P&T Committee Meeting Minutes
Commercial/Exchange/CHIP
July 16, 2024

Present (via Teams):	**Absent:**
Amir Antonius, Pharm.D.	Kristen Bender, Pharm.D.
Emily Bednarz, Pharm.D.	Alyssa Cilia, RPh
Jeremy Bennett, MD	Michael Dubartell, MD
Kim Castelnovo, RPh	Michael Evans, RPh
Kimberly Clark, Pharm.D.	Nichole Hossler, MD
Bhargavi Degapudi, MD	Jason Howay, Pharm.D.
Kelly Faust, Pharm.D.	Kelli Hunsicker, Pharm.D.
Tricia Heitzman, Pharm.D.	Perry Meadows, MD
Keith Hunsicker, Pharm.D.	Jamie Miller, RPh
Derek Hunt, Pharm.D.	William Seavey, Pharm.D.
Emily Jacobson, Pharm.D.	Michael Shepherd, MD
Dennis Janosczyk, Pharm.D.	Leslie Shumlas, Pharm.D.
Alexanda Kempf-Malys	Todd Sponenberg, Pharm.D.
Kerry Ann Kilkenny, MD	Jill Stone, Pharm.D.
Philip Krebs, R.EEG T	Kevin Szczecina, RPh
Briana LeBeau, Pharm.D.	Margaret Whiteash, Pharm.D.
Ted Marines, Pharm.D.	Bret Yarczower, MD, MBA – Chair
Lisa Mazonkey, RPh	Sherry Beagle, LPN (non-voting participant)
Tyreese McCrea, Pharm.D.	Marika Bergenstock, DO (non-voting participant)
Mark Mowery, Pharm.D.	Abigail Chua, DO (non-voting participant)
Austin Paisley, Pharm.D.	Andrei Nemoianu, MD (non-voting participant)
Jonas Pearson, RPh	
Lauren Pheasant, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Sartori, Pharm.D.	
Kristen Scheib, Pharm.D.	
Kirsten Smith, Pharm.D.	
Aubrielle Smith-Masri, Pharm.D.	
Michael Spishock, RPh	
Luke Sullivan, DO	
Amanda Taylor, MD	
Ariana Wendoloski, Pharm.D.	
Brandon Whiteash, Pharm.D.	
Benjamin Andrick, Pharm.D. (non-voting participant)	
Birju Bhatt, MD (non-voting participant)	
Alfred Denio, MD (non-voting participant)	
Keri Jon Donaldson, MD (non-voting participant)	
Jeremy Garris, Pharm.D. (non-voting participant)	
Nikolas Norman, Pharmacy Student	
Katelyn Kinczel, Pharmacy Student	
Shannon Brown, Pharm.D. (pharmacy resident)	
Lindsey Kisielewsi, Pharm.D. (pharmacy resident)	
Ciera Helsel, Pharm.D. (pharmacy resident)	
Anye Stevenson, Pharm.D. (pharmacy resident)	
Abigail Perriello, Pharm.D. (pharmacy resident)	
Tina Cao, Pharm.D. (pharmacy resident)	

Call to Order:
Kimberly Clark called the meeting to order at 1:03 p.m., Tuesday, July 16, 2024.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the April 2024 e-vote and May 21, 2024 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

ALVAIZ (eltrombopag)

Review: Alvaiz is a thrombopoietin receptor agonist indicated for the following:

- for the treatment of thrombocytopenia in adult and pediatric patients 6 years and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Alvaiz should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.
- for the treatment of thrombocytopenia in adult patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. Alvaiz should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy.
- for the treatment of adult patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Limitations of Use:

- Alvaiz is not indicated for the treatment of patients with myelodysplastic syndrome (MDS).
- Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection.

Alvaiz (eltrombopag choline) is a new salt form of Promacta (eltrombopag). The approval of Alvaiz is based on safety and efficacy findings for Promacta tablets. No additional clinical efficacy or safety data was performed for Alvaiz. Tentative approval was granted for an additional indication for first-line treatment of severe aplastic anemia in adult and pediatric patients 2 years and older for which Promacta currently has exclusivity.

The recommended dosage of Alvaiz is initiated at a dosage of 36 mg orally once daily for refractory severe aplastic anemia and for persistent or chronic immune thrombocytopenia. The recommended initial dosage for chronic hepatitis C-associated thrombocytopenia is 18 mg orally once daily. The dosage is adjusted to achieve the target platelet counts. Maximum recommended dosages are 54 mg/day for persistent or chronic immune thrombocytopenia, 72 mg in thrombocytopenia due to chronic hepatitis C, and 108 mg in refractory severe aplastic anemia. Alvaiz is supplied as 9 mg, 18 mg, 36 mg, and 54 mg tablets for oral administration.

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 (27 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (28 approvals). None were opposed.

