P&T Committee Meeting Minutes
Commercial, Exchange, CHIP
May 16, 2023

Present (via Teams):	Absent:
Bret Yarczower, MD, MBA – Chair	Kristen Bender, Pharm.D.
Amir Antonius, Pharm.D.	Jeremy Bennett, MD
Emily Antosh, Pharm.D.	Alyssa Cilia, RPh
Kim Castelnovo	Holly Bones, Pharm.D.
Kimberly Clark, Pharm.D.	Michael Evans, RPh
Bhargavi Degapudi, MD	Jason Howay, Pharm.D.
Michael Dubartell, MD	Briana LeBeau, Pharm.D.
Rajneel Farley, Pharm.D.	Tyreese McCrea, Pharm.D.
Kelly Faust Pharm.D.	Jonas Pearson, RPh
Tricia Heitzman, Pharm.D.	William Seavey, Pharm.D.
Nichole Hossler, MD	Michael Shepherd, MD
Emily Hughes, Pharm.D.	Robert Strony, MD, MBA
Keith Hunsicker, Pharm.D.	
Kelli Hunsicker, Pharm.D.	
Derek Hunt, Pharm.D.	
Kerry Ann Kilkenny, MD	
Philip Krebs, R.EEG T	
Ted Marines, Pharm.D.	
Lisa Mazonkey, RPh	
Perry Meadows, MD	
Jamie Miller, RPh	
Mark Mowery, Pharm.D.	
Austin Paisley, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Sartori, Pharm.D.	
Angela Scarantino	
Kristen Scheib, Pharm.D.	
Leslie Shumlas, Pharm.D.	
Aubrielle Smith Pharm.D.	
Kirsten Smith, Pharm.D.	
Michael Spishock, RPh	
Todd Sponenberg, Pharm.D.	
Jill Stone, Pharm.D.	
Luke Sullivan, DO	
Kevin Szczecina, RPh	
Amanda Taylor, MD	
Ariana Wendoloski, Pharm.D.	
Brandon Whiteash, Pharm.D.	
Margaret Whiteash, Pharm.D.	
Birju Bhatt, MD (non-voting participant)	
Jeremy Garris, Pharm.D. (non-voting participant)	
Marianne Linko, LPN (non-voting participant)	
Dionardo Medina Encarnacion, MD (non-voting participant)	
Tiffany O'Hagan, Pharm.D. (non-voting participant)	

Call to Order:
Dr. Bret Yarczower called the meeting to order at 1:02 p.m., Tuesday, May 16, 2023.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the March 21st, 2023 and April 2023 e-vote minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

HEMGENIX (etranacogene dezaparvovec-drlb)

Review: Hemgenix is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with hemophilia B (congenital Factor IX deficiency) who: currently use Factor IX prophylaxis therapy, or have current or historical life-threatening hemorrhage, or have repeated, serious spontaneous bleeding episodes.

People with hemophilia A have a deficiency in factor VIII and patients with hemophilia B have a deficiency in Factor IX. Between 30,000 to 33,000 people are living with hemophilia in the United States, and hemophilia B is four times less common than hemophilia A. The estimated incidence of hemophilia B is 1 per 19,283 male births. Based on CDC data from federally funded HTCs reported from January 1, 2012 through March 31, 2022, there are an estimated 6,073 male patients with hemophilia B in the United States.

About 44% of patients with hemophilia B have severe disease. Severe disease is defined as FIX levels <1 IU/dL or <1% of normal; moderate disease is defined as FIX levels of 1–5 IU/dL or 1%–5% of normal; and mild disease is defined as FIX levels of 5–40 IU/dL or 5% to <40% of normal. About 1% to 4% of patients with severe hemophilia B may develop an inhibitor to FIX replacement therapy.

The standard of care for hemophilia B is aimed at preventing bleeds, which would also prevent long-term adverse outcomes related to joints and targets a FIX trough level of at least 1% of normal between doses. Prior to the approval of Hemgenix, standard-of-care treatment for moderate to severe hemophilia included prophylaxis with Factor IX replacement therapy, self-administered intravenously multiple times a week. Hemgenix is an adeno-associated virus serotype 5 (AAV5)–based gene therapy designed to deliver a copy of a gene encoding the Padua variant of human coagulation FIX (hFIX-Padua) to the patient's hepatic cells, which is where the production of clotting factors occurs.

Prior to administering Hemgenix, Factor IX inhibitor testing should be completed. In case of a positive result for Factor IX inhibitors, a re-test should be performed within 2 weeks. If both the initial and re-test results are positive, Hemgenix should not be administered to the patient. Also, liver health assessment should be completed prior to administration of Hemgenix. In case of radiological liver abnormalities and/or sustained liver enzyme elevations, a consultation with a hepatologist should be completed to assess eligibility for Hemgenix.

Hemgenix is supplied as sterile, preservative-free, clear, and colorless suspension. Hemgenix has a nominal concentration of 1 x 103 genome copies (gc)/mL. Hemgenix is supplied as a customized kit to meet dosing requirements for each patient, with each kit containing 10 to 48 single-use vials. The total number vials in each kit corresponds to the patient's body weight, see Table 1. The recommended dose of Hemgenix is 2 x 103 gc/kg of body weight (or 2 mL/kg body weight) administered as an intravenous infusion after dilution with 0.9% sodium chloride solution. The dose in mL is calculated as patient body weight (in kg) x 2. The multiplication factor 2 represents the per kilogram dose (2 x 1013 gc/kg divided by the amount of genome copies per mL of the Hemgenix solution (1 x 1013 gc/mL). The number of Hemgenix vials needed is calculated by dividing the dose in mL by 10 (rounded up to the next whole number of vials) (each vial is 10 mL). So for example, a 72 kg patient would need a dose of 144 mL, which would be 15 vials. Hemgenix should be administered as an IV infusion at a constant infusion rate of 500 mL/hour (8 mL/min).
Dr. Moe Samour, hematologist/oncologist at Geisinger, agreed with the proposed criteria. We discussed the preexisting neutralizing anti-AAV5 antibodies and how one patient that had preexisiting neutralizing anti-AAV5 antibody titer of 1:3212 had no human Factor IX expression and had to restart Factor IX

prophylaxis. However, subjects with and without neutralizing anti-AAV5 antibodies demonstrated hemostatic protection. Since there is no guidance on this in the standard of care setting yet, he agreed we should not include any limitations around preexisiting neutralizing anti-AAV5 antibodies in our policy. However, he suggested adding a comment to our policy regarding this so it can be a reminder for clinicians/pharm to consider.

Matthew Silecchia, Regional Sales Manager for CSL Behring, informed me of the distribution of Hemgenix. At this point, the administration is limited to hemophilia treatment centers and most of the distribution is buy and bill through direct contracts with hospitals and hemophilia treatment centers. However, due to the cost of the product, Hemgenix is able to be distributed through a limited distribution specialty network that includes Accredo, CVS Specialty, and Orsini. They are entering value-based/ outcome-based contracts with insurers, where insurers receive a percentage of payback in the event the gene therapy does not work as promised.

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

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

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

Outcome: Hemgenix will be a medical benefit. Hemgenix will be added to the medical benefit cost share list. If processed at a specialty pharmacy, Hemgenix will process at the Specialty tier or Brand Non-Preferred tier for those with a three tier benefit of the pharmacy formulary. Hemgenix will require a prior authorization with the following criteria:

- Prescription written by or in consultation with a hematologist **AND**
- Medical record documentation that the member is a male based on assigned sex at birth and age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of moderate or severe hemophilia B with Factor IX level < 2 IU/dL or ≤ 2% of normal **AND**
- Medical record documentation of one of the following:
    - Member has current use of Factor IX prophylaxis therapy for at least 2 months with > 150 exposure days^ of treatment with Factor IX protein
    - Member has current of historical life-threatening hemorrhage
    - Member has repeated, serious spontaneous bleeding episodes

  AND
- Medical record documentation that the member has a recent negative inhibitor status to Factor IX prior to administration of Hemgenix **AND**
- Medical record documentation that the member does not have an active hepatitis B or hepatitis C infection* assessed within the last 6 months **AND**
- Medical record documentation that the member does not have uncontrolled HIV** assessed within the last 6 months **AND**
- Medical record documentation that the member does not have evidence of advanced cirrhosis*** assessed within the last 6 months **AND**
- Medical record documentation that the member has not received any previous gene therapy for hemophilia B **AND**
- Medical record documentation that Hemgenix is being dosed according to the Food and Drug Administration approved labeling**** **AND**
- Medical record documentation of the frequency of bleeds within the previous 12 months **AND**
- Medical record documentation of therapeutic failure on Factor IX prophylaxis therapy

^Exposure days is the number of days a patient was exposed to exogenous factor.

*In the Hope-B trial members were excluded at screening if they were currently receiving antiviral therapy

for this/these infection(s) and/or positive for any of the following: Hepatitis B surface antigen, except if in the opinion of the investigator this is due to a previous Hepatitis B vaccination rather than an active Hepatitis B infection, Hepatitis B virus deoxyribonucleic acid (HBV DNA), Hepatitis C virus ribonucleic acid (HCV RNA)

**In the Hope-B trial members were excluded at screening and the last lead-in visit if they had a positive human immunodeficiency virus (HIV) serological test, not controlled with anti-viral therapy as shown by CD4+ counts ≤200/microL

***In the Hope-B trial members were excluded at screening and the last lead-in visit if they had ALT > 2 times upper limit of normal (ULN), AST > 2 times ULN, total bilirubin > 2 times ULN, alkaline phosphatase (ALP) > 2 times ULN, creatinine > 2 times ULN. Also patients were excluded at screening if they had any known significant medical condition that may significantly impact the transduction of the vector and/or expression and activity of the protein, including but not limited to: disseminated intravascular coagulation, accelerated fibrinolysis, advanced liver fibrosis (suggestive of or equal to METAVIR Stage 3 disease; e.g., a FibroScan™ score of ≥9 kPa is considered equivalent)

****Hemgenix is administered as a single IV infusion. To calculate the Hemgenix dose use the following equation:

Hemgenix dose (in mL)= patient body weight (in kilogram) X 2
Number of vials needed= Hemgenix dose (in mL) / 10 (round up to the next whole number of vials)

Note to Reviewer: In the HOPE-B study, patients were assessed for AAV5 neutralizing antibodies using a clinical laboratory test, but patients were not excluded based on their test results nor are they excluded in our approved indication. The subject sub-group with detectable preexisting neutralizing anti-AAV5 antibodies up to titers of 1:678 showed mean Factor IX activity that was numerically lower compared to that subject sub-group without detectable preexisting neutralizing anti-AAV5 antibodies. In one subject with a preexisting neutralizing anti-AAV5 antibody titer of 1:3212, no human Factor IX expression was observed. Patients who intend to receive treatment with Hemgenix are encouraged to enroll in a study to measure pre-existing anti-AAV5 neutralizing antibodies by calling CSL Behring at 1-800-504-5434. Although there is no FDA-approved AAV5 NAb assay, CSL will make available a laboratory developed, CLIA-validated test that was used during the clinical trial. If a provider is interested in ordering this kit, free of charge, they can call 1-833-436-0021, Mon–Fri, 8 AM–8 PM ET (https://labeling.cslbehring.com/PRODUCT-DOCUMENT/US/Hemgenix/HEMGENIX-Patient-Eligibility-Brochure.pdf).

Authorization Duration: One (1) time approval per lifetime; Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

Require RPH Sign off: Yes

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

RAYALDEE (calcifediol)

Review: Rayaldee is FDA-approved for treatment of secondary hyperparathyroidism in adults with stage 3 or 4 CKD and serum total 25-hydroxyvitamin D levels < 30 ng/mL. It is available as 30 mcg extended-release capsules. The initial dose of Rayaldee is 30 mcg PO once daily at bedtime. Serum calcium (corrected for low albumin) should be < 9.8 mg/dL before starting treatment. After 3 months of initiating treatment, increase the dose to 60 mcg once daily if intact PTH is above treatment goal. Serum calcium (corrected for low albumin) should be < 9.8 mg/dL, phosphorus < 5.5 mg/dL, and 25-hydroxyvitamin D < 100 ng/mL before increasing the dose. Temporarily stop treatment if intact PTH is persistently abnormally

low, serum calcium (corrected for low albumin) is consistently above the normal range, or serum 25-hydroxyvitamin D is consistently > 100 ng/mL.

According to the KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease—Mineral and Bone Disorder, in patients with CKD stages 3 through 5 not on dialysis, the optimal PTH level is not known. The guideline suggests that patients with levels of intact PTH progressively rising or persistently above the upper normal limit be evaluated for modifiable factors, including hyperphosphatemia, hypocalcemia, high phosphate intake, and vitamin D deficiency. Due to the risk of hypercalcemia, the guideline suggests that calcitriol and vitamin D analogs, including doxercalciferol and paricalcitol, not be routinely used to treat SHPT, but it is reasonable to reserve these agents for patients with CKD stages 4 and 5 with severe and progressive hyperparathyroidism. As an alternative to these agents, the guideline suggests nutritional vitamin D supplementation, which includes cholecalciferol and ergocalciferol, to suppress PTH. The guideline does not provide recommendations on the use of calcifediol for management of SHPT.

Rayaldee is not indicated in patients with stage 5 CKD or ESRD on dialysis. Excessive administration of Rayaldee may cause hypercalcemia and hyperuricemia. Symptoms of elevated calcium to be of aware of include tiredness, difficulty thinking clearly, loss of appetite, nausea, vomiting, constipation, increased thirst, increased urination, and weight loss. Hypercalcemia may also potentiate digitalis toxicity. Monitor serum calcium and symptoms of digitalis toxicity in patients who use concomitant digitalis compounds. Rayaldee may also suppress intact PTH levels to abnormally low levels, increasing the risk for adynamic bone disease and fractures. Monitor intact PTH levels and adjust the dose of Rayaldee if needed.

The most common adverse reactions of Rayaldee are anemia, nasopharyngitis, increased serum creatinine, dyspnea, cough, congestive heart failure, and constipation. Be aware of drug interactions with Rayaldee. Concomitant thiazides may cause hypercalcemia. CYP450 inhibitors like ketoconazole may alter serum calcifediol levels. Cholestyramine may reduce calcifediol absorption. Lastly, drugs that stimulate microsomal hydroxylation, including phenobarbital and other anticonvulsants, may reduce calcifediol's half-life.

There is no human data evaluating calcifediol use in pregnant or lactating women. Infants who may be exposed to calcifediol through breast milk should be monitored for signs of hypercalcemia, including seizures, vomiting, constipation, and weight loss. The safety and efficacy of Rayaldee have not been established in pediatric patients. There were no differences in safety and efficacy of Rayaldee between geriatric patients over 65 years and younger patients. There were no differences in safety and efficacy of Rayaldee between patients with stage 3 CKD and those with stage 4 CKD. Safety and efficacy in patients with stage 2 or stage 5 CKD or in those with ESRD on dialysis have not been established.

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

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

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

Outcome: Rayaldee is a pharmacy benefit and will not be added to Commercial, Exchange, or CHIP formularies. Prior authorization criteria are as follows:

- Medical record documentation of age ≥ 18 years **AND**
- Medical record documentation of a diagnosis of secondary hyperparathyroidism **AND**
- Medical record documentation of stage 3 or stage 4 CKD **AND**
- Medical record documentation that patient is not on dialysis **AND**
- Medical record documentation of serum total 25-hydroxyvitamin D levels < 30 ng/mL **AND**
- Medical record documentation of serum calcium (corrected for low albumin) < 9.8 mg/dL before starting treatment **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to (1) vitamin D supplement (cholecalciferol, ergocalciferol) **AND** (1) vitamin D analog (calcitriol, doxercalciferol, paricalcitol)

GPI Level: GPI-12

Quantity Limit: 60 mcg per day (2 capsules per day)

Authorization Duration: 12 months

- Medical record documentation of a diagnosis of secondary hyperparathyroidism **AND**
- Medical record documentation of stage 3 or stage 4 CKD **AND**
- Medical record documentation that patient is not on dialysis **AND**
- Medical record documentation that intact PTH is not consistently and abnormally low, serum calcium (corrected for low albumin) is not consistently above normal range, and 25-hydroxyvitamin D is not consistently > 100 ng/mL

Formulary Alternatives: cholecalciferol (OTC), ergocalciferol (Rx or OTC), calcitriol, doxercalciferol, paricalcitol

Require RPH Sign off: Yes

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

LUNSUMIO (mosunetuzumab-axgb)

Review: Lunsumio is a bispecific CD20-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy. This indicated is an accelerated approval based on response rate. Lunsumio binds the CD3 receptor expressed on the surface of T-cells and CD-20 expressed on the surface of lymphoma cells and some healthy B-lineage cells. In-vitro, the activated T-cells caused the release of pro-inflammatory cytokines and induced lysis of B-cells. NCCN recommends Lunsumio as a third-line or later treatment for follicular lymphoma (Category 2A).

Lunsumio is administered as in intravenous infusion for 8 to 17 cycles. Patients achieving a complete response after 8 cycles do not require further treatment. Patients with a partial response or stable disease after 8 cycles should receive and additional 9 cycles of treatment (17 in total) unless there is disease progression or unacceptable toxicity. The recommended dosage and schedule for the 21 day treatment cycles are shown in Table 4. Premedication prior to each dose in Cycle 1 and Cycle 2 is recommended to reduce the risk of cytokine release syndrome and infusion-related reactions (Table 5). Table 6 shows the recommendations for restarted Lunsumio therapy following dose delays. Lunsumio is suppled as 1mg/mL single-dose vials and 30 mg/30 mL single dose vials.

There is a black box warning for Lunsumio for the risk of cytokine release syndrome, including serious or life-threatening reactions. Step-up dosing is recommended to reduce the risk of CRS and patients who experience CRS should withhold Lunsumio until CRS resolves or permanently discontinue treatment based on severity. During clinical trials, CRS occurred in 39% of patients treated with Lunsumio at the recommended dosage. Recurrent CRS occurred in 11% of patients. Most patients experienced CRS following doses of 1 mg on Cycle 1 Day 1, 2 mg on Cycle 1 Day 8, and 60 mg on Cycle 1 Day 15. The median duration of CRS was 3 days. Clinical signs and symptoms included fever, chills, hypotension, tachycardia, hypoxia, and headache. Concurrent neurologic adverse reactions occurred in 6% of patients and included headache, confusional state, and anxiety. Lunsumio can cause serious neurologic toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome. Neurological toxicity occurred in 39% of patients, most frequently headache, peripheral neuropathy, dizziness, and mental status changes.

ICANS was reported in 1% of patients.

Lunsumio can also cause serious or fatal infections. In clinical trials, serious infections, including opportunistic infections occurred in 17% of patients, with Grade 3 or 4 infections in 14% of patients and fatal infections in 0.9% of patients. The most common Grade 3 or higher infections were pneumonia, sepsis, and upper respiratory tract infection. Other warnings and precautions for Lunsumio included cytopenia, tumor flare, and embryo fetal toxicity.

During clinical trials, serious adverse reactions occurred in 47% of patients, including CRS, infection, renal insufficiency, pyrexia, and tumor flare. Discontinuation occurred in 3% of patients due to CRS, and EBV viremia. Dose interruptions due to adverse reactions occurred in 37% of patients, most commonly due to neutropenia, infection, and cytokine release syndrome. The most common adverse reactions occurring with Lunsumio treatment were cytokine release syndrome, fatigue, rash, pyrexia, and headache. The most common Grade 3 or 4 laboratory abnormalities were decreased lymphocyte count, phosphate, neutrophil count, white blood cell count, hemoglobin, and platelets, and increased glucose and uric acid.

The safety and efficacy of Lunsumio has not been established in pediatric patients. Among the 90 patients with relapsed or refractory follicular lymphoma treated with Lunsumio, 39% were 65 years or older and 8% were 75 years or older. There was an insufficient number of patients 65 years and older to determine whether there were differences in safety and efficacy between older and younger patients.

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

Clinical Discussion: We considered a quantity limit but opted not to propose a quantity limit as dose delays requiring re-titration would make operationalizing anything very difficult. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

Outcome: Lunsumio is a medical benefit and will require a prior authorization. Lunsumio will be added to the medical benefit cost share list. When Lunsumio is processed at a specialty pharmacy, it will process at the specialty tier or the brand non-preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation that Lunsumio is written by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years of age **AND**
- Medical record documentation of a diagnosis with relapsed or refractory follicular lymphoma **AND**
- Medical record documentation of prior treatment with two or more lines of therapy

Authorization duration: Approval of Lunsumio will be given for an initial authorization of 6 months or less if the reviewing provider feels it is medically appropriate. One subsequent approval will be given for 12 months or less if the reviewing provider feels it is medically appropriate, not to exceed the limitations outlined below.

Authorization of Lunsumio for the treatment of relapsed or refractory follicular lymphoma should not exceed the FDA-approved treatment duration of 8 total cycles for patients who are in complete remission following 8 cycles of Lunsumio treatment.

Authorization of Lunsumio for the treatment of relapsed or refractory follicular lymphoma should not exceed the FDA-approved treatment duration of 17 total cycles for patients who are in partial remission or stable disease following 8 cycles of Lunsumio treatment.

For requests exceeding the above limit, medical record documentation of the following is required:

- Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration

Formulary Alternatives: Aliqopa

GPI Level: GPI-12

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

ADUHELM (aducanumab-avwa)

Review: Aduhelm is an amyloid beta-directed antibody indicated for the treatment of Alzheimer's Disease (AD). Treatment should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease (the population studied in clinical trials). There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. The indication was approved under accelerated approval based on the reduction in amyloid beta plaques observed, and continued approval may be based upon confirmation of clinical benefit in confirmatory trials. The recommended dose of Aduhelm is 10 mg/kg to be given after initial titration. Initial titration is 1mg/kg on infusions one and two, 3 mg/kg on infusions three and four, 6 mg/kg on infusions five and six, and 10mg/kg on infusion seven and beyond. All titration and maintenance doses should be administered as an intravenous (IV) infusion given over approximately one hour, every 4 weeks (at least 21 days apart). Aduhelm is supplied in either one of two cartons. One carton (NDC 64406-101-01) contains one single-dose vial at a strength of 170mg/1.7mL (red cap). Another carton (NDC 64406-102-02) contains one single-dose vial at a strength of 300mg/3mL (blue cap). Aduhelm is the first drug for AD approved in over 18 years, the first drug approved to slow the progression of AD, and the first anti-amyloid monoclonal antibody approved for the treatment of AD.

