P&T Committee Meeting Minutes
GHP Family
January 15, 2019

Present:	**Absent:**
Bret Yarczower, MD, MBA – Chair	Kenneth Bertka, MD
Kristen Bender, PharmD – via phone	Beverly Blaisure, MD
Rajneel Chohan Pharm.D.	Holly Bones, PharmD
Alyssa Cilia, RPh – via phone	Kim Castelnovo, RPh
Kimberly Clark, PharmD	Dean Christian, MD
Kristi Clarke, PharmD, MHA – via phone	Michael Evans, RPh
Tricia Heitzman, PharmD.	Patrick Ferguson, RPh, MBA
Jason Howay, PharmD. – via phone	Sandra Garrett, RPh, MBA
Keith Hunsicker, PharmD.	Perry Meadows, MD
Kelli Hunsicker, PharmD. – via phone	Stephen Moscello, RPh
Steven Kheloussi, PharmD – via phone	Jonas Pearson, RPh
Phillip Krebs, R.EEG T. – via phone	Richard Silbert, MD
Jamie Miller, RPh	
Aubrielle Prater PharmD.	
Kristen Scheib, PharmD. – via phone	
William Seavey, PharmD. – via phone	
Michael Spishock, RPh – via phone	
Todd Sponenberg, PharmD.	
Jill Stone, Pharm.D. – via phone	
Kevin Szczecina, RPh	
Kelly Yelenic PharmD	
Matthew Seltzer – student	
Zachary Koehler - student	

Call to Order:
Dr. Bret Yarczower called the meeting to order at 1:02 p.m., Tuesday, January 15, 2019.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the November 20, 2018 minutes as written. Kim Clark accepted the motion and Todd Sponenberg seconded the motion. None were opposed.

DRUG REVIEWS

Lorbrena (lorlatinib)

Review: Lorbrena indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on: crizotinib and at least one other ALK inhibitor for metastatic disease; or alectinib as the first ALK inhibitor therapy for metastatic disease; or Ceritinib as the first ALK inhibitor therapy for metastatic disease. Lorbrena is the fifth ALK-targeted TKI to market, competing with other FDA-approved ALK inhibitors, including Xalkori (crizotinib), Zykadia (ceritinib), Alecensa (alectinib), and Alunbrig (brigatinib). Lorbrena, however, is unique in that it was specifically designed to inhibit tumor mutations that drive resistance to other ALK inhibitors and to penetrate the blood brain barrier, allowing for use in treatment of brain metastases. Additionally, Lorbrena is the first ALK-directed targeted therapy to be approved as a third line option for patients with metastatic disease. Xalkori has poor CNS penetration, however Alecensa and Alunbrig have both shown promising results in the setting of brain metastases. The NCCN Panel recommends Alecensa, Alunbrig, or Zykadia for patients with brain lesions. Lorbrena will likely compete against Alecensa and Alunbrig for ALK- positive metastatic NSCLC with the presence of intracranial metastases.

Lorbrena is supplied as 25 mg and 100 mg tablets. The recommended dosage of Lorbrena is 100 mg orally once daily, with or without food, until disease progression or unacceptable toxicity. Tablets should be swallowed whole and should not be chewed, crushed or split. For adverse reactions, the first dose reduction would be Lorbrena 75 mg orally once daily and the second dose reduction would be Lorbrena 50 mg orally once daily. Lorbrena should be permanently discontinued in patients who are unable to tolerate 50 mg orally once daily.

The efficacy of Lorbrena was evaluated in Study B7461001, a phase 2, non-randomized, dose-ranging and activity-estimating, multi-cohort, multicenter study in ALK-positive metastatic NSCLC patients. Forty-eight percent of patients experienced an overall response rate (4% complete and 44% partial). The median duration of response was 12.5 months. In patients with measurable intracranial lesions, the intracranial response rate was 60% (21% complete; 38% partial) with a median duration of response of 19.5 months.

Lorbrena is contraindicated in patients taking strong CYP3A inducers, due to potential for serious hepatotoxicity. Use of Lorbrena has been associated with an increased risk of serious hepatotoxicity when used with strong CYP3A4 inducers, central nervous system (CNS) effects, hyperlipidemia, atrioventricular block, interstitial lung disease/pneumonitis, and embryo-fetal toxicity. In clinical trials, the most commonly reported adverse events included edema, peripheral neuropathy, cognitive effects, dyspnea, fatigue, weight gain, arthralgia, mood effects, and diarrhea. The safety and effectiveness of Lorbrena in pediatric patients have not been established.

Per NCCN, Lorbrena is indicated as a single-agent therapy for ALK rearrangement-positive recurrent, advanced or metastatic disease following disease progression on first-line therapy with crizotinib and subsequent therapy with alectinib, brigatinib, or ceritinib and as subsequent therapy following disease progression on first-line therapy with alectinib, brigatinib, or ceritinib. Lorbrena is also indicated as a single therapy for recurrent, advanced or metastatic disease in patients with ROS1 rearrangement-positive tumors as subsequent therapy, following disease progression on crizotinib or ceritinib.

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 questions or comments. Tricia Heitzman made a motion to accept the criteria as written. Kevin Szczecina seconded the motion. None were opposed.

Financial Discussion: No questions or comments. Tricia Heitzman made a motion to accept the criteria as written. Kevin Szczecina seconded the motion. None were opposed.

Outcome: For GHP Family, Lorbrena will be a pharmacy benefit. It is recommended that Lorbrena be added to the Geisinger GHP Family formulary at the Brand tier. The following prior authorization criteria should apply.

- Prescription written by or in consultation with an oncologist or hematologist AND
- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation of anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) AND
- Medical record documentation of disease progression on one of the following:
    - Crizotinib (Xalkori) and at least one other ALK inhibitor for metastatic disease; OR
    - Alectinib (Alecensa) as the first ALK inhibitor therapy for metastatic disease; OR
    - Ceritinib (Zykadia) as the first ALK inhibitor therapy for metastatic disease

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 medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

Quantity Limit: Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).

25 mg tablet: 3 tablets per day

100 mg tablet: 1 tablet per day

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

ZEMDRI (plazomicin)

Review: Zemdri is an aminoglycoside anti-infective agent indicated for the treatment of patients 18 years of age and older with complicated urinary tract infections (cUTI), including pyelonephritis caused by the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, and Enterobacter cloacae. Due to limited clinical safety and efficacy data, Zemdri is recommended to be reserved for use in cUTI patients who have limited or no alternative treatment options. Zemdri is administered via the intravenous route at a dose of 15mg/kg over 30 minutes every 24 hours for a maximum of 7 days. Due to the nephrotoxic nature of Zemdri, renal dosage adjustments may be necessary.

In clinical trials, Zemdri was proven to be non-inferior to meropenem based on the 5-day composite cure rate and Test of Cure visit rate of a microbiological modified intent-to-treat population. The average Zemdri length of therapy was 6 days during clinical trials. The safety profile of Zemdri is significant for four black box warnings (nephrotoxicity, ototoxicity, neuromuscular blockage, and fetal harm), one contraindication (known hypersensitivity to aminoglycoside products), and three additional warnings and precautions (hypersensitivity reactions, including anaphylaxis, Clostridium difficile-associated diarrhea, and potential development of drug-resistant bacteria). The most common adverse effects not already mentioned included decreased renal function, diarrhea, hypertension, headache, nausea, vomiting, and hypotension.

Zemdri has not been studied in patients less than the age of 18 years. The geriatric population may be subject to a higher incidence of adverse effects, which may be due to the higher probability of having decreased renal function. Patients with renal impairment require close monitoring as well as dosage adjustments; however, there is insufficient evidence to make dosing recommendations for patients with a CrCl less than 15mL/min. Ricky

Rampulla, a Geisinger Infectious Disease pharmacist, does not anticipate high utilization of plazomicin as he expects it to be used for only "super resistant" multi-drug resistant organisms. He anticipates patients requiring plazomicin to be hospitalized due to the complicated nature of the patients who would qualify for this treatment.

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

Clinical Discussion: Bret Yarczower asked if the reason for drug failures (i.e., was it resistance, etc) was known? Response was that it was not specified in the trial. No other questions or comments. Kevin Szczecina made a motion to accept the recommendations as presented. Kelly Yelenic seconded the motion. None were opposed.

Financial Discussion: No questions or comments. Todd Sponenberg made a motion to accept the recommendations as presented. Kim Clark seconded the motion. None were opposed.

Outcome: For GHP Family, Zemdri will be a medical benefit requiring prior authorization.The following prior authorization criteria should apply.

- Age of 18 years or greater **AND**
- Medical record documentation of a diagnosis of complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis,* and *Enterobacter cloacae* **AND**
- Medical record documentation of culture and sensitivity showing the patient's infection is not susceptible to ALL alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to ALL other antibiotics shown to be susceptible on the culture and sensitivity **OR**
- If initiated during an inpatient say: Medical record documentation of a culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity

Authorization Duration: up to a maximum of 7 days

Other Recommendations: Vabomere (Meropenem/Vaborbactam Injection): To ensure consistency between anti-infective policies, it is recommended that the following criteria be added to the respective Vabomere policies for all lines of business:

- … **OR**
- If initiated during an inpatient say: Medical record documentation of a culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity

Other Recommendations: Sivextro (Tedizolid): To ensure consistency between anti-infective policies and lines of business, it is recommended that the following be added to (or replace the existing inpatient stay criteria) the respective Sivextro policies for all lines of business:

- … **OR**

- If initiated during an inpatient say: Medical record documentation of a culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity

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

LOKELMA (sodium zirconium cyclosilicate)

Review: Lokelma is a potassium binder indicated for the treatment of hyperkalemia in adults. Lokelma is not to be used in emergency treatment for life threatening hyperkalemia. Lokelma is dosed as 10 g three times a day for up to 48 hours as a starting dose, then as 5 g every other day to 15 g once daily for maintenance treatment. Lokelma can be stored at room temperature compared to Veltassa, which needs to be stored in the refrigerator. Other medications with pH dependent solubility must be administered at least 2 hours before or 2 hours after Lokelma administration. Lokelma has been shown to significantly decrease serum potassium in the first 48 hours and maintain normal levels during the extended phase. Lokelma does not have any black box warnings or contraindications. It has a warning for patients with motility disorders due to possible gastrointestinal adverse events. The adverse events of Lokelma include edema and hypokalemia. Lokelma is safe in pregnancy, lactation, and geriatrics, however safety in pediatrics has not been established. UpToDate recommends the use of dietary modification, diuretics (if otherwise appropriate), and reversal of factors that can cause hyperkalemia (e.g., NSAIDs, hypovolemia, RAAS inhibitors) before using a gastrointestinal cation exchanger, like Lokelma and Veltassa for patients without an urgent need to lower their potassium levels (most patients with serum potassium levels $\leq$ 6.5 mEq/L). Veltassa and Lokelma are recommended over SPS for chronic hyperkalemia due to multiple warnings and contraindications with SPS, particularly intestinal necrosis, which may be fatal.