Outcome: Alvaiz will not be added to the Commercial, Marketplace, or GHP Kids formulary. The following prior authorization criteria will apply:

For Chronic Immune Thrombocytopenic Purpura (ITP)

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

AUTHORIZATION DURATION: If an exception is made, Alvaiz will be authorized for an initial period of three (3) months and continued coverage will require medical record documentation of improvement in symptoms and platelet count response above 20,000/µL. Subsequent authorizations will be for a period of six (6) months and will then require medical record documentation of dosing to maintain a platelet count between 50,000/µL and 100,000/µL.

For Chronic Hepatitis C

- Medical record documentation of a diagnosis of chronic hepatitis C and plan to initiate or continue interferon-based therapy **AND**
- Medical record documentation of a platelet count of less than 50,000/µL **AND**
- Medical record documentation that Alvaiz is prescribed by a gastroenterologist, hematologist, hepatologist or infectious disease specialist

AUTHORIZATION DURATION: If approved, the authorization will be for a time period of 6 months.

For Severe Aplastic Anemia

- Medical record documentation that Alvaiz is prescribed is written by a hematologist AND
- Medical record documentation of a platelet count less than or equal to 30,000/µL AND
- Medical record documentation of a diagnosis of severe aplastic anemia AND
- Medical record documentation of an inadequate response to at least one prior immunosuppressive therapy (e.g., cyclosporine, mycophenolate mofetil, sirolimus, Atgam® [lymphocyte immune globulin, anti-thymocyte globulin [equine] sterile solution for intravenous use only])

AUTHORIZATION DURATION: If an exception is made, Alvaiz will be authorized for an initial period of six (6) months and continued coverage will require medical record documentation of improvement in symptoms and a hematological response. Subsequent authorizations will be for a period of six (6) months and will then require medical record documentation of continued hematological response.

NOTE: Per UpToDate, hematologic response is defined as independence from transfusion, no need for additional immunosuppressive therapy, and/or improvement or peripheral blood counts to the point that they no longer meet criteria for severe aplastic anemia.

GPI LEVEL: GPI-12

FORMULARY ALTERNATIVES: Promacta* (*prior authorization required)

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

EOHILIA (budesonide)

Review: Eohilia is a glucocorticoid steroid with high topical potency and limited systemic effects. It is used to help reduce inflammation in patients 11 years and older with eosinophilic esophagitis (EoE). The exact mechanism on how Eohilia reduces inflammation is not known. Eohilia is an immediate release oral suspension that is supplied as a premixed single-dose stick pack. It is dose at 2mg/10mL (1 stick pack) orally twice daily for 12 weeks. The administration of the medication is done by shaking the stick pack for at least 10 seconds. The pack of medication is then squeezed into the patient's mouth and swallowed. The patient must wait 30 minutes before eating or drinking. After 30 minutes, the patient rinses their mouth with water and should spit the remaining contents out without swallowing.

Current management of EoE includes a combination strategy with dietary management, acid suppression, topical glucocorticoids, Dupixent, and endoscopic interventions. Prior to the approval of Eohilia, respiratory glucocorticoids such as fluticasone inhalers swallowed not inhaled or budesonide nebulizer respules made into a slurry would be used off label to deliver steroid to the esophagus. Eohilia is the first topical steroid formulated specifically for esophageal delivery and provide standardized dosing.

The only labeled contraindication to Eohilia is in patients with hypersensitivity to budesonide. There are warnings on the FDA label for hypercortisolism and adrenal axis suppression, immunosuppression and increased risk of infection, erosive esophagitis, effects on growth, symptoms of steroid withdrawal in patients transferred from other systemic corticosteroids, Kaposi syndrome, and other corticosteroid effects that should be monitored in patients that have certain conditions such as hypertension, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma or cataracts where corticosteroids may have unwanted side effects. The most common reported adverse effects of the medication are respiratory tract infection (13%), gastrointestinal mucosal candidiasis (8%), headache (5%), gastroenteritis (3%), and throat irritation (3%).

There are no dosage adjustments recommended for kidney impairment. For patients with moderate to severe hepatic impairment, there is a theoretical increased risk of hypercortisolism and adrenal axis suppression due to an increased systemic exposure to budesonide. Caution is recommended in those with moderate dysfunction and use is not recommended in patients with severe hepatic impairment.

The available with oral budesonide use in pregnant women has not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal outcomes. Infants exposed to in-utero corticosteroids, including Eohilia, are at risk for hypoadrenalism. Infants should be carefully observed for signs of hypoadrenalism, such as poor feeding, irritability, weakness, and vomiting, and managed accordingly. Budesonide is known to be present in breast milk following maternal inhalation. Lactation studies have not been conducted with oral budesonide, including Eohilia, and no information is available on the effects of the drug on the breastfed infant or the effects of the drug on milk production.

The safety and efficacy of Eohilia in pediatric patients less than 11 years of age has not been established. Clinical studies of Eohilia did not include enough subjects 65 years of age and older to determine whether they respond differently from younger adult subjects.