Alzheimer's Disease (AD) is a progressive, neurodegenerative disease that causes cognitive, functional, and behavioral impairments. Dementia is the umbrella term for the loss of memory and other thinking abilities severe enough to interfere with daily life. The Alzheimer's Association (AA) estimates 6.2 million Americans have AD, with 1-2 million Americans having mild dementia or mild cognitive impairment, the stages of disease Aduhelm is indicated for. According to the AA, every state across the country is expected to experience an increase of at least 6.7% in the number of people with Alzheimer's between the years 2020 and 2025. Average survival time after a diagnosis of AD is 8-10 years (range 3-20 years), with patients generally succumbing to complications such as dehydration, malnutrition and infection related to advanced debilitation.

AD is thought to be caused by the progressive accumulation of amyloid beta (Aβ) plaques and neurofibrillary tangles (NFTs), formed by aggregated tau protein. The mechanism of action section in the prescribing information states that the accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of AD. Aduhelm is a recombinant human immunoglobulin gamma 1 monoclonal antibody which is directed against aggregated soluble and insoluble forms of amyloid beta, thereby reducing amyloid beta plaques, which has been observed in clinical studies. To detect abnormal amyloid protein in the brain, either an amyloid-PET scan or a cerebrospinal fluid (CSF) amyloid level can be used. The CSF amyloid level is done through a lumbar puncture and is not often used in diagnosis due the invasive nature of this method. The amyloid PET scan uses injectable radioactive tracers that bind to β-amyloid plaques in the brain and produces a positron signal that is detected by the PET scanner. Brand names of the injectable radiopharmaceuticals used for amyloid PET scans are Amyvid (florbetapir F 18), Neuraceq (florbetaben F 18), Tauvid (flortaucipir F 18), and Vizamyl (flutemetamol F 18). A fluorodeoxyglucose (FDG)-PET scan is also used in the diagnosis of AD, however this particular scan measures the concentration of glucose in the brain and helps to distinguish between AD and frontotemporal dementia.

When diagnosing AD, it is helpful to rule out other types of dementia not related to AD. These other

causes of dementia account for up to 40% of all dementia, as summarized in *Table 1* above. Also, specifying the stage of disease is helpful when diagnosing AD as it relates to starting treatment with Aduhelm. The National Institute on Aging (NIA, part of the National Institutes of Health [NIH]) and Alzheimer Association (AA) 2011 guidelines separated AD into three phases: preclinical stage, mild cognitive impairment (MCI) stage, and dementia caused by AD stage. Preclinical stage is defined as no symptoms, but changes in the brain have occurred which may result in symptoms later on. The MCI stage is defined as deficits in thinking beginning to surface (e.g. difficulty with learning, retaining new information) but can still live a relatively normal life. The NIA-AA article stated that differentiating the severity of dementia was beyond the scope of the workgroup. In addition to the NIA-AA, several other organizations use varying nomenclature to describe the stages of AD, which is summarized in *Figure 3* above. In an article published by *The Journal of Prevention of Alzheimer's Disease*, referenced in the drug review above, it states individuals with MCI may struggle to find the right word (language), forget recent conversations (episodic memory), struggle with completing familiar tasks (executive function), or get lost in familiar surroundings (visuospatial function), with symptomology varying widely but tending to remain relatively independent. Individuals who progress to AD dementia will have severe cognitive deficits that interfere with social functioning and require assistance with activities of daily living. The article goes on to state that because biomarkers can be detected decades before onset of symptoms, they represent an important opportunity for early detection and can support the diagnosis of AD, especially when symptoms can be subtle. Lastly, the article recommends stages, in a stepwise infographic summarized in *Figure 7* below, to be completed prior to a diagnosis. As seen in the infographic, the initial diagnosis of dementia should include cognitive tests, which can include a series of questions, memorization exercises, and simple tasks, such as clock drawing. Cognitive tests include the Mini-Mental State Exam (MMSE; short set of questions), Clinical Dementia Rating Scale (CDR-SB or CDR-GS; measures 4 cognitive domains and 3 functional domains), Montreal Cognitive Assessment (MoCA; checks language, memory, orientation, visual and spatial thinking), Quick Dementia Rating System (QDRS; for comprehensive diagnosis and staging), and Repeatable Battery for Assessment of Neuropsychological Status (RBANS; measures attention, language, spatial/constructional abilities, intermediate and delayed memory).

Aduhelm has no listed contraindications. Warnings and precautions are significant for hypersensitivity reactions and amyloid related imaging abnormalities (ARIA). ARIA with edema (ARIA-E) ARIA with hemosiderin deposition (ARIA-H), which includes microhemorrhage and superficial siderosis are subtypes of ARIA. ARIA-E can be observed on MRI as brain edema or sulcal effusions. ARIA-H can occur spontaneously in patients with Alzheimer's disease, however ARIA-H usually occurs in association with an occurrence of ARIA-E in patients taking monoclonal antibodies against beta amyloid. ARIA is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. A causal relationship between ARIA and fatal outcomes has not been established, however fatal events in the setting of ARIA have occurred rarely. ARIA symptoms may include headache, confusion, visual changes, dizziness, nausea, gait difficulty and neurologic defects, which usually resolve over time. Common adverse events, including ARIA-E and ARIA-H are summarized in Figure 6 above. Of the 1105 patients treated with Aduhelm, 110 (10%) had symptomatic ARIA and 0.3% had serious symptoms associated with ARIA.

The incidence of symptomatic ARIA was higher in ApoE ε4 homozygotes (16%) as opposed to heterozygote carriers (11%) and noncarriers (5%) in patient who received Aduhelm, although the incidence of serious adverse reactions with ARIA-E was similar across all three groups (2%, 1%, 2%, respectively). The prescribing information states testing for ApoE ε4 carrier status should be considered to inform of the risk of developing ARIA. The majority of ARIA-E occurred early in treatment (within first 8 doses), however ARIA can occur at any time and can be recurrent. ARIA-E resolved in 98% of cases after detection, while the prescribing information does not comment on resolution of ARIA-H in trials.

There was no increased risk of ARIA or intracerebral hemorrhage in patients who received Aduhelm and an antithrombotic medication versus patients who received placebo and an antithrombotic medication. The majority of the exposures were to aspirin, and few patients were exposed to antiplatelet or anticoagulant drugs, limiting any meaningful conclusions about the risk of ARIA or intracerebral hemorrhage in patients taking other antiplatelet or anticoagulant drugs. Caution should be exercised

when considering the administration of antithrombotics or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with Aduhelm. Caution should be exercised when considering Aduhelm in patients with prior intracerebral hemorrhage greater than 1 cm in diameter, more than 4 microhemorrhages, superficial siderosis, and history of diffuse white matter disease. The prescribing information recommends baseline brain MRI and periodic monitoring with MRI, enhanced clinical vigilance for ARIA in the first 8 doses, and if symptoms are suggestive of ARIA, clinical evaluation should be performed, including MRI if indicated. There is limited experience in continuing Aduhelm in symptomatic ARIA-E or asymptomatic moderate to severe ARIA-E. The prescribing information does have dosing recommendations for varying severities of ARIA-E and ARIA-H. A summary of dosing recommendations in ARIA-E and ARIA-H is listed in the prescribing information.

In clinical trials, 5% (66 of 1386) of patients in the 10 mg/kg group withdrew due to adverse reactions. The most common reaction leading to a withdrawal was ARIA-H superficial siderosis. Common adverse reactions are summarized in *Figure 6* above. There is not adequate data for Aduhelm use in pregnant women or in pediatrics. No drug interactions are listed in the prescribing information.

Dr. Glenn Finney, Geisinger Director of Neurology, suggests there is a consensus between the manufacturer, the Alzheimer's Association, and professionals in the area of dementia that only patients that resemble the study population should be considered for Aduhelm at this time. The population to receive Aduhelm includes: 1) Must be able and willing to have serial MRIs of the brain done, 2) Should have evidence of abnormal amyloid in the central nervous system, 3) Should be in the mildest stages of cognitive decline (mild cognitive impairment to mild stage dementia).

Dr. Bradford C. Dickerson, professor of neurology, Harvard Medical School, recommends the ideal population to receive Aduhelm is patients with a diagnosis of Mild Cognitive Impairment likely due to AD (Albert et al., 2011) or mild dementia likely due to AD (McKhann et al., 2011) with biomarker evidence of cerebral amyloidosis based on CSF or amyloid PET. Dr. Dickerson also recommends the diagnosis of AD should be made as early as possible after symptom onset. He recommends confirmatory biomarker diagnosis of cerebral amyloidosis since some patients who present with symptoms consistent with AD do not have elevated amyloid and therefore likely do not have a diagnosis of AD and would not benefit from Aduhelm. If Aduhelm therapy is to be potentially helpful, it should be started as early as possible after diagnosis. Lastly, Dr. Dickerson suggested it would be helpful to have a follow-up amyloid biomarker to confirm that the primary biological target of the treatment is being reduced. He also states it would be helpful to have follow-up cognitive testing and functional assessment to determine whether the patient's trajectory of decline is being slowed relative to their trajectory prior to starting the treatment (if that information is available).

The National Institute on Aging and Alzheimer Association (NIA-AA) created a workgroup in 2011 to develop criteria for the symptomatic predementia phase of Alzheimer's. The workgroup created core clinical criteria to be used by healthcare providers without access to imaging and cerebrospinal fluid measures. The clinical criteria for MCI includes: A concern regarding cognition or observed, objective evidence of impairment in domains that is not explained by age or education, preservation of independence in functional abilities, and not demented. Differentiation of AD from other systemic or brain diseases is recommended. Other causes can include Parkinsonism, vascular cognitive impairment, prominent behavior or language disorders, prion disease, neoplasm or metabolic disorders. Lastly, mutations in APP, PS1 and PS2 can indicate MCI is most likely the prodrome to AD dementia. The workgroup states that biomarkers can be used to create increasing levels of certainty that AD pathology is the cause. Amyloid beta and neuronal injury (tau, FDG and sMRI) are two biomarkers that are considered to be the determinant factors for level of certainty, per NIA-AA workgroup guidelines.

The NIA-AA charged a workgroup in 2011 to develop and refine criteria for all-cause dementia and AD dementia. Several changes were made to the currently existing clinical criteria, as well as the addition of biomarkers for enhancement of specificity. The goal of the workgroup was to make criteria flexible enough to be used by healthcare professionals of varying access to neuropsychological testing. The determination of dementia from MCI includes if there is significant interference in the ability to function at work or in usual daily activities. The criteria for determining dementia can be found in the guidelines,

differentiating severity of dementia was beyond the scope of the workgroup. In terms of biomarkers, the workgroup states amyloid beta can be detected by low CSF-$A\beta_{42}$ or a positive PET scan, and neuronal injury biomarkers include elevated CSF tau (total tau and p-tau), decreased fluorodeoxyglucose (FDG)-PET and sMRI. These biomarkers, as indicated in MCI, can increase the certainty that dementia is following AD pathophysiology. If amyloid beta and neuronal injury biomarker results are negative, a diagnosis of dementia unlikely due to AD should be made regardless of meeting clinical criteria for dementia caused by AD.

The NIA-AA charged a workgroup in 2018 to complete a “research framework” for defining and staging the disease across its entire spectrum. The research framework is not to be used as diagnostic criteria or guidelines until it can be thoroughly examined and modified. The workgroup states an individual with only biomarker evidence of Aβ deposition and normal tau would be labeled with “Alzheimer’s pathologic change”. An individual with both Aβ and pathologic tau would be labeled with “Alzheimer’s disease”, representing a spectrum rather than separate entities, applied independently of symptoms. If an individual does not have either Aβ deposition or pathologic tau, then they are not considered to be apart of the Alzheimer’s continuum. The workgroup documents the syndromal staging of the cognitive continuum, independent of biomarkers, which defines mild cognitive impairment and dementia. The workgroup goes on to define stage 4 as “mild dementia” and defines it as “clearly evident functional impact on daily life, affecting mainly instrumental activities. No longer fully independent/requires occasional assistance with daily life activities.”

The controversies surrounding Aduhelm are summarized above, and include a broad label, lack of prescribing requirements, accelerated approval, FDA Advisory Committee vote and feedback, government review, drug cost, reimbursement, patient cost, and sites of care. Aduhelm’s label does not require patients to have confirmed amyloid pathology, does not indicate how to identify the target population to treat, and does not provide guidance on how to measure clinical efficacy once started on Aduhelm. In an unprecedented way, the FDA decided to add clarification to the labeled indication 30 days after the original approval to indicate only patients with MCI and mild dementia stage of disease should receive treatment. The accelerated approval was based on the ability to lower amyloid, which the FDA states is “reasonably likely” to predict clinical benefit. The FDA’s Peripheral and Central Nervous System Drugs Advisory Committee voted 10 to 0 against Aduhelm, and since the FDA approval, three members have quit the committee due to their views not being taken into consideration. Regarding the approval process, the Oversight Committee and the Energy and Commerce Committee conducted a joint investigation in the House of Representatives (see results below). Finance Committee member Ron Wyden has spoken out against the price and has been asked by U.S. Senate members Elizabeth Warren and Bill Cassidy to convene hearings. The FDA conducted an internal federal investigation on staff and the interactions they had with Biogen. The Institute for Clinical and Economic Review (ICER) reported that despite uncertainty surrounding trial results, that a price between $3,000 and $8,400 annually would make Aduhelm cost-effective for patients with early AD. Aduhelm has the potential to double the $37 billion that Medicare currently spends per year on all Part B drugs combined. Also, Medicare beneficiaries would be required to pay more than $10,000 each year to receive Aduhelm in addition to any noncovered amyloid PET scans. Finally, there may not be enough specialists (e.g. neurologists, geriatricians, and geriatric psychiatrists) to service the 1-2 million patients that can potentially receive Aduhelm.
The Committee on Oversight and Reform and the Committee on Energy and Commerce completed an 18-month investigation in December 2022. They uncovered the FDA’s interactions with Biogen were atypical and failed to follow protocol. All interactions between the FDA and drug sponsor are meant to be documented, however the investigation revealed 66 additional calls and emails were not appropriately documented. In addition, Biogen and the FDA jointly collaborated on a briefing document where the FDA helped to draft Biogen’s responses to then take to the Peripheral and Central Nervous System Drugs (PCNS) Advisory Committee meeting. The briefing document also did not represent the differing views within the FDA. The FDA’s own internal review stated this “was not an appropriate approach in this instance.” In addition, the FDA pivoted to using the accelerated approval pathway on a substantially abbreviated timeline. The FDA then approved a broad indication for Aduhelm, which Biogen accepted despite their own reservations about the lack of evidence of clinical benefit for patients outside the disease severity seen in clinical trials. Related to pricing, Biogen estimated the cost of Aduhelm to Medicare would be $12 billion in one year (or 36% of Medicare’s 2018 Part B budget and knew that early

pricing models showed some Medicare patients would struggle to afford the medication. Lastly, Biogen planned to spend billions on marketing even though the financial impact on patients and the health care system was expected to be large.

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

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

Financial Discussion: Given that the clinical benefit of Aduhelm isn't well supported, is Leqembi better clinically and can we consider preferring the other product based on efficacy? As of right now they're both approved through accelerated approval, but in general most people would likely agree that Leqembi has better efficacy results compared to Aduhelm. If Leqembi is fully approved in the future, it will be likely that Leqembi will be clinically superior to Aduhelm. Because the outcomes of current clinical trials measured for both products were the same, we don't have the data to support at this point. Additional approval for Leqembi is anticipated in the next two months and policy changes may be necessary. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Aduhelm is a medical benefit which will be excluded from coverage for the Commercial, Exchange, and CHIP lines of business.

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

LEQEMBI (lecanemab-irmb)

Review: Leqembi is an amyloid beta-directed antibody indicated for the treatment of Alzheimer's disease (AD). Treatment should be initiated in patients with mild cognitive impairment (MCI) or mild dementia stage of disease (the population studied in clinical trials). There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied. The indication was approved under accelerated approval based on the reduction in amyloid beta plaques observed, and continued approval may be based upon confirmation of clinical benefit in confirmatory trials. The recommended dose of Leqembi is 10mg/kg to be given over approximately one hour, once every two weeks. Leqembi is supplied in either one of two cartons. One carton (NDC 62856-215-01) contains one single-dose vial at a strength of 500mg/5mL (white cap). A second carton (NDC 62856-212-01) contains one single-dose vial at a strength of 200mg/2mL (dark grey cap). Leqembi is the second anti-amyloid monoclonal antibody approved for AD and the second drug approved to slow the progression of AD. The first anti-amyloid monoclonal antibody being Biogen's Aduhelm, which received a controversial approval in June 2021.

Alzheimer's disease (AD) is a progressive, irreversible neurodegenerative disease that causes cognitive, functional, and behavioral impairments. AD is the most common cause of dementia, causing an estimated 60% to 80% of cases. About 6.5 million Americans are estimated to have Alzheimer's dementia, with 5 million Americans estimated to have mild cognitive impairment (MCI) due to AD. Eisai estimates that about 100,000 patients will be eligible for Leqembi within 3 years, while an estimated 2.5 million patients will be eligible for Leqembi within about 7 years (2030). Projected patients with AD is summarized in *Figure 2* above. Average survival time after a diagnosis of AD is 8-10 years, dependent upon disease progression and age at onset of symptoms.
AD is thought to be caused by the progressive accumulation of amyloid beta (Aβ) plaques and neurofibrillary tangles (NFTs), formed by aggregated tau protein. The mechanism of action in the prescribing information states that the accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of AD. Leqembi is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody which is directed against aggregated soluble and insoluble forms of amyloid beta, thereby

reducing amyloid beta plaques, which has been observed in clinical studies. Before the approval of Aduhelm, amyloid levels were only measured in clinical trials, however now measurement of cerebrospinal fluid (CSF) in combination with MRI has become the standard for diagnosis of AD when considering an anti-amyloid antibody. To measure amyloid, the accepted methods are either a positron emission tomography (PET) scan or a CSF analysis from a lumbar puncture. CSF tests are often not the method used due to the invasive nature of a lumbar puncture. Blood-based marker (BBM) tests are being studied and developed, but they are not ready for widespread use in clinical practice to replace the invasive or expensive tests. Biomarkers used in an AD diagnosis are summarized in *Table 1* above.

Specifying the stage of disease is important when diagnosing AD as it relates to Leqembi. AD starts with an asymptomatic phase then progresses to MCI, then progresses to AD dementia. The asymptomatic phase (preclinical AD) consists only of biomarker evidence of AD and typically lasts for 6-10 years. MCI due to AD typically includes initial clinical symptoms of short-term memory impairment, followed by subsequent decline in additional cognitive domains. AD dementia will include severe cognitive deficits that interfere with social functioning and will require assistance with activities of daily living. Several organizations define the AD stages using different terminology, which is summarized in *Figure 3* above. Another portion of the initial diagnosis of dementia is cognitive tests, which can include a series of questions, memorization exercises, and simple tasks, such as clock drawing. Cognitive tests include the Mini-Mental State Exam (MMSE; short set of questions), Clinical Dementia Rating Scale (CDR-SB or CDR-GS; measures 4 cognitive domains and 3 functional domains), Montreal Cognitive Assessment (MoCA; checks language, memory, orientation, visual and spatial thinking), Quick Dementia Rating System (QDRS; for comprehensive diagnosis and staging), and Repeatable Battery for Assessment of Neuropsychological Status (RBANS; measures attention, language, spatial/constructional abilities, intermediate and delayed memory).

Leqembi has no listed contraindications. Warnings and precautions are significant for infusion related reactions and Amyloid Related Imaging Abnormalities (ARIA). ARIA with edema (ARIA-E) ARIA with hemosiderin deposition (ARIA-H), which includes microhemorrhage and superficial siderosis are subtypes of ARIA. ARIA-E can be observed on MRI as brain edema or sulcal effusions. ARIA-H can occur spontaneously in patients with Alzheimer's disease, however ARIA-H usually occurs in association with an occurrence of ARIA-E in patients taking monoclonal antibodies against beta amyloid. ARIA is usually asymptomatic, although serious and life-threatening events, including seizure and status epilepticus, rarely can occur. ARIA symptoms may include headache, confusion, visual changes, dizziness, nausea, gait difficulty and neurologic defects, which usually resolve over time. Of the 161 patients treated with Leqembi, 3% (5/161) had symptomatic ARIA. Asymptomatic or symptomatic ARIA-E was observed in 10% (16/161) of Leqembi treated patients and 1% (2/245) of placebo treated patients. Asymptomatic or symptomatic ARIA-H was observed in 6% (10/161) of Leqembi treated patients and 5% (12/245) of placebo treated patients. There was no increase in isolated ARIA-H in the Leqembi group compared to the placebo group. In Study 201, the incidence of ARIA was higher in ApoE e4 homozygotes as compared to heterozygotes and noncarriers in patients receiving Leqembi. Of the 5 patients with symptomatic ARIA in trials, 4 were ApoE e4 homozygotes, and 2 of the 4 homozygotes experienced severe symptoms. The prescribing information states testing for ApoE e4 carrier status should be considered to inform of the risk of developing ARIA. Radiographic ARIA-E resolved on MRI by some time after detection for 94% of patients, while the prescribing information does not comment on resolution rate of ARIA-H. There was no increased risk of ARIA or intracerebral hemorrhage in patients who received Leqembi and an antithrombotic medication versus patients who received placebo and an antithrombotic medication. The majority of the exposures were to aspirin, and few patients were exposed to antiplatelet or anticoagulant drugs, limiting any meaningful conclusions about the risk of ARIA or intracerebral hemorrhage in patients taking other antiplatelet or anticoagulant drugs. Caution should be exercised when considering the administration of antithrombotics or a thrombolytic agent (e.g., tissue plasminogen activator) to a patient already being treated with Leqembi. Additionally, caution should be exercised when considering Aduhelm in patients with prior intracerebral hemorrhage greater than 1 cm in diameter, more than 4 microhemorrhages, superficial siderosis, evidence of vasogenic edema, evidence of cerebral contusion, aneurysm, vascular malformation, infective lesions, multiple lacunar infarcts or stroke involving a major vascular territory, and severe small vessel or white matter disease. There is no experience in patients who continued dosing through symptomatic ARIA-E or through asymptomatic, but

radiographically severe, ARIA-E. There is limited experience in patients who continued dosing through asymptomatic but radiographically mild to moderate ARIA-E, and dosing in patients with recurrent ARIA-E. A summary of dosing recommendations in ARIA-E and ARIA-H is listed in the prescribing information.