A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented. For geriatric members, no overall difference in safety or effectiveness were observed between elderly and younger patients.

Clinical Discussion: No comments or questions. Tricia Heitzman made a motion to accept the recommendations as written. Keith Hunsicker seconded the motion. None were opposed

Financial Discussion: No comments or questions. Rajneel Chohan made a motion to accept the recommendations as written. Tricia Heitzman seconded the motion. None were opposed.

Outcome: Lokelma is a pharmacy benefit and should be added to the Brand tier of the GHP Family formulary at this time. The following prior authorization criteria should apply.

- Medical record documentation of a diagnosis of mild to moderate hyperkalemia (greater than or equal to 5.1 mEq/L and less than 6.5 mEq/L) **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that attempt has been made to identify and correct the underlying cause of the patient's hyperkalemia **OR** rationale as to why the underlying cause cannot be corrected **AND**
- <u>For mild hyperkalemia (serum potassium greater than or equal to 5.1 mEq/L and less than 5.5 mEq/L)</u>: Medical record documentation that a low potassium diet has been tried and was unsuccessful at controlling the patient's serum potassium level **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to loop diuretic or thiazide diuretic therapy

Quantity Limit:5 g packet: 1 packet daily; 10 g packet: 34 packets/30 days

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

LUMOXITI (moxetumomab pasudotox-tdfk)

Review: Lumoxiti is a CD22-directed cytotoxin indicated for the treatment of adult patients with relapsed or refractory hairy cell leukemia (HCL) who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA).

Hairy Cell Leukemia (HCL) is a rare form of chronic lymphocytic leukemia (CLL), a cancer that originates in the bone marrow. HCL affects about 1,000 people per year in the United States and comprises about 2% of all leukemias. Approximately 40% of patients relapse after responding to initial treatment with a purine nucleoside analog after being in remission for 10 to 15 years. Lumoxiti marks the first new treatment option for patients with hairy cell leukemia in over 20 years. Lumoxiti is a CD22-directed cytotoxin that works by delivering a bound toxic substance directly to the cancer cells, limiting its effects on healthy cells by virtue of its targeted delivery. This is the first drug of this type approved for the treatment of HCL. Lumoxiti is given via intravenous infusion on Days 1, 3, and 5 of each 28-day cycle, for a maximum of 6 cycles, or until disease progression or unacceptable toxicity.

Safety and Efficacy were established in a phase 3, single arm, open-label, multicenter trial of Lumoxiti in relapsed or refractory HCL. Patients had a diagnosis of HCL and had received prior treatment with at least two systemic therapies, including one purine nucleoside analog (PNA). Efficacy was shown with a Complete Response (CR) rate of 30% (24/80 patients; 95% CI: 20-41%). Complete Response was confirmed by maintenance of hematologic remission (hemoglobin $\geq$ 11 g/dL, neutrophils $\geq$ 1,500/mm3, and platelets $\geq$ 100,000/mm3 without transfusions or growth factor for at least 4 weeks) more than 180 days after internal review committee assessed CR. Lumoxiti has a black box warning for the risk of capillary leak syndrome (CLS) and hemolytic uremic syndrome (HUS), which can be life-threatening. There are additional warnings and precautions for renal toxicity, infusion related reactions, and electrolyte abnormalities. The most common adverse reactions occurring in $\geq$20% of patients are infusion related reactions, edema, nausea, fatigue, headache, pyrexia, constipation, anemia, and diarrhea. The most common laboratory abnormalities occurring in $\geq$ 50% of patients are hypoalbuminemia, hypocalcemia, hypophosphatemia, and increased creatinine, ALT and AST.

NCCN Guidelines consider purine nucleoside analogs (PNA) (e.g. cladribine, pentostatin) first-line therapy for initial treatment of previously untreated classic HCL. Patients with disease relapse after > 2 years after achieving CR to initial PNA may benefit from retreatment with the same PNA with or without rituximab. Other options include treatment with an alternative PNA with or without rituximab or rituximab monotherapy (if unable to receive PNA). Options for patients with disease relapse within 2 years after achieving CR to initial therapy, or who do not attain CR on first-line therapy, include enrollment in clinical trials, treatment with interferon alfa, alternate PNA + rituximab monotherapy (if unable to receive PNA), and vemurafenib. For further disease progression of relapsed or refractory HCL, second-line therapy options include enrollment in clinical trials, ibrutinib or vemurafenib + rituximab or Lumoxiti.

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

Clinical Discussion: Keith Hunsicker suggested amending the reauthorization requirement beyond six months to require literature support for dosing that exceeds product labeling. Keith Hunsicker made a motion to accept the recommendations as amended. Rajneel Chohan seconded the motion. None were opposed

Financial Discussion: No comments or questions. Kevin Szczecina made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed

Outcome: Lumoxiti will be a medical benefit requiring prior authorization as outlined below for Geisinger GHP Family members.

Hairy Cell Leukemia

- Prescription is written by a hematologist/oncologist **AND**
- Medical record documentation that member is 18 years of age or older **AND**
- Medical record documentation of a diagnosis of relapsed or refractory hairy cell leukemia (HCL) **AND**
- Medical record documentation that member has received at least two prior systemic therapies, one of which must be a purine nucleoside analog (e.g., cladribine, pentostatin (Nipent), etc.)

Authorization Duration: Initial approval will be limited to **6 cycles (6 months)** or less if the reviewing provider feels it is medically necessary. Subsequent approval for treatment past 6 cycles (6 months) will require documentation of well-controlled, peer-reviewed literature with evidence to support this request.

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

ONPATTRO (patisiran)

Review: Onpattro is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. Onpattro is the first approved agent for the treatment of hereditary transthyretin amyloidosis (hATTR), a rare, genetic, and progressive multi-organ disorder. Onpattro is also the first FDA approval of a new class of drugs called small interfering ribonucleic acid (siRNA) treatment, which work by silencing a portion of the RNA involved in causing the disease. Onpattro causes degradation of mutant and wild-type TTR mRNA through RNA interference, which results in a reduction in serum TTR protein and TTR protein deposits in tissues. Onpattro is available as a lipid complex solution for intravenous infusion and is supplied as a 10 mg/5 mL single-dose vial. Onpattro requires administration only by a healthcare professional. Dosing is based on actual body weight. For patients weighing less than 100 kg, the recommended dosage is 0.3 mg/kg once every 3 weeks. For patients weighing 100 kg or more, the recommended dosage is 30 mg once every 3 weeks. All patients should receive pre-medications (corticosteroid, acetaminophen, H1 blocker, H2 blocker) 60 minutes prior to Onpattro to reduce the risk of infusion-related reactions.

The safety and efficacy for Onpattro was demonstrated in a Phase 3 randomized, double-blind, placebo-controlled clinical trial in adult patients with polyneuropathy caused by hATTR. To be included in the clinical trial patients had to have a diagnosis of hATTR amyloidosis with polyneuropathy caused by an TTR mutation and neuropathy impairment score (NIS) of 5-130. About half of the patients were previously treated with tafamidis or diflunisal. Patients who were wheelchair-bound or bedridden were excluded from the trial. Patients with a history of liver transplant, those planning to undergo a liver transplant, or those with NYHA class III or IV heart failure were excluded. Patients were randomized in a 2:1 ratio to receive Onpattro 0.3 mg/kg (N=148) or placebo (N=77) intravenously once every 3 weeks for 18 months. The change from baseline to month 18 on both endpoints met statistical significance in favor of Onpattro, as well as did other secondary endpoints. Patients who received Onpattro had similar improvements relative to placebo in mNIS+7 and Norfolk QoL-DN across all subgroups of patients (age, sex, race, region, mutation type, NIS score, prior tafamidis or diflunisal use, and disease stage). The effects were seen as early as 9 months. The mNIS +7 is an objective assessment of neuropathy that measures

deficits in cranial nerve function, muscle strength, and reflexes, as well as postural blood pressure, quantitative sensory testing, and peripheral nerve electrophysiology (higher scores indicate a greater severity of disease). The QoL-DN score is a patient-reported assessment that evaluates the experience of neuropathy in functioning, large-fiber/small-fiber neuropathy, activities of daily living, and autonomic neuropathy (higher scores indicate a greater impairment). There were changes in BMI and gait speed that significantly favored Onpattro. Patients receiving Onpattro experienced a statistically significant reduction in autonomic symptoms such as dizziness, constipation, diarrhea, vomiting, and incontinence. Those receiving Onpattro saw a significant benefit in the ability to perform activities of daily living and everyday function (eating, bathing, dressing, motor strength, standing, mobility, self-care, usual activities, and pain/discomfort and anxiety/depression. The polyneuropathy disability score was stable in 65% of patients and improved in 8% of patients receiving Onpattro. This included transition from assisted to unassisted walking. Among patients whose polyneuropathy disability score worsened at 18 months, worsening by more than 1 level was observed in 17% of patients in the patisiran group as compared to 50% in the placebo group. Patisiran was also associated with better cardiac structure and function compared to placebo.

There are no black box warnings or contraindications to Onpattro. There are warnings for infusion-related reactions and reduced serum vitamin A levels. Supplementation of recommended daily allowances of vitamin A is advised for patients taking Onpattro. Upper respiratory tract infections and infusion-related reactions were the most common adverse reactions. Four serious adverse reactions of atrioventricular (AV) heart block (2.7%) occurred in Onpattro-treated patients, including 3 cases of complete AV block. No serious adverse reactions of AV block were reported in placebo-treated patients. Safety and effectiveness in pediatric patients have not been established.