The most up to date guidelines for the treatment of EoE are the AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis, which were last updated in May 2022. The guidelines provide a conditional recommendation to use proton pump inhibitors over no treatment. They also provide a strong recommendation of use of topical glucocorticoids over no treatment and conditionally suggest topical steroids should be used over oral steroids. The American college of Gastroenterology current is in the process of updating their EoE guidelines last published in May 2013. They currently recommend using a PPI trial to see if symptoms resolve or overlap of GERD or other GI disease is occurring. If symptoms remain persistent and present, then they also recommend topical steroid use over oral steroids.

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 (29 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (27 approvals). None were opposed.

Outcome: Eohilia will not be added to the Commercial, Marketplace, or GHP Kids formulary. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of eosinophilic esophagitis **AND**
- Medical record documentation of greater than or equal to 15 intraepithelial eosinophils per high-power field (eso/hpf) **AND**
- Medical record documentation of age greater than or equal to 11 years **AND**
- Medical record documentation that Eohilia is prescribed by or in consultation with an allergist, immunologist, or gastroenterologist **AND**
- Medical record documentation that the member is experiencing symptoms of dysphasia (for example: food refusal, food impaction, vomiting, coughing, pain with swallowing) **AND**
- Medical record documentation of contraindication to, intolerance to or therapeutic failure on a proton pump inhibitor **AND**
- Medical record documentation of contraindication to, intolerance to or therapeutic failure of on an inhaled respiratory glucocorticoid

GPI LEVEL: GPI-12

AUTHORIZATION DURATION: 12 weeks. Subsequent approval will require peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA 12-week approved treatment duration.

QUANTITY LIMIT: 60 packets (600 mL) per 30 days

RPH SIGNOFF REQUIRED: Yes

FORMULARY ALTERNATIVES:
Proton pump inhibitors: omeprazole capsule, pantoprazole tablet, lansoprazole capsule, rabeprazole tablet, esomeprazole capsule
Inhaled respiratory glucocorticoids: budesonide inhalation suspension, Fluticasone propionate HFA

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

LIKMEZ (metronidazole)

Review: Likmez is a nitroimidazole antimicrobial indicated for trichomoniasis in adults, amebiasis in adults and pediatric patients, and anaerobic bacterial infections in adults. It is provided in a 200 mL oral suspension with a concentration of 500 mg/5 mL. Likmez is stored at room temperature and should be discarded 60 days after opening container. Max dose is 4 grams per day for treatment of anaerobic infections but other indications have no well established maximum doses. According to Study 1 and Study 2, pharmacokinetic properties were similar with oral solution were similar to that of oral tablets with peak plasma concentrations occurring between 0.25 and 6 hours after administration in fasting adults. Contraindications include hypersensitivity reactions, psychotic reactions with disulfiram, and Cockayne syndrome where severe irreversible hepatotoxicity/acute liver failure with fatal outcomes have been reported. Likmez is indicated off label for pediatric patients. Severe hepatic impairment should have a dose reduction by 50% and no dose adjustment for kidney impairment. Likmez does have a boxed warning for been shown carcinogenic in mice and rats.

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 (28 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (29 approvals). None were opposed.

Outcome: Likmez is a pharmacy benefit and will not be added to Commercial, Marketplace, or GHP Kids formulary. With its broad indications, each review should be done with an administrative policy to assess specific indications and alternatives tried.

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

HEPZATO KIT (melphalan/helatic delivery system [HDS])

Review: Hepzato is indicated as a liver-directed treatment for adult patients with uveal melanoma with unresectable hepatic metastases affecting less than 50% of the liver and no extrahepatic disease, or extrahepatic disease limited to the bone, lymph nodes, subcutaneous tissues, or lung that is amenable to resection or radiation. Melphalan is an alkylating drug that works by targeting both resting and rapidly dividing tumor cells.

Ocular melanomas represent 3-5% of all melanomas and about 85% of those are reported to be uveal melanomas arising in the anterior (iris) or the posterior (ciliary body or choroid) uveal tract. While most are initially asymptomatic, the tumor may enlarge and cause distortion of the pupil, blurred vision, or markedly decreased visual acuity caused by secondary retinal detachment. The U.S. incidence of primary metastatic uveal melanoma is approximately 2000 cases per year. Up to 50% of patients with UM will have recurrence of distant metastases and 90% of these patients with have metastases predominantly within the liver. Liver failure is most often the cause of death for patients with mUM. Patients typically have poor prognosis and those with metastatic disease have a mean overall survival (OS) of approximately 1 year. Prior to the approval of Hepzato, the only treatment option for mUM was Kimmtrak, which is indicated as a systemic treatment for HLA-A*02:01–positive adult patients with unresectable or metastatic UM. HLA-A*02:01–positive only makes up about 45% of patients with mUM which leaves approximately 55% of patients with no FDA approved treatment options. Off-label FDA options include Opdivo and Yervoy, however early clinical trials have shown limited efficacy with response rates of up to 18%, median PFS of up to 5.5 months, and median OS of up to 19.1 months.

