weighing less than 30 kg, although based on the FDA approved dosing it may be cheaper. She said that a lot of her patients are on 40 mg/kg

(of actual body weight) every 2 weeks of Lumizyme, despite the labeling suggesting a dose of 20 mg/kg every 2 weeks for all patients. She also mentioned that if a patient is stable on a higher dose of Nexviazyme 40mg/kg every 2 weeks, it would not be clinically appropriate to make them go to the lower dose (20 mg/kg) once they are over 30 kg, despite the labeling. She has had many conversations with insurance companies regarding the dosing of Lumizyme and Nexviazyme. She said the dosing is very patient specific. She suggested we remove the ideal body weight requirement from our Lumizyme policies as that is not what is being followed in practice.

She suggested that we require muscle strength evaluations, including GSGC (gait, stairs, gower, chair), and biomarker trends instead of specifically calling out 6-Minute Walk Test, since a 13-month old would not be able to complete that. The GSGC scale is used in Pompe disease providing a quantitative (timed performance) and qualitative evaluation (severity grades) of 4 motor performances usually compromised in patients with proximal muscle weakness: G=Gait by walking for 10 m, S= climbing 4 steps, G= Gowers' maneuver, C= rising from a Chair.

She said in general, Nexviazyme may be more effective based on its mechanism of action and the trends in the studies, although it was not statistically significant. Also, Nexviazyme may be less immunogenic.

It is essential to start treatment early in patients with Pompe disease to prevent damage. She believes that from the insurance perspective, we need to make sure we are provided with a baseline assessment and re-assessments to confirm the efficacy of treatment.

Recommendation: There are no changes to formulary status or authorization duration. However, it is recommended to update the prior authorization criteria for Lumizyme based on Dr. Kishnani's feedback.

Nexviazyme:

- Medical record documentation of a diagnosis of late-onset Pompe disease supported by:
  - Acid alpha-glucosidase (GAA) assay performed on dried blood spots, skin fibroblasts or muscle biopsy AND
  - Genetic testing showing a mutation in the *GAA* gene
- Medical record documentation of a consultation with a metabolic specialist and/or biochemical geneticist AND
- Medical record documentation of age greater than or equal to 1 year AND
- Medical record documentation of baseline pulmonary function testing and muscle strength evaluation (e.g. percent-predicted forced vital capacity (% FVC), 6-minute walk test (6MWT), GSGC (gait stairs, gower, chair)) AND
- Medical record documentation that the member is receiving an appropriate dose* based on patient's weight AND
- Medical record documentation that Nexviazyme will not be used in combination with other enzyme replacement therapy (e.g. Lumizyme)

Authorization Duration: Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require the following:

- Medical record documentation of improvement or stabilization in pulmonary function testing and/or muscle strength evaluation (e.g. percent-predicted forced vital capacity (% FVC), 6-minute walk test (6MWT), GSGC (gait stairs, gower, chair)) AND
- Medical record documentation that the member is receiving an appropriate dose* based on patient's weight AND
- Medical record documentation that Nexviazyme will not be used in combination with other enzyme replacement therapy (e.g. Lumizyme)

*Note to reviewing pharmacist: For patients weighing ≥30 kg, the recommended dosage is 20 mg/kg (of actual body weight) every two weeks. For patients weighing < 30 kg, the recommended dosage is 40 mg/kg (of actual body weight) every two weeks.

Lumizyme:

- Physician provided documentation of a diagnosis of late-onset (non-infantile) Pompe disease OR a diagnosis of infantile-onset Pompe disease supported by:
  - GAA assay performed on dried blood spots, skin fibroblasts or muscle biopsy; and
  - Baseline pulmonary function testing (PFT) and muscle strength evaluation (e.g. percent-predicted forced vital capacity (% FVC), 6-minute walk test (6MWT), GSGC (gait stairs, gower, chair)); and
  - For late-onset Pompe disease only – Genetic testing to identify the specific mutation to confirm the diagnosis of late-onset Pompe disease; and
- Physician provided documentation of a consultation with a metabolic specialist and/or biochemical geneticist; and
- Medical record documentation that the member is receiving an appropriate dose* based on patient's weight AND
- Medical record documentation that Lumizyme will not be used in combination with other enzyme replacement therapy (e.g. Nexviazyme)