Nathan Sauers, clinical pharmacist at Geisinger, had some discussions with cardiologists regarding the use of Onpattro in patients with wild type ATTR cardiac amyloid. At this time, they believe that the approval for wild type ATTR cardiac amyloid is years away. Until further studies are completed, they believe the FDA approved indication is the most appropriate use for Onpattro at this time. Dan Grassi, neurology clinical pharmacist at Geisinger, had discussions regarding Onpattro with Dr, Friedenberg and Dr. Avila. They agree that treatment of Onpattro should be avoided in patients that are wheelchair bound or bedridden, based on the inclusion criteria in the APOLLO study. Patients with TTR genotype with hATTR amyloidosis neuropathy (confirmed via genetic testing) with FAP stage 1-2 and PND scores I-IIIb should meet criteria for treatment. For these patients, initial treatment would be Onpattro, not diflunisal.

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

Clinical Discussion: No comments or questions. Tricia Heitzman made a motion to accept the recommendations as written. Kevin Szczecina seconded the motion. None were opposed

Financial Discussion: Bret Yarczower asked if it was known if Geisinger Medical Center was able to obtain the medication. It was not known at this time. No other comments or questions. Tricia Heitzman make a motion to accept the recommendations as written. Kevin Szczecina seconded the motion. None were opposed

Outcome: Onpattro will be covered as a medical benefit for Geisinger GHP Family members. The following prior authorization criteria should apply.

- Prescription written by or in consultation with a neurologist, specialist at a hereditary transthyretin-mediated amyloidosis treatment center, or geneticist AND
- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation of diagnosis of hereditary transthyretin-mediated amyloidosis as confirmed by <u>all</u> of the following:
    - Biopsy of tissue/organ to confirm amyloid presence AND
    - Immunohistochemistry or mass spectroscopy to differentiate ATTR amyloidosis from amyloid light-chain amyloidosis AND

- Genetic testing to differentiate between hereditary and wild-type ATTR amyloidosis AND
- Medical record documentation of Onpattro being used to treat polyneuropathy AND
- Medical record documentation of familial amyloid polyneuropathy (FAP) stage 1-2 and/or polyneuropathy disability score of I, II, IIIA, or IIIB AND
- Medical record documentation that Onpattro will not be used in combination with other RNA interference treatment

Note:
FAP stage:
1-unimpairmend ambulation
2- assistance with ambulation
3- wheelchair-bound or bedridden
Polyneuropathy disability score:
I- preserved walking, sensory disturbances
II- impaired walking without need for stick/crutches
IIIa- walking with 1 stick/crutch
IIIb- walking with 2 sticks/crutches
IV-wheelchair-bound or bedridden

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. The medication will no longer be covered if the member progresses to FAP stage 3 and/or polyneuropathy disability score IV (wheelchair-bound or bedridden).

Quantity Limit: 15 mL per 21 days

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

PLENVU (polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride and potassium chloride for oral solution)

Review: Plenvu (polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride and potassium chloride for oral solution) is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults.

Plenvu (polyethylene glycol 3350, sodium ascorbate, sodium sulfate, ascorbic acid, sodium chloride and potassium chloride for oral solution) is supplied as a white to yellow powder for reconstitution.

Two doses of Plenvu are required for a complete preparation for colonoscopy, using a "Two-Day" or "One-Day" dosing regimen. Plenvu must be reconstituted in water prior to ingestion. Additional clear liquids must be consumed after each dose of Plenvu in both dosing regimens. Patients should be instructed to not take oral medications within 1 hour of starting each dose. The Two-Day Split-Dosing Regimen commences in the evening of the day before the colonoscopy. Instruct adult patients that on the day before the clinical procedure, they can consume a light breakfast followed by a light lunch, which must be completed at least 3 hours prior to the start of the first Plenvu dose. Instruct patients to take two separate doses in conjunction with clear liquids. The One-Day Morning Dosing Regimen commences in the morning of the day of the colonoscopy. Instruct adult patients that on the day before the clinical procedure, they can consume a light breakfast followed by a light lunch, and clear broth soup and/or plain yogurt for dinner, which should be completed by approximately 8 pm. Instruct patients to take two separate doses in conjunction with clear liquids.

Approval was based on multiple Phase III clinical trials, including the NOCT study, a multicenter, randomized, parallel-group trial that enrolled 540 patients across two arms. The study compared Plenvu with a trisulfate bowel cleansing solution (sodium sulfate, potassium sulfate, and magnesium sulfate for oral solution [Suprep]) using a 2-day split-dosing regimen in adults. Participants met both primary endpoints, achieving noninferior overall bowel cleansing success and "excellent plus good" cleansing of the ascending colon according to the Harefield Cleansing Scale. The Phase III program also included two clinical trials in Europe.

The MORA study compared Plenvu to a standard 2-liter PEG with ascorbate (sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate, and ascorbic acid for oral solution [Moviprep]) using a 2-day evening/morning split-dosing regimen and a 1-day, morning-only split-dosing regimen in adults. The study met both of its primary endpoints: when administered using either dosing regimen, Plenvu was as effective as Moviprep in achieving overall bowel cleansing success and superior to Moviprep in achieving "high-quality" cleansing of the ascending colon.

In the other European study, DAYB, Plenvu achieved statistically significant improvements in adequate cleansing rates using a day-before-only dosing regimen in adults when compared with a sodium picosulfate and magnesium salt solution.

The most common adverse reactions (>2% of participants) are nausea, vomiting, dehydration, and abdominal pain/discomfort. Patients should stop drinking Plenvu temporarily or drink each portion at longer intervals if they develop severe abdominal discomfort or distention

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

Clinical Discussion: Keith Hunsicker made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed

Financial Discussion: No comments or questions. Tricia Heitzman made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed

Outcome: Plenvu will be non-formulary for Geisinger GHP Family members.

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

MULPLETA (lusutrombopag)

Review: Mulpleta (lusutrombopag) joins Doptelet (avatrombopag) as the second FDA-approval oral thrombopoietin receptor agonist (TPO-RA) approved specifically for use in chronic liver disease (CLD) adult patients with thrombocytopenia anticipating an invasive procedure. Promacta (eltrombopag) is another oral TPO-RA used for the treatment of thrombocytopenia; however, it is indicated to allow initiation and maintenance of interferon treatment in hepatitis C patients with low platelets. It is anticipated that Mulpleta will share the same place in therapy as Doptelet. Mulpleta provides an additional treatment option for adult CLD patients with thrombocytopenia and it may offer several advantages over Doptelet: Doptelet's dosing is based on a patient's platelet count whereas Mulpleta has a fixed dose for all patients. Additionally, Mulpleta's one-tablet-per-day dosing may be a more desirable option for patients with a high pill burden, as patients on Doptelet may be required to take up to 3 tablets per day. However, Mulpleta is taken for a longer duration (7 days) compared to Doptelet (5 days).

The efficacy of Mulpleta was evaluated in L-PLUS 1 and L-PLUS 2; two randomized, multicenter, double-blind, placebo-controlled clinical trials. To be included in the trials, patients had to have CLD with thrombocytopenia defined as $<50 \times 10^9$ platelets/L with a scheduled procedure. Patients were randomized 1:1 to

receive 3 mg of Mulpleta or placebo once daily for up to 7 days. Randomization was stratified by procedure: liver ablation/coagulation or other procedure, with the majority (57% in L-PLUS 1 and 98% in L-PLUS 2) undergoing a procedure other than liver ablation/coagulation. Patients were excluded if their procedure included laparotomy, thoracotomy, open-heart surgery, craniotomy, or organ resection. Patients were also excluded if they had a history of splenectomy, partial splenic embolization, thrombosis, Child-Pugh class C liver disease, absence of hepatopetal blood flow, or a prothrombotic condition other than CLD. The primary endpoint was met in both L-PLUS 1 and 2, and more patients in the Mulpleta group showed response in platelet increase compared to their corresponding placebo group. There are no black box warnings or contraindications associated with the use of Mulpleta. Safety and effectiveness in pediatric patients have not been established. Clinical studies of Mulpleta did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. A population pharmacokinetic analysis did not find a clinically meaningful effect of mild) and moderate renal impairment on the pharmacokinetics of Mulpleta. No clinically significant differences in the pharmacokinetics of lusutrombopag were observed based on mild to moderate hepatic impairment. The mean observed Mulpleta Cmax and AUC0-τ decreased by 20% to 30% in patients with severe hepatic impairment compared to patients with Child-Pugh class A and class B liver disease. However, the ranges for Cmax and AUC0-τ overlapped among patients with mild, moderate, and severe liver disease. There are no dosage adjustments due to renal or hepatic insufficiency provided in the manufacturer's labeling.

Sandra Gaines, PharmD, Clinical Pharmacist at Geisinger Medical Center was consulted, and she stated there is very little utilization of Mulpleta or Doptelet and she does not prefer one agent over the other.

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

Clinical Discussion: Todd Sponenberg made a motion to accept the recommendations as written. Tricia Heitzman seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Tricia Heitzman made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

Outcome: Mulpleta is a pharmacy benefit and should be added to the Geisinger GHP Family Formulary on the Brand tier requiring prior authorization. The following prior authorization criteria should apply:

- Medical record documentation of thrombocytopenia in adult patients with chronic liver disease **AND**
- Medical record documentation of member's age being $\geq$ 18 years old **AND**
- Medical record documentation of a platelet count of $< 50 \times 10^9$/L measured within the past 30 days **AND**
- Medical record documentation of a planned invasive procedure to be performed 8-14 days after initiation date for Mulpleta treatment **AND**
- Medical record documentation that the prescription for Mulpleta is written by or in consultation with a hematologist, gastroenterologist, hepatologist, immunologist, transplant specialist, or endocrinologist **AND**
- Medical record documentation that the member is not receiving other TPO-RAs (Nplate/romiplostim, Promacta/eltrombopag) **AND**
- Medical record documentation of the correct dose being used (3 mg orally once daily for 7 days)

Authorization Duration: 30 days

Quantity Limit: 7 tablets per fill, one fill per Rx.