Hepzato is administered by intra-arterial infusion into the hepatic artery at a recommended dosage of 3 mg/kg based on ideal body weight (Table 3), with a maximum absolute dose of 220 mg during a single Hepzato treatment. Hepzato should only be administered to patients weighing 35 kg or greater due to potential size limitations with percutaneous catheterization. The drug is infused over 30 minutes followed by a 30-minute washout period. Treatments should be administered every 6 to 8 weeks but can be delayed for toxicity recovery if needed. Hepzato can be administered for up to 6 total infusions. Dosages should be reduced to 2 mg/kg for Grade 4 neutropenia lasting greater than 5 days, despite growth factor support or Grade 4 thrombocytopenia lasting greater than 5 days or associated with a hemorrhage that require a transfusion.

Hepzato is supplied in the Hepzato Kit which contains 5 single dose vials of melphalan for injection, containing 50 mg of powder and a closed circuit of catheters and drug-specific filters utilized to deliver Hepzato (melphalan) to the hepatic artery and to lower the concentration of melphalan in the blood before it is returned to systemic circulation.

Prior to the initiation of Hepzato, patients should discontinue oral anticoagulation, drugs affecting platelet function, ACE-inhibitors, calcium channel blockers, or alpha-1 adrenergic blockers. Hematologic testing should be conducted at baseline and Hepzato should only be administered to patients with hemoglobin ≥ 10 g/dL, platelets ≥ 100,000/microliter, and neutrophils > 2000/microliter.

Hepzato is contraindicated in patients with active intracranial metastases or brain lesions with propensity to bleed; liver failure, portal hypertension, or known varices at risk for bleeding; surgical or medical treatment of the liver in the previous 4 weeks; uncorrectable coagulopathy; inability to safety undergo general anesthesia; allergies/hypersensitivity to melphalan, natural rubber latex, heparin, or severe allergic reaction to iodinated contrast not controlled by premedication.

Hepzato has a black box warning for severe peri-procedural complications and myelosuppression, including hemorrhage, hepatocellular injury, and thromboembolic events which may occur via hepatic intra-arterial administration of Hepzato. Patients should be assessed for these adverse reactions for at least 72 hours following administration of Hepzato. Myelosuppression may also occur with Hepzato resulting in severe infection, bleeding, or symptomatic anemia. Hematologic laboratory parameters should be monitored and treated should be delayed until blood counts have improved. Due to these risks, Hepzato Kit is only available through a restricted REMS program and should only be used by a trained healthcare professionals and certified healthcare facilities must ensure that healthcare providers who perform Percutaneous Hepatic Perfusion (PHP) procedure are trained on the use of Hepzato and must ensure that patients are assessed for severe peri-procedural complications during the procedure and for at least 72 hours following the procedure.

Other warnings include risk of hypersensitivity reactions, including anaphylaxis; gastrointestinal adverse reactions, including nausea, vomiting, abdominal pain, and diarrhea; secondary malignancies, including acute nonlymphocytic leukemia, myeloproliferative syndrome, and carcinoma; and embryo-fetal toxicity based on genotoxic properties of melphalan which targets actively dividing cells. Hepzato also carries a warning for infertility based on reports of melphalan-based chemotherapy regimens causing suppression of ovarian function in premenopausal women which resulted in persistent amenorrhea in approximately 9% of patients. Reversible or irreversible testicular suppression has also been reported.

During clinical trials, serious adverse reactions occurred in 45% of patients who received Hepzato, most commonly thrombocytopenia, neutropenia, febrile neutropenia, decreased platelet count, leukopenia, cardiac arrest, decreased neutrophil count, hypoxia, pleural effusion, pulmonary edema, and deep vein thrombosis. Fatal adverse reactions occurred in 3 patients and included cardiac arrest, acute hepatic failure, and bacterial peritonitis. Hepzato was permanently discontinued in 14% of patients who received Hepzato, most commonly due to decreased platelet count, neutropenia, anemia, and thrombocytopenia. Dosage reductions due to adverse reactions occurred in 14% of patients, most commonly caused by decreased platelet count, neutropenia, anemia, and thrombocytopenia. During clinical trials, the most common adverse reactions and laboratory abnormalities were thrombocytopenia, fatigue, anemia, nausea, musculoskeletal pain, leukopenia, abdominal pain, neutropenia, vomiting, increased alanine aminotransferase, prolonged activated partial thromboplastin time, increased aspartate aminotransferase, increased blood alkaline phosphates, and dyspnea.