Common adverse events were infusion-related reactions (Leqembi 20%; placebo 3%), headache (Leqembi 14%; placebo 10%), ARIA-E (Leqembi 10%; placebo 1%), cough (Leqembi, 9%; placebo, 5%) and diarrhea (Leqembi, 8%; placebo, 5%). Treatment was discontinued in 6% of patients receiving placebo and 15% of patients receiving Leqembi. There is not adequate data for Leqembi use in pregnant women or in pediatrics. No drug interactions are listed in the prescribing information.

The National Institute on Aging and Alzheimer Association (NIA-AA) created a workgroup in 2011 to develop criteria for the symptomatic predementia phase of Alzheimer's. The workgroup created core clinical criteria to be used by healthcare providers without access to imaging and cerebrospinal fluid measures. The clinical criteria for MCI includes: A concern regarding cognition or observed, objective evidence of impairment in domains that is not explained by age or education, preservation of independence in functional abilities, and not demented. Differentiation of AD from other systemic or brain diseases is recommended. Other causes can include Parkinsonism, vascular cognitive impairment, prominent behavior or language disorders, prion disease, neoplasm or metabolic disorders. Lastly, mutations in APP, PS1 and PS2 can indicate MCI is most likely the prodrome to AD dementia. The workgroup states that biomarkers can be used to create increasing levels of certainty that AD pathology is the cause. Amyloid beta and neuronal injury (tau, FDG and sMRI) are two biomarkers that are considered to be the determinant factors for level of certainty, per NIA-AA workgroup guidelines.

The NIA-AA charged a workgroup in 2011 to develop and refine criteria for all-cause dementia and AD dementia. Several changes were made to the currently existing clinical criteria, as well as the addition of biomarkers for enhancement of specificity. The goal of the workgroup was to make criteria flexible enough to be used by healthcare professionals of varying access to neuropsychological testing. The determination of dementia from MCI includes if there is significant interference in the ability to function at work or in usual daily activities. The criteria for determining dementia can be found in the guidelines, differentiating severity of dementia was beyond the scope of the workgroup. In terms of biomarkers, the workgroup states amyloid beta can be detected by low CSF-$A\beta_{42}$ or a positive PET scan, and neuronal injury biomarkers include elevated CSF tau (total tau and p-tau), decreased fluorodeoxyglucose (FDG)-PET and sMRI. These biomarkers, as indicated in MCI, can increase the certainty that dementia is following AD pathophysiology. If amyloid beta and neuronal injury biomarker results are negative, a diagnosis of dementia unlikely due to AD should be made regardless of meeting clinical criteria for dementia caused by AD.

The NIA-AA charged a workgroup in 2018 to complete a "research framework" for defining and staging the disease across its entire spectrum. The research framework is not to be used as diagnostic criteria or guidelines until it can be thoroughly examined and modified. The workgroup states an individual with only biomarker evidence of Aβ deposition and normal tau would be labeled with "Alzheimer's pathologic change". An individual with both Aβ and pathologic tau would be labeled with "Alzheimer's disease", representing a spectrum rather than separate entities, applied independently of symptoms. If an individual does not have either Aβ deposition or pathologic tau, then they are not considered to be apart of the Alzheimer's continuum. The workgroup documents the syndromal staging of the cognitive continuum, independent of biomarkers, which defines mild cognitive impairment and dementia. The workgroup goes on to define stage 4 as "mild dementia" and defines it as "clearly evident functional impact on daily life, affecting mainly instrumental activities. No longer fully independent/requires occasional assistance with daily life activities."

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

Clinical Discussion: Did clinical trials differentiate how they attributed brain volume loss due to Leqembi vs. the progressive nature of Alzheimer's disease. Study investigators are still unsure how to interpret the

loss of brain volume. No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

Outcome: Leqembi is a medical benefit and will be excluded from coverage for the Commercial, Exchange, and CHIP lines of business. Leqembi will be monitored and coverage adjusted as warranted.

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

REBYOTA (fecal microbiota, live-jslm)

Review: Rebyota is the first fecal microbiome therapy to be approved for the prevention of recurrence of *Clostridium difficil*e infections (CDI) in individuals 18 years of age and older, following antibiotic treatment for recurrent CDI. Rebyota is not indicated for the treatment of CDI. Rebyota is manufactured from human fecal matter sourced from qualified donors. The human fecal matter is tested for a panel of transmissible pathogens. Donors do not have dietary restrictions with respect to potential food allergens. The fecal microbiota suspension is the filtrate generated by processing the fecal matter in a pre-defined ratio with a solution of polyethylene glycol (PEG) 3350 and saline. Each 150 ml dose is Rebyota contains between $1x10^8$ and $5x10^{10}$ colony forming units (CFU) per mL of fecal microbes including > $1x10^5$ CFU/mL of *Bacteroides*, and contains not greater than 5.97 grams of PEG 3350 in saline. The mechanism of action of Rebyota has not been established.

CDI is one of the most common hospital-acquired infections and is an increasingly frequent cause of morbidity and mortality among older adult hospitalized patients. *Clostridium difficil*e colonizes the human intestinal tract after the normal gut flora has been disrupted (frequently in association with antibiotic therapy) and is the causative organism of antibiotic-associated colitis. *Clostridioides difficile* produces a toxin that causes diarrhea and inflammation of the colon.

The diagnosis of CDI should be suspected in patients with acute diarrhea (≥ 3 loose stools in 24 hours) with no obvious alternative explanation, particularly in the setting of relevant risk factors (including recent antibiotic use, hospitalization, and advanced age). Patients with suspected CDI should be placed in contact precautions until test results return. There are numerous laboratory stool tests available to diagnose CDI. These include: NAAT, enzyme immunoassay for *C. difficile* toxin A and B, enzyme immunoassay for *C. difficile* GDH, cell culture cytotoxicity assay, and selective anaerobic culture.

Recurrent CDI is defined by resolution of CDI symptoms while on appropriate therapy, followed by reappearance of symptoms within two to eight weeks after treatment has been stopped. Up to 25% of patients experience recurrent CDI within 30 days of treatment. Once patients have experienced one recurrence, they are at significantly increased risk for further recurrences.

The American College of Gastroenterology (ACG) recommends that oral metronidazole, oral vancomycin, and oral fidaxomicin all have a role in first-line treatment of initial nonsevere CDI. Metronidazole should not be used for the treatment of severe CDI because it was shown to be inferior to oral vancomycin and oral fidaxomicin in multiple studies. Another course of antibiotics is generally required for the treatment of a first recurrence of CDI, and the choice of treatment is dependent on what was used to treat the initial episode. Preventative strategies for recurrent CDI include fecal microbiota transplant (FMT), which is recommended by the ACG for recurrent CDI. Other preventative strategies include prophylactic oral vancomycin and Zinplava.

Dr. Jeff Hosry, infectious disease specialist at Geisinger Wyoming Valley, was consulted regarding the role Rebyota may have in clinical practice. He explained that as the stool transplant bank was depleted due to Covid, we were unable to do fecal transplant at Geisinger, therefore all possible medical options

were exhausted. In 2 years at Geisinger, Dr. Hosry encountered probably up to 5 patients with more than 3 recurrences of CDI, and all of them improved with a prolonged taper of oral vancomycin and Zinplava, which Dr. Hosry feels is effective in preventing recurrences of CDI. He stated that he will continue to do the same with oral vancomycin and Zinplava, and if that fails, he will proceed with a possible GI referral for Rebyota.

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

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

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

Outcome: Rebyota will be a medical benefit and will require prior authorization. Rebyota will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Rebyota will process at the specialty tier or the brand non-preferred tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- Documentation of age greater than or equal to 18 years **AND**
- Prescribed by or in consultation with an infectious disease specialist or gastroenterologist **AND**
- Medical record documentation that Rebyota will be used for the prevention of recurrence of C. difficile infections **AND**
- Medical record documentation of a diagnosis of recurrent C. difficile infection based on the results of an appropriate laboratory stool test within 30 days of prior authorization request **AND**
- Medical record documentation that an appriopriate standard-of-care antibacterial regimen was used for the treatment of recurrent C. difficile infection (e.g., oral fidaxomicin, oral vancomycin, oral metronidazole) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Zinplava **AND**
- Medical record documentation of a prescribed dose and administration that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

Authorization duration: If approved, authorization shall be for the authorization of one (1) Rebyota dose with an authorization duration of 30 days.

NOTE: Rebyota is not indicated for the treatment of C. difficile infection infections. There is no information currently available indicating that an individual is unable to receive more than one dose of Rebyota.

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

TZIELD (teplizaumab-mzwv)

Review: Tzield (teplizumab-mzwv) is indicated to delay the onset of Stage 3 Type 1 Diabetes (T1D) in adults and pediatric patients aged 8 years and older with Stage 2 T1D. Stage 2 T1D should be confirmed by documenting at least 2 positive pancreatic islet autoantibodies in those who have dysglycemia without overt hyperglycemia using an oral glucose tolerance test (OGTT) or alternative method if appropriate and OGTT is not available. If the patient meets the criteria for a diagnosis of Stage 2 T1D, providers should ensure that the clinical history of the patient does not suggest Type 2 Diabetes (T2D). Prior to initiation of Tzield, providers should obtain a complete blood count (CBC) and liver enzyme tests. Tzield is administered by intravenous (IV) infusion (over a minimum of 30 minutes) once daily for 14 days. Patients taking Tzield should be premedicated with: (1) a non-steroidal anti-inflammatory drug (NSAID) or

acetaminophen, (2) an antihistamine, and/or (3) an antiemetic before each Tzield dose for at least the first 5 days of the 14-day treatment course.

The Centers for Disease Control and Prevention (CDC) describes T1D as occurring when your pancreas doesn't make insulin or makes very little insulin. T1D was previously called insulin-dependent or juvenile diabetes since it usually develops in children, teens, and young adults, but it can happen at any age. T1D is an autoimmune reaction that destroys the beta cells in the pancreas that are responsible for making insulin. According to the American Diabetes Association (ADA), management of an adult with suspected T1D begins by measuring islet autoantibodies. If the autoantibodies are negative, based on age, the differential is maturity onset diabetes of the young (MODY) or T2D. If MODY and T2D are ruled out, a clinical diagnosis of T1D can be assumed. The ADA has not yet updated the guidelines to include the use of Tzield.

There are no contraindications for use of Tzield. Tzield has warnings and precautions for cytokine release syndrome, serious infections, lymphopenia, hypersensitivity reactions, and vaccinations. The most common adverse reactions were lymphopenia, rash, leukopenia, and headache.

The safety and effectiveness of Tzield have not been established in pediatric patients younger than 8 years of age. The safety and effectiveness of Tzield to delay the onset of Stage 3 T1D have been established in pediatric patients 8 years of age and older with Stage 2 T1D. Adverse reactions observed in pediatric patients 8 years of age and older who received Tzield were consistent with those reported in adult patients. Stage 2 T1D is largely a condition that occurs in pediatric and younger adult patients. Clinical studies of Tzield to delay the onset of Stage 3 T1D did not include patients 65 years of age and older.

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

Clinical Discussion: Do we need to add a note or authorization duration to ensure members are not approved for more than one dose per lifetime? Leslie and Keith will work together to craft language to include. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

Outcome: Tzield is a medical benefit. Tzield will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Tzield will process at the specialty tier or the brand non-preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of Stage 2 Type 1 Diabetes (T1D) confirmed by both of the following:
    - Medical record documentation at least two positive pancreatic islet cell autoantibodies **AND**
    - Medical record documentation of dysglycemia without overt hyperglycemia using an oral glucose tolerance test (OGTT) [if an OGTT is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate]

  AND
- Medical record documentation **OR** provider attestation that the clinical history of the patient does not suggest Type 2 Diabetes (T2D) **AND**
- Medical record documentation that member is 8 years of age or older **AND**
- Medical record documentation that Tzield is prescribed by or in consultation with an endocrinologist

NOTE: Pancreatic Islet Autoantibodies include:

- Glutamic Acid Decarboxylase 65 (GAD) Autoantibodies

- Insulin Autoantibodies (IAA)
- Insulinoma-Associated Antigen 2 Autoantibodies (IA-2A)
- Zinc Transporter 8 Autoantibodies (ZnT8A)
- Islet Cell Autoantibodies (ICA)

AUTHORIZATION DURATION: 14 days

GPI Level: GPI- 12

Require RPH Sign off: Yes

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

XACIATO (clindamycin phosphate)

Review: Xaciato is a lincosamide antibacterial indicated for the treatment of bacterial vaginosis (BV) in female patients 12 years of age and older. Xaciato is supplied as a clear, colorless, viscous vaginal gel that contains 2% clindamycin (present as clindamycin phosphate) in an 8 g tube. One user-filled single-dose disposable applicator delivers 5 g of gel containing 100 mg of clindamycin. The recommended dosage of Xaciato is one applicatorful administered once intravaginally as a single dose at any time of the day. Current regimens for BV include metronidazole 500mg twice daily for 7 days, metronidazole gel 0.75% intravaginally once daily for 5 days, and clindamycin cream 2% once at bedtime for 7 days. Solosec (secnidazole) and tinidazole are also alternative options for treatment but are higher cost and lack long-term outcomes compared with the other regimens. Xaciato affords low peak serum levels and systemic exposure of clindamycin compared to an oral or intravenous dose of clindamycin. Data, however, from well-controlled trials directly comparing orally administered clindamycin to vaginally administered clindamycin are not available. Data comparing the efficacy of single-day gel with multiday regimens are also not yet available. Xaciato is not included in the CDC's Sexually Transmitted Infections Treatment Guidelines as a recommended regimen or an alternative regimen and given the availability of low-cost generics, Xaciato is not considered first-line.

Adverse reactions were reported by 76/202 (38%) of patients who received Xaciato and 28/103 (27%) of patients who received placebo. The most common side effects (occurring in >2% of patients and at a higher rate in the Xaciato group) included vulvovaginal candidiasis (17% [35/202]) and vulvovaginal discomfort (6% [13/202]).

Contraindications include history of hypersensitivity to clindamycin or lincomycin. Other warnings and precautions include *Clostridioides difficile*-associated diarrhea (CDAD) and decreased efficacy of polyurethane condoms when used during Xaciato treatment. Xaciato has not been studied in pregnant women, however based on the low systemic absorption of Xaciato, maternal use is not likely to result in significant fetal exposure of the drug. The safety and effectiveness of Xaciato have been established in females aged 12 years and older for the treatment of BV. Use of Xaciato for this indication is supported by the extrapolation of clinical trial data from adequate and well-controlled clinical studies in adult women. The safety and effectiveness of Xaciato have not been established in pediatric patients younger than 12 years of age for the treatment of BV. Clinical studies with Xaciato did not include any subjects 65 years of age or older to determine whether they respond differently than younger subjects.

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

Clinical Discussion: No comments or questions. The committee voted to accept the recommendations as presented by majority vote. One was opposed.

Financial Discussion: No comments or questions. The committee voted to accept the recommendations as presented by majority vote. One was opposed.

Outcome: Xaciato is a pharmacy benefit and will not be added to the Commercial/Exchange/CHIP formularies. The following prior authorization criteria will apply:

- Medical record documentation of bacterial vaginosis **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives, one of which must be clindamycin 2% vaginal cream

GPI Level: GPI-12

Quantity Limit: 5 grams (1 tube) per 30 days

Formulary Alternatives: metronidazole tablets, metronidazole vaginal gel, clindamycin vaginal cream, Clindesse vaginal cream, Cleocin vaginal suppositories, tinidazole

Require RPH Sign off: No

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

CAYSTON (aztreonam inhalation solution)

Review: Cayston is a monobactam antibacterial FDA approved and indicated for improvement in respiratory symptoms in cystic fibrosis (CF) patients with Pseudomonas aeruginosa. It should only be used in those with confirmed Pseudomonas aeruginosa to maintain effectiveness and reduce drug resistance. Use has not been established or approved in those below 7 years of age.
Cayston is supplied as a 28-day supply kit containing 84 -75 mg single-use ampule vial with Cayston medication and 88- 1 mL ampule vials of sterile diluent packaged into 2 cartons containing 14 days-supply each. It is to be administered by inhalation only. Cayston should be stored in a refrigerator at 2oC to 8oC until needed. Reconstitution should only occur at time of administration. Reconstituted solution must be administered using the Altera Nebulizer System. To reconstitute, open one amber glass vial of Cayston by removing blue cap, metal ring, a gray rubber stopper. Twist tip off the diluent ampule and squeeze into glass vial. Rubber stopper should be replaced, and contents swirled until medication is dissolved.

Cayston is administered 3 times a day at least 4 hours apart for 28 days, followed by 28 days off therapy. Dosing is not based on weight or age. Patients should use a short-acting bronchodilator 15 minutes to 4 hours before Cayston administration or use long-acting bronchodilator 30 minutes to 12 hours before Cayston administration. To administer, pour reconstituted solution into handset of Altera Nebulizer System. Turn unit on and place mouthpiece of handset in mouth. Patient should breathe normally through mouth only for 2 to 3 minutes. It is noted that Cayston should not be mixed with any other drug in the nebulizer machine. If patient is taking multiple inhaled therapies, the recommended order of administration is bronchodilator, mucolytics, and lastly, Cayston.

Cystic fibrosis airways are particularly susceptible to P. aeruginosa, where prevalence increases with age. More than 60% of adults are chronically infected. Prophylactic antibiotics targeting P. aeruginosa is not recommended. Early eradication and treatment is recommended regardless of clinical symptoms or age when detection is made during routine 3 month sputum or throat swabs. If detected, 28-day course of inhaled tobramycin is used. And repeated if repeated cultures still show bacteria presence. With chronic P. aeruginosa infection, cyclic inhaled antibiotic treatment is recommended. First line therapy is inhaled tobramycin due to its' extensive studies and good safety record. Inhaled aztreonam lysine (Cayton) is a second-line alternative for those who do not tolerate tobramycin, have deteriorating pulmonary status despite tobramycin, or is or may soon become pregnant. Last line therapy due to lack of FDA approval is

colistin and is reserved for those who are not responding to or not tolerating tobramycin and aztreonam. For those with deteriorating pulmonary status or frequent exacerbations, tobramycin and aztreonam may be continuously alternated for 28-day periods.

Adverse reactions were evaluated in a placebo-controlled trial, as listed in the table.

Special considerations should be given to certain populations. For those who are pregnant or lactating, caution is advised due to insufficient data on associated risk and defects. However, it is preferred over the first line treatment, and has little absorption through its' route of inhaled administration. Clinical need and benefits of breastfeeding should be weighed when making decision. For pediatric patients, use is not advised in those under 7 years of age fur to lack of safety and effectiveness not established. For geriatric patients 65 and older, safety and effectiveness were not established, and caution should be taken. Cayston is okay in those with mild to severe renal impairment due to clinically irrelevant accumulation due to inhaled administration even though aztreonam is excreted via the kidneys.

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

Clinical Discussion: No comments or questions. The committee voted to accept the recommendations as presented by majority vote. One was opposed.

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

Outcome: Cayston is a pharmacy benefit that will not be added to Commercial, Exchange, or CHIP formularies. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of cystic fibrosis **AND**
- Medical record documentation that pseudomonas aeruginosa is positive in sputum, mouth swab or other cultures of the airway **AND**
- Medical record documentation that member is at least 7 years of age or older **AND**
- Prescription is written by a pulmonologist or infectious disease specialist **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to the use of tobramycin inhalation solution

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT: 84 vials per 56 days

Require RPh signoff: Yes

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

KORSUVA (difelikefalin)

Review: Korsuva is the first treatment for moderate-to-severe pruritis associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD). Currently, there are no formalized treatment guidelines for treatment of CKD-aP because of a lack of supportive evidence for use of currently utilized therapies.
The efficacy of Korsuva compared to placebo was evaluated in two randomized, double-blind, placebo-controlled trials in a total of 851 adult patients undergoing HD who had moderate-to-severe pruritis. Efficacy was assessed based on the proportion of patients achieving a 4-point or greater improvement from baseline in the weekly mean of the daily 24-hour WI-NRS score at Week 12. In trial one, 40% of patients treated with Korsuva achieved the primary endpoint compared to 21% of placebo treated

patients. In trial 2, 37% of patients treated with Korsuva achieved the primary endpoint compared to 26% of placebo treated patients. Itch reduction was seen by Week 4 and sustained through Week 12.

There are no black box warnings for Korsuva. Warnings and Precautions include dizziness, somnolence, mental status changes, and gait disturbances, including falls, and risk of driving and operating machinery. In clinical trials of Korsuva, 17% of patients randomized to receive Korsuva reported at least one of these adverse reactions compared to 13% of patients who received placebo. The most common adverse reactions were diarrhea, dizziness, nausea, gait disturbances, including falls, hyperkalemia, headache, somnolence, and mental status changes.

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

Clinical Discussion: No comments or questions. The committee voted to accept the recommendations as presented by majority vote. One was opposed.

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

Outcome: Korsuva is a medical benefit and will be added to the medical benefit cost share list. When Korsuva is processed at a Specialty Pharmacy, it will process on the specialty tier or brand non-preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Korsuva is prescribed by a nephrologist **AND**
- Medical record documentation of moderate-to-severe pruritis associated with chronic kidney disease (CKD-aP) **AND**
- Medical record documentation that member is undergoing hemodialysis **AND**
- Medical record documentation that the member was assessed for and determined to have no other causes of pruritis

GPI Level: GPI-12

Require RPH Sign off: Yes

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

TASCENSO ODT (fingolimod)

Review: Tascenso ODT is a sphingosine 1-phosphate receptor modulator and binds with high affinity to sphingosine 1-phosphate receptors. This in turn blocks lymphocytes from leaving the lymph nodes and reduces the number of lymphocytes in peripheral blood. It is believed that this decrease of lymphocyte migration into the central nervous system serves as the therapeutic mechanism of action for Tascenso ODT by reducing inflammatory damage to nerve cells.