Authorization Duration: Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require the following:

- Medical record documentation of improvement or stabilization in pulmonary function testing and/or muscle strength evaluation (e.g. percent-predicted forced vital capacity (% FVC), 6-minute walk test (6MWT), GSGC (gait stairs, gower, chair)) AND
- Medical record documentation that the member is receiving an appropriate dose* based on patient's weight AND
- Medical record documentation that Lumizyme will not be used in combination with other enzyme replacement therapy (e.g. Nexviazyme)

*Note to reviewing pharmacist: The recommended dose is 20 mg/kg intravenously every 2 weeks.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

KISQALI & KISQALI FEMARA COPACK

Recommendation: The following change is recommended for Commercial Policy 447.0:

- Medical record documentation that Kisqali is prescribed by an oncologist **AND**
- Medical record documentation of diagnosis of hormone-receptor (HR) positive, HER2- negative, advanced or metastatic breast cancer **AND**
- Medical record documentation that Kisqali is being prescribed as initial endocrine therapy **AND**
- Medical record documentation that Kisqali will be used in combination with an aromatase inhibitor or fulvestrant **AND**
- Medical record documentation of one of the following:
  - Medical record documentation of postmenopausal status **OR**

- Medical record documentation of pre/perimenopausal status or member is male **AND** that member will be treated ~~with ovarian ablation or suppression~~ with a luteinizing hormone-releasing hormone (LHRH) agonist AND

Kisqali Following Disease Progression on Endocrine Therapy

- Medical record documentation that Kisqali is prescribed by an oncologist **AND**
- Medical record documentation of diagnosis of hormone-receptor (HR) positive, HER2- negative, advanced or metastatic breast cancer **AND**
- Medical record documentation that Kisqali is being prescribed after disease progression following endocrine therapy **AND**
- Medical record documentation that Kisqali will be used in combination with fulvestrant **AND**
- Medical record documentation of one of the following:
  - Medical record documentation of postmenopausal status **OR**
  - Medical record documentation of pre/perimenopausal status or member is male **AND** that member will be treated ~~with ovarian ablation or suppression~~ with a luteinizing hormone-releasing hormone (LHRH) agonist

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

UPTRAVI INTRAVENOUS FORMULATION

Background: Uptravi now has a formulation for intravenous infusion for patients who are temporarily unable to take oral therapy. Uptravi is available in a single-dose vial for reconsitution which contains 1800 mcg of selexipag. The dosage of Uptravi corresponds to the patient's current dose of Uptravi tablets (Table 1) and is administered twice daily as an 80-minute intravenous infusion. Adverse reactions reported with Uptravi for injection were infusion site reactions, including erythema, redness, pain and swelling.

Table 1. Dosing Table for UPTRAVI intravenous based on current UPTRAVI tablets dose[1]

UPTRAVI tablets dose (mcg) for twice daily dosing	Corresponding IV UPTRAVI Dose (mcg) for twice daily dosing	Reconstituted transfer volume (mL) for dilution
200	225	1.0
400	450	2.0
600	675	3.0
800	900	4.0
1000	1125	5.0
1200	1350	6.0
1400	1575	7.0
1600	1800	8.0

Cost:

Drug	AWP/MAC per unit ($)	AWP/MAC per 28-day supply ($)
Uptravi SDV for reconstitution, 1800 mcg	$404.74	$22,665
Uptravi Tablets, 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1000 mcg, 1200 mcg, 1400 mcg, 1600 mcg	$405.51	$22,708

Recommendation: Uptravi Intravenous will be a medical benefit. It will require a prior authorization and should be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Uptravi Intravenous should process at the Specialty tier or Brand Non-Preferred tier for members with a three tier benefit. The following prior authorization, quantity limit, and authorization duration criteria will apply:

- Medical record documentation that Uptravi is prescribed by a cardiologist or pulmonologist **AND**
- Medical record documentation of a diagnosis of World Health Organization (WHO) Group I, function class II or III pulmonary hypertension **AND**
- Medical record documentation of use in combination with, or failure on, intolerance to, or contraindication to sildenafil and/or an endothelin receptor antagonist (Tracleer [bosentan], Letairis [ambrisentan], or Opsumit [macitentan]) **AND**
- Medical record documentation that request is for temporary use of intravenous formulation and member is unable to take oral Uptravi tablets

QUANTITY LIMIT: 2 vials per day, 30 day supply per fill

AUTHORIZATION DURATION: 3 months. **Reauthorization** for Uptravi Intravenous beyond 3 months will be for an additional 3 months and will require documentation that request is for temporary use of intravenous formulation and member continues to be unable to take oral Uptravi tablets

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

TALZENNA QUANTITY LIMIT UPDATE

Background: Talzenna is now available in 0.5 mg and 0.75 capsules. Previously Talzenna was available in 0.25 mg and 1 mg capsules

Dosing Regimen: The recommended dose of Talzenna is 1 mg taken orally once daily, with or without food.

- Dose modifications for adverse reactions

Dose Level Dose	Dose Level Dose
Recommended starting dose	1 mg once daily
First dose reduction	0.75 mg once daily
Second dose reduction	0.5 mg once daily
Third dose reduction	0.25 mg once daily

- Dose modifications for patients with renal impairment
    - For patients with moderate renal impairment (CLcr 30 - 59 mL/min), the recommended dose of Talzenna is 0.75 mg once daily.
- Dose modifications for use with P-glycoprotein (P-gp) inhibitors
    - Reduce the Talzenna dose to 0.75 mg once daily when coadministered with certain P-gp inhibitors. For additional information on interacting P-gp inhibitors. When the P-gp inhibitor is discontinued, increase the Talzenna dose (after 3–5 half-lives of the P-gp inhibitor) to the dose used prior to the initiation of the P-gp inhibitor.

Current Formulary Status:

- Commercial/Exchange/CHIP: $0 Oncology Brand NP tier, PA required
    - 1 mg capsule: 30 capsules per 30 days
    - 0.25 mg capsules: 90 capsules per 30 days

Recommendation: It is recommended that Talzenna 0.5 mg and 0.75 mg capsules are added to the same tier as existing strengths with the same prior authorization criteria. Quantity limits should be added/modified as follows:

- 0.25 mg capsules: 30 capsules per 30 days (2023 for Gold)
- 0.5 mg capsules: 30 capsules per 30 days
- 0.75 mg capsules: 30 capsules per 30 days

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

SKYRIZI & STELARA LOOKBACK UPDATE

Background: Skyrizi and Stelara are currently configured as a prior authorization for new starts only with a 90 day lookback period. Due to their extended dosing intervals slight inconsistencies with fill dates members are denying as requiring a new prior authorization if their refill is just outside the 90 day window. Geisinger Specialty Pharmacy confirmed that they see most fills within 2 weeks +/- the calculated next fille date.

Recommendation: It is recommended that the lookback period for Skyrizi and Stelara are extended to 105 days in order to capture additional fills and eliminate unnecessary prior authorizations.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

CONTINUITY OF CARE UPDATE

Background: The Commercial continuity of care policy currently states:

Continuity of Care – Classes of Clinical Concern

For initial requests, Geisinger Health Plan will not require members to meet prior authorization or step therapy criteria if they are currently taking a medication in one of the following drug classes:

- Immunosuppressants (for prophylaxis of organ transplant rejection)
- Antidepressants
- Antipsychotics
- Anticonvulsants
- Antiretrovirals
- Antineoplastics
- Tumor Necrosis Factor Blockers
- Multiple Sclerosis
- Attention Deficit Hyperactivity Disorder/Attention Deficit Disorder

If members are currently receiving one of these medications requests for coverage will be approved as long as there is medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature.