The safety and efficacy of Hepzato has not been evaluated in pediatric patients. Clinical trials of Hepzato did not include sufficient numbers of subjects aged 65 years and over to determine if they respond differently from younger patients. In the FOCUS trial, 30 of the 91 patients (33%) were 65 years 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: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Outcome: Hepzato is a medical benefit and will require a prior authorization to ensure appropriate utilization. Hepzato will be added to the medical benefit cost share list. Hepzato will not be dispensed by specialty pharmacies. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of unresectable metastatic uveal melanoma **AND**
- Medical record documentation of unresectable hepatic metastases affecting less than 50% of the liver **AND**
    - Documentation of no extrahepatic disease **OR**
    - Documentation of extrahepatic disease limited to bone, lymph nodes, subcutaneous tissues, or lung that is amenable to resection or radiation

GPI LEVEL: GPI-12

QUANTITY LIMIT: 6 Kits per lifetime, Facets RX Count 1500

RPH SIGNOFF REQUIRED: yes

AUTHORIZATION DURATION: 24 months

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

REZDIFFRA (resmetirom)

Review: Rezdiffra is a thyroid hormone receptor-beta (THR-beta) agonist indicated in conjunction with diet and exercise for the treatment of adults with noncirrhotic nonalcoholic steatohepatitis (NASH) with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). Rezdiffra should be avoided in patients with decompensated cirrhosis. NASH is the most severe form of nonalcoholic fatty liver disease (NAFLD). As of June 2023, the nomenclature changed from NAFLD and NASH to metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH), respectively. This review will match the old nomenclature to coincide with language used in the Rezdiffra prescribing information. Rezdiffra was approved under accelerated approval based on NASH and fibrosis improvement, but continued approval may be contingent on verification and description of clinical benefit from additional trials.

NAFLD is a condition where fat builds up in the liver, typically associated with comorbid obesity and type 2 diabetes (T2D) but can develop with no risk factors. About 25% of the U.S. population is estimated to have NAFLD, however many people do not know they have it. NASH is the most severe form of NAFLD, characterized by accumulating fat causing swelling and damage to the liver. Patients with NASH, compared to patients with NAFLD without NASH, are more likely to have serious liver complications such as cirrhosis or liver cancer. It is estimated that about 1.5-6.5% of U.S. adults have NASH. The prevalence of NASH is projected to increase by 63% by 2030 and expected to become the leading cause of liver transplantation between 2020 and 2025. The progression of NAFLD is reversible until NASH progresses to cirrhosis, at which point it becomes irreversible liver damage.

Diagnosis of NASH and staging of fibrosis is most accurately done by liver biopsy. However, biopsies are not commonly used in real-world clinical practice for this diagnosis due to risk for complications, pathologist variability in reading the biopsy, and patient hesitation for an invasive procedure while asymptomatic. Therefore, non-invasive tests (NITs) are an alternative diagnostic tool for NASH and staging of fibrosis and are generally preferred by providers due to lower risk and ease of use. NITs are an area of active research, with no current test or combination of tests replacing liver biopsy as most accurate diagnostic tool for NASH/fibrosis staging. The 2023 AASD NAFLD guidelines outline when to

use NITs and biopsy in the management of fatty liver disease. Per the algorithm, biopsy is limited to more intermediate- and high-risk patients with suspected cirrhosis or NITs that were inconclusive, diagnostic uncertainty, or ALT and AST that is persistently elevated. NITs include imaging (ultrasounds, computed tomography [CT], and magnetic resonance imaging [MRI]) and laboratory paneling (Enhanced Liver Fibrosis [ELF] tests, Fibrosure, etc.).

Rezdiffra is the first FDA-approved treatment for NASH. Rezdiffra is a partial agonist of THR-beta, the major form of THR in the liver. In patients with NASH, the function of THR-beta is impaired which causes a reduction in mitochondrial function, a reduction in beta-oxidation of fatty acids, and an increase in fibrosis. Rezdiffra works by stimulating THR-beta in the liver, leading to a reduction in intrahepatic triglycerides. Prior to Rezdiffra, off-label use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been strongly recommended in treating NASH in the guidelines due to the association of obesity and T2D with NAFLD. It is thought that GLP-1 RAs will continue to be useful in earlier stages of disease, but Rezdiffra will be more appropriate as a liver-directed therapy in patients with more progressed liver-disease. There are four GLP-RAs in Phase 2 and Phase 3 clinical trials for NASH (semaglutide [estimated approval 2025], and tirzepatide, survodutide, efinopegdutide [all estimated approval 2027]).

Rezdiffra is supplied as an oral tablet in 60 mg (white oval), 80 mg (yellow oval), and 100 mg (beige/pink oval) strengths that can be administered with or without food. The recommended dosage is based on actual body weight. For patients weighing less than 100 kg, the recommended dosage is 80 mg once daily. For patients weighing 100 kg or more, the recommended dosage is 100 mg once daily. Concomitant use with strong CYP2CB inhibitors (e.g., gemfibrozil) is not recommended. If administered concomitantly with a moderate CYP2CB inhibitor (e.g., clopidogrel), the dose should be reduced to 60 mg or 80 mg dependent on if they weigh under 100 kg or greater than or equal to 100 kg, respectively.

There is no data on use of Rezdiffra in pregnancy or breastfeeding. Rezdiffra safety and efficacy has not been evaluated in pediatric patients. Of the patients in the clinical trial, 25% were 65 years or older and 2% were 75 years or older; there is no evidence suggesting effectiveness is different in the geriatric population but there was a higher incidence of adverse reactions compared to younger adult patients. No dosage adjustments recommended in mild or moderate renal impairment; Rezdiffra has not been studied in patient with severe renal impairment. No dosage adjustment recommended for patients with mild hepatic impairment; Rezdiffra should be avoided in patients with decompensated cirrhosis (consistent with moderate to severe hepatic impairment).