Tascenso ODT is approved for the treatment of relapsing forms of multiple sclerosis including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients > 10 years of age. Tascenso ODT is available as a 0.25 mg and 0.5 mg orally disintegrating tablet. The recommended dosage for adults and pediatric patients (10 years of age and older) weighing more than 40 kg is dissolve 0.5 mg on tongue once daily with or without food. The recommended dosage for pediatric patients (10 years of age and older) weighing less than or equal to 40 kg is dissolve 0.25 mg on tongue once daily with or without food. Tascenso ODT requires first dose monitoring. It is recommended that patients undergo 6-hour monitoring after administration of the first dose of Tascenso ODT, if switching from 0.25 mg to 0.5 mg in pediatric patients or scenarios where there has been a therapy

interruption for greater than 14 days. This monitoring is done to ensure that if a patient begins to experience symptomatic bradycardia it can be managed with appropriate resources quickly. Some patients may be observed overnight if they have a higher risk of symptomatic bradycardia, heart block, prolonged QTc interval or if they are taking medications with known risk of torsades de pointes. Tascenso ODT contains the same active ingredient as Gilenya but provides a different formulation of the widely used MS medication. Gilenya's package insert does not currently provide any guidance on whether it can be crushed or chewed. Tascenso ODT is the first orally disintegrating tablet for the treatment of MS and may be beneficial for patients with issues swallowing.

No specific dosage adjustments are recommended for the geriatric population or those with renal or hepatic impairment but per the package insert Tascenso ODT should be used with caution in these patients and they should be monitored closely throughout therapy. Patients with severe hepatic impairment may see an increase in fingolimod exposure which can increase the risk of adverse reactions. Tascenso ODT can increase the risk of infections due to its mechanism of action and for this reason live vaccines should not be administered while on Tascenso ODT therapy.

A complete cardiac evaluation is needed prior to initiating therapy. Warnings and precautions include: Bradyarrhythmia's and AV blocks, infections, PML, macular edema, liver injury, posterior reversible encephalopathy syndrome, respiratory effects, fetal risk, severe increase in disability after stopping Tascenso ODT, tumefactive MS, increased blood pressure and malignancies.

Contraindications include: myocardial infarction, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, NYHA class III/IV heart failure in the past 6 months, Mobitz type II second- or third-degree AV block or sick sinus syndromes (unless patient has a functioning pacemaker); baseline QTc interval of 500 msec or more, and concurrent use of class Ia or III antiarrhythmics.

To note, Tascenso ODT has an accompanying patient support program, Cycle Vita, which assists patients in getting their medications and provides educational support. This includes initial evaluation prior to therapy initiation. I also wanted to mention that per IPD, Gilenya 0.25 mg will have loss of exclusivity in 2024.

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

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

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

Outcome: Tascenso ODT is a pharmacy benefit and will not be added to the Commercial/Exchange/CHIP formularies. The following prior authorization criteria will apply:

- Medical record documentation that the prescribed dose is appropriate for patients age and weight **AND**
- Medical record documentation of trouble swallowing **OR**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to fingolimod capsules (generic Gilenya)

***NOTE:** 0.25 mg strength is indicated for those greater than or equal to 10 years of age with a weight less than or equal to 40 kg.
MediSpan Authorization Level: GPI-12

Quantity Limit: 1 tablet per day

RPh sign-off: yes

Other Recommendations:

- Fingolimod 0.5 mg capsules are now available as a generic and it is recommended to move Gilenya 0.5 mg capsules to NF for Commercial/Exchange/CHIP and Gold
- Generic Aubagio (Teriflunomide) is also now available in 7 mg and 14 mg strengths, I recommend adding Teriflunomide to the generic tier. In turn I also recommend removing Brand Aubagio from formulary for Commercial/Exchange/CHIP and Medicare.

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

SKYSONA (elivaldogene autotemcel)

Review: Skysona is indicated to slow the progression of neurologic dysfunction in male patients 4 to 17 years of age with early, active cerebral adrenoleukodystrophy (CALD). Early, active CALD refers to asymptomatic or mildly symptomatic (neurologic function score ≤1) males who have gadolinium enhancement on brain MRI and Loes scores of 0.5 to 9. Skysona was approved under the accelerated approval pathway, and continued approval will be based on longer term confirmatory trials. Adrenoleukodystrophy (ALD) is a rare genetic condition characterized by progressive loss of white matter in the nervous system and degradation of adrenal glands. It is caused by a mutation in the ABCD1 gene on the X chromosome. The diagnosis of ALD can be established based on clinical findings, elevated very-long-chain fatty acids (VLCFAs) and confirmed via genetic testing. CALD is a specific subtype of ALD, and the most severe and neurodegenerative form of the disease. Boys with CALD typically present with neurologic symptoms between 3 and 10 years old. After an initial period of normal development, symptoms typically include behavioral problems, such as ADHD and learning disabilities. Progressive symptoms include diminished visual acuity, hearing loss, gait instability, weakness and stiffness of limbs, and seizures. Within 2-3 years symptoms progress to a loss of most neurologic function and total disability, with death often occurring by the second decade of life. The overall prevalence of adrenoleukodystrophy is approximately 1 in 17,000 newborns. According to bluebird's estimates, about 40 patients are diagnosed with CALD in the United States each year.

Allogenic hematopoietic stem cell transplantation (HSCT) is the treatment of choice for boys with early stages (no or mild symptoms) of cerebral involvement in ALD who have an appropriate matched related donor. Observational studies have reported 5- and 8-year survival rates of 56% in patients treated with HSCT (without regard to severity of disease at time of transplant) with 5-year survival rates as high as 92% among patients treated at very early stages of the illness. In addition to the risks associated with the required myeloablative therapy prior to transplant, there are additional transplant-related risks, including graft versus-host disease (GVHD), graft failure, and transplant-related mortality. Risks are higher when matched unrelated donors and unmatched donors are used and when patients are older and have more advanced disease at the time of transplant. Bluebird has stated that only about 30% of patients with CALD are able to find a matched sibling donor.

With newborn screening, some patients can be diagnosed with CALD before symptoms occur. If the results of the newborn screening are positive for CALD, patients can be monitored before the onset of symptoms, increasing their chance of undergoing HSCT in time to stabilize the disease. Early diagnosis is critical, as untreated CALD is life threatening and HSCT offers little clinical benefit for patients with late-stage disease. Approximately 50% of boys with CALD are diagnosed too late to be effectively treated with HSCT. In February 2016, the U.S. Department of Health and Human Services recommended that screening for ALD be made a part of routine newborn screening. While Pennsylvania did adapt this recommendation and does mandate that screening for ALD be part of the newborn screening process, as of February 2023, 14 states (AK, AL, IA, HI, KS, LA, MD, MS, MT, ND, NV, SC, SD, WI) still have not initiated this recommendation and do not mandate routine screening. Besides HSCT, no other disease-modifying treatments have historically existed for CALD. Symptomatic and supportive treatments for CALD include physical therapy, psychological support, and special education.

Skysona is intended to be a one-time gene therapy and is designed to treat the underlying cause of CALD. Skysona adds functional copies of the ABCD1 cDNA into patients' hematopoietic stem cells (HSCs) through transduction of autologous CD34+ cells with a Lenti-D lentiviral vector (LVV). After Skysona infusion, transduced CD34+ HSCs engraft in the bone marrow and differentiate into various cell types, including monocytes (CD14+) capable of producing functional adrenoleukodystrophy protein (ALDP). Functional ALDP can then participate in the local degradation of very-long-chain fatty acids (VLCFAs), which is believed to slow or possibly prevent further inflammation and demyelination. Skysona is composed of one or two infusion bags which contain 4 to 30 × 106 CD34+ cells/mL suspended in cryopreservation solution. Each infusion bag contains approximately 20 mL. A single dose of Skysona contains a minimum of 5 × 106 CD34+ cells/kg suspended in cryopreservation solution. The dose is calculated based on the patient's weight prior to first apheresis. The target number of CD34+ cells to be collected is ≥ 12 X 106 CD34+ cells/kg. The minimum recommended dose is 5 × 106 CD34+ cells/kg.

In the two trials, the most common non-laboratory adverse reactions (all 20% or more) in patients treated with Skysona (between the start of conditioning and 24 months after Skysona administration) included mucositis, nausea, vomiting, febrile neutropenia, alopecia, decreased appetite, abdominal pain, constipation, pyrexia, diarrhea, headache, and rash. The most common grade 3/4 laboratory abnormalities (all 40% or more) included leukopenia, lymphopenia, thrombocytopenia, neutropenia, anemia, and hypokalemia. These reactions are comparable to that of the agents used for mobilization and conditioning. There are no contraindications, but several warnings and precautions for serious infections, prolonged cytopenias, delayed platelet engraftment, and risk of neutrophil engraftment failure. There is a Black Box warning for hematologic malignancy. Hematologic malignancy, including life-threatening cases of myelodysplastic syndrome, have occurred in patients treated with Skysona. The cancers appear to be the result of the Skysona lentiviral vector, Lenti-D, integration into proto-oncogenes. Patient should be monitored closely for evidence of malignancy through complete blood counts at least every 6 months and through assessments for clonal expansion or predominance at least twice in the first year and annually thereafter.

Patients should not take anti-retroviral medications for at least one month prior to initiating medications for stem cell mobilization and for the expected duration for elimination of the medications, and until all cycles of apheresis are complete because these medications may interfere with the manufacturing of the apheresed cells. Skysona also affects PCR assays for HIV and PCR-based assays should not be used to avoid false positives when testing for HIV in patients treated with Skysona.
Following completion of the two clinical trials, participants may enroll in LTF-304, a long-term follow-up study to continue monitoring safety and efficacy outcomes in boys treated with Skysona through 15 years post treatment. As a condition of the accelerated approval of Skysona, bluebird will provide confirmatory long-term clinical data to the FDA, including results of this ongoing study and data from commercially treated patients.

Currently Skysona is the only FDA approved treatment for CALD. Another drug, leriglitazone, is currently being studied for the same indication. Leriglitazone is an orally administered selective peroxisome proliferator-activated receptor (PPAR) agonist and metabolite of pioglitazone that aims to modify pathways leading to oxidative stress, neuroinflammation, mitochondrial dysfunction, demyelination, and axonal degeneration. The approval timeline for treatment of CALD is unclear at this time.

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

Clinical Discussion: Even though this is an inpatient medication, it is likely we will be consulted for approval prior to administration which is why it is necessary to create a policy. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

Outcome: Skysona will be a medical benefit, limited to administration in the inpatient hospital setting. Skysona will require a prior authorization with the following criteria and will be added to the medical benefit cost share list.

- Prescription written by a hematologist, neurologist and/or stem cell transplant specialist **AND**
- Medical record documentation that the patient is a male based on assigned sex at birth, age greater than or equal to 4 years and less than or equal to 17 years **AND**
- Medical record documentation of a diagnosis of adrenoleukodystrophy (ALD) confirmed by BOTH of the following:
    - Medical record documentation of the presence of a mutation (variant) in the adenosine triphosphate binding cassette, sub family D member 1 (ABCD1) gene confirmed by genetic testing, **AND**
    - Medical record documentation of elevated plasma concentrations of very long chain fatty acids (VLCFA) levels **AND**
- Medical record documentation that the patient has early, active cerebral disease (Cerebral adrenoleukodystrophy (CALD)) as evidenced by ALL of the following:
    - Central radiographic review of Brain MRI demonstrating BOTH of the following:
        - Loes score between 0.5 and 9 (inclusive) on the 34-point scale **AND**
        - Gadolinium enhancement on MRI of demyelinating lesions **AND**
    - Neurologic function score (NFS) of less than or equal to 1 **AND**
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant **AND**
- Medical record documentation the member is a candidate for an allogenic hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has not received Skysona, or any other gene therapy previously **AND**
- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV) **AND**
- Medical record documentation that the member will have treatment administered at a Skysona Qualified Treatment Center

NOTE: The package insert recommends confirming that hematopoietic stem cell transplantation (HSCT) is appropriate prior to Skysona since patients will be going through similar steps (mobilization, apheresis, and myeloablation) required for a HSCT. However, the ALD-102 clinical trial excluded patients who had a known and available HLA-matched family donor. Considering that HSCT has been available for longer and has more evidence supporting its use, it may be appropriate to require HSCT as an alternate to Skysona. While it is possible for patients to have a matched unrelated donor, outcomes are best with matched related donors.

AUTHORIZATION DURATION: One (1) time approval per lifetime; Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

RPh Sign Off: Yes

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

ZYNYZ (retifanlimab-dlwr)

Review: Zynyz is a programmed death-receptor-1 (PD-1)- blocking antibody indicated for the treatment of adult patients with metastatic or recurrent locally advanced Merkel cell carcinoma. This indication was an accelerated approval based on tumor response rate and duration of response. Zynyz binds the PD-1

receptor and blocks its interaction with the ligands PD-L1 and PD-L2 and potentiates T-cell activity. NCCN recommends Zynyz as single-agent treatment of locally advanced, region disease, and metastatic disease in patients who are not amenable to surgery or radiation therapy (Category 2A).
The recommend dosage of Zynyz is 500 mg administered as an intravenous infusion over 30 minutes every 4 weeks until disease progression, unacceptable toxicity, or up to 24 months. There are no dosage reductions recommended. Zynyz can be withheld for severe (Grade 3) immune-mediated adverse reactions. It should be permanently discontinued for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids. Zynyz is available as a 500 mg/20 mL (25 mg/mL) in a single-dose vial.

Warnings and precautions include severe and fatal immune-mediated adverse reactions, infusion-related reactions, complications of allogeneic HSCT, and embryo-fetal toxicity. Immune-mediated reactions can include immune-mediated pneumonitis, colitis, hepatitis, and endocrinopathies.

During clinical trials of Zynyz, serious adverse reactions occurred in 22% of patients, most frequently fatigue, arrythmia, and pneumonitis. Permanent discontinuation due to adverse reaction occurred in 11% of patients, including asthenia , atrial fibrillation, concomitant disease progression of chronic lymphocytic leukemia, demyelinating polyneuropathy, eosinophilic fasciitis, increased transaminases, infusion-related reaction, lung disorder, pancreatitis, polyarthritis, and radiculopathy. Dose interruptions due to adverse reactions occurred in 25% of patients, including pneumonitis, pyrexia, and increased lipase, transaminase, and amylase. The most common adverse reactions were fatigue, musculoskeletal pain, pruritis, diarrhea, rash, pyrexia, and nausea.

The safety and efficacy of Zynyz has not been established in pediatric patients. Of the 65 patients with metastatic or recurrent locally advanced MCC treated with Zynyz, 79% were 65 years or older and 37% were 75 years or older. Clinical studies of Zynyz did not include sufficient numbers of younger adult patients to determine if old patients respond differently than younger adult patients.

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

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

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

Outcome: Zynyz is a medical benefit and will require a prior authorization. It will be added to the medical benefit cost share list. When Zynyz is processed at a Specialty Pharmacy, it will process at the specialty tier or the brand non-preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation that Zynyz is written by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years of age **AND**
- Medical record documentation of a diagnosis of metastatic or recurrent locally advanced Merkel cell carcinoma

Quantity Limit: 20 mL per 28 days

Authorization Duration: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 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 patient experiences toxicity or worsening of disease.

GPI Level: GPI-12

Require RPh Signoff: Yes

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

KYZATREX (testosterone undecanoate)

Review: Kyzatrex is an oral capsule of testosterone undecanoate indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone. This includes both primary hypogonadism (low serum testosterone, FSH and LH above the normal range) and hypogonadotropic hypogonadism (low testosterone, FSH and LH in normal to low range).

Diagnosis is confirmed by measuring serum testosterone levels in the morning on at least two separate days prior to initiation of treatment. The recommended starting dose is 200mg twice daily, in the morning and evening with food. After starting treatment, the dosage can be adjusted according to Table 1, based on serum testosterone concentrations taken 7 days after initial dosing or dosage adjustments. Kyzatrex is not substitutable with other oral testosterone undecanoate products, such as Jatenzo and Tlando.

The safety profile of Kyzatrex is similar to that of Jatenzo and Tlando, which have a black box warning for increased blood pressure. During clinical trials, Kyzatrex treatment increased systolic blood pressure, by an average of 1.7 mmHG based on ambulatory blood pressure monitoring after 4 months and 2.7 mmHg after 4 months of treatment based on blood pressure cuff measurements. Increased blood pressure can increase the risk of MACE, with greater risk in patients with established cardiovascular disease or risk factors. After initiating Kyzatrex treatment or adjusting the dose, blood pressure should be monitored periodically and benefits vs. risks should be re-evaluated in patietnts who develop cardiovascular risk factors. Other warnings and precautions are consistent with Jatenzo, Tlando, and other testosterone replacement therapy products. Safety and efficacy of Kyzatrex have not been established in patients under the age of 18.

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

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

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

Outcome: Kyzatrex is a pharmacy benefit and will be added to the brand non-preferred tier of the Commercial, Marketplace, and CHIP formularies. It will be added to the Commercial Policy 722.0 Jatenzo and Tlando, which has the following prior authorization criteria:

- Medical record documentation of use for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
    - Primary hypogonadism (congenital or acquired) **OR**
    - Hypogonadotropic hypogonadism (congenital or acquired)

AND

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three formulary alternatives

MediSpan GPI Level: GPI-12

Quantity Limit:

- 100mg capsule: 2 capsules per day
- 150mg and 200mg capsule: 4 capsules per day

Formulary Alternatives: testosterone gel, testosterone transdermal gel, testosterone transdermal solution, testosterone cypionate, testosterone enanthate, Androderm, Aveed*

RPh Sign Off: No

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

XENPOZYME (olipudase alfa-rpcp)

Review: Xenpozyme is a hydrolytic lysosomal sphingomyelin-specific enzyme indicated for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD) in adult and pediatric patients. Xenpozyme provides and exogenous from of the enzyme acid sphingomyelinase (ASM) which has reduced activity in ASMD cause by pathogenic variants in the sphingomyelin phosphodiesterase 1 gene. Xenpozyme is not expected to cross the blood brain barrier and therefore is not likely to modulate CNS manifestations associated with ASMD.

Xenpozyme is administered by intravenous infusion every 2 weeks with a dose escalation and maintenance dose based on weight and age. For adult patients the recommended starting dose is 0.1 mg/kg gradually increased to a maintenance dosage of 3 mg/kg (Table 5). Pediatric patients initiate Xenpozyme at a dosage of 0.03 mg/kg and gradually increase to a maintenance dosage of 3 mg/kg (Table 6).

Warnings and precautions include precautions for hypersensitivity reactions including anaphylaxis, infusion related reactions, elevated transaminase levels, and risk of fetal malformations during initiation or escalation in pregnancy. During the pooled data from clinical trials of Xenpozyme, serious adverse reactions of anaphylactic reaction were reported in 2 patients. The most frequent adverse reactions in adults were headache, cough, diarrhea, hypotension, and ocular hyperemia. The most frequently reported adverse reactions in pediatric patients were pyrexia, cough, diarrhea, rhinitis, abdominal pain, vomiting, headache, urticaria, nausea, rash, arthralgia, pruritus, fatigue and pharyngitis.
The safety and efficacy of Xenpozyme has been established in pediatric patients down to birth. Compared to adults, a higher percentage of pediatric patients experienced treatment related serious adverse reactions, anaphylaxis, hypersensitivity reactions, and IARs that occurred within 24 hours of infusion.

Of the adult patients included in trial 1, only 1 patient was 65 to 74 years of age and no patients were 75 years of age and older. Clinical trials didn't include sufficient numbers of patients 65 years and older to determine whether they respond differently from younger adult patients.

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

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

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

Outcome: Xenpozyme is a medical benefit and will require a prior authorization. It will be added to the medical benefit cost share list. When processed at Specialty pharmacy, Xenpozyme will process on the specialty tier or the brand non-preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of acid sphingomyelinase deficiency (ASMD) **AND**
- Medical record documentation of clinical presentation consistent with ASMD type B OR ASMD type A/B **AND**
- Medical record documentation of one of the following:
    - Documentation of sphingomyelin phosphodiesterase-1 (SMPD1) genetic mutation **OR**
    - Documentation of enzyme assay demonstrating a deficiency of acid sphingomyelinase activity

  AND
- Medical record documentation that Xenpozyme will be used for the treatment of non-central nervous system manifestations of acid sphingomyelinase deficiency (ASMD)

Authorization Duration: Initial approval will be for 6 months. Subsequent approvals will be for an additional 12 months and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

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

HYFTOR (sirolimus)

Review: Hyftor is an (mTOR) inhibitor immunosuppressant indicated for the treatment of facial angiofibroma associated with tuberous sclerosis in adults and pediatric patients 6 years of age and older. All age-appropriate vaccinations recommended by current guidelines should be completed prior to Hyftor initiation. Hyftor is available as a topical 0.2% gel (2 mg of sirolimus per gram). The maximum daily dose is 600 mg (2 cm) for patients 6 to 11 years of age and 800 mg (2.5 cm) for patients 12 years of age and older.

Tuberous sclerosis complex (TSC) is a rare genetic disease that causes benign tumor growth throughout the body, including in the brain, spinal cord, nerves, eyes, lungs, heart, kidneys, and skin. In the United States, approximately 1 in 6,000 children are born with TSC each year, affecting all races, ethnic groups, and genders, with symptoms and severity being highly variable. Genetic mutations at either the TSC1 or TSC2 gene leads to development of TSC. The TSC1 and TSC2 genes produce proteins, hamartin and tuberin, respectively. When the mutation is present in either gene, the production of these proteins is affected. Without these proteins the mTOR pathway goes unregulated, causing abnormal cell changes and enlarged cell generation. Diagnosis can be made clinically or through genetic testing, but genetic testing is recommended to support clinical diagnosis. Patients with TSC are at risk for many life-threatening conditions, including neurological conditions (brain tumors, seizures), kidney lesions, and lung lesions. Additionally, patients may suffer from cognitive and behavioral problems, Autism Spectrum Disorder, skin conditions, and cardiac complications. TSC is a lifelong disease with no current cure. Treatment is supportive and symptom driven, requiring individualized treatment plans for each person. Skin conditions affect more than 90% of patients with TSC, with facial angiofibromas occurring in approximately 75 to 80% of TSC patients. Facial angiofibromas are pinkish-reddish skin bumps on the cheeks, nose, and chin, typically in a butterfly pattern. The bumps can bleed, block nasal openings, and cause disfigurement as they become rough and thick. Prior to Hyftor, only invasive treatment options were available to treat facial angiofibromas which include surgical removal, laser therapy, and dermabrasion.
Hyftor is the first FDA-approved therapy for the treatment of facial angiofibroma associated with TSC. The mechanism of action of Hyftor in the treatment of angiofibromas associated with TSC is unknown. However, it is known that in TSC the loss of regulation of mTOR leads to abnormal cell changes. Hyftor inhibits mTOR activation, treating symptoms of TSC including facial angiofibromas. There are no alterative treatments FDA-approved for facial angiofibromas associated with TSC.