Continuity of Care – All Others

For initial requests, Geisinger Health Plan will not require new members (members who have enrolled with the plan in the last 120 days) to meet prior authorization or step therapy criteria if medical record documentation of the following is provided:

- Member has been utilizing the requested medication for greater than or equal to six (6) months **AND**
- Member was not stabilized on samples of the requested medication **AND**
- Medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature

The following medications are specifically excluded from continuity of care. All other categories are subject to the discretion of the reviewing provider.

• Acthar	• GLP-1 Agonists
• Active Ingredients on Formulary as a Different Formulation (e.g., Lialda vs. Delzicol)	• High Risk Medications in the Elderly • Insulin
• Allergy Eye Drops	• Nasal Steroids
• Asthma/COPD Inhalers	• Oral Contraceptives
• Brands with a Generic	• Pancreatic Enzymes
• Combination Agents when all ingredients are on formulary (e.g., Vytorin)	• Proton Pump Inhibitors • SGLT2 Inhibitors
• Compounds	• Testosterone Products
• Diabetic Testing Supplies When Not Used in Conjunction with a Pump	• Topical Acne Products • Topical Antifungals
• DPP4 Inhibitors	• Topical Steroids

Recommendation: In order to improve consistency and to allow reviewers the ability to exercise their clinical judgement for continuity request, it is recommended that the policy is updated as follows:

Continuity of Care – Classes of Clinical Concern

For initial requests, Geisinger Health Plan will not require members to meet prior authorization or step therapy criteria if they are currently taking a medication in one of the following drug classes:

- Immunosuppressants (for prophylaxis of organ transplant rejection)
- Antidepressants
- Antipsychotics
- Anticonvulsants
- Antiretrovirals
- Antineoplastics
- Tumor Necrosis Factor Blockers
- Multiple Sclerosis
- Attention Deficit Hyperactivity Disorder/Attention Deficit Disorder

If members are currently receiving one of these medications requests for coverage will be approved as long as there is medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature.

Continuity of Care – All Others

Requests for continuity of care for all other medications will be at the discretion of the reviewer and may be considered if being used for a medically acceptable indication and the member is stable on therapy.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

NPLATE & PROMACTA UPDATE

Recommendation: It is recommended to update the prior authorization criteria for Nplate (MBP 68.0) and Promacta (Commercial Policy 185.0) to align policies for the indication of Chronic ITP across all applicable products.

MBP 68.0 Nplate (romiplostim)

Immune Thrombocytopenia (ITP)

- Physician supplied documentation of a diagnosis of immune thrombocytopenia (ITP); **AND**
- Physician supplied documentation of a therapeutic failure on, intolerance to, or contraindication to corticosteroids, immunoglobulins*, rituximab*, splenectomy, and eltrombopag (Promacta)*; **AND**
- Physician supplied documentation of:
    - symptomatic ITP with platelets less than 30,000/µL and bleeding symptoms; **OR**
    - ITP with platelets less than 30,000/µL and a documented history of significant bleeding; **OR**
    - a platelet count of less than 20,000/µL ~~and an increased risk of bleeding~~

*requires prior authorization

Commercial Policy 185.0 Promacta

For Chronic Immune Thrombocytopenic Purpura (ITP)

- Medical record documentation of a diagnosis of chronic immune (idiopathic) thrombocytopenic purpura (ITP) **AND**
- Medical record documentation that Promacta is prescribed by a hematologist **AND**
- Medical record documentation of a therapeutic failure on, or contraindication to ALL of the following: corticosteroids, immunoglobulins, and ~~Rituxan~~ rituximab* **AND**
- Symptomatic ITP with bleeding symptoms and a platelet count of less than 30,000/ µL; **OR** a documented history of significant bleeding and a platelet count of less than 30,000/µL; **OR** a platelet count of less than 20,000/µL ~~and an increased risk of bleeding~~

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

MEDICAL BENEFIT POLICY UPDATES

Recommendation:

MBP 48.0 Rituxan (rituximab), Truxima (rituximab-abbs), Ruxience (rituximab-pvvr), and Riabni (rituximab-arrx):

9. **For Pemphigus Vulgaris (PV)**
    - Prescription written by a dermatologist **AND**
    - Member is 18 years of age or older **AND**
    - Medical record documentation of a diagnosis of moderate to severe pemphigus vulgaris **AND**

- ~~Medical record documentation of a contraindication to, intolerance to, or therapeutic failure on corticosteroids AND a 12-week trial of at least one (1) nonsteroidal immunomodulatory medication (e.g. azathioprine, cyclophosphamide, or mycophenolate).~~
- Medical record documentation of use in combination with corticosteroids or a contraindication or intolerance to corticosteroids.