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 (29 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (28 approvals). None were opposed.

Outcome: Rezdiffra 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 18 years or older **AND**
- Medical record documentation of a diagnosis of metabolic dysfunction-associated steatohepatitis (MASH) [formerly known as noncirrhotic nonalcoholic steatohepatitis (NASH)] **AND**
- Medical record documentation of moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) **AND**
- Medical record documentation of chart notes showing that diagnosis is confirmed by 1 of the following:
    - Liver biopsy **OR**

    - Non-invasive test (NIT) (e.g. – ultrasound elastography [i.e., Fibroscan], magnetic resonance elastography [MRE], biomarker labs [i.e., Enhanced Liver Fibrosis (ELF) test, Fibrosure]) **AND**
- Medical record documentation that Rezdiffra will be used in combination with diet and exercise **AND**
- Medical record documentation that the patient does not have decompensated cirrhosis **AND**
- Medical record documentation that Rezdiffra is prescribed by or in consultation to an appropriate specialist (hepatologist or gastroenterologist)

NOTE: As of June 2023, the nomenclature changed from nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) to metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH), respectively. There is not yet an ICD-10 code for MASH or MASLD. The wording used in the review matches the old nomenclature as used in the package labeling. Either NASH or MASH should be accepted during clinical review.

QUANTITY LIMIT: 1 tablet per day

AUTHORIZATION DURATION: Initial approval will be for 6 months. Subsequent approvals will be for 12 months and will require:

- Medical record documentation of continued disease improvement or lack of disease progression as evidenced by one of the following:
    - NASH (MASH) resolution **AND** no worsening of fibrosis **OR**
    - No worsening of NASH (MASH) AND improvement in fibrosis by at least 1 stage

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: yes

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

RIVFLOZA (nedosiran)

Review: Rivfloza is a double-stranded small interfering RNA (siRNA) indicated to lower urinary oxalate levels in children 9 years of age and older and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function (e.g., estimated glomerular filtration rate [eGFR] ≥30 mL/min/ 1.73 m2).

Primary hyperoxaluria (PH) is a rare, severe disease characterized by an overproduction of oxalate. Three biochemically defined types of PH exist. PH1 is the most common type of PH. It is estimated there are 2,000 people living with PH1 and an estimated prevalence of 1 to 3 cases per 1 million people. Though, the exact prevalence is unknown because many cases are undiagnosed or misdiagnosed. PH1 is the most severe type of PH as patients are more likely to progress to end stage kidney disease (ESKD) at an earlier age with a median age of approximately 5 to 5.5 years at diagnosis. PH1 is characterized by mutations of the alanine--glyoxylate aminotransferase (AGXT) gene, which can result in a deficiency of alanin:glyoxylate aminotransferase (AGT). The deficiency of AGT leads to an increase in the glyoxylate pool, which is converted by lactate dehydrogenase (LDH) to oxalate. The overproduction of oxalate causes increased urinary oxalate excretion, resulting in formation of kidney stones, and leads to progressive kidney damage.

Standard management of PH1 includes increasing fluid intake (greater than 3 L/day per 1.73 m2) to decrease oxalate concentration via high urinary output, administration of oral calcium oxalate crystallization inhibitors (potassium citrate, neutral phosphate, or magnesium oxide) to reduce kidney stone formation, and dietary oxalate restriction to reduce oxalate absorption. Pyridoxine (vitamin B-6)

supplementation is recommended with a trial given at diagnosis for at least three months to help promote conversion of glyoxylate to glycine rather than oxalate. Pyridoxine is recommended as ongoing treatment in combination with ribonucleic acid interference (RNAi) drugs, Oxlumo or Rivfloza. Liver transplant provides a definitive cure for PH1, but there is hope that the RNAi drugs will restore oxalate production and slow the progression of kidney damage to where liver transplant is no longer necessary in the future. Oxlumo (lumasiran) was the first RNAi drug that was FDA-approved for treatment of PH1 with no age or kidney function restrictions. It is currently recommended as first-line therapy. Oxlumo reduces levels of glycolate oxidase by targeting the HAO1 messenger ribonucleic acid (mRNA) by RNA interference resulting in the depletion of the substrate glyoxylate for oxalate synthesis and thus a reduction in oxalate production. Oxlumo is administered subcutaneously every 3 months by a health care provider only and dosing is weight-based.

Rivfloza works to reduce levels of hepatic LDH by targeting the LDHA mRNA by RNA interference, and thus reduces the production of oxalate. Rivfloza is a subcutaneous monthly injection supplied as a single-dose 80mg vial and single-dose 128mg and 160mg pre-filled syringes. The vial is intended for children 9 to 11 years of age weighing less than 50kg and should be administered by a healthcare professional or a trained caregiver. The pre-filled syringes can be administered by a healthcare professional, caregiver, or patient 12 years of age and older. Rivfloza should be refrigerated at 36°F to 46°F until expiration date or at room temperate (59°F to 86°F) for a maximum of 28 days. Recommended dosing for Rivfloza is based on age and actual body weight.