Hyftor is absorbed systemically after topical administration and may result in fetal exposure and harm when administered during pregnancy. Breastfeeding is not recommended during treatment with Hyftor

due to the potential for serious adverse reactions in the breastfed infant. Females of reproductive potential are recommended to avoid becoming pregnant and should be initiated on contraception prior to starting Hyftor therapy and continued through treatment and for 12 weeks after the final Hyftor dose. Female and male infertility may be compromised by Hyftor, based on clinical findings and animal studies. Clinical studies did not include enough patients over 65 to determine response in geriatric patients. Safety and effectiveness of Hyftor for facial angiofibroma associated with TSC have not been established in pediatrics patients less than 6 years of age.

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

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

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

Outcome: Hyftor is a pharmacy benefit and will be added to the Commercial, Marketplace, and GHP Kids pharmacy formularies at the specialty tier or brand non-preferred tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of age 6 years or older **AND**
- Medical record documentation of a diagnosis of facial angiofibroma associated with tuberous sclerosis **AND**
- Medical record documentation of age appropriate dosing (less than or equal to 600 mg per day for patients 6 to 11 years of age OR less than or equal to 800 mg per day for patients 12 years of age and older)

MediSpan Authorization Level: GPI-12

Quantity Limit: 3 tubes (30 grams) per 30 days

Authorization Duration: Initial approval will be for 3 months. Subsequent approvals will be for an additional 6 months and will require medical record documentation of clinical improvement or lack of progression in symptoms of facial angiofibromas on Hyftor therapy is required.

Require RPh Signoff: No

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

VIVJOA (oteseconazole)

Review: Vivjoa is an azole antifungal indicated to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are NOT of reproductive potential. It is supplied as an oral 150 mg capsule and comes as an 18-capsule packet with directions on the packet. Vivjoa is an azole metalloenzyme inhibitor of the fungal sterol, 14 alpha-demethylase, which results in accumulation of membrane disrupting 14-methylated sterols.
Treatment of RVVC consists of an induction phase to attempt to achieve mycologic remission, followed by a maintenance phase. An extended duration of topical (clotrimazole, tioconazole, butoconazole, terconazole, or miconazole) or oral (fluconazole) antifungals is recommended for initial treatment from the CDC and IDSA. CDC recommends initial treatment with 7 to 14 days of topical therapy or three doses (administered 3 days apart) of oral fluconazole, followed by maintenance treatment of once-weekly oral fluconazole for 6 months.

Dosing for Vivjoa consists of two different dosing regimens, one with Vivjoa only and a second with Vivjoa and Fluconazole.

Vulvovaginal candidiasis (VVC) is the second most common type of vaginal infection in the United States, after bacterial vaginosis. It is estimated that 1.4 million American women visit a healthcare provider each year for this condition. VVC affects women of all ethnicities, social classes, and ages, although it is more common in women of childbearing age. Vivjoa is the first FDA-approved medication for RVVC which is also referred to as a chronic yeast infection. RVVC is defined by the CDC as three or more symptomatic acute episodes of RVVC in 12 months. RVVC is characterized as acute inflammation of the vulva and vaginal mucosa caused or accompanied by overgrowth of Candida yeast.

Most common reported adverse reactions were headache and nausea. No dosage adjustments are recommended in patients with mild to moderate renal impairment (eGFR 30-89 mL/min) but not recommended in severe renal impairment (eGFR 15-29 mL/min) because there were not sufficient numbers of patients with severe renal impairment and end-stage-renal disease to determine safety of Vivjoa. Vivjoa is contraindicated in lactating women and females of reproductive potential as well as anyone with known hypersensitivity to oteseconazole. Ocular abnormalities were observed in a pre and postnatal study in the offspring of rats administer oteseconazole from Gestation Day 6 through lactation day 20 at doses approximately 2.5 times the recommended human dose based on AUC comparisons. The drug exposure window is 690 days (based on 5 times the half-life of oteseconazole). Females who are NOT of reproductive potential are defined as: persons who are biological females who are postmenopausal or have another reason for permanent infertility (tubal ligation, hysterectomy, salpingo-oophorectomy).

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

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

Financial Discussion: Give the high cost it was recommended that Vivjoa be added to the brand non-preferred tier of the formulary. Additionally, it was recommend that the authorization duration be deleted from the recommendations. No additional comments or questions. The committee unanimously voted to accept the recommendations as amended. None were opposed.

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

- Medical record documentation of history of recurrent vulvovaginal candidiasis (RVVC) (>3 acute VVC episodes within 12 months) **AND**
- Medical record documentation of one of the following:
    - Medical record documentation that member is postmenopausal **OR**
    - Medical record documentation that member is 12 years of age or older AND both of the following:
        - Medical record documentation that member is post-menarchal **AND**
        - Medical record documentation that member is not of reproductive potential (i.e., history of tubal ligation, salpingo-oophorectomy, or hysterectomy) **AND**
- Medical record documentation of therapeutic failure, contraindication, or intolerance to oral fluconazole tablets

MediSpan Authorization Level: GPI-12

Quantity Limit: 18 capsules per 84 days, RX count 1

Require RPh Signoff: Yes

Formulary Alternatives: fluconazole

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

VIVIMUSTA & BELRAPZO (bendamustine)

Review: Vivimusta and Belrapzo are alkylating drugs indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) and adult patients with indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within six months of treatment with rituximab or a rituximab-containing regimen. Other than efficacy relative to chlorambucil, efficacy relative to other first line therapies for CLL has not been established.

Vivimusta and Belrapzo for CLL are dosed at 100 mg/m2 intravenously on Day 1 and Day 2 of a 28-day cycle, for up to 6 cycles. Vivimusta and Belrapzo for NHL is dosed at 120 mg/m2 intravenously on Day 1 and Day 2 of a 21-day cycle for up to 8 cycles. Vivimusta and Belrapzo are supplied in multiple-dose vials as a clear, colorless to yellow solution for intravenous use providing 100 mg per 4 mL (NDC 71225-120-01).

Vivimusta and Belrapzo are the fourth and third branded bendamustine products approved, respectively. Other brands already on the market include Treanda and Bendeka. Treanda (Teva) was approved in March 2008. Teva then partnered with Eagle Pharmaceuticals to launch Bendeka in December 2015 as a next-generation version of Treanda. The generic for Treanda was recently launched on December 7th, 2022 by Accord. Other generic manufacturers are expected to launch their products on the 180-day exclusivity expiration date of June 5th, 2023.

The five bendamustine products currently available differ in regard to how they are supplied and their durations of infusion. Table 1 summarizes the differences between the products. Treanda and its generic are supplied as a powder to be reconstituted, while Bendeka, Belrapzo and Vivimusta are supplied as a solution to be diluted. The duration of infusion is 20 minutes for Vivimusta, 30 minutes for Treanda and Belrapzo, and 10 minutes for Bendeka.

No new safety information was included in the Vivimusta and Belrapzo prescribing information as compared to the other branded bendamustine products. Vivimusta has a contraindication significant for known hypersensitivity to bendamustine, polyethylene glycol 400, dehydrated alcohol or monothioglycerol. Belrapzo has a contraindication significant for hypersensitivity to bendamustine, polyethylene glycol 400, propylene glycol or monothioglycerol. Warnings and precautions are significant for myelosuppression, infections, progressive multifocal leukoencephalopathy (PML), anaphylaxis and infusion-related reactions, tumor lysis syndrome, skin reactions, hepatotoxicity, other malignancies, and extravasation injury. Common adverse reactions in clinical trials for CLL included pyrexia (24%), nausea (20%) and vomiting (16%). Common adverse reactions in clinical trials for NHL included nausea (75%), fatigue (57%), vomiting (40%), diarrhea (37%) and pyrexia (34%). Drug interactions include CYP1A2 inhibitors and inducers, alternative treatment options should be considered.

For pregnancy and lactation, there is no available data on bendamustine to evaluate for a drug-associated risk of major birth defects, miscarriage, adverse maternal or fetal outcomes, metabolites in either human or animal milk, the effects on the breastfed child, or the effects on milk production. Safety and effectiveness has not been established in pediatric patients. No overall differences in safety were observed between patients aged 65 year and older compared to younger patients. Efficacy was lower in patients aged 65 and older in regard to overall response rate and progression free survival for CLL. No overall differences in efficacy were observed between patients aged 65 and older compared to younger patients in NHL.

The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium groups Vivimusta and Belrapzo with Treanda and Bendeka for the medically accepted clinical indications. At the time of this review, NCCN includes Vivimusta in recommendations for B-cell lymphomas, CLL, Hodgkin

Lymphoma, Multiple Myeloma, Pediatric Hodgkin Lymphoma, and T-Cell Lymphoma. Belrapzo is also indicated for Hematopoietic Cell Transplantation, Small Cell Lung Cancer, Systemic Light Chain Amyloidosis and Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma within NCCN guidelines.

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

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

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

Outcome: Vivimusta and Belrapzo are medical benefits and will not require a prior authorization. Vivimusta and Belrapzo will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Vivimusta and Belrapzo will process on the specialty tier or the brand non-preferred tier for members with a three tier benefit.

MediSpan Authorization Level: GPI-12

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

CLASS REVIEWS

ATOPIC DERMATITIS CLASS REVIEW

Agents for Atopic Dermatitis			
Brand Name	**Generic**	**Generic Available?**	**Manufacturer**
Monoclonal Antibodies			
Dupixent	dupilumab	No	Regeneron
Adbry	tralokinumab	No	LEO
Janus Kinase Inhibitors			
Cibinqo	abrocitinib	No	Pfizer
Rinvoq	upadacitinib	No	AbbVie
Opzelura	ruxolitinib	No	Incyte
Phosphodiesterase-4 Enzyme Inhibitors			
Eucrisa	crisaborole	No	Pfizer
Calcineurin Inhibitors			
Elidel	pimecrolimus	Yes	Bausch Health
Protopic	tacrolimus	Yes	LEO
Other			
Zonalon	doxepin	Yes	Mylan

Review: Atopic dermatitis (AD), also known as eczema, is a chronic inflammatory disease of the skin that causes erythema, irritation, and pruritus. Rashes may form on the skin and can appear anywhere on the body. Atopic dermatitis often appears in babies and children but can develop at any point in a person's life. The cause is unknown but is believed to be linked to gene mutations, weakened immune systems, and environmental exposures. Treatment includes proper skin care with moisturizers, medications, and/or phototherapy.

American Academy of Dermatology

- Emollients and moisturizers should be considered first-line in chronic management of AD as a non-pharmacological option and should be continued during acute flares.
- Topical corticosteroids are considered first-line in anti-inflammatory therapy and should be used during acute flares or in those who fail to respond to good skin care and regular use of emollients and moisturizers.
- Topical calcineurin inhibitors are a second-line option in anti-inflammatory therapy.
- Topical phosphodiesterase-4 enzyme inhibitor crisaborole is recommended for adults with mild-to-moderate AD.
- Topical Janus Kinase inhibitor ruxolitinib is recommended for adults with mild-to-moderate AD.

European Academy of Dermatology

- Emollients are the mainstay of management and should be considered first-line in chronic management of AD as a non-pharmacological option.
- Topical corticosteroids are considered first-line in anti-inflammatory therapy and should be used during acute flares or in those who fail to respond to good skin care and regular use of emollients and moisturizers.
- Topical calcineurin inhibitors are a second-line option in anti-inflammatory therapy.
- Topical phosphodiesterase-4 enzyme inhibitor crisaborole ointment is currently not licensed in Europe.
- Topical Janus Kinase inhibitors are not currently licensed in Europe.

Recommendations:

Commercial (Traditional)/ Exchange (Marketplace)/ CHIP (Kids)		
Medication	**Current Policy**	**Recommendations**
Dupixent (dupilumab)	**Dupixent Policy 457.0** • Medical record documentation that Dupixent is prescribed by or in consultation with an allergist, dermatologist, or immunologist AND • Medical record documentation of age greater than or equal to 6 months AND • Medical record documentation of a diagnosis of moderate to severe atopic dermatitis AND • Medical record documentation of one of the following: o Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid OR o For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable (use on sensitive areas, age between 2 and 15 years): Therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) AND • Medical record documentation that the member is receiving an appropriate dose based on patient's age and weight.	No changes recommended.
Adbry (tralokinumab)	**Adbry Policy 701.0** • Medical record documentation of a diagnosis of moderate to severe atopic dermatitis AND • Medical record documentation that Adbry is prescribed by or in consultation with an allergist, dermatologist, or immunologist AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) AND • Medical record documentation of one of the following: o Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid OR	No changes recommended.

	○ For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable, therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor.	
Cibinqo (abrocitinib)	**Cibinqo Policy 711.0** • Medical record documentation of a diagnosis of moderate to severe atopic dermatitis AND • Medical record documentation that Cibinqo is prescribed by or in consultation with an allergist, dermatologist, or immunologist AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of one of the following: • Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid OR • For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable: Therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure to Dupixent AND • Medical record documentation that Cibinqo will not be used in combination with another Janus kinase (JAK) inhibitor, biologic immunomodulator or with other immunosuppressants including but not limited to azathioprine and cyclosporine.	**Cibinqo Policy 711.0** • Medical record documentation of a diagnosis of moderate to severe atopic dermatitis AND • Medical record documentation that Cibinqo is prescribed by or in consultation with an allergist, dermatologist, or immunologist AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of one of the following: • Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid OR • For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable: Therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor OR • Medical record documentation of contraindication to, intolerance to, or therapeutic failure to one systemic therapy (e.g., Dupixent, Adbry) • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) AND ~~• Medical record documentation of contraindication to, intolerance to, or therapeutic failure to Dupixent AND~~ • Medical record documentation that Cibinqo will not be used in combination with another Janus kinase (JAK) inhibitor, biologic immunomodulator or with other immunosuppressants including but not limited to azathioprine and cyclosporine.
Rinvoq (upadacitinib)	**Rinvoq Policy 605.0** • Medical record documentation of a diagnosis of moderate to severe atopic dermatitis AND • Medical record documentation that Rinvoq is prescribed by an allergist, dermatologist, or immunologist AND	**Rinvoq Policy 605.0** • Medical record documentation of a diagnosis of moderate to severe atopic dermatitis AND • Medical record documentation that Rinvoq is prescribed by an allergist, dermatologist, or immunologist AND

	• Medical record documentation of age greater than or equal to 12 years AND • Medical record documentation of one of the following: • Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid OR • For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable (use on sensitive areas, age between 2 and 15 years): Therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure to Dupixent AND • Medical record documentation that Rinvoq will not be used in combination with another Janus kinase (JAK) inhibitor, biologic immunomodulator, or with other immunosuppressants including but not limited to azathioprine and cyclosporine.	• Medical record documentation of age greater than or equal to 12 years AND • Medical record documentation of one of the following: • Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid OR • For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable (use on sensitive areas, age between 2 and 15 years): Therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor OR • Medical record documentation of contraindication to, intolerance to, or therapeutic failure to one systemic therapy (e.g., Dupixent, Adbry) • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) AND ~~• Medical record documentation of contraindication to, intolerance to, or therapeutic failure to Dupixent AND~~ • Medical record documentation that Rinvoq will not be used in combination with another Janus kinase (JAK) inhibitor, biologic immunomodulator, or with other immunosuppressants including but not limited to azathioprine and cyclosporine.
Opzelura (ruxolitinib)	**Opzelura 695.0** • Medical record documentation that Opzelura is prescribed by or in consultation with a dermatologist, allergist, or immunologist AND • Medical record documentation of a diagnosis of mild to moderate atopic dermatitis AND • Medical record documentation of age greater than or equal to 12 years AND • Medical record documentation that member is immunocompetent AND • Medical record documentation of Body Surface Area (BSA) less than or equal to 20% AND • Medical record documentation that Opzelura is NOT being used in combination with therapeutic biologics, other Janus-associated	No changes recommended.

	kinase (JAK) inhibitors or potent immunosuppressants such as azathioprine or cyclosporine AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ALL of the following: o One formulary topical calcineurin inhibitor AND o One formulary topical corticosteroid unless deemed inadvisable due to potential risks such as (a) use on sensitive skin areas (face, axillae, or groin) OR (b) member is less than 15 years of age AND o Eucrisa.	
Eucrisa (crisaborole)	**Eucrisa Policy 456.0** • Medical record documentation that Eucrisa is prescribed by or in consultation with a dermatologist AND • Medical record documentation of a diagnosis of mild to moderate atopic dermatitis AND • For members 2 years of age and older: Medical record documentation of contraindication to, intolerance to, or therapeutic failure on tacrolimus ointment AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on at least two (2) formulary topical corticosteroids unless deemed inadvisable due to potential risks such as (a) use on sensitive skin areas (face, axillae, or groin) or (b) member is less than 15 years of age.	No changes recommended.
Elidel (pimecrolimus)	**Pimecrolimus Policy 67.0** • Medical record documentation of a diagnosis of atopic dermatitis AND • Medical record documentation of contraindication to, intolerance to, or therapeutic failure on tacrolimus ointment AND • Medical record documentation of contraindication to, intolerance to or therapeutic failure on at least two formulary topical corticosteroids unless deemed inadvisable due to potential risks such as (a) use on sensitive skin areas (face, axillae, or groin) or (b) patient is between 2 and 15 years of age.	No changes recommended.
Protopic (tacrolimus)	No prior authorization required.	No changes recommended.
Zonalon (doxepin)	No prior authorization required.	No changes recommended.

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

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

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

HEPATITIS C CLASS REVIEW

Agents for **Hepatitis C (Direct Acting Antivirals)**			
Brand Name	**Generic**	**Generic Available?**	**Manufacturer**
NS3/4A Protease Inhibitor/ NS5A Inhibitor			
Mavyret	Glecaprevir/Pibrentasvir	No	AbbVie Inc
Zepatier	Elbasvir/Grazoprevir	No	Merck, Sharp & Dohme
NS5A Inhibitor/ NS5B RNA Polymerase Inhibitor			
Epclusa	Sofosbuvir/Velpatasvir	Yes	Gilead Sciences Inc.
Harvoni	Ledipasvir/Sofosbuvir	Yes	Gilead Sciences, Inc.
NS3/4A Inhibitor/ NS5A Inhibitor/ NS5B RNA Polymerase Inhibitor			
Vosevi	Sofosbuvir, Velpatasvir, and Voxilaprevir	No	Gilead Sciences, Inc.
NS5B RNA Polymerase Inhibitor			
Sovaldi	Sofosbuvir	No	Gilead Sciences, Inc

Review: Hepatitis C is a virus that causes inflammation and damage to the liver. It is a blood-borne pathogen that can infect people in an acute or progress to a chronic stage. Its severity can range from a mild to serious infection that can lead to liver cirrhosis and cancer. In 2016, it was estimated that 2.4 million people had an active HCV infection. People infected with Hepatitis C usually have no symptoms. Symptoms usually do not occur until people have an advanced form of disease. Its most common risk factors are sharing needles or unsafe tattoo practices. Other methods of transmission are from mother to child, receiving a Hepatitis C infected organ, blood transfusions or transplantation before 1992, or sharing personal items like razors, toothbrushes, etc with an infected person. It can be transmitted via sex, but this is rare.

Tests are usually performed to check the Hepatitis C antibody in patients greater than 18 years and older (at least once in a lifetime), are pregnant, are injecting drugs or have ever injected drugs in the past, coinfected with HIV, have abnormal liver function, are on dialysis, received donated organs or transfusions before 1992, have been exposed to blood of a person infected with Hepatitis C, or were born to a mother with Hepatitis C. If the HCV antibody is positive, they will test to see if there is active virus in

a PCR test called the HCV RNA. If positive, treatment is recommended. It is possible for our bodies to clear Hepatitis C without treatment; this happens frequently in babies infected with HCV from their mother. The CDC recommends people with risk factors to be tested regularly. The Hepatitis C antibody will always remain positive, even after the active infection is eradicated. Also, there is no immunity to Hepatitis C. People can be reinfected with risky behavior.

If the HCV RNA is positive, treatment is recommended regardless of fibrosis. The guidelines still recommend patients to be evaluated by a healthcare provider with expertise in assessment of liver disease severity and HCV treatment. Direct acting antiviral therapy (DAA) is recommended for all people infected with HCV, except those with a short life expectancy or during pregnancy. Treatment has really progressed in the last few years, and HCV can be cured in as little as 8 to 12 weeks in most cases. DAA therapy is greater than 90% effective with little to no side effects. Before the initiation of treatment, patients should be educated about how to prevent further liver damage, including abstinence of alcohol. Other tests that are routinely recommended include analyzing fibrosis and evaluation of coexisting Hepatitis B and/or HIV. Hepatitis B that lays dormant can reactivate when initiating Hepatitis C treatment. HIV is transmitted in a similar form to HCV, and drugs used to treat HIV can interact with DAA. The genotype used to be routinely recommended, but it not always necessary now that they are pangenotypic regimens on the market. With that being said, some regimens may differ by genotype in those with cirrhosis or with treatment experience, and genotype is thus recommended in these instances. Also, this may play a role in treatment failure versus reinfection in those who get lost to follow up and never get official SVR12. Previous treatments and results should always be assessed and documented. Vaccination against Hepatitis A and Hepatitis B is recommended with for all patients with an HCV infection. In addition, all patients should be educated on how to prevent HCV transmission to others.

The staging of hepatic fibrosis is essential to treatment. Also, potential drug interactions should be assessed prior to treatment. Other recommended laboratory tests include CBC, INR, hepatic function panel, and eGFR. Treatment is recommended using the AASLD (American Association for the Study of Liver Diseases) and IDSA (Infectious Diseases Society of America) Guidelines. Patients with advanced liver disease (Metavir Stage 3 or 4) are at more risk of developing complications of liver disease, including hepatic decompensation. These cases are specially treated, and recommendations can be found in the Guidelines under special populations. The regimens usually include the addition of ribavirin, which comes with its own set of monitoring parameters. Resistance testing should be performed when recommended. In addition, special populations such as transplants and treatment in children ≥ 3 years old are discussed under the Unique and Key populations tab. Patients that have been previously treated with a Hepatitis C regimen have recommendations under the Treatment Experienced tab.

The SVR (Sustained Virologic Response) is the goal of HCV treatment. The SVR12 is defined as the absence of detectible HCV RNA at least 12 weeks after the end of treatment. It is the marker of cure of HCV. Touchpoints between a healthcare professional and patient are known to improve compliance and therefore cure.

WHO 2030 has a goal of Hepatitis C eradication target. This is defined as a 90% reduction in new chronic infections and a 65% reduction in mortality, compared with the 2015 baseline. Because of increased recommendation of screening, IPD estimates this could increase DAA use between 10-25%.