Additional formulary recommendation:

Add the following criterion to the Doptelet policy for all lines of business:

- Medical record documentation of therapeutic failure on, intolerance to or contraindication to Mulpleta

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

ILUMYA (tildrakizumab-asmn)

Review: Ilumya is an IgG1/k monoclonal antibody indicated for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy, which joins 12 other biologic agents used to treat the same indication. Ilumya must be provider administered and is dosed as a subcutaneous injection at weeks 0, 4, and every 12 weeks thereafter. While the frequency of dosing makes Ilumya preferable among some of the alternatives, the requirement of provider administration may be a drawback for patients who prefer self-administration.

In clinical trials, Ilumya consistently outperformed placebo and etanercept in the achievement of PASI (Psoriasis Area and Severity Index) 75 improvement, PASI 90 improvement, PASI 100 improvement, clear or minimal PGA (Physician's Global Assessment), and DLQI (Dermatology Life Quality Index) score at week 12. These results were maintained out to week 28 and were also maintained when switching from placebo to tildrakizumab. Switching from etanercept to tildrakizumab was not tested. At week 28, patients responding to tildrakizumab were re-randomized to an additional 36 weeks of either Ilumya or placebo. 84% of patients who continued to receive Ilumya maintained PASI 75 compared to 22% of patients who received placebo at week 64. 69% of patients who continued to receive Ilumya compared to 14% of patients who received placebo maintained a PGA of 0 or 1 from week 28 to 64. The median time to loss of PASI 75 in patients who transitioned from tildrakizumab to placebo was about 20 weeks. The median time to loss of PGA of 0 or 1 in these patients was about 16 weeks.

The safety profile of Ilumya is relatively benign. Ilumya's warnings and precautions are significant for hypersensitivity reactions, infections, and tuberculosis. The most common adverse reactions included upper respiratory infections, injection site reactions, and diarrhea.

Guidelines generally reserve biologic treatments for patients with extensive disease or if patients do not have extensive disease but have other risk factors such as poor quality of life or ineffectiveness of other therapies. The American Academy of Dermatology guidelines only discuss the role of IL-12/23 blockade in the pathophysiology of psoriasis. The guidelines have not been updated since the introduction of these agents to make recommendations on non-TNF biologics. The Geisinger Psoriasis ProvenCare Pathway generally reserves biologic treatment for patients with extensive disease after failure of light therapy and oral therapies and for patients with less extensive disease after failure of topical, light, and oral therapies. The pathway prefers Humira as a first-line biologic and Cosentyx as a second-line biologic due to the lack of clear evidence that one therapy is more clinically significant than another.

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

Clinical Discussion: No comments or questions. Kim Clark made a motion to accept the recommendations as written. Kelly Yelenic seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Kevin Szczecina made a motion to accept the recommendations as written. Todd Sponenberg Heitzman seconded the motion. None were opposed.

Outcome: For GHP Family, Ilumya will be a medical benefit and should not be added to the Geisinger GHP Family pharmacy formulary. A prior authorization with the following criteria should apply.

1. Prescribed by a dermatologist **AND**
2. Medical record documentation that the patient is 18 years of age or older **AND**
3. Medical record documentation of a diagnosis of moderate to severe plaque psoriasis characterized by greater than or equal to 5% body surface area involved or disease affecting crucial body areas such as the hands, feet, face, or genitals **AND**
4. Medical record documentation that Ilumya is not being used concurrently with a TNF blocker or other biologic agent **AND**
5. Medical record documentation of an inadequate response to, contraindication to, or failure on at least 3 months of Humira **AND** Cosentyx

Authorization Duration: Approval will be given for an initial duration of six (6) months. For continuation of coverage, medical record documentation of clinical improvement or lack of progression in the signs and symptoms of the treated indication at six (6) months of Ilumya therapy is required.

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 of continued or sustained improvement in the signs and symptoms of the treated indication while on Ilumya therapy.

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

GALAFOLD (migalastat)

Review: Galafold is an alpha-galactosidase A (alpha-Gal A) pharmacological chaperone indicated for the treatment of adults with a confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data. Galafold is the first oral medication for the treatment of Fabry disease. As an alpha-Gal A pharmacological chaperone, Galafold reversibly binds to the active site of the alpha-Gal A protein. This selective binding stabilizes and coaxes alpha-Gal A into its proper conformation, enabling augmented enzymatic function of residual alpha-Gal A and, thereby, clearance of glycosphingolipids including GL-3. The management of Fabry disease currently centers around enzyme replacement therapy (ERT) with Fabrazyme (agalsidase beta), a recombinant form of the alpha-Gal A enzyme. Fabrazyme can be used in all variants of Fabry disease for the treatment of both children (8 years and older) and adults. In contrast, Galafold is only indicated in a subset of adult patients with amenable GLA mutations (with FDA approval for 348 amenable variants) as Galafold works by stabilizing and enhancing the activity of residual alpha-Gal A. Galafold offers the advantage of being an oral medication with no significant safety concerns, whereas Fabrazyme requires administration via intravenous infusion by a healthcare professional and is associated with a risk of anaphylactic and infusion reactions.

Galafold is available as 123 mg capsules in a blister pack containing 14 capsules for a 28-day supply. The recommended dosage of Galafold is 123 mg orally once every other day (Galafold should not be taken on two consecutive days). Doses should be taken on an empty stomach.

The efficacy and safety of Galafold was evaluated in a 6-month, randomized, double-blind, placebo-controlled trial followed by a 6-month, open-label treatment phase and a 12-month, open-label extension phase. In the initial 6-month phase, a total of 67 participants were randomized in a 1:1 ratio to receive either placebo or Galafold at the recommended dosing regimen. In the 6-month, open-label phase, all patients were treated with Galafold. Of the 67 enrolled patients, 50 had amenable GLA variants based on the in vitro amenability assay. The primary efficacy endpoint of the average number of GL-3 inclusions per kidney interstitial capillary (KIC) in renal biopsy samples was assessed by light microscopy before and after treatment. Efficacy was evaluated after 6 months

of treatment. A greater proportion of patients receiving Galafold experienced ≥ 50% reduction from baseline in the average number of GL-3 inclusions per KIC. Patients with non-amenable GLA variants had no change from baseline in the average number of GL-3 inclusions per KIC at 6 months.

There are no black box warnings, contraindications, or warnings and precautions associated with the use of Galafold. The safety and effectiveness of Galafold have not been established in pediatric patients.

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

Clinical Discussion: No comments or questions. Kevin Szczecina made a motion to accept the recommendations as written. Kelly Yelenic seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Todd Sponenberg made a motion to accept the recommendations as written. Keith Hunsicker seconded the motion. None were opposed.

Outcome: Galafold will be a pharmacy benefit and should not be added to the Geisinger GHP Family pharmacy formulary. The following prior authorization criteria will apply:

- Patient is 18 years of age or older **AND**
- Prescription written by or in consultation with a geneticist, nephrologist, cardiologist, or a physician who specializes in the treatment of Fabry disease **AND**
- Medical record documentation of a diagnosis of Fabry disease as confirmed by one of the following:
    - Enzyme assay indicating deficiency of Alpha Gal-A (if male) OR
    - Genetic test documenting galactosidase alpha gene mutation

  AND
- Medical record documentation of in vitro assay data confirming the presence of an amenable galactosidase alpha gene (GLA) variant, in accordance with the FDA-approved prescribing information **AND**
- Medical record documentation that Galafold will not be used concurrently with enzyme replacement therapy intended for the treatment of Fabry disease, such as agalsidase beta (Fabrazyme).

Quantity Limit: 14 capsules per 28 days

Authorization Duration:

Initial approval will be for a duration of **six (6) months.** For continuation of coverage, medical record documentation of clinical improvement or lack of progression in signs and symptoms of Fabry disease on six (6) months of migalastat is required. 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 of clinical improvement or lack of progression in signs and symptoms of Fabry disease while on migalastat therapy.

Note: Examples of disease improvement may include:

- Decreased symptoms of Fabry disease (e.g., pain, hypohidrosis/anhidrosis, exercise intolerance, GI symptoms, angiokeratomas, abnormal cornea, tinnitus/hearing loss)
- Imaging (brain/cardiac MRI, DEXA, renal ultrasound)
- Laboratory testing (e.g., GL-3 in plasma/urine) or histological tests (e.g., renal biopsy)

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

TAKHZYRO (lanadelumab-flyo)

Review: Takhzyro (lanadelumab-flyo) joins Cinryze and Haegarda as the third agent to be approved for prophylaxis against attacks caused by HAE. It offers several advantages over Cinryze and Haegarda: it is longer-acting, allowing for a dosing frequency of every 2 weeks. Additionally, Takhzyro provides a different mechanism for preventing bradykinin production: inhibition of plasma kallikrein. Bradykinin is a potent vasodilator that increases vascular permeability resulting in swelling and pain associated with HAE.

Takhzyro is administered as a 300mg subcutaneous injection, given once every 2 weeks. Its efficacy was demonstrated in a randomized, placebo-controlled clinical trial in patients 12 years and older with HAE. Patients in the study were allowed to continue use of rescue medication and were randomized to placebo, Takhzyro 150mg every 4 weeks, Takhzyro 300mg every 4 weeks, or Takhzyro 300mg every 2 weeks. All treatment arms produced clinical and statistically significant reductions in HAE attack rate versus placebo. The mean reduction in attack rates was consistently greater for patients treated with Takhzryo regardless of baseline history of prior long-term prophylaxis, laryngeal attacks, or attack rate during run in period.

There are no black box warnings or contraindications to Takhzyro. The most common adverse reactions seen in studies were injection site reaction, upper respiratory infection, headache, rash, myalgia, dizziness, and diarrhea.

Plasma derived C1-INH is currently the preferred long-term prophylaxis for prevention of HAE attacks, per the 2017 guidelines. Lanadelumab, the first kallikrein inhibitor, is not included in these guidelines. Up To Date also does not provide any specific recommendations regarding lanadelumab's place in therapy.

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

Clinical Discussion: Tricia Heitzman made a motion to accept the recommendations as written. Kevin Szczecina seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Kevin Szczecina made a motion to accept the recommendations as written. Keith Hunsicker seconded the motion. None were opposed.