Rivfloza should be administered as soon as possible if a dose is missed. Monthly dosing should resume from the most recently administered dose if the dose is missed by more than 7 days. Since Rivfloza has a slightly different mechanism from Oxlumo, patients 9 years of age and older may switch from Oxlumo to Rivfloza depending on their clinical response to Oxlumo (e.g., no reduction in urine or plasma oxalate levels).

The safety of Rivfloza was evaluated in the placebo-controlled PHYOX2 trial and the open-label extensions study PHYOX3 with patient age ranging from 9 to 46 years. The most common adverse reaction was injection site reactions (erythema, pain, bruising, and rash), which was experienced in 39% of Rivfloza-treated patients versus no patients on placebo. The injection site reactions were generally mild and did not lead to any discontinuation of treatment. There are no contraindications or warnings for Rivfloza.

Safety and efficacy of Rivfloza have not been established in patients less than 9 years of age. No studies were completed in patients aged 65 and older, but no dose adjustment is recommended for these patients. There is insufficient data on the risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes associated with the use of Rivfloza in pregnant patients. No dose adjustment is recommended for patients with mild hepatic impairment and no studies were completed in patients with moderate or severe hepatic impairment or severe renal impairment.

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 (30 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (29 approvals). None were opposed.

Outcome: Rivfloza will be a pharmacy benefit and will not be added to the Commercial, Exchange, and CHIP Formulary. The following prior authorization criteria will apply

- Medical record documentation of a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH)
- Medical record documentation of primary hyperoxaluria type 1 (PH1) as confirmed by one of the following:
    - Molecular genetic testing that confirms a mutation of alanin:glyoxylate aminotransferase

(*AGXT*) gene* **OR**
    - A liver biopsy to confirm absent or significantly reduced alanin:glyoxylate aminotransferase (AGT)

*Note: *AGXT* genotypes include but are not limited to: PR/RR, PR/M, PR/N, M/M, M/N, N/N
AND

- Medical record documentation that Rivfloza is prescribed by or in consultation with an appropriate specialist with experience managing hyperoxaluria (i.e., a nephrologist, urologist, geneticist, or hepatologist) **AND**
- Medical record documentation of age greater than or equal to 9 years **AND**
- Medical record documentation of increased urinary oxalate excretion (i.e., generally greater than 0.7 mmol/1.73 m^2 per day or greater than the upper limit of normal) **AND**
- Medical record documentation of relatively preserved kidney function as defined by one of the following:
    - Medical record documentation patient has an eGFR ≥30 mL/min/1.73m^2 **OR**
    - If eGFR is not calculated due to age limitations, a serum creatine within the normal age-specific reference range

  AND
- Medical record documentation that the patient does not have a history of a liver transplant **AND**
- Medical record documentation that the member will not be receiving Rivfloza in combination with Oxlumo **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 **AND**
- Medical record documentation of failure, contraindication, or intolerance to Oxlumo

AUTHORIZATION DURATION: Approval will be given for an **initial duration of six (6) months** or less if the reviewing provider feels it is medically appropriate. After the initial six (6) month approval, subsequent approvals will be for a **duration of twelve (12) months** or less if the reviewing provider feels it is medically appropriate, requiring:

- Medical record documentation of reduction in urinary oxalate excretion from baseline AND
- Medical record documentation of relatively preserved kidney function as defined by ONE of the following:
    - Medical record documentation patient has an eGFR ≥30 mL/min/1.73m^2 **OR**
    - If eGFR is not calculated due to age limitations, a serum creatine within the normal age-specific reference range **AND**
- Medical record documentation that the patient does not have a history of liver transplant **AND**
- Medical record documentation that the member will not be receiving Rivfloza in combination with Oxlumo

Ongoing subsequent approvals will be for a duration of twelve (12) months or less if the reviewing provider feels it is medically appropriate, requiring:

- Medical record documentation of reduction in urinary oxalate excretion from baseline **AND**
- Medical record documentation of relative preserved kidney function as defined by ONE of the following:
    - Medical record documentation patient has an eGFR ≥30 mL/min/1.73m^2 **OR**
    - If eGFR is not calculated due to age limitations, a serum creatine within the normal age-specific reference range **AND**
- Medical record documentation that the patient does not have a history of liver transplant **AND**
- Medical record documentation that the member will not be receiving Rivfloza in combination with Oxlumo

QUANTITY LIMIT:

- For 160mg/mL prefilled syringe: 1 syringe per 28 days (1ml per 28 days)
- For 128mg/0.8mL prefilled syringe: 1 syringe per 28 days (0.8ml per 28 days)
- For 80mg/0.5mL vial: 2 vials per 28 days (1mL per 28 days)

GPI LEVEL: GPI-10

RPH SIGNOFF REQUIRED: yes

FORMULARY ALTERNATIVES: Oxlumo* (*prior authorization required)

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

ZORYVE TOPICAL FOAM (roflumilast)

Review: Zoryve (roflumilast) 0.3% topical foam is a phosphodiesterase-4 (PDE4) inhibitor indicated for the treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older. Roflumilast and its active metabolite (roflumilast N-oxide) selectively inhibit PDE4, leading to accumulation of cyclic AMP (cAMP). The specific mechanism(s) by which roflumilast exerts its therapeutic action is not well defined.