Recommendations:

Mavyret Policy 461.0 (Comm/Exchange/Chip)

Recommendations: I would like move Mavyret packets for Commercial and Chip lines to Tier 2 to be in line with the Mavyret tablets. All other tiering would remain the same.

Rationale: Mavyret packets are the most cost effective non-tablet form of Hepatitis C Treatment.

- Medical record documentation of age greater than or equal to 3 years **AND**
- Medical record documentation of a diagnosis of a hepatitis C infection **AND**
- ~~Medical record documentation of the member's hepatitis C genotype **AND**~~

- Medical record documentation of a diagnosis of hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) **AND**
- Medical record documentation of METAVIR liver scoring or cirrhosis assessment by a non-invasive test **AND**
- Medical record documentation of a hepatocellular carcinoma screening in those with cirrhosis (METAVIR score F4) **AND**
- Medical record documentation of the member receiving a Food and Drug Administration (FDA) approved medication regimen that is inside the parameters of use approved by the FDA or supported in the widely used compendia available ~~**OR**~~ **AND**
- ~~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 a hepatitis C virus (HCV) NS5A inhibitor or an NS3/4A protease inhibitor, but not both **OR**~~
    - ~~Liver or kidney transplant recipients with Hepatitis C infection **AND**~~
- Medical record documentation of appropriate duration of treatment **AND**
- Medical record documentation of previous treatment and treatment response **AND**
- Medical record documentation of any potential drug interactions addressed by the prescriber (such as discontinuation of the interacting drug, dose reduction of the interacting drug, or counseling of the recipient of the risks associated with the use of both medications when they interact) **AND**
- Medical record documentation of receiving the following within the past ~~3 months~~ 6 months:
    - Hepatic function panel
    - Complete blood count ~~including differential~~
    - Basic metabolic panel
- Medical record documentation of receiving the following within a reasonable timeframe:
    - Baseline hepatitis C virus (HCV) RNA viral load **AND**
- If actively abusing alcohol or intravenous (IV) drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment **AND**
- Medical record documentation that member received pre-treatment readiness education about hepatitis C treatment expectations by a health care provider **AND**
- Medical record documentation that the member commits to the documented planned course of treatment including anticipated blood tests and visits, during and after treatment **AND**
- Medical record documentation that member does not have a limited life expectancy of less than 12 months due to non-liver related co-morbid conditions **AND**

- Medical record documentation of completed:
    - Hepatitis B immunization series **OR**
    - Hepatitis B screening (sAb/sAg and cAb/cAg) **AND** Quantitative hepatitis B virus (HBV) DNA if positive for hepatitis B sAg or cAb or cAg **AND**
        - If there is detectable hepatitis B virus (HBV) DNA, will be treated for Hepatitis B **OR**
        - If negative for hepatitis B sAb, is being vaccinated against Hepatitis B **AND**

- Medical record documentation of human immunodeficiency virus (HIV) screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay:
    - Is being treated for human immunodeficiency virus (HIV) **OR**
    - If not being treated for human immunodeficiency virus (HIV), the medical record documents the rationale for the beneficiary not being treated **AND**
- Medical record documentation that member has been evaluated and treated by a contracted Center of Excellence in hepatitis C management **AND**
- If member is under the age or 12 years or weighs less than 45 kilograms, medical record documentation that proper weight-based dosing is prescribed **AND**
- If member is greater than or equal to 12 years of age or weighs greater than or equal to 45 kilograms and the request is for packets, medical record documentation of why tablets cannot be used

OR

- Medical record documentation of a hepatitis C negative recipient receiving a transplant from a hepatitis C positive donor

~~**NOTE:** Center of Excellence (COE) requirements do not apply to strategic partner TPA plans (i.e., Northern Light Health).~~

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

- QL FOR LETTER ONLY:
    - Tablets: three (3) tablets per day, 28 day supply per fill
    - Packets: six (6) packets per day, 28 day supply per fill

Approval language: Meets criteria, auth x (?) weeks, rx count= (?), (28 day supply/fill), QL: 3 tabs/day (QL for LETTER only)

AUTHORIZATION DURATION: 8, 12, or 16 weeks consistent with current AASLD/IDSA guidelines or Food and Drug Administration (FDA) recommendations

NOTES TO REVIEWER

1. Center of Excellence (COE) requirements do not apply to strategic partner TPA plans (i.e., Northern Light Health).
2. Mavyret is pangenotypic, although advised to get Genotype, it is not always necessary and do not have to list this in denial rationale.

3. Per the prescribing information, treatment duration for liver or kidney transplant recipients is 12 weeks. Geisinger has been treating kidney transplant recipients for 8 weeks with success. Please refer to Guidelines.

Guidelines can be referenced at https://www.hcvguidelines.org/

FORMULARY ALTERNATIVES:

~~None~~ sofosbuvir-velpatasvir 400-100mg tablets*

*prior authorization required

Epclusa and Sofosbuvir/Velpatasvir Policy 434.0 (Comm/Exchange/Chip)

Recommendations: I would like to make Sofosbuvir/Velpatasvir 400-100mg tablets at parity with Mavyret. It should be added to the Specialty tier or the Brand Preferred tier for members with a three tier benefit. The quantity limits would remain, with the following updates to the prior authorization criteria:

Rationale: There are certain instances where sofosbuvir-velpatasvir is a preferred option over Mavyret. It can be used in decompensated cirrhosis and an option when patients are on estrogen containing contraceptives. It has a 12 week treatment period, but offers cost savings over other agents due to availability of generics and MAC pricing.

- Medical record documentation of age greater than or equal to 3 years **AND**
- Medical record documentation that proper weight-based dosing is being prescribed **AND**
- Medical record documentation of a diagnosis of hepatitis C infection **AND**
- ~~Medical record documentation of the member's hepatitis C genotype **AND**~~
- Medical record documentation of a diagnosis of hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis or in combination with ribavirin in patients with decompensated cirrhosis (if eligible) **AND**
- Medical record documentation of METAVIR liver scoring or cirrhosis assessment by a non-invasive test **AND**
- Medical record documentation of a hepatocellular carcinoma screening in those with cirrhosis (METAVIR score F4) **AND**
- Medical record documentation of the member receiving a Food and Drug Administration (FDA) approved medication regimen that is inside the parameters of use approved by the FDA or supported in the widely used compendia available ~~**OR**~~ **AND**
  - ~~Medical record documentation of:~~
    - ~~Genotype 1, 2, 3, 4, 5, 6~~
      - ~~As monotherapy if treatment-naïve or peginterferon alfa + ribavirin based regimen experienced **OR**~~
      - ~~Concurrent therapy with ribavirin if decompensated cirrhosis **AND**~~
- Medical record documentation of appropriate duration of treatment **AND**
- Medical record documentation of previous treatment and treatment response **AND**
- ~~Medical record documentation of concurrent therapy with appropriate dose and duration of weight-based ribavirin, if indicated **AND**~~
- Medical record documentation of any potential drug interactions addressed by the prescriber (such as discontinuation of the interacting drug, dose reduction of the interacting drug, or counseling of the recipient of the risks associated with the use of both medications when they interact) **AND**
- Medical record documentation of receiving the following within the past ~~3 months~~ 6 months:
  - Hepatic function panel
  - Complete blood count ~~including differential~~
  - Basic metabolic panel
- Medical record documentation of receiving the following within ~~the past 3 months~~ a reasonable timeframe:
  - Baseline hepatitis C virus (HCV) RNA viral load **AND**
- Medical record documentation of concurrent therapy with appropriate dose and duration of weight-based ribavirin, if indicated **AND**

- Medical record documentation of a negative pregnancy test if member is female of childbearing potential and receiving ribavirin **AND**
- When concurrent ribavirin therapy is indicated and prescribed, medical record documentation for male members that their female partner is not pregnant **AND**
- If the member or their partner are of childbearing potential, medical record documentation that the member was instructed to practice effective contraception during therapy with ribavirin and for 6 months following discontinuation of ribavirin therapy **AND**
- If actively abusing alcohol or intravenous (IV) drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment **AND**
- Medical record documentation that member received pre-treatment readiness education about hepatitis C treatment expectations by a health care provider **AND**
- Medical record documentation that the member commits to the documented planned course of treatment including anticipated blood tests and visits, during and after treatment **AND**
- Medical record documentation that member does not have a limited life expectancy of less than 12 months due to non-liver related co-morbid conditions **AND**
- Medical record documentation of completed:
    - Hepatitis B immunization series **OR**
    - Hepatitis B screening (sAb/sAg and cAb/cAg) **AND** Quantitative hepatitis B virus (HBV) DNA if positive for hepatitis B sAg or cAb or cAg **AND**
        - If there is detectable hepatitis B virus (HBV) DNA, will be treated for Hepatitis B **OR**
        - If negative for hepatitis B sAb, is being vaccinated against Hepatitis B **AND**
- Medical record documentation of human immunodeficiency virus (HIV) screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay:
    - Is being treated for human immunodeficiency virus (HIV) **OR**
    - If not being treated for human immunodeficiency virus (HIV), the medical record documents the rationale for the beneficiary not being treated **AND**
- ~~Medical record documentation of a therapeutic failure on, intolerance to Mavyret, if clinically appropriate **AND**~~
- Medical record documentation that member has been evaluated and treated by a contracted Center of Excellence in hepatitis C management
- If member is greater than or equal to 18 years or weighs greater than or equal to 30 kilograms and the request is for 200/50 mg or 150 mg/37.5 mg strength, medical record documentation of why 400/100 mg tablets cannot be used

OR

- Medical record documentation of a hepatitis C negative recipient receiving a transplant from a hepatitis C positive donor ~~**AND**~~
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret, if clinically appropriate **AND**~~
- ~~If member is greater than or equal to 18 years or weighs greater than or equal to 30 kilograms and the request is for 200/50 mg or 150 mg/37.5 mg strength, medical record documentation of why 400/100 mg tablets cannot be used~~

NOTES TO REVIEWER:

1: Center of Excellence (COE) requirements do not apply to strategic partner TPA plans (i.e., Northern Light Health).
2: Treatment naïve, genotype 3 patients with compensated cirrhosis require NS5A RAS Y93H testing for velpatasvir.
3. Sometimes sofosbuvir-velpatasvir is preferred over Mavyret in cases when patients have decompensating features such as portal hypertension, low platelets, encephalopathy, etc.
4: Sofosbuvir-velpatasvir is pangenotypic, although advised to get Genotype, it is not always necessary and do not have to list this in denial rationale.
5: Per the prescribing information, treatment duration for liver or kidney transplant recipients is 12 weeks. Please refer to Guidelines.

Guidelines can be referenced at https://www.hcvguidelines.org/

MEDISPAN AUTHORIZATION LEVEL: GPI-14, if request is for sofosbuvir/velpatasvir 400/100 include generic only.

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

- QL FOR LETTER ONLY:
  - Tablets: one (1) tablet per day, 28 day supply per fill
  - 150/37.5 mg packets: one (1) packet per day, 28 day supply per fill
  - 200/50 mg packets: two (2) packets per day, 28 day supply per fill

AUTHORIZATION DURATION: According to IDSA/AASLD Guidelines (longer treatment duration is recommended when ribavirin ineligible)

Approval language: Meets criteria, auth x (?) weeks, rx count= (?), (28 day supply/fill), generic only [when applicable]. QL: 1 tab/day (QL for LETTER only)

FORMULARY ALTERNATIVES:
Mavyret*, ~~ledipasvir-sofosbuvir 400/90 mg*~~
*prior authorization required

Harvoni and Ledipasvir/Sofosbuvir 90/400 mg tablet Policy 358.0 (Comm/Exchange/Chip)

Recommendations: For Harvoni (Ledipasvir/sofosbuvir) for Marketplace: Remove Harvoni 33.75mg-150mg Oral Packet, Remove Harvoni 45-200mg Oral Packet, Remove Harvoni 45-200 Oral Tablet, and Remove ledipasvir-sofosbuvir 90-400mg oral tablet from the Marketplace Formulary.
Rationale: Harvoni has fallen out of favor due to pangenotypic regimens such as Mavyret and Epclusa (sofosbuvir-velpatasvir) and is associated with a higher cost than both agents. We have Mavyret packets on formulary with prior auth, and they are more cost effective.

- Medical record documentation of age greater than or equal to 3 years using weight-based dosing **AND**
- Medical record documentation of a diagnosis of hepatitis C infection **AND**
- Medical record documentation of the member's hepatitis C genotype **AND**
- Medical record documentation of a diagnosis of hepatitis C virus (HCV) genotype 1, 4, 5 or 6 infection without cirrhosis or with compensated cirrhosis; with decompensated cirrhosis, in combination with ribavirin (if eligible) **AND**
- Medical record documentation of METAVIR liver scoring fibrosis or cirrhosis assessment by a non-invasive test **AND**
- Medical record documentation of a hepatocellular carcinoma screening in those with cirrhosis (METAVIR score F4) **AND**
- ~~Medical record documentation of:~~
  - ~~Genotype 1~~
    - ~~As monotherapy **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment experienced with cirrhosis **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment naïve or experienced with decompensated cirrhosis **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment naïve or experienced with or without compensated cirrhosis in liver transplant recipients **OR**~~
  - ~~Genotype 4~~
    - ~~As monotherapy **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment naïve or experienced with decompensated cirrhosis **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment naïve or experienced with or without compensated cirrhosis in liver transplant recipients **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment experienced with compensated cirrhosis **OR**~~
  - ~~Genotype 5~~
    - ~~As monotherapy **OR**~~
  - ~~Genotype 6~~
    - ~~As monotherapy **AND**~~
- Medical record documentation of the member receiving a Food and Drug Administration (FDA) approved medication regimen that is inside the parameters of use approved by the FDA or supported in the widely used compendia available **AND**

- Medical record documentation of appropriate duration of treatment **AND**
- Medical record documentation of previous treatment and treatment response **AND**
- ~~Medical record documentation of concurrent therapy with appropriate dose and duration of ribavirin (weight-based dosing of ribavirin 1200 mg per day if greater than or equal to 75 kg, or 1000 mg per day if less than 75 kg, or 15 mg/kg in pediatric patients less than 47 kg), if indicated **AND**~~
- Medical record documentation of any potential drug interactions addressed by the prescriber (such as discontinuation of the interacting drug, dose reduction of the interacting drug, or counseling of the recipient of the risks associated with the use of both medications when they interact) **AND**
- Medical record documentation of receiving the following with the past ~~3 months~~ 6 months:
  - Hepatic function panel
  - Complete blood count ~~including differential~~
  - Basic metabolic panel
- Medical record documentation of receiving the following ~~with the past 3 months~~ within a reasonable timeframe:
  - Baseline hepatitis C virus (HCV) RNA viral load **AND**
- Medical record documentation of concurrent therapy with appropriate dose and duration of ribavirin, if indicated **AND**
- Medical record documentation of a negative pregnancy test if member is female of childbearing potential and receiving ribavirin **AND**
- When concurrent ribavirin therapy is indicated and prescribed, medical record documentation for male members that female partner is not pregnant **AND**
- If the member or their partner are of childbearing potential, medical record documentation that the member was instructed to practice effective contraception during therapy with ribavirin and for 6 months following discontinuation of ribavirin therapy **AND**
- If actively abusing alcohol or intravenous (IV) drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment **AND**
- Medical record documentation that member received pre-treatment readiness education about hepatitis C treatment expectations by a health care provider **AND**
- Medical record documentation that the member commits to the documented planned course of treatment including anticipated blood tests and visits, during and after treatment **AND**
- Medical record documentation that member does not have a limited life expectancy of less than 12 months due to non-liver related co-morbid conditions **AND**

- Medical record documentation of completed:
  - Hepatitis B immunization series **OR**
  - Hepatitis B screening (sAb/sAg and cAb/cAg) **AND** Quantitative hepatitis B virus (HBV) DNA if positive for hepatitis B sAg or cAb or cAg **AND**
    - If there is detectable hepatitis B virus (HBV) DNA, will be treated for Hepatitis B **OR**
    - If negative for hepatitis B sAb, is being vaccinated against Hepatitis B **AND**

- Medical record documentation of human immunodeficiency virus (HIV) screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay:
    - Is being treated for human immunodeficiency virus (HIV) **OR**
    - If not being treated for human immunodeficiency virus (HIV), the medical record documents the rationale for the beneficiary not being treated **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret OR sofosbuvir-velpatasvir tablets, if clinically appropriate **AND**
- Medical record documentation that member has been evaluated and treated by a contracted Center of Excellence in hepatitis C management

OR

- Medical record documentation of a hepatitis C negative recipient receiving a transplant from a hepatitis C positive donor **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret OR sofosbuvir-velpatasvir , if clinically appropriate

NOTE: Center of Excellence (COE) requirements do not apply to strategic partner TPA plans (i.e., Northern Light Health).

Guidelines can be referenced at https://www.hcvguidelines.org/

TREATMENT DURATION:
Consistent with AASLD/ IDSA Guidelines (8 weeks, 12 weeks, 24 weeks)

**8 weeks duration is only for treatment-naïve, Genotype 1 patients who are HIV-uninfected and whose HCV RNA level is < 6million IU/ml

MEDISPAN AUTHORIZATION LEVEL: GPI-10, if request is for ledipasvir/sofosbuvir 90/400 mg tablet include generic only.
QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

- QL FOR LETTER ONLY:
    - 90-400 mg and 45-200 mg tablets: 1 tablet per day, 28 day supply per fill
    - 45-200 mg pellets: 2 packets per day, 28 day supply per fill
    - 37.5-150 mg pellets: 1 packet per day, 28 day supply per fill

Approval language: Meets criteria, auth x (?) weeks, rx count= (?), (28 day supply/fill), generic only [when applicable]. QL: 1 tab/day (QL for LETTER only)

If an exception is made, Harvoni or ledipasvir/sofosbuvir 90/400 mg tablet will be paid for under the member's prescription drug benefit.

Reviewer should refer to the process and procedure in Pharmacy Policy 3.0 (Geisinger Health Plan (GHP) Formulary Exception) for additional information.

FORMULARY ALTERNATIVES:
Mavyret*, sofosbuvir-velpatasvir tablets*
*prior authorization required

Vosevi Policy 460.0 (Comm/Exchange/Chip)

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of hepatitis C infection **AND**
- Medical record documentation of the member's hepatitis C genotype **AND**
- Medical record documentation of a diagnosis of hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis **AND**
- Medical record documentation of METAVIR liver scoring or cirrhosis assessment by a non-invasive test **AND**
- Medical record documentation of a hepatocellular carcinoma screening in those with cirrhosis (METAVIR score F4) **AND**
- Medical record documentation that Vosevi is prescribed by a board-certified gastroenterologist, hepatologist, infectious disease specialist, or transplant specialist **AND**
- Medical record documentation of the member receiving a Food and Drug Administration (FDA) approved medication regimen that is inside the parameters of use approved by the FDA or supported in the widely used compendia available ~~**OR**~~ **AND**
  - ~~Medical record documentation of:~~
    - ~~Genotype 1, 2, 3, 4, 5, or 6~~
      - ~~As monotherapy if treatment experienced with an NS5A inhibitor (daclatasvir, elbasvir, ledipasvir, ombitasvir, or velpatasvir) **OR**~~
    - ~~Genotype 1a or 3 As monotherapy if treatment experienced with a prior treatment regimen including sofosbuvir with or without any of the following:~~
      - ~~peginterferon alfa/ribavirin, ribavirin, HCV NS3/4A protease inhibitor (boceprevir, simeprevir, or telaprevir) **AND**~~
- Medical record documentation of appropriate duration of treatment **AND**
- Medical record documentation of previous treatment and treatment response **AND**
- Medical record documentation of any potential drug interactions addressed by the prescriber (such as discontinuation of the interacting drug, dose reduction of the interacting drug, or counseling of the recipient of the risks associated with the use of both medications when they interact) **AND**
- Medical record documentation of receiving the following within the past ~~3 months~~ 6 months:
  - Hepatic function panel
  - Complete blood count ~~including differential~~
  - Basic metabolic panel
- Medical record documentation of receiving the following within a reasonable timeframe:
  - Baseline hepatitis C virus (HCV) RNA viral load **AND**
- Medical record documentation of concurrent therapy with appropriate dose and duration of weight-based ribavirin, if indicated **AND**
- Medical record documentation of a negative pregnancy test if member is female of childbearing potential and receiving ribavirin **AND**
- When concurrent ribavirin therapy is indicated and prescribed, medical record documentation for male members that their female partner is not pregnant **AND**
- If the member or their partner are of childbearing potential, medical record documentation that the member was instructed to practice effective contraception during therapy with ribavirin and for 6 months following discontinuation of ribavirin therapy **AND**

- ~~Medical record documentation that member does not have severe renal impairment (estimated glomerular filtration rate less than 30 mL/min/1.73 m^2) or end stage renal disease requiring hemodialysis **AND**~~
- If actively abusing alcohol or intravenous (IV) drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment **AND**
- Medical record documentation that member received pre-treatment readiness education about hepatitis C treatment expectations by a health care provider **AND**
- Medical record documentation that the member commits to the documented planned course of treatment including anticipated blood tests and visits, during and after treatment **AND**
- Medical record documentation that member does not have a limited life expectancy of less than 12 months due to non-liver related co-morbid conditions **AND**
- Medical record documentation of completed:
    - Hepatitis B immunization series **OR**
    - Hepatitis B screening (sAb/sAg and cAb/cAg) **AND** Quantitative hepatitis B virus (HBV) DNA if positive for hepatitis B sAg or cAb or cAg **AND**
        - If there is detectable hepatitis B virus (HBV) DNA, will be treated for Hepatitis B **OR**
        - If negative for hepatitis B sAb, is being vaccinated against Hepatitis B **AND**
- Medical record documentation of human immunodeficiency virus (HIV) screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay:
    - Is being treated for human immunodeficiency virus (HIV) **OR**
    - If not being treated for human immunodeficiency virus (HIV), the medical record documents the rationale for the beneficiary not being treated **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Mavyret OR sofosbuvir-velpatasvir tablets, if clinically appropriate **AND**
- Medical record documentation that member has been evaluated and treated by a contracted Center of Excellence in hepatitis C management

  OR
- Medical record documentation of a hepatitis C negative recipient receiving a transplant from a hepatitis C positive donor **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret, OR sofosbuvir-velpatasvir tablets, if clinically appropriate

NOTES TO REVIEWER

1. Center of Excellence (COE) requirements do not apply to strategic partner TPA plans (i.e., Northern Light Health).
2. Vosevi is usually reserved for treatment-experienced patients. It is an IIa recommendation according to the AASLD/IDSA Guidelines which is equivalent to Mavvret + sofosbuvir + ribavirin in most scenarios. Ribavirin is sometimes avoided due to frequent lab work.