Outcome: Takhzyro is a pharmacy benefit and should be added to the Geisinger GHP Family formulary at the Brand Tier. The following prior authorization criteria should apply:

- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation that Takhzyro is prescribed by an allergist, immunologist, hematologist, or dermatologist **AND**
- Medical record documentation of a diagnosis of hereditary angioedema (HAE) established and supported by documentation of:
    - Recurrent, self-limiting, non-inflammatory subcutaneous angioedema without urticaria which lasts more than 12 hours **OR**
    - Laryngeal edema **OR**
    - Recurrent, self-remitting abdominal pain which lasts more than 6 hours, without clear organic etiology **AND**
- Medical record documentation of specific abnormalities in complement proteins, in the setting of a suggestive clinical history or episodic angioedema without urticaria; supported by:
    - Medical record documentation of two (2) or more sets of complement studies, separated by one month or more, showing consistent results of:

    - Low C4 levels **AND**
    - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
    - Less than 50% of the lower limit of normal C1-INH functions levels **AND**
- Medical record documentation of history of more than one (1) severe event per month **OR** a history of laryngeal attacks **AND**
- Medical record documentation that Takhzyro is being used as prophylactic therapy for hereditary angioedema (HAE) attacks **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to danazol

Reauthorization info: 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 12 months or less if the reviewing provider feels it is medically appropriate and will required medical record documentation of continued disease improvement or lack of disease progression. Takhzyro will no longer be covered if the member experiences unacceptable toxicity or worsening of disease

Authorization Duration: Initial approval: 6 months, Reauthorization: 12 months

Quantity Limit: 4ml per 28 days

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

TALZENNA (talazoparib)

Review: Talzenna is indicated for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer. Select patients for therapy based on an FDA-approved companion diagnostic for Talzenna. Talzenna (talazoparib) joins Lynparza (olaparib) as the second FDA-approved poly (ADP-ribose) polymerase (PARP) inhibitor to treat breast cancer. Lynparza is indicated in patients with deleterious or suspected deleterious gBRCAm HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Per NCCN, both agents are recommended as single agents (preferred regimen) for recurrent or stage (IV) (M1) HER2-negative, BRCA 1/2- germline mutated disease with symptomatic visceral disease or visceral crisis and that is hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory.

Talzenna is available as 0.25 mg and 1 mg oral capsules. The recommended dosage is 1 mg taken as a single oral dose daily, with or without food. For patients with moderate renal impairment (CLcr 30-59 mL/min) the recommended dose is 0.75 mg daily.

Talzenna was approved based upon data from the EMBRACA study, an open-label clinical trial in 431 patients with gBRCAm HER2-negative locally advanced or metastatic breast cancer. Patients received Talzenna 1 mg or healthcare provider's choice of chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine) until disease progression or unacceptable toxicity. Talzenna demonstrated a statistically significant improvement in median PFS, with a median PFS of 8.6 months in the Talzenna arm compared to 5.6 months in the chemotherapy arm. Consistent PFS results were observed across patient subgroups defined by study stratification factors (line of therapy, triple-negative breast cancer status, and history of CNS metastases).

There are no contraindications or black box warnings associated with the use of Talzenna. Like Lynparza, Talzenna has warnings and precautions for myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) and embryo-fetal toxicity; Talzenna has an additional warning for myelosuppression. Unlike Lynparza, the labeling for Talzenna does not contain a warning for pneumonitis. The most common adverse reactions reported in clinical studies (incidence ≥20%) were fatigue, anemia, nausea, neutropenia, headache, thrombocytopenia, vomiting, alopecia, diarrhea, decreased appetite. The most common laboratory abnormalities (incidence ≥25%) were: Decreases in hemoglobin, platelets, neutrophils, lymphocytes, leukocytes, and calcium. Increases in glucose, alanine

aminotransferase, aspartate aminotransferase, and alkaline phosphatase. The safety and effectiveness of Talzenna have not been established in pediatric patients.

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

Clinical Discussion: No comments or questions. Todd Sponenberg made a motion to accept the recommendations as written. Kelly Yelenic seconded the motion. None were opposed.

Financial Discussion: No comments or questions. Kevin Szczecina made a motion to accept the recommendations as written. Kim Clark seconded the motion. None were opposed.

Outcome: Talzenna will be a pharmacy benefit. It is recommended that Talzenna be added to the Geisinger GHP Family formulary at the Brand tier. The following prior authorization criteria should apply.

- Prescription written by or in consultation with an oncologist or hematologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative locally advanced or metastatic breast cancer as verified by an FDA-approved test

Note: Information on the FDA-approved test for the detection of BRCA mutations is available at http://www.fda.gov/companiondiagnostics

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 medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

Quantity Limit: Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).

0.25 mg capsule: 3 capsules per day

1 mg capsule: 1 capsule per day

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

QBREXZA (glycopyrronium)

Review: Qbrexza is an anticholinergic agent that is only approved to be used in adults and pediatric patients 9 years and older with primary axillary hyperhidrosis. It comes as a pre-moistened, single use cloth that should be used on both axillae once daily. It is contraindicated in patients with medical conditions that may be exacerbated by the anticholinergic effect of Qbrexza. The most common side effects seen with Qbrexza include urinary hesitation, dry mouth, mydriasis, oropharyngeal pain, headache, blurred vision, nasal dryness, dry throat/eye/skin, and constipation. Local reactions such as erythema, burning/stinging, and pruritus were also common. Qbrexza, aluminum chloride hexahydrate, and onabotulinumtoxin A are the only three medications that are FDA-approved for treating primary axillary hyperhidrosis. Guidelines suggest that Qbrexza and topical antiperspirants, including aluminum chloride (OTC) and aluminum chloride hexahydrate (prescription-only) are appropriate first line options. Qbrexza can also be

used as a 2nd, 3rd, or 4th line agent after any combination of topical antiperspirants, microwave thermolysis, and/or onabotulinumtoxin.

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

Clinical Discussion: No comments or questions. Tricia Heitzman made a motion to accept the recommendations as written. Kevin Szczecina seconded the motion. None were opposed.

Financial Discussion: There was discussion about certain OTC products not containing high enough concentrations of aluminum chloride to be acceptable as a required prerequisite medication. Rajneel Chohan made a motion to accept the recommendations as amended. Kevin Szczecina seconded the motion. None were opposed.

Outcome: Qbrexza is a pharmacy benefit and should be added to the formulary on the Brand Tier requiring prior authorization. The following criteria should apply:

- Medical record documentation that the patient is 9 years of age and older **AND**
- Medical record documentation of the diagnosis of primary axillary hyperhidrosis **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to at least one prescription antiperspirant (aluminum chloride hexahydrate 6.25% [Xerac AC], 20% [Drysol])

Quantity Limit (all LOB): 1 per day

Additional formulary/criteria changes

- GHP Family
    - It is recommended that Xerac (aluminum chloride hexahydrate 6.25%) is added to the GHP Family formulary on the brand tier without a prior authorization.

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

FAST FACTS

KEYTRUDA (pembrolizumab)

Updated Indication: Keytruda is now indicated for the treatment of patients with non-small cell lung cancer (NSCLC) in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of patients with metastatic squamous NSCLC.

Keytruda is also now indicated under the accelerated approval process for the treatment of patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib.

Keytruda is also now indicated under the accelerated approval process for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).

In addition to the indications mentioned above, Keytruda maintains its previously approved indications of non-small cell lung cancer, melanoma, head and neck squamous cell cancer, classical Hodgkin lymphoma, primary

mediastinal large B-cell lymphoma, urothelial carcinoma, microsatellite instability-high cancer, gastric cancer, and cervical cancer.

Recommendations: No changes are recommended to the formulary status of Keytruda at this time. It is recommended that the current policies are updated to account for the new indications as outlined below.

Metastatic Non-Small Cell Lung Cancer (NSCLC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of a diagnosis of metastatic NSCLC meeting one of the following situations:
  - Medical record documentation that Keytruda is being given as monotherapy **AND**
  - Medical record documentation that tumors have high PD-L1 expression (Tumor Proportion Score (TPS)≥50% as determined by an FDA-approved test **AND**
  - Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

  OR
  - Medical record documentation that Keytruda is being given as monotherapy **AND**
  - Medical record documentation that tumors express PD-L1 (TPS)≥1% as determined by an FDA-approved test **AND**
  - Medical record documentation of disease progression on or after platinum-containing chemotherapy **AND**
  - For patients with EGFR or ALK genomic tumor aberrations: medical record documentation of disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.

  OR
  - Medical record documentation of metastatic nonsquamous NSCLC **AND**
  - Medical record documentation that Keytruda will be given in combination with pemetrexed AND either carboplatin or cisplatin **AND**
  - Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

  OR
  - Medical record documentation that Keytruda will be given in combination with carboplatin AND either paclitaxel or nab-paclitaxel **AND**
  - Medical record documentation that Keytruda, carboplatin, and paclitaxel (or nab-paclitaxel) are being used as first-line treatment.

Hepatocellular Carcinoma (HCC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of a diagnosis of hepatocellular carcinoma **AND**
- Medical record documentation of a therapeutic failure on or intolerance to sorafenib (Nexavar)

Merkel Cell Carcinoma (MCC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of Merkel Cell Carcinoma **AND**
- Medical record documentation of metastatic and/or recurrent disease

Discussion: No comments or questions

Outcome: Kevin Szczecina made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

KALYDECO (ivacaftor)

Updated Indication:
Kalydeco is now indicated for the treatment of CF in patients age 12 months and older who have one mutation in the *CFTR* gene that is responsive to ivacaftor based on clinical and/or in vitro assay data.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

Note: Previously, Kalydeco was indicated in patients 2 years and older.

Summary of Updated Clinical Studies[1]: The efficacy of Kalydeco in patients 12 months to less than 24 months was extrapolated from patients 6 years of age and older with support from population pharmacokinetic analyses showing similar drug exposure levels in adults and children 12 months to less than 24 months of age. The safety in this patient population was derived from a cohort of 19 patients aged 12 months to less than 24 months in a 24-week open label clinical study, administered either 50 mg or 75 mg of ivacaftor granules twice daily. The safety profile in this trial was similar to patients 2 years of age and older.

Recommendation:
There are no recommended changes to formulary status at this time. However, it is recommended to update the age restriction to the following.

"Medical record documentation of member age **≥ 12 months**
Discussion: No comments or questions.