A thin layer of Zoryve 0.3% topical foam should be applied once daily to affected areas on skin and/or scalp when not wet. The can should be shaken prior to each use. The medication should be rubbed in completely. Patients should wash hands after each application. Avoid fire, flame, and smoking during and immediately following application due to flammability of the propellants in Zoryve foam. Zoryve is supplied as a 0.3% topical foam containing 3 mg of roflumilast per gram of foam in 60-gram pressurized cans.

Zoryve topical foam is the first PDE4 inhibitor indicated for seborrheic dermatitis (SD) and offers the first new mechanism to treat seborrheic dermatitis in over two decades. Seborrheic dermatitis is a form of dermatitis that is generally mild. Severity varies from minimal, asymptomatic scaliness of the scalp (dandruff) to more widespread involvement. The exact pathogenesis of seborrheic dermatitis is not known, however it is theorized that it may result from an immune response to fungi of the genus Malassezia which can be found on the skin. Seborrheic dermatitis is chronic and relapsing with a biphasic incidence, occurring in infants between the ages of 2 weeks and 12 months and later during adolescence and adulthood. The prevalence of clinically significant seborrheic dermatitis is approximately 3 percent, with peak prevalence in the third and fourth decade of life. Males are generally affected more frequently than females. Individuals with HIV infection have an increased prevalence (35% among those with early HIV infection and up to 85% among those with acquired immunodeficiency syndrome (AIDS)). Patients with parkinsonism also frequently present with seborrheic dermatitis.

Management of scalp seborrheic dermatitis includes topical antifungal shampoos: ketoconazole 2%, ciclopirox 1%, zinc pyrithione, and selenium sulfide 2.5%. Management of non-scalp seborrheic dermatitis includes topical antifungals, low- to high-potency topical steroids (depending on severity and location), topical calcineurin inhibitors, systemic antifungals, crisaborole, and roflumilast. Topical calcineurin inhibitors, crisaborole, and roflumilast may be appropriate alternatives to topical corticosteroids as they lack the local adverse effects of topical corticosteroids. The available treatments do not cure seborrheic dermatitis and must be continued or repeated intermittently to prevent recurrence.

It is important to note that while roflumilast cream is also branded as Zoryve, Zoryve topical cream is indicated solely for plaque psoriasis, whereas Zoryve topical foam is indicated solely for seborrheic dermatitis.

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

Clinical Discussion: Kim Clark shared that Zoryve recently was approved as 0.15% cream for the treatment of atopic dermatitis. It was suggested that the policy be updated to indicate that the criteria for

psoriasis are specific to Zoryve 0.3% cream. No additional comments or questions. The committee unanimously voted to accept the recommendations as amended (29 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

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

Policy 744.0 Zoryve
An exception for coverage of Zoryve topical cream or Zoryve topical foam may be made for members who meet the following:

Zoryve 0.3% topical cream

Age 12 Years and Above

- Medical record documentation that Zoryve is prescribed by or in consultation with a dermatologist or rheumatologist **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation of a diagnosis of chronic plaque psoriasis **AND**
- Medical record documentation of BSA involvement less than or equal to 20% **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to at least one of the following:
    - A high- to ultrahigh-potency TCS used concurrently with a generic topical calcipotriene product **OR**
    - A generic calcipotriene/betamethasone combination product **OR**
    - A high- to ultrahigh-potency TCS used concurrently with generic tazarotene 0.1%

Age 6 to 11 Years

- Medical record documentation that Zoryve is prescribed by or in consultation with a dermatologist or rheumatologist **AND**
- Medical record documentation of age 6 to 11 years **AND**
- Medical record documentation of a diagnosis of chronic plaque psoriasis **AND**
- Medical record documentation of BSA involvement less than or equal to 20% **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to a medium to high-potency topical corticosteroid used concurrently with a generic topical calcipotriene product [calcipotriene should be avoided on the face, genitalia, intertriginous areas/flexures]

Zoryve topical foam

- Medical record documentation that Zoryve topical foam is prescribed by or in consultation with a dermatologist **AND**
- Medical record documentation of age greater than or equal to 9 years **AND**
- Medical record documentation of a diagnosis of seborrheic dermatitis **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to:
    - At least one low- to high-potency topical corticosteroid **AND**
    - At least one topical antifungal

QUANTITY LIMIT: 60 grams (1 can) per 30 days

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 the following:

Zoryve 0.3% topical cream

- Medical record documentation of clinical improvement based on signs and symptoms of plaque psoriasis

Zoryve topical foam

- Medical record