Guidelines can be referenced at https://www.hcvguidelines.org/

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

- QL FOR LETTER ONLY: one (1) tablet per day, 28 day supply per fill

AUTHORIZATION DURATION: 12 weeks **OR** ~~medical record documentation of the member receiving a Food and Drug Administration (FDA) approved medication regimen that is inside the parameters of use approved by the FDA or supported in the widely used compendia available~~ as per Consistent with AASLD/ IDSA Guidelines (12 weeks, 24 weeks) for Treatment Experienced patients

Approval language: Meets criteria, auth x (?) weeks, rx count= (?), (28 day supply/fill), generic only [when applicable]. QL: 1 tab/day (QL for LETTER only)

FORMULARY ALTERNATIVES:
Mavyret*, sofosbuvir-velpatasvir tablets*
*prior authorization required

Sovaldi Policy 326.0 (Comm/Exchange/Chip)

- Medical record documentation of age greater than or equal to 3 years using weight-based dosing **AND**
- Medical record documentation of a diagnosis of hepatitis C infection **AND**
- Medical record documentation of the member's hepatitis C genotype **AND**
- Medical record documentation of a diagnosis of Hepatitis C Virus (HCV) genotype 1, 2, 3, or 4 infection in adults **OR** HCV genotype 2 or 3 in pediatric patients ≥ 3 years of age, without cirrhosis or with compensated cirrhosis, as a component of a combination antiviral treatment regimen AND
- Medical record documentation of METAVIR liver scoring or cirrhosis assessment by a non-invasive test **AND**
- Medical record documentation of a hepatocellular carcinoma screening in those with cirrhosis (METAVIR score F4) **AND**
- Medical record documentation of the member receiving a Food and Drug Administration (FDA) approved medication regimen that is inside the parameters of use approved by the FDA or supported in the widely used compendia available **AND**
- Medical record documentation of appropriate duration of treatment **AND**
- Medical record documentation of previous treatment and treatment response **AND**
- ~~Medical record documentation of concurrent therapy with appropriate dose and duration of ribavirin (weight-based dosing of ribavirin 1200 mg per day if greater than or equal to 75 kg, or 1000 mg per day if less than 75 kg, or 15 mg/kg in pediatric patients less than 47 kg), if indicated **AND**~~
- Medical record documentation of any potential drug interactions addressed by the prescriber (such as discontinuation of the interacting drug, dose reduction of the interacting drug, or counseling of the recipient of the risks associated with the use of both medications when they interact) **AND**
- Medical record documentation of receiving the following with the past ~~3 months~~ 6 months:
  - Hepatic function panel
  - ~~o~~ Complete blood count ~~including differential~~
  - Basic metabolic panel
- Medical record documentation of receiving the following within a reasonable timeframe:
  - Baseline Hepatitis C Virus (HCV) RNA viral load **AND**
- ~~Medical record documentation that member does not have severe renal impairment (estimated glomerular filtration rate less than 30 mL/min/1.73 m^2) or end stage renal disease requiring hemodialysis **AND**~~
- Medical record documentation of concurrent therapy with appropriate dose and duration of weight-based ribavirin, if indicated **AND**
- Medical record documentation of a negative pregnancy test if member is female of childbearing potential and receiving ribavirin **AND**
- When concurrent ribavirin therapy is indicated and prescribed, medical record documentation for male members that female partner is not pregnant **AND**
- If the member or their partner are of childbearing potential, medical record documentation that the member was instructed to practice effective contraception

during therapy with ribavirin and for 6 months following discontinuation of ribavirin therapy **AND**
    - If actively abusing alcohol or intravenous (IV) drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment **AND**
    - Medical record documentation that member received pre-treatment readiness education about hepatitis C treatment expectations by a health care provider **AND**
    - Medical record documentation that the member commits to the documented planned course of treatment including anticipated blood tests and visits, during and after treatment **AND**
    - Medical record documentation that member does not have a limited life expectancy of less than 12 months due to non-liver-related co-morbid conditions **AND**
- Medical record documentation of completed:
    - Hepatitis B immunization series **OR**
    - Hepatitis B screening (sAb/sAg and cAb/cAg) **AND** Quantitative hepatitis B virus (HBV) DNA if positive for hepatitis B sAg or cAb or cAg **AND**
        - If there is detectable hepatitis B virus (HBV) DNA, will be treated for Hepatitis B **OR**
        - If negative for hepatitis B sAb, is being vaccinated against Hepatitis B **AND**
- Medical record documentation of human immunodeficiency virus (HIV) screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay:
    - Is being treated for human immunodeficiency virus (HIV) **OR**
    - If not being treated for human immunodeficiency virus (HIV), the medical record documents the rationale for the beneficiary not being treated **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret OR sofosbuvir-velpatasvir tablets, if clinically appropriate **AND**
- Medical record documentation that member has been evaluated and treated by a contracted Center of Excellence in hepatitis C management

OR

- Medical record documentation of a hepatitis C negative recipient receiving a transplant from a hepatitis C positive donor **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret OR sofosbuvir-velpatasvir tablets, if clinically appropriate

NOTES TO REVIEWER

1. Center of Excellence (COE) requirements do not apply to strategic partner TPA plans (i.e., Northern Light Health).
2. The AASLD/IDSA Guidelines only recommend single-agent sofosbuvir, in combination with other appropriate agents, for HCV infection (all genotypes) in limited situations.

Guidelines can be referenced at https://www.hcvguidelines.org/

TREATMENT DURATION: Consistent with AASLD/ISDA Guidelines

MEDISPAN AUTHORIZATION LEVEL: GPI-10

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

- QL FOR LETTER ONLY:
  - 200 mg and 400 mg tablets: 1 tablet per day, 28 day supply per fill
  - 200 mg pellets: 2 packets per day, 28 day supply per fill
  - 400 mg pellets: 1 packet per day, 28 day supply per fill

Approval language: Meets criteria, auth x (?) weeks, rx count= (?), (28 day supply/fill), generic only [when applicable]. QL: 1 tab/day (QL for LETTER only)

FORMULARY ALTERNATIVES (if applicable):

Mavyret*, sofosbuvir-velpatasvir tablets*

*prior authorization required

Zepatier Policy 419.0 (Comm/Exchange/Chip)

- Medical record documentation of age greater than or equal to 12 years of age **OR** weighing at least 30 kilograms **AND**
- Medical record documentation of a diagnosis of hepatitis C infection **AND**
- Medical record documentation of the member's hepatitis C genotype **AND**
- Medical record documentation of a diagnosis of hepatitis C virus (HCV) genotype 1 or 4 infection **AND**
  - Medical record documentation of METAVIR liver scoring **AND**
  - Medical record documentation of a hepatocellular carcinoma screening in those with cirrhosis (METAVIR score F4) **AND**
  - Medical record documentation that the member does not have moderate or severe hepatic impairment (Child-Pugh B or C) **AND**
- ~~Medical record documentation of:~~
  - ~~Genotype 1a~~
    - ~~As monotherapy if treatment-naïve or peginterferon alfa + ribavirin experienced without baseline NS5A polymorphisms **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment-naïve or peginterferon alfa + ribavirin experienced with baseline NS5A polymorphisms **OR**~~
    - ~~Concurrent therapy with ribavirin if peginterferon alfa + ribavirin + hepatitis C virus (HCV) NS3/4A protease inhibitor experienced **OR**~~
  - ~~Genotype 1b~~
    - ~~As monotherapy if treatment-naïve or peginterferon alfa + ribavirin experienced **OR**~~
    - ~~Concurrent therapy with ribavirin if peginterferon alfa + ribavirin + hepatitis C virus (HCV) NS3/4A protease inhibitor experienced **OR**~~
  - ~~Genotype 4~~
    - ~~As monotherapy if treatment naïve or if treatment experienced with peginterferon alfa + ribavirin who experienced virologic relapse following treatments **OR**~~
    - ~~Concurrent therapy with ribavirin if treatment experienced with peginterferon alfa + ribavirin who experienced virologic failure during treatment **AND**~~
- Medical record documentation of the member receiving a Food and Drug Administration (FDA) approved medication regimen that is inside the parameters of use approved by the FDA or supported in the widely used compendia available **AND**
- Medical record documentation of appropriate duration of treatment **AND**
- Medical record documentation of previous treatment and treatment response **AND**
- ~~Medical record documentation of concurrent therapy with appropriate dose and duration of ribavirin (less than 66 kilograms – 800 milligrams per day, 66 to 80 kilograms = 1000 milligrams per day, 81 to 105 kilograms = 1200 milligrams per day, greater than 105 kilograms = 1400 milligrams per day), if indicated **AND**~~
- Medical record documentation of any potential drug interactions addressed by the prescriber (such as discontinuation of the interacting drug, dose reduction of the interacting drug, or counseling of the recipient of the risks associated with the use of both medications when they interact) **AND**
- Medical record documentation of receiving the following within the past ~~3 months~~ 6 months:
  - Hepatic function panel

    - ~~o~~ Complete blood count ~~including differential~~
    - Basic metabolic panel
- Medical record documentation of receiving the following within ~~the past 3 months~~ a reasonable timeframe:
    - Baseline hepatitis C virus (HCV) RNA viral load **AND**
- Medical record documentation of concurrent therapy with appropriate dose and duration of ribavirin AND
- Medical record documentation of a negative pregnancy test if member is female of childbearing potential and receiving ribavirin **AND**
- When concurrent ribavirin therapy is indicated and prescribed, medical record documentation for male members that female partner is not pregnant **AND**
- If the member or their partner are of childbearing potential, medical record documentation that the member was instructed to practice effective contraception during therapy with ribavirin and for 6 months following discontinuation of ribavirin therapy **AND**
- If actively abusing alcohol or intravenous (IV) drugs, or has a history of abuse, has documentation of prescriber counseling regarding the risks of alcohol or IV drug abuse, and an offer of a referral for substance use disorder treatment **AND**
- Medical record documentation that member received pre-treatment readiness education about hepatitis C treatment expectations by a health care provider **AND**
- Medical record documentation that the member commits to the documented planned course of treatment including anticipated blood tests and visits, during and after treatment **AND**
- Medical record documentation that member does not have a limited life expectancy of less than 12 months due to non-liver related co-morbid conditions **AND**
- Medical record documentation of completed:
    - Hepatitis B immunization series **OR**
    - Hepatitis B screening (sAb/sAg and cAb/cAg) **AND** Quantitative hepatitis B virus (HBV) DNA if positive for hepatitis B sAg or cAb or cAg **AND**
        - If there is detectable hepatitis B virus (HBV) DNA, will be treated for Hepatitis B **OR**
        - If negative for hepatitis B sAb, is being vaccinated against Hepatitis B **AND**
- Medical record documentation of human immunodeficiency virus (HIV) screening (HIV Ag/Ab) and if confirmed positive by HIV-1/HIV-2 differentiation immunoassay:
    - Is being treated for human immunodeficiency virus (HIV) **OR**
    - If not being treated for human immunodeficiency virus (HIV), the medical record documents the rationale for the beneficiary not being treated **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret OR sofosbuvir-velpatasvir tablets, if clinically appropriate **AND**
- Medical record documentation that member has been evaluated and treated by a contracted Center of Excellence in hepatitis C management

OR

- Medical record documentation of a hepatitis C negative recipient receiving a transplant from a hepatitis C positive donor **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Mavyret OR sofosbuvir-velpatasvir tablets, if clinically appropriate

NOTE: Center of Excellence (COE) requirements do not apply to strategic partner TPA plans (i.e., Northern Light Health).

Guidelines can be referenced at https://www.hcvguidelines.org/

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*

- QL FOR LETTER ONLY: 1 tablet per day, 28 day supply per fill

AUTHORIZATION DURATION: Per AASLD/IDSA guidelines

Approval language: Meets criteria, auth x (?) weeks, rx count= (?), (28 day supply/fill), generic only [when applicable]. QL: 1 tab/day (QL for LETTER only)

FORMULARY ALTERNATIVES (if applicable):

Mavyret*, sofosbuvir-velpatasvir tablets*
*prior authorization required

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

Financial Discussion: A concern was raised that moving generic Epclusa to parity with Mavyret would eliminate rebates for Mavyret. Exponent confirmed this would be the case. We will table and re-evaluate this recommendation. No additional comments or questions. The committee unanimously voted to accept the other recommendations as presented. None were opposed.

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

FAST FACTS

TAFINLAR & MEKINIST (dabrafenib & trametinib)

Review: Tafinlar and Mekinist are now indicated in combination for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600 E mutation who require systemic therapy. An FDA-approved test for detection of this mutation in LGG is not currently available. The recommended dosage of Tafinlar and Mekinist in pediatric patients is based on body weight (Table 1 and Table 2). New formulations of Tafinlar (10 mg tablets for oral suspension) and Mekinist (powder for oral solution containing 4.7 mg per bottle, each mL of reconstituted solution containing 0.05 mg) were approved with the new indication. The formulations are not currently on the market and pricing is unavailable at this time.

No new warnings and precautions were added for Tafinlar and Mekinist for treatment in pediatric patients based on the results of Study G2201. The most common adverse reactions were pyrexia, rash, headache, vomiting, musculoskeletal pain, fatigue, diarrhea, dry skin, nausea, hemorrhage, abdominal pain, dermatitis acneiform, dizziness, upper respiratory tract infection, and weight increased.

Current Formulary Status: Tafinlar capsules: Oral Oncology Brand Non-Preferred tier ($ copay), Prior authorization required for new starts only, QL: 4 capsules per day, 30 day supply per fill

Mekinist tablets: Oral Oncology Brand Non-Preferred tier ($ copay), Prior authorization required, QL: Mekinist 1 mg and 2 mg: 1 tablet per day, 30 day supply per fill ,Mekinist 0.5 mg: 3 tablets per day, 30 day supply per fill

Recommendation: When available, the new formulations of Tafinlar and Mekinist will be added to match the placement of Tafinlar Capsules and Mekinist tablets.
GPI-12, QL: Tafinlar Tablets for Oral Suspension: 30 tablets per day, 30 day supply per fill
GPI-12, QL Mekinist for Oral Solution: 40 milliliters per day, 30 day supply per fill

The following prior authorization criteria will be added to Commercial Policy 304.0 for Tafinlar and Mekinist and Part D Policies 303.0D and 306.0D for Tafinlar and Mekinist.
Low Grade Glioma (LGG)

- Medical record documentation that Tafinlar and Mekinist are prescribed by a hematologist or oncologist **AND**
- Medical record documentation of low-grade glioma (LGG) **AND**
- Medical record documentation of age greater than or equal to one year and less than 18 years **AND**
- Medical record documentation of BRAF V600E mutation **AND**
- Medical record documentation that Mekinist and Tafinlar will be used in combination

Authorization duration: Each treatment period will be defined as 12 months. Re-review will occur every 12 months. Tafinlar and/or Mekinist will no longer be covered if there is medical record documentation of disease progression.

Discussion: No comments or questions.

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

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

UPDATES

BUDESONIDE & FORMOTEROL INHALATION UPDATE

Background: In the past, GHP was told that preferring generic Symbicort, budesonide-formoterol, would negatively impact current ICS-LABA inhalers on formulary. However, we confirmed that adding the authorized generic of Symbicort will not impact rebates of the others in the market basket. It is currently on formulary for Gold but requires a step through fluticasone-salmeterol. It is non-formulary for commercial plans. Pulmonology is interested in prescribing a single inhaler for both maintenance and rescue therapy. The newer GINA guidelines recommend for patients 12 years and older to use Symbicort as a rescue inhaler in addition to the BID dosing, SMART approach. SABAs are no longer preferred. For patients 6-11 years old, the reliever option can be as-needed SABA or as-needed ICS-formoterol. Budesonide-formoterol is the only agent indicated for this use in the guidelines, so they would be interested in this agent as a preferred product. Budesonide-formoterol for PRN use allows up to 12 inhalations per day. Also, from an Asthma Medication Ratio (AMR) HEDIS measure perspective, the addition of budesonide-formoterol would potentially make a positive impact on the measure rates. Members would hopefully replace their SABAs with Symbicort and decrease their rescue inhaler fills, which would improve the AMR measure.

Recommendation: It is recommended to add budesonide-formoterol inhalation to formulary at the generic tier. Budesonide-formoterol inhalation will not require a prior authorization/step therapy. The following quantity limit will apply:

> **QUANTITY LIMIT:** Budesonide-Formoterol Fumarate Inhalation 80-4.5 mcg/act and 160-4.5 mcg/act: 1.02 grams per day

Discussion: No comments or questions.

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

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

PROLIA UPDATE

Background: During an update to Tymlos, it was identified that guidelines recommending treatment of osteoporosis in men with high risk of fracture have been updated to match the recommendations for post-menopausal women at high risk of fractures. The following updates are recommended for Medical Benefit Policy 81.0:

Recommendation:
For the treatment of men at high risk for fractures:

- Physician provided documentation of a diagnosis of osteoporosis; **AND**
- Physician provided documentation of previous osteoporotic fracture or high risk of fracture (defined as spine or hip DXA T-score of less than or equal to -2.0 -2.5, supporting clinical factors, and/or FRAX calculation showing a >3% probability of hip fracture OR >20% probability of major osteoporosis-related fracture); **OR**
- Physician provided documentation of a failed attempt of therapy with or contraindication to one oral bisphosphonate

Discussion: No comments or questions.

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

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

MEDICAL BENEFIT POLICY UPDATE

Background: Policies updated at the direction of DHS during PARP submission process:

MBP: 275.0 Pedmark (sodium thiosulfate) – THE COG ACCL0431 (NCT00716976) study included patients 18 years of age [The median age was 8 years (range: 1 to 18)]. Please revise to include patients less than or equal to 18 years of age.

Recommendation:

MBP 275.0 Pedmark (sodium thiosulfate)

- Documentation of age greater than or equal to 1 month but less than or equal to 18 years of age **AND**

Discussion: No comments or questions.

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

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

MIFEPRISTONE UPDATE

Background: It was recently identified that Geisinger is the only insurer offering Commercial coverage in the state of Pennsylvania which does not cover mifepristone as part of the drug formulary. Mifepristone is used in combination with misoprostol to terminate a pregnancy up to 70 days (10 weeks) gestation. Since its original approval in 2000, mifepristone has been used approximately 5.6 million times and the FDA has found it to have a very low rate of complications and a high rate of effectiveness.

Recommendation: In order to ensure our members have access to mifepristone when deemed medically necessary, it is recommended that mifepristone is added to the prescription drug formulary:

- Commercial/CHIP: generic, tier 1
- Marketplace: non-preferred generic, tier 2

Discussion: Dr. Yarczower how it was identified that we were an outlier. Kim C. responded that the Pennsylvania Insurance Department completed a survey of commercial insurers following Roe vs. Wade being overturned. No additional comments or questions.

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

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

MAY 2023 P&T DUR/ADHERENCE UPDATE

Drug Use Evaluations (DUEs)

- Overutilization of albuterol and levalbuterol
    - This is our 2022 3rd quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, Chip
    - For this report, we identified members who had greater than a 180-day cumulative day supply of Albuterol and/or levalbuterol (based on pharmacy claims from 1/1/2022-12/23/22) with a diagnosis of Asthma (based on medical claims from 4/1/2021 through 12/23/22)
        - See below for the number of members identified:
            - For COMM: **61**
            - For D6: **66**
        - Letters were sent to the MI attributed PCP of each member with their medication fill history of both their controller and rescue inhalers to help providers identify members that may be overutilizing their rescue inhalers and to identify potential compliance concerns with their controller inhaler.
        - We will be re-running this data in June 2023 to analyze effectiveness of the letter
- Use of Opioids at High Dosage
    - This is our 2022 2nd quarter Geisinger Health Plan DUE for Commercial, Exchange, TPA, Medicaid, Medicare
    - From this report, we identified members 18 years and older with 15+ opioid covered days and had an MME of 90 or greater per day based on claims from 1/1/2022 through 7/27/2022
        - See below for the number of members that were identified with an MME of 90 or greater per day:
            - For COMM: **13**
            - For D6: **19**
            - For TP45: **2**
            - For TPE0: **1**
            - For SASN: **1**
            - For TG48/TG51: **18**
        - Letters were sent to the MI attributed PCP of each member with the respective medication fill history for providers to evaluate their patients current pain regimen and ensure lowest effective doses are utilized.
        - Letters were mailed out on 9/15/2023
        - Adam K. re-ran this data on 5/5/2023 to analyze the effectiveness of the letter. The following number of members had not filled an opioid within the past 60 days, had an MME less than 90, and/or had an average MME decrease:
            - For COMM: Of the 13 members originally identified, 7 were still active. Of those members, **2 members** did not fill an opioid in the past 60 days, **4 members** had an average MME decrease
            - For D6: Of the 19 members originally identified, 15 were still active. Of those members, **1 member** did not fill an opioid in the past 60 days, **1 member** had an average MME less than 90, **8 members** had an average MME decrease

        - For TG48: Of the 18 members originally identified, 15 were still active. Of those members, **1 member** did not fill an opioid in the past 60 days, **1 member** had an average MME less than 90, **8 members** had an average MME decrease
        - For TG45: Of the 2 members originally identified, 2 were still active. Of those members, **1 member** had an average MME decrease
        - For TPE0: Of the 1 member originally identified, 1 was still active. Of those members, **1 member** had an average MME decrease
        - For SASN: Of the 1 member originally identified, 1 was still active. Of those members, **1 member** had an average MME decrease
- Asthma Medication Ratio
    - This is our 2022 1st quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, CHIP
    - From this report, we used proactive HEDIS data and identified members aged 5-64 with an AMR<0.5. Pharmacy claims from the prior 6 months (9/2021-3/2022) were pulled into the report.
        - See below for the number of members that were identified with an AMR<0.5
            - For **COMM:** 6
            - For **D6: 6**
        - Letters were sent to the MI attributed PCP of each member with the respective medication fill history to encourage conversation around the importance of controller medications.
    - Letters were mailed out on 4/20/2022
    - Adam K. re-ran this data on 8/29/2022 to analyze the effectiveness of the letter. Of the 12 members initially identified, 9 members were still active. Of those members, **4 members** showed an AMR increase compared to 4/2022.
- Use of Opioids from Multiple Providers (UOP) DUE
    - This is our 2021 3rd quarter Geisinger Health Plan DUE for Medicare, Medicaid, Commercial
    - From this report, we identified members 18 years of age and older with a total day supply of all opioid claims to be 15 day or greater based on claims from 1/1/2021 through 9/27/2021:
        - See below for the number of **members** who were identified who were seeing 4 or more providers from different offices for their opioid prescriptions
            - For COMM: **15**
            - For D6: 5
        - See below for the number of **members** who were identified who were seeing 4 or more providers within the same office for their opioid prescriptions
            - For COMM: **0**
            - For D6: **0**
        - We sent letters to the member's MI attributed PCP with the respective medication fill history to encourage medication evaluation of the opioid medications
    - Mitch Kocen completed the mail merge via Quadient on 10/14/2021 and the print shop sent out the letters on 10/18/2021
    - Adam K. re-ran this data on 3/10/2022 to analyze the effectiveness of the letter. Of the 20 members initially addressed, 13 members were still active. Of those members, **all 13**

members showed a decrease in the number of prescribers they were seeing compared to 10/2021