Outcome: Kevin Szczecina made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

TECENTRIQ (atezolizumab)

Updated Indication: In combination with bevacizumab, paclitaxel, and carboplatin, Tecentriq is now indicated for the first-line treatment of patients with metastatic non-squamous non-small cell lung cancer (NSq NSCLC) with no EGFR or ALK genomic tumor aberrations**.**

Previously, Tecentriq was only indicated for NSCLC (after progression on platinum chemotherapy) and urothelial carcinoma.

Recommendation: No changes are recommended to the formulary placement of Tecentriq at this time. It is recommended that applicable policies are updated to account for the updated indication as outlined below for all lines of business.

Non-Small Cell Lung Cancer:

- Prescription written by an oncologist **AND**
- Medical record documentation of a diagnosis of metastatic non-small cell lung cancer meeting one of the following situations:
    - Medical record documentation of disease progression during or following platinum-containing chemotherapy

    OR
    - Medical record documentation of disease progression on at least one FDA-approved therapy targeting EGFR or ALK if the patient has EGFR or ALK genomic tumor aberrations (e.g. mutation, deletion, insertion, etc.)

    OR
    - Medical record documentation of a non-squamous histologic subtype **AND**
    - Medical record documentation that Tecentriq will be given as first-line treatment **AND**
    - Medical record documentation that Tecentriq will be given in combination with bevacizumab, paclitaxel, AND carboplatin **AND**
    - Medical record documentation that the patient does not have an EGFR or ALK genomic tumor aberration.

Discussion: No comments or questions.

Outcome: Kevin Szczecina a motion to accept the recommendations as written. Kelly Yelenic seconded the motion. None were opposed.

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

PREPOPIK (sodium picosulfate/magnesium oxide/anhydrous citric acid)

Updated Indication: Prepopik is a combination of sodium picosulfate, a stimulant laxative, and magnesium oxide and anhydrous citric acid which form magnesium citrate, an osmotic laxative, indicated for cleansing of the colon as a preparation for colonoscopy in adults and pediatric patients ages 9 years and older.

Previously, Prepopik was approved for this indication in adults only.

Recommendation: No formulary changes are recommended at this time.

Discussion: No comments or questions

Outcome: Todd Sponenberg made a motion to accept the recommendations as amended. Tricia Heitzman seconded the motion. None were opposed.

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

GRANIX (tbo-filgrastim)

Updated Indication: Granix is now indicated to reduce the duration of severe neutropenia in adult and pediatric patients 1 month of age and older with nonmyeloid malignancies receiving myelosuppressive anticancer drugs associated with a clinically significant incidence of febrile neutropenia.

Previously, Granix only maintained this indication for the adult population.

Recommendation: No changes are recommended to the formulary placement of Granix at this time for all lines of business. No changes are recommended to the prior authorization criteria in the existing policies at this time as age is not addressed in the existing policies.

It is recommended that the A(N)CVB chemotherapy regimen be removed from the list of high risk regimens for febrile neutropenia as vindesine is not available within the United States.

Discussion: No comments or questions.

Outcome: Rajneel Chohan made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

ZOMACTON (somatropin)

Updated Indication: Zomacton is now indicated for the treatment of pediatric patients with

- short stature associated with Turner syndrome,
- idiopathic short stature (ISS), height standard deviation score (HSDS) ≤-2.25 and associated with growth rates unlikely to permit attainment of adult height in the normal range,
- short stature or growth failure in short stature homeobox-containing gene (SHOX) deficiency,
- short stature born small for gestational age (SGA) with no catch-up growth by 2 years to 4 years of age.

Zomacton was previously indicated only for the treatment of pediatric and patients who have growth failure due to inadequate secretion of endogenous growth hormone.

FDA Approved Indications

	Genotropin	Humatrope	Norditropin	Nutropin AQ	Omnitrope	Saizen	Zomacton
Pediatric GHD	✓	✓	✓	✓	✓	✓	✓
Prader-Willi Syndrome	✓		✓		✓		
Small for Gestational Age	✓[a]	✓[b]	✓[b]		✓[a]		✓[b]
Turner Syndrome	✓	✓	✓	✓	✓		✓
Idiopathic Short Stature	✓	✓	✓	✓	✓		✓
SHOX Deficiency		✓					✓
Noonan Syndrome			✓				
Growth Failure Secondary to CKD				✓[c]			
Adult GHD[d]	✓	✓	✓	✓	✓	✓	✓

GHD – Growth Hormone Deficiency; CKD – Chronic Kidney Disease

a. Indicated for the treatment of pediatric patients with short stature born SGA with no catch-up growth by age 2 years.
b. Indicated for the treatment of pediatric patients with short stature born SGA with no catch-up growth by age 2 to 4 years.
c. Up to the time of renal transplantation
d. Includes "Adult or Childhood Onset GHD" and "Replacement of endogenous growth hormone in adults with GHD"
e. Not included from this point on due to unique indications not related to growth failure.

Recommendation: No changes are recommended to the formulary at this time. The following updates should be made to the FDA-approved indications note in the existing growth hormone policies

FDA-Approved Indications

- **Growth failure associated with Turner syndrome**: (Genotropin, Humatrope, Norditropin FlexPro, Omnitrope, Nutropin AQ, and Zomacton)
- **For the treatment of children with short stature born SGA with no catch-up growth by 2 to 4 years of age**: (Humatrope, Norditropin FlexPro, and Zomacton)
- **Growth hormone deficiency in adults**: (Genotropin, Humatrope, Norditropin FlexPro, Nutropin AQ, Omnitrope, Saizen, and Zomacton)
    - Note – Zomacton is currently included for this indication in the existing Commercial policy, but not in the GHP Family.
- **Idiopathic short stature**: (Genotropin, Humatrope, Omnitrope, Norditropin FlexPro, Nutropin AQ, and Zomacton)
- **Short stature homeobox-containing gene (SHOX) deficiency**: (Humatrope and Zomacton)

Discussion: No comments or questions.

Outcome: Kim Clark made a motion to accept the recommendations as written. Kelly Yelenic seconded the motion. None were opposed.

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

ASTAGRAF XL (tacrolimus)

Updated Indication: Astagraf XL is now indicated for prophylaxis of organ rejection in kidney transplant patients in combination with immunosuppressants in pediatric patients aged 4 and older.

Recommendation: Astagraf XL is currently available on the Geisinger GHP Family formulary at the Brand Tier and does not require prior authorization. No changes are recommended at this time.

Discussion: No comments or questions.

Outcome: Kim Clark made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

KYMRIAH (tisagenlecleucel)

Updated Indication: Kymriah is now indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitation of Use: Kymriah is not indicated for the treatment of patients with primary central nervous system lymphoma.

Previously, Kymriah was only indicated for the treatment of patients up to the age of 25 years with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

Recommendations: No changes are recommended to the formulary placement of Kymriah at this time. Kymriah will continue to be a medical benefit for all lines of business (Kymriah remains GHP Family excluded). It is recommended that the prior authorization criteria outlined by MBP 159.0 are edited as outlined below.

Acute Lymphoblastic Leukemia (ALL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is less than 26 years of age **AND**
- Medical record documentation of a diagnosis of B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second (or later) relapse **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

Note: The indication of Kymriah is intended to treat patients up to the age of 25 years 364 days. Upon reaching 26 years of age the patient is no longer a candidate for Kymriah treatment. Per Novartis, Kymriah will not be manufactured for any patient who does not meet the specific FDA approved indication, including these age restrictions.

AUTHORIZATION DURATION: Approved requests will be for a one-time authorization for one administration of Kymriah.

Large B-Cell Lymphoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or greater **AND**
- Medical record documentation of one of the following diagnoses:
    - High grade B-cell lymphoma **OR**
    - Diffuse Large B-Cell Lymphoma (DLBCL) arising from follicular lymphoma **OR**
    - Diffuse Large B-cell Lymphoma (DLBCL) not otherwise specified

  AND
- Medical record documentation of relapsed or refractory disease after at least two lines of systemic therapy **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

Limitation of use: Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

AUTHORIZATION DURATION: Approved requests will be for a one-time authorization for one administration of Kymriah

Other Recommendations: Repeated administrations of CAR-T cell therapy have not been studied. Furthermore, NCCN recommendations to treat with Kymriah or Yescarta are contingent upon the patient not having received previous treatment with one of these therapies. To promote consistency between policies for CAR-T cell therapies, it is recommended that the following changes are made to the Yescarta medical benefit policy (MBP 162.0).

MBP 162.0

Large B-Cell Lymphoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or older **AND**
- Medical record documentation of one of the following diagnoses:
    - Relapsed or refractory diffuse large B-cell lymphoma (DLBCL) **OR**
    - Relapsed or refractory primary mediastinal large B-cell lymphoma **OR**
    - Relapsed or refractory high-grade B-cell lymphoma

  AND
- Medical record documentation of a therapeutic failure on two or more previous lines of therapy **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

Note: Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

AUTHORIZATION DURATION: Yescarta will be approved for a one-time authorization for one administration of Yescarta.

Discussion: No comments or questions.

Outcome: Kevin Szczecina made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

VIREAD (tenofovir disoproxil fumarate)

Updated Indication: Treatment of chronic hepatitis B in adults and pediatric patients 2 years and older weighing at least 10 kg.

Treatment of HIV-1 infection in adults and pediatric patients 2 years and older weighing at least 10 kg, in combination with other antiretroviral agents.

Recommendation: Recommend adding Viread 40 mg/scoop to the formulary on the Brand Tier.

Dis**cussion:** No comments or questions.

Outcome: Kelly Yelenic made a motion to accept the recommendations as written. Aubrielle Prater seconded the motion. None were opposed.

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

VENCLEXTA (venetoclax)

Updated Indication: Venclexta is now FDA approved for use in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of adult patients, aged 75 years and older, with newly diagnosed acute myeloid leukemia (AML) who have comorbidities that preclude use of intensive induction chemotherapy.

Updated Dosing for New Indication:[1]

	Venclexta Daily Dose	
Day 1	100mg	
Day 2	200mg	
Day 3	300mg	
Days 4 and beyond	400mg when used in combination with **azacitidine** or **decitabine**	600mg when used in combination with **low-dose cytarabine**

* Initiate therapy with azacitidine, decitabine, or low-dose cytarabine on Day 1 of treatment.