MBP 92.0 Off-Label Drug Use for Oncologic Indications

4. The proposed drug use is supported by any one or more of the following:
   - The National Comprehensive Cancer Network Practice Guidelines™ in Oncology category 1, 2A, or 2B recommendation; **OR**
   - The National Comprehensive Cancer Network Drug & Biologics Compendium™ category of Evidence and consensus 1, 2A, or 2B; **OR**
   - The American Hospital Formulary Service – Drug Information; **OR**
   - Thompson Micromedix DrugDEx Compendium (DrugDex®) class I or IIa indication; or
   - Elsevier Gold Standard's Clinical Pharmacology Compendium (Clinical Pharmacology®)

MBP 198.0 Gamifant (emapalumab-lzsg)

- Medical record documentation of a diagnosis of primary hemophagocytic lymphohistiocytosis (HLH) based on one of the following:
  - A molecular diagnosis (HLH gene mutations) **OR**
  - A family history consistent with primary HLH (X-linked lymphoproliferative syndrome) **OR**
  - 5 out of the following 8 criteria fulfilled:
    - Fever ≥ 38.5ºC
    - Splenomegaly
    - Cytopenias affecting 2 of 3 lineages in the peripheral blood; hemoglobin <9 g/dL, platelets <100 x 10^9/L, neutrophils <1 x 10^9/L
    - Hypertriglyceridemia (fasting triglycerides > 3 mmol/L or ≥ 265 mg/dL) and/or ~~hyper~~hypofibrinogenemia (≤1.5 g/dL)
    - Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy
    - Low or absent NK-cell activity
    - Ferritin ≥ 500 mcg/L
    - Soluble CD25 level (i.e. soluble IL-2 receptor) of ≥ 2,400 U/mL or two standard deviations above age-adjusted laboratory-specific norms

MBP 230.0 Darzalex Faspro (daratumumab/hyaluronidase)

- Medical Record documentation that the patient does NOT have New York Heart Association (NYHA) Class IIIB (defined by marked limitation of physical activity, comfortable at rest, less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain, symptomatic with recent history of dyspnea at rest) or Class IV heart failure, or mayo cardiac stage IIIB* **AND**

MBP 249.0 Saphnelo (anifrolumab-fnia)

- Medical record documentation that Saphnelo is being prescribed by or in consultation with a rheumatologist **AND**

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

QUARTERLY CASE AUDIT

The Quarterly Case Audit for 4th quarter 2021 was held on March 3, 2022. It was decided to create a policy for duloxetine 40mg based on the number of requests we had that were reviewed with the Commercial Administrative policy. The policy will help to ensure consistency among reviewers. We will continue to look for opportunities to create more drug specific policies at future quarterly case audit meetings.

Discussion: No comments or questions.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

KERENDIA UPDATE

Background: DHS noted that members started on Kerendia prior to coverage through Geisinger could be maintained on a 10 mg or 20 mg dose as long as serum potassium is less than or equal to 5.5 mEq/L and questioned our rationale for failure on three different SGLT-2 inhibitors.

Recommendation: It is recommended that the potassium criterion be updated as follows:

- Medical record documentation of serum potassium ≤ 5.0 mEq/L or ≤ 5.5 mEq/L if previously established on therapy **AND**

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed.

Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

Meeting adjourned at 4:37 pm

Future Scheduled Meetings

The next bi-monthly scheduled meeting will be held on May 17th, 2022 at 1:00 p.m.

All of these meetings are scheduled to be held at Geisinger Health Plan, Hughes Center North and South Buildings; 108 Woodbine Lane; Danville, PA 17821 or will be held virtually.