- Statin Use in Persons with Diabetes DUE
    - This is our 2021 2nd quarter Geisinger Health Plan DUE for all LOBs
    - From this report, we identified **1,564 members** age 40 to 75 with at least 2 distinct fills of any diabetic medication(s) without a statin claim. We sent an educational letter to providers to encourage prescribing of a statin to members, if medically appropriate.
    - The Print Shop completed the mail merge and sent out letters to the member's providers on 8/2/2021.
    - Adam K. re-ran this data on 11/19/2021 to analyze the effectiveness of the letter. Of the **1564 members** initially addressed, **1430** are still active. Of those members, **128** now have a claim for a statin medication. This equates to about **9%** of the targeted members.
    - See below for the number of letters sent:
        - For COMM: **613**
        - For D6: **372**
        - For TP23: **4**
        - For TP33: **2**
        - For TP41: **2**
        - For TP45: **34**
        - For TP46: **11**
        - For TP49: **2**
        - For TP50: **11**
        - For TP56: **2**
        - For TP64: **3**
        - For TPA6: **2**
        - For TPA7: **3**
        - For TPB3: **1**
        - For TPD2: **1**
        - For TPE0: **4**
        - For TPF0: **1**
        - For TPF2: **2**
        - For TPH2: **0**
        - For TPI0: **4**
        - For TPI2: **4**
        - For TPL0: **0**
        - For TPM2: **2**
        - For TPN1: **1**
        - For TPU1: **2**
        - For TPW1: **2**
        - For WF89: **11**
        - For EMYD: **0**
        - For SASE: **6**
        - For SAI1: **1**
        - For SASF: **1**
        - For SASN: **55**
        - For SASX: **5**
        - For PM70: **2**
        - For PM71: **1**
        - For TG48/TG51: **397**

In Progress

- For Exchange: HEDIS PQA Adherence Reports for the following measures:
    - Renin Angiotensin System Antagonists (PDC-RASA)
    - Diabetes All Class (PDC-DR)
    - Statins (PDC-STA)
- For Exchange: HEDIS PQA Long term Opioid use report
    - Annual Monitoring for Persons on Long-Term Opioid Therapy (AMO)
- DPP-4/GLP-1 Diabetes Duplicate Therapy Report

Ongoing

- TNF and Oral Oncology Agent Report
    - We get this report monthly for the Commercial/Exchange, TPA, and CHIP LOBs from Adam Kelchner.
    - This report was generated in response to removing the renewal prior authorization requirement for these agents.

- This report identifies members who are on a TNF or Oral Oncology agent and may not have been seen by their applicable specialist in the last 15 months.
- We research these members and reach out to the offices/members as necessary to ensure the member has been seen within the last 15 months, an appointment has been scheduled or will be scheduled with the member to ensure the member continues to be able to receive their medication.
- For 2023:
  - For COMM
    - Members Reviewed: **9**
    - Outreaches Made: **2**
    - Letters Sent: **2**
    - Negative Overrides Entered: **0**
  - For D6
    - Members Reviewed: **11**
    - Outreaches Made: **3**
    - Letters Sent: **1**
    - Negative Overrides Entered: **1**
  - For TG48
    - Members Reviewed: **7**
    - Outreaches Made: **3**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TG51
    - Members Reviewed: **1**
    - Outreaches Made: **0**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TGW2
    - Members Reviewed: **1**
    - Outreaches Made: **0**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TP45
    - Members Reviewed: **1**
    - Outreaches Made: **0**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**

- <u>Cystic Fibrosis Adherence Report</u>
  - We get this report monthly for all LOBs from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.
    - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence
    - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
    - And for all members we send a letter discussing the importance of medication adherence

        - For 2023, please see below for the number of **members** an adherence letter was sent to:
            - Letters are only sent to members every 6 months
                - For COMM: **2**
                - For D6: **2**
                - For TG48: **2**
                - For WF89: **2**
        - Please see below for the number of letters sent to non-GHS pulmonologists
            - For D6: **0**
        - Please see below for the number of members referred to the CF coordinators:
            - For COMM: **8**
            - For D6: **8**
            - For TG48: **7**
            - For WF89: **3**
- Duplicate Anticoagulant Report
    - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
    - For 2023:
        - For COMM (Commercial): **3 members** reviewed and **0 interventions** made
        - For D6 (Exchange): **6 members** reviewed and **0 interventions** made
        - For TG48/GH51: **1 member** reviewed and **1 intervention** made
        - For TP23: **0 members** reviewed and **0 interventions** made
        - For TP45: **0 members** reviewed and **0 interventions** made
        - For TP56: **0 members** reviewed and **0 interventions** made
        - For EMYD: **0 members** reviewed and **0 interventions** made
        - For MT38: **0 members** reviewed and **0 interventions** made
        - For TP74: **0 members** reviewed and **0 interventions** made
        - For SASN: 0 **member** reviewed and **0 interventions** made
        - For SASF: 0 **member** reviewed and **0 interventions** made
        - For TPH3: **1 member** reviewed and **0 interventions** made
- Duplicate Specialty Therapy
    - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Smith. These members are identified and written up and sent to a medical director if follow up is needed.
        - For Commercial/Exchange/TPA for, **0 members** were referred to Dr. Yarczower for additional follow-up.
- Duplicate Buprenorphine Therapy
    - We get this report **quarterly** 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 and Dr. Hossler for further outreach.
        - For Commercial/Exchange, TPAs for 2023, we have reviewed **0 members** and **0 members** were referred to Dr. Meadows
- Suboxone with an Opioid Report
    - We get this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each new member that flags on the report. These members are being discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both medical directors look into whether it

is appropriate to end the opioid authorizations still in place or if further intervention is required.
    - For Commercial/Exchange/TPA for 2023, see below for the new members reviewed and those referred to the MDs:
        - For COMM: we have reviewed **0 new members** and **0 members** were referred to MDs
        - For D6: we have reviewed **1 new member** and **0 members** were referred to MDs
        - For EMYD: we have reviewed **0 new members** and **0 members** were referred to MDs
        - For TG48: we have reviewed **3 new members** and **0 members** was referred to MDs
        - For SASE: we have reviewed **0 new members** and **0 members** was referred to MDs
        - For SASN: we have reviewed **0 new members** and **0 members** was referred to MDs
        - For TPI2: we have reviewed **0 new members** and **0 members** was referred to MDs
- 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 Commercial/Exchange/TPA for 2023, see below for the number of letters we sent to members notifying them that we are ending their opioid authorization(s):
        - For D6: **0**
        - For COMM: **0**
        - For TG48/TG51: **0**
        - For SASN: **0**
- Opioid Overutilization Report
    - We get this report **monthly** from PerformRx and we write 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 Commercial/Exchange/TPA for 2023, see below for the number of reviewed cases.
        - For COMM: we have reviewed **0 members** and sent **0 cases** to MDs for review
        - For EMYD: we have reviewed **2 members** and sent **0 cases** to MDs for review
        - For TG48: we have reviewed **1 member** and sent **0 cases** to MDs for review
- FWA Reports
    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For COMM for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $1,543.86**
        - For D6 for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $2,103.84**

        - For TPJ0 for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
        - For TPH2 for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
        - For TPE0 for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
        - For TPN2 for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
        - For EMYD for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $783.62**
        - For TG48, TG51 for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $4,464.49**
        - For SASE for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $1**
        - For SASN for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $778.06**
        - For SASK for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
        - For TP23 for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $32.91**
        - For TP45 for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
        - For WF89 for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $312.96**
        - For TPD2 for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $286.50**
        - For TP49 for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $27.91**
        - For TGW2 for 2023, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
- Duplicate Antipsychotics
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - We have sent the following provider letters in 2023
            - For COMM: **13**
            - FOR D6: **14**
            - FOR TG48, TG51: **15**
            - For TP45: **2**
            - For TP56: **0**
            - For EMYD: **0**
            - For MT38: **0**
            - For TP74: **0**
            - For SASN: **0**
            - For SASF: **0**
            - For TGW2: **1**
- Severity Report
    - We get this report **monthly** 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 Commercial/Exchange/TPA for 2023 see below for the number of members identified and had sent letters to their MI attributed PCP:
            - For COMM: **22**
            - For D6: **18**
            - For EMYD: **0**
            - For SASF: **0**
            - For SASN: **2**
            - For SASE: **0**
            - For TG48: **17**
            - For TG51: **2**
            - For TGW2: **1**
            - For TPB3: **0**
            - For TPE0: **0**
            - For TPH2: **0**
            - For TPM2: **0**
            - For TP23: **0**
            - For TP41: **1**
            - For TP45: **1**
            - For TP46: **0**
            - For TP50: **0**
            - For TP56: **0**
            - For TP88: **0**
            - For TPU1: **1**
            - For TPA6: **0**
            - For WF89: **0**
- Tobacco Cessation Program
    - We get this report **monthly** to identify members on prolonged tobacco cessation treatment. We send a letter and resource pamphlet to provide additional behavioral health support through Geisinger Health and Wellness.
    - For Commercial/Exchange/TPA for 2023, we sent letters to the below number of members:
        - For COMM: **2**
        - For D6: **0**
        - For EMYD: **5**
        - For SASN: **0**
        - For SASE: **0**
        - For TG48, TG51: **0**
        - For TPB3: **0**
        - For TP23: **0**
        - For TP33: **0**
        - For TP45: **1**
        - For TP46: **0**
        - For TP50: **0**
        - For TP56: **0**
        - For TP64: **0**
        - For TP88: **0**
        - For TPA6: **0**
        - For TPT2: **0**

        - For WF89: **0**

- <u>STENT Adherence Report</u>
    - We get this report **<u>monthly</u>** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
    - In 2023, we have sent letters encouraging adherence to the below number of members:
        - **Members for Antiplatelet:**
            - COMM: **0**
            - D6: **0**
            - EMYD: **0**
            - SASN: **0**
            - TG48, TG51: **0**
            - TP41: **0**
            - TP23: **0**
            - TP33: **0**
            - TP45: **0**
            - TP46: **0**
            - TP50: **0**
            - TP56: **0**
            - TP64: **0**
            - TP74: **0**
            - PM71: **0**
            - TP88: **0**
            - TPA6: **0**
            - WF89: **0**
            - TPD2: **0**
            - SASE: **0**
            - SASF: **0**
            - SASK: **0**
            - TPB3: **0**
            - TPF2: **0**
            - TPI0: **0**
            - TPL0: **0**
            - TPM2: **0**
            - **P**M70: **0**
            - PM71: **0**
        - **Members for Beta-Blocker:**
            - COMM: **0**
            - D6: **0**
            - EMYD: **0**
            - SASN: **0**
            - TG48, TG51: **0**
            - TP23: **0**
            - TP45: **0**
            - TP46: **0**
            - TP50: **0**
            - TP56: **0**
            - TP88: **0**
            - TPA6: **0**
            - WF89: **0**
            - TPI0: **0**
            - SASK: **0**
            - TPB3: **0**
            - TPR1: **0**
            - TPT2: **0**
            - TPU1: **0**
            - SASE: **0**
        - **Members for Statin:**
            - COMM: **0**
            - D6: **0**
            - EMYD: **0**
            - SASN: **0**
            - SASF: **0**
            - TG48, TG51: **0**
            - TP23: **0**
            - TP45: **0**
            - TP46: **0**
            - TP56: **0**
            - PM71: **0**
            - SASK: **0**
            - SAQ2: **0**
            - TPI0: **0**
            - TPM2: **0**
            - TPR1: **0**
            - TP88: **0**
            - TPA6: **0**
            - TPU1: **0**
            - WF89: **0**
            - TP50: **0**
            - TP64: **0**
            - PM70: **0**
            - TP74: **0**
            - SASE: **0**
            - TPB3: **0**
            - TPH2: **0**
            - TPT2: **0**
            - TP41: **0**

        - *member may flag for more than one measure and are included in the count for each measure
    - In 2023, we have attempted telephonic outreach to the below number of members non-adherent in all 3 measures and reached the below members to encourage adherence.
        - COMM:
            - Attempted:**0**
            - Reached: **0**
        - D6:
            - Attempted: **0**
            - Reached:**0**
        - SASN:
            - Attempted: **0**
            - Reached: **0**
- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
        - For Commercial/Exchange for 2023, see below for the number of letters sent to members:
            - COMM: **0**
            - D6: **0**
- Asthma Medication Ratio (AMR) Member Calls
    - Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. The RPHs call Commercial/Exchange members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication.
    - For Commercial/Exchange for 2023, see below for the number of members we have outreached to and the number of members that have been reached:
        - COMM:
            - Outreached to: **34**
            - Reached: **21**
        - D6:
            - Outreached to: **42**
            - Reached: **34**
- Antidepressant Medication Management (AMM)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
        - For Commercial/Exchange for 2023, see below for the number of letters sent to members:
            - Effective Acute Phase:
                - COMM: **0**
                - D6: **0**
            - Effective Continuation Phase:
                - COMM: **0**
                - D6: **0**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.

        - For Commercial/Exchange for 2023, see below for the number of letters sent to members:
            - COMM: **0**
            - D6: **0**
- Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange in 2023, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **0**
            - D6: **0**
        - For Commercial/Exchange in 2023, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **0**
            - D6: **0**
- Statin Therapy for Patients with Diabetes (SPD)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange for 2023, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **0**
            - D6: **0**
        - For Commercial/Exchange for 2023, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **0**
            - D6: **0**
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)
    - We get this report **monthly** to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For Commercial/Exchange for 2023, see below for the number of letters sent to **members:**
            - COMM: **0**
            - D6: **0**
- Use of Opioids from Multiple Providers (UOP)
    - We get this report quarterly to identify members 18 years of age and older with a total day supply of all opioid claims to be 15 days or greater
        - See below for the number of members that were identified who were seeing 4 or more providers from different offices for their opioid prescriptions for 2023
            - **COMM: 4**
            - **D6: 6**
        - See below for the number of members that were identified who were seeing 4 or more providers within the same office for their opioid prescriptions for 2023
            - **COMM: 0**
            - **D6: 0**
        - We sent letters to the MI attributed PCP of each member with the respective medication fill history to encourage medication evaluation of the opioid medications

- **HEDIS PQA Initiatives:**
- HEDIS PQA- INR Report
    - We get this report **weekly** for the Exchange population from Adam Kelchner
    - This report looks at the percentage of members 18 years of age and older who had at least one 56-day interval of warfarin therapy and who received at least one international normalized ratio (INR) monitoring test during each 56-day interval with active warfarin therapy.
        - For Exchange for 2023, we have performed telephonic outreach to providers for **0 members** that had not had an INR level drawn.

Fliers/Letters

- Commercial/Exchange DUR/FWA Program internal Fliers
    - Last updated 11/2022 next update 6/2023
- Current Provider Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Congestive Heart Failure DUE
        - Coronary Artery Disease DUE
        - Statin Use in Persons with Diabetes DUE
        - Opioid Overutilization
        - Duplicate Antipsychotic medication
        - Severity Report
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - HEDIS: Statin Therapy for Patients with Diabetes (SPD)
        - HEDIS: Asthma Medication Ratio (AMR)
        - HEDIS: Use of Opioids from multiple providers (UOP)
        - HEDIS: Use of Opioids at High Dosage (HDO)
- Current Member Letters
        - Exchange PQA Adherence Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Ending Opioid Authorizations
        - Tobacco Cessation Letter
        - STENT Adherence Report
        - HEDIS: Asthma Medication Ratio (AMR)
        - HEDIS: Antidepressant Medication Management (AMM)
        - HEDIS: Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - HEDIS: Statin Therapy for Patients with Diabetes (SPD)
        - HEDIS: Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)

CHIP (CHBQ)

- All of our Medicaid adherence/DUR reports include logic to identify the CHIP population

Drug Use Evaluations (DUEs)

- Overutilization of albuterol and levalbuterol
  - This is our 2022 3rd quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, Chip
  - For this report, we identified members who had greater than a 180-day cumulative day supply of Albuterol and/or levalbuterol (based on pharmacy claims from 1/1/2022-12/23/22) with a diagnosis of Asthma (based on medical claims from 4/1/2021 through 12/23/22)
    - **5 members** were identified with overutilization of their inhalers
    - Letters were sent to the MI attributed PCP of each member with their medication fill history of both their controller and rescue inhalers to help providers identify members that may be overutilizing their rescue inhalers and to identify potential compliance concerns with their controller inhaler.
    - We will be re-running this data in June 2023 to analyze effectiveness of the letter
- Asthma Medication Ratio
  - This is our 2022 1st quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, CHIP
  - From this report, we used proactive HEDIS data and identified members aged 5-64 with an AMR<0.5. Pharmacy claims from the prior 6 months (9/2021-3/2022) were pulled into the report.
    - **0 members** were identified with an AMR<0.5
    - Letters were sent to the MI attributed PCP of each member with the respective medication fill history to encourage conversation around the importance of controller medications.
- Statin Use in Persons with Diabetes DUE
  - This is our 2021 2nd quarter Geisinger Health Plan DUE for all LOBs
  - From this report, we identified **0 members** age 40 to 75 with at least 2 distinct fills of any diabetic medication(s) without a statin claim. We sent an educational letter to providers to encourage prescribing of a statin to members, if medically appropriate.

In Progress

- DPP-4/GLP-1 Diabetes Duplicate Therapy Report

Ongoing

- Cystic Fibrosis Adherence Report
  - We get this report **monthly** for **all LOBs** from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.
    - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence with the member
    - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
    - And for all members we send a letter discussing the importance of medication adherence
    - For CHBQ for 2023, we sent **0 members** an adherence letter

        - Letters are only sent to members every 6 months
        - There were **0 members** who saw a non-GHS pulmonologist and a letter was sent to that pulmonologist
        - There were **0 members** who saw GHS pulmonologists and were sent to the CF coordinators for follow up
- Duplicate Anticoagulant Report
    - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
        - For CHBQ in 2023, we have reviewed **0 members** and have made interventions for **0 members**
- Duplicate Specialty Therapy
    - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Smith. These members are identified and written up and sent to a medical director if follow up is needed.
        - For CHBQ for 2023, **0 members** were referred to Dr. Yarczower for additional follow-up.
- Duplicate Buprenorphine Therapy
    - We get this report **quarterly** 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 and Dr. Hossler for further outreach.
        - For CHBQ for 2023, we have reviewed **0 members** and **0 members** were referred to MDs
- Suboxone with an Opioid Report
    - We get 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 discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both MDs look into whether it is appropriate to end the opioid authorizations still in place or if further intervention is required.
        - For CHBQ for 2023, we have reviewed **0 new members**, and **0 members** were referred to MDs
- 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 CHBQ for 2023, we sent **0 members** a letter notifying them of the end of their opioid authorization(s).
- 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 CHBQ for 2023, letters have been sent to MI attributed providers of **2 CHIP members**
- FWA Reports

    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For CHBQ for 2023, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $1,041.16**
- Tobacco Cessation Program
    - We get this report **monthly** to identify members on prolonged tobacco cessation treatment. We send a letter and resource pamphlet to provide additional behavioral health support through Geisinger Health and Wellness.
        - For CHBQ for 2023, we have not sent any letters
- STENT Adherence Report
    - We get this report **monthly** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
    - For CHBQ for 2023, we have sent letters encouraging adherence to:
        - Members for Antiplatelet:
            - CHBQ: **0**
        - Members for Beta-blocker:
            - CHBQ: **0**
        - Members for Statin:
            - CHBQ: **0**
        - *member may flag for more than one measure and are included in the count for each measure
- Antipsychotic with Opioid Report
    - We get this report **quarterly** to identify **CHIP** members with an overlap of 8 or more days between an opioid and antipsychotic medication.
    - We send a letter with claims data to both the opioid prescriber and the antipsychotic prescriber to encourage collaboration in medication management.
        - For CHBQ for 2023, we sent **0 letters** to **opioid and antipsychotic prescribers**
- Duplicate Antipsychotics
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - For CHBQ in 2023, we have sent letters to **3 providers**
- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR)
    - Jesse Barsh runs this proactive HEDIS report **monthly,** and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
        - For CHBQ for 2023, we sent **0 letters** to members
- Asthma Medication Ratio (AMR) Member Calls
    - Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. we send CHIP members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication to the Respiratory Therapists for direct telephonic outreach.
        - For CHBQ for 2023, we have referred **5 members** to the Respiratory Therapists for outreach.
        - For CHBQ for 2023, our pharmacy technician and the STAR reps have outreached to **5 members** and reached **4 members**

- Antidepressant Medication Management (AMM)
    - Jesse Barsh runs this proactive HEDIS report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
        - For CHBQ for 2023, we sent **0 letters** to members in the **Effective Acute Phase**, and **0 letters** to members in the **Effective Continuation Phase**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
        - For CHBQ for 2023, we have sent **0 letters** to members
- Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ for 2023, we have sent **0 letters** to providers
        - For CHBQ for 2023, we have sent **0 letters** to members
- Statin Therapy for Patients with Diabetes (SPD)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ for 2023, we have sent **0 letters** to providers
        - For CHBQ for 2023, we have sent **0 letters** to members
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)
    - This is a **monthly** report to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For CHBQ for 2023, we have sent **0 letters** to members

Fliers/Letters

- Chip DUR/FWA Program internal Fliers
    - Last updated 11/2022 next update 6/2023
- Current Provider Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Duplicate Antipsychotic medication
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        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - HEDIS: Statin Therapy for Patients with Diabetes (SPD)

Meeting adjourned at 5:16 pm.

The next bi-monthly scheduled meeting will be held on July 18th, 2023 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.