Recommendation: No changes to formulary status are recommended at this time. Recommend updating the existing policy to include the following criteria:

- Medical record documentation that Venclexta is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of newly-diagnosed acute myeloid leukemia (AML) **AND**
- Medical record documentation of age 75 years or older **OR**
- Medical record documentation of a comorbidity that precludes patient from receiving intensive induction chemotherapy **AND**
- Medical record documentation that Venclexta is being used in combination with azacitidine, decitabine, or low- dose cytarabine.

Quantity Limits: Increase QL for 100mg tablet to 6 tablets per day

Authorization Duration: **Duration**: Initial approval will be for twelve (12) months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional twelve (12) 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 the member experiences unacceptable toxicity or worsening of disease.

Discussion: No comments or questions.

Outcome: Kelly Yelenic made a motion to accept the recommendations as written. Keith Hunsicker seconded the motion. None were opposed.

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

MAVYRET (glecaprevir/pibrentasvir)

Indication: Mavyret is a fixed-dose combination of glecaprevir, a hepatitis C virus (HCV) NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor, and is indicated for the treatment of:

- adult patients with chronic HCV genotype (GT) 1, 2, 3, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A).
- adult patients with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both.

New Patient Population[1]**:**
Recommendations for Liver or Kidney Transplant Recipients:

- Genotype 1-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A PI:
    - Mavyret for 16 weeks

- Genotype 3-infected patients who are PRS* treatment-experienced:
    - Mavyret for 16 weeks
- All other liver or kidney transplant recipients:
    - Mavyret for 12 weeks

*PRS=Prior treatment experience with regimens containing (peg) interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor.

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

- Medical record documentation of:
    - Genotype 1, 2, 3, 4, 5, or 6 without cirrhosis or with compensated cirrhosis who are treatment naïve or experienced with peginterferon/ribavirin or Sovaldi/ribavirin +/- peginterferon **OR**
    - Genotype 1 previously treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both **OR**
    - Liver or kidney transplant recipients with Hepatitis C infection **AND**

It is also recommended to add a note after the treatment duration.

Treatment Duration: 8, 12, or 16 weeks consistent with current AASLD/IDSA guidelines or FDA recommendations

Note to reviewer: Per the prescribing information, treatment duration for liver or kidney transplant recipients is 12 weeks except for genotype 1-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A PI and genotype 3-infected patients who are prior treatment experienced with regimens containing (peg) interferon, ribavirin, and/or sofosbuvir, but no prior treatment experience with an HCV NS3/4A PI or NS5A inhibitor. Treatment duration is 16 weeks in these 2 cases.

Discussion: No comments or questions.

Outcome: Tricia Heitzman made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

COMPLERA (emtricitabine/rilpivirine/tenofovir disoproxil fumarate)

Updated Indication: Complera is now indicated for use as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing at least 35 kg as initial therapy in those with no antiretroviral treatment history and with HIV-1 RNA less than or equal to 100,000 copies/mL at the start of therapy, or to replace a stable antiretroviral regiment in those who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen for at least 6 months with no treatment failure and no known substitutions associated with resistance to the individual components of Complera.[1]

- Complera was previously approved for this indication in patients 12 years of age or older weighing at least 35 kg.

No new study data was presented related to the expanded indication.

Recommendation: No changes are recommended at this time based on the new, expanded indication.

Discussion: No comments or questions.

Outcome: Kelly Yelenic made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

ODEFSEY (emtricitabine, rilpivirine, and tenofovir alafenamide)

Updated Indication: Odefsey is now indicated as a complete regimen for the treatment of HIV-1 infection in adult and pediatric patients weighing at least 35 kg, regardless of age, as initial therapy in those with no antiretroviral treatment history with HIV-1 RNA less than or equal to 100,000 copies per mL or to replace a stable antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Odefsey.[1]

- Odefsey previously was only approved for use in adults and pediatric patients 12 years and older.

No new study data was presented related to the expanded indication.

Recommendation: No changes are recommended at this time based on the new, expanded indication

Discussion: No comments or questions.

Outcome: Kevin Szczecina made a motion to accept the recommendations as written. Todd Sponenberg seconded the motion. None were opposed.

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

NUVESSA (metronidazole 1.3%)

Updated Indication: Nuvessa is a nitroimidazole antimicrobial indicated for the treatment of bacterial vaginosis in females 12 years of age and older.

Dosing:
A single-dose, pre-filled disposable applicator administered once intravaginally at bedtime

Recommendation: Do not recommend any changes in formulary status (remain non-formulary)

The following prior authorization criteria should apply:

For patients 18 years of age and older:

- Medical record documentation of failure on, intolerance to, or contraindication to Clindamycin 2% and Metronidazole 0.75% vaginal gel

OR

For patients between age 12 and <18 years old:

- Medical record documentation of failure on, intolerance to, or contraindication to Clindamycin Phosphate 2%

Note: Pediatric dosing is based on adult dosing for Clindamycin Phosphate 2% **ONLY** in postmenarchal female pediatric patients. Safety and effectiveness in premenarchal females have not been established.
Astagraf XL is currently available on the Geisinger GHP Family formulary at the Brand Tier. A prior authorization is only required to determine if the drug is covered under the Part B or GHP Family benefit. No changes are recommended at this time.

Discussion: No comments or questions.

Outcome: Keith Hunsicker made a motion to accept the recommendations as written. Tricia Heitzman seconded the motion. None were opposed.

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

ADCETRIS (brentuximab vedotin)

Updated Indication: Adcetris is now indicated for the treatment of adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD-30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone.

The indication for previously untreated classical Hodgkin lymphoma (cHL) has been updated to the following: Adcetris is indicated for the treatment of adult patients with previously untreated Stage III or IV cHL, in combination with doxorubicin, vinblastine, and dacarbazine. Previously, this indication only specified "in combination with chemotherapy."

Adcetris maintains its other indications of cHL consolidation, relapsed cHL, relapsed sALCL, and relapsed pcALCL.

Current Formulary Status/Prior Authorization Criteria:
GHP Family: Medical benefit requiring PA

Recommendation: No changes are recommended to the formulary status of Adcetris at this time. It is recommended that the exisiting Adcetris policy be updated as outlined below to account for the updated indications and to aid in clarity to the reviewing provider. It is recommended that the authorization duration criteria be updated to reflect the FDA approved dosing regimens as outlined below.

Classical Hodgkin Lymphoma (cHL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is at least 18 years of age **AND**
- Medical record documentation of a diagnosis of classical Hodgkin Lymphoma meeting one of the following situations:
    - Medical record documentation of failure of autologous hematopoietic stem cell transplant (auto-HSCT)

  OR
    - Medical record documentation of failure of at least 2 multi-agent chemotherapy regimens in patients who are not candidates for auto-HSCT

OR

- Medical record documentation of use as consolidation treatment following auto-HSCT in patients with high risk of relapse or progression post-auto-HSCT (high risk patients include: refractory to first line therapy, relapse within 12 months of first line therapy, presence of extranodal disease)

OR

- Medical record documentation of previously untreated Stage III or IV cHL AND
- Medical record documentation that Adcetris will be used in combination with doxorubicin, vinblastine, and dacarbazine.

Systemic Anaplastic Large Cell Lymphoma (sALCL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is at least 18 years of age **AND**
- Medical record documentation of a diagnosis of systemic anaplastic large cell lymphoma (sALCL) meeting one of the following situations:
  - Medical record documentation of failure of at least 1 prior multi-agent chemotherapy regimen

OR

- Medical record documentation of previously untreated sALCL AND
- Medical record documentation that Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone

Peripheral T-cell Lymphomas (PTCL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is at least 18 years of age **AND**
- Medical record documentation of a diagnosis of a CD30-expressing peripheral T-cell lymphoma (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified **AND**
- Medical record documentation that Adcetris will be used in combination with cyclophosphamide, doxorubicin, and prednisone

Primary Cutaneous Anaplastic Large Cell Lymphoma (pcALCL)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is at least 18 years of age **AND**
- Medical record documentation of a diagnosis of primary cutaneous anaplastic large cell lymphoma (pcALCL) OR CD30-expressing mycosis fungoides (MF) **AND**
- Medical record documentation of failure of prior radiation or systemic therapy

AUTHORIZATION DURATION:

Indication	Initial Authorization	Subsequent Authorizations
Previously Untreated Stage III or IV cHL	Initial approval will be limited to 12 doses (6 months) or less if the reviewing provider feels it is medically appropriate.	Subsequent approval for treatment past the initial 12 doses will require documentation of well-controlled, peer-reviewed literature with evidence to support this request.
cHL Consolidation	Initial approval will be limited to 6 months or less if the reviewing provider feels it is medically appropriate.	Subsequent approval will be for one additional 6-month authorization to allow for a total of 16 cycles of treatment. Subsequent approval for treatment past 16 cycles will require documentation of well-

		controlled, peer-reviewed literature with evidence to support this request.
Previously Untreated sALCL or Other CD30-expressing PTCLs	Initial approval will be limited to 8 doses (6 months) or less if the reviewing provider feels it is medically appropriate.	Subsequent approval for treatment past the initial 8 doses will require documentation of well-controlled, peer-reviewed literature with evidence to support this request.
Relapsed cHL	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 12 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. Adcetris will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.
Relapsed sALCL		
Relapsed pcALCL or CD30-expressing MF		

Discussion: No comments or questions.

Outcome: Kevin Szczecina made a motion to accept the recommendations as written. Kelly Yelenic seconded the motion. 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

Lenvima quantity limits

Discussion: All Lenvima quantity limits were previously listed as 90 capsules per 30 days.

Recommendation: Quantity limits to be changed to be appropriate based on the daily dose as follows:

- Lenvima 4 mg daily dose pack (30 x 4 mg capsules)
  - 30 capsules per 30 days
- Lenvima 8 mg daily dose pack (60 x 4 mg capsules)
  - 60 capsules per 30 days
- Lenvima 10 mg daily dose pack (30 x 10 mg capsules)
  - 30 capsules per 30 days
- Lenvima 12 mg daily dose pack (90 x 4 mg capsules)
  - 90 capsules per 30 days
- Lenvima 14 mg daily dose pack (30 x 4 mg capsules, 30 x 10 mg capsules)
  - 60 capsules per day
- Lenvima 18 mg daily dose pack (60 x 4 mg capsules, 30 x 10 mg capsules)

- 90 capsules per day

- Lenvima 20 mg daily dose pack (60 x 10 mg capsules)
  - 60 capsules per 30 days

- Lenvima 24 mg daily dose pack (30 x 4 mg capsules, 60 x 10 mg capsules)
  - 90 capsules per 30 days

Discussion: Changes to be effective in 2020 for GHP Family. No comments or questions.

Outcome: Tricia Heitzman made a motion to accept the recommendations as presented. Kevin Szczecina seconded the motion. None were opposed.

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

Inhaled Corticosteroids Formulary and Policy updates

Discussion: A recent analysis of the inhaled corticosteroid class has revealed an opportunity to configure the current formulary placement to improve access and decrease costs to the plan and members by expanding our formulary agents.

Recommendations:

- QVAR 40 mcg and 80 mcg is no longer available replaced by QVAR RediHaler
- Add ArmonAir Respiclick, Asmanex HFA, Pulmicort Flexhaler, and QVAR RediHaler to the Brand Preferred Tier
- Create a policy for Non-formulary agents Alvesco and Asmanex Twisthaler
  - Medical record documentation of failure on, intolerance to, or contraindication to Arnuity Ellipta, QVAR RediHaler and one additional formulary agent.
  - Add a note to Reviewing Pharmacist: Alvesco and QVAR RediHaler are both small particle inhalers. It has been believed that the smaller particle size distribution is an advantage of these agents however there is no concrete evidence to indicate that this is clinically justified. Currently, per the guidelines, there is not one ICS inhaler preferred over the other.
- Update Flovent Policy 1317.0F
  - Currently states: Prior authorization of Flovent Diskus for members age 12 and older and for Flovent HFA for members age 18 and older will be made for members who meet the following criteria:
  - Update to state: Prior authorization of Flovent Diskus for members age ***5*** and older and for Flovent HFA for members age 18 and older will be made for members who meet the following criteria:
    - Medical record documentation of a therapeutic failure on, intolerance to or contraindication to Arnuity Ellipta OR
    - Medical record documentation of a diagnosis of Eosinophilic Esophagitis

Discussion: No comments or questions.

Outcome: Keith Hunsicker made a motion to accept the recommendations as amended. Kelly Yelenic seconded the motion. None were opposed.

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

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DUR update January 2019

Discussion: Current and completed drug utilization review items were discussed:

In Progress

- Polypharmacy DUE
  - This is the 2018 4th quarter Medimpact DUE for all LOBs
  - From this report, we identified **95 members** who are receiving more than 10 unique, chronic medications from 3 or more prescribers over a 3-month timeframe
  - Brandy P. completed the mail merge and sent out the letters to their providers on 12/17/2018.
  - We will run a report on the members who we sent a letter, in March 2019, to determine the effectiveness of the initial letter
- Statin Use in Persons with Diabetes (SUPD)
  - This is the 2018 3rd quarter MedImpact DUE for Commercial/Exchange and GHP Family
  - From this report, we identified **99 members** whose medication history was suggestive of the presence of diabetes and who were not receiving a statin drug during the previous three-month period.
  - Brandy P. completed the mail merge and sent out the letters to their providers on 09/13/2018.
  - We will run a report on the members who were sent a letter in March 2019 to determine the effectiveness of the initial letter
- Asthma Med Ratio DUE
  - This is the 2018 2nd quarter MedImpact DUE for Commercial/Exchange and GHP Family
  - From this report, we identified **92 members** with a ratio of controller medications to total asthma medications of greater than 0.2 (HEDIS threshold is greater than or equal to 0.5) and sent letters to their providers.
    - Adam was able to run this data again October 2018 (**53 members** now analyzed) and of those members **29 members** had a AMR Ratio increase and **5 of those members** now have an AMR greater than 0.6.
- Adherence to Antidepressants DUE
  - This is the 2018 1st quarter MedImpact DUE
  - From this report, we identified **187 members** with MPR < 50% and sent out letters to their prescribers. These letters were mailed out to providers 3/6/18.
    - Adam was able to run this data again August 2018 (**100 members** now analyzed) and of those members **83%** had an increase in their PDC with **19 members** who more than doubled their PDC.
- Tobacco Cessation Program
  - Monthly meeting with Wellness/MTDM RPhs to create a program that identifies GHP members who may benefit from tobacco cessation interventions/medications.
  - We gathered drug utilization data to determine which medications are being commonly prescribed and assessed proper utilization. We also informed the group of the Chantix updates approved at the March 2018 P&T meeting: Chantix was added to the Brand Tier for GHP Family without prior authorization.

- We are in the process of making changes to the report and should start sending out letters/brochures to patients February 2019 as both the brochure and letter have been approved by DHS

- DUR Duplicate Anticoagulant Report
  - We are working with Sally and Krista to build a **weekly** report for **all LOBs** flagging members filling duplicate anticoagulant medications. We are working to functionalize this report and will be personally reaching out to the providers of the flagged members to confirm proper medication therapy. We have a Marketing/Legal approved letter to send to providers if further outreach is needed.
- FWA with MedImpact
  - We are working with MedImpact to see if we can implement pharmacy compliance audits and implement a policy for billing lotions/eye drops. We sent a document in the beginning of July 2018, to MI, of common types of medications that are flagging on the FWA reports for further pharmacy level outreach/education.

Ongoing

- Duplicate Buprenorphine Therapy
  - We are getting this report **monthly** with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows for outreach.
    - For Family in 2018 we reviewed **11 members**, and all have switched to monotherapy.
- Duplicate Specialty Therapy
  - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Prater. These members are identified and written up and sent to a medical director if follow up is needed.
  - For Family 1Q2018 report, **1 intervention** resulting in a **cost savings of $3,103.30**
- Suboxone with an Opioid Report
  - We are getting this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each member that flags on the report. These members are being forwarded to Dr. Meadows, and he is looking into whether it is appropriate to end the opioid authorizations still in place
  - For Family in 2018, we reviewed **223 members**, and **40 members** were referred to Dr. Meadows
- Ending Opioid Authorizations
  - We are working on identifying members who have active opioid authorizations in place but have since started Buprenorphine therapy. The letter is sent to the members notifying them the opioid authorization has been ended due to the start of buprenorphine therapy.
  - For Family in 2018, we sent **8 members** letters notifying them of the end of their opioid authorization
- Medicaid Opioid Overutilization Report
  - We are getting this report **monthly** from MedImpact and we are writing up each member that flags on the report. We have been monitoring the members that are continuously showing up on the report by any change in their MED. For those members we deem appropriate we will send a letter to their PCP.
  - For Family in 2018, we reviewed **47 cases** and did not send any prescriber letters
- FWA Reports
  - We are getting this report **weekly** for **all LOBs** from Marie Strausser. We prepare this report by determining which claims need to be verified, and the Wilkes pharmacy students/GHP technicians have been making the calls to pharmacies.
  - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
  - For Family in 2018, we **reviewed 580 cases** so far and **corrected 291 claims**, resulting in a **cost savings of $25,984.32**
- Stent Antiplatelet Adherence Program

- We continue to identify new stent patients for **all LOBs** at GMC/GWV/CMC/Susq and follow these members for 1 year after discharge to ensure adherence to their aspirin, beta blocker, antiplatelet, and statin therapy regimens.
- For Family in 2018, we identified and outreached to **95 new stent patients**

- Severity Report
  - This is a **monthly** report for **all LOBs** on members who have filled a medication that has a level one interaction with another medication they have a claim for
  - For Family in 2018, we sent letters to providers on **207 GHP Family members**
- Duplicate Antipsychotics
  - Adam Kelchner runs this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
  - 1Q2018 report was received on 4/17/18 included **133 members** with multiple antipsychotics. We sent these members to Brandy Powell who completed the mail merge and sent letters 4/18/18.
  - 2Q2018 report received on 07/18/18 included **147 members** with multiple antipsychotic claims. We sent these members to Brandy Powell who completed the mail merge and sent letters the week of 7/23/18.
  - 3Q2018 report received on 10/16/18 included **158 members** with multiple antipsychotic claims. We sent these members to Brandy Powell who completed the mail merge and sent letters the week of 10/22/18
- Adherence to Antipsychotics
  - Kayla Stanishefski runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
  - For Family in 2018, we sent letters to **170 members**
- Enbrel Overutilization for Treating Plaque Psoriasis
  - A report was created to determine members who have been overutilizing Enbrel twice weekly dosing as outlined by the FDA approved dose. One (1) members flagged on the July report, and it was written up and sent to Dr. Yarczower on 7/10/18.
    - Working on follow up to ensure members are on proper therapy.

Completed

- Medicaid DUR/FWA Program Fliers
  - Last updated 12/2018
- Current Provider Letters
    - Polypharmacy DUE
    - Statin Use in Persons with Diabetes DUE
    - Adherence to Antidepressants DUE
    - Asthma Med Ratio DUE
    - Opioid Overutilization
    - Duplicate Antipsychotics
    - Severity Report
    - Duplicate Anticoagulant Report
- Current Member Letters
    - Ending opioid Authorizations
    - Stent Antiplatelet Adherence Program
    - Adherence to Antipsychotics
    - Tobacco Cessation

Discussion: No comments or questions. Informational only

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

January 2019 GHP Family Formulary Update

Recommendations: it is recommended that the following medication(s) be added to the GHP Family formulary:

Medication	Cost	Formulary Placement
Valganciclovir 450 mg Tablet	$7.99 per tablet (MAC)	Generic Tier, QL of 4 per day

Discussion: No comments or questions.

Outcome: Rajneel Chohan made a motion to accept the recommendations as amended. Kelly Yelenic seconded the motion. None were opposed.

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

2019 GHP Family Formulary

Recommendations: it is recommended that the Committee approve the 2019 GHP Family Formulary.

Discussion: No comments or questions.

Outcome: Kim Clark made a motion to accept the recommendations as amended. Kelly Yelenic seconded the motion. 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 4:01 pm.

Future Scheduled Meetings
An electronic ad-hoc Pharmacy and Therapeutics session will be sent out to voting members on February 22nd, 2019.
The next bi-monthly scheduled meeting will be held on Tuesday, March 19, 2019 at 1:00 HCN3A & 3B Conference room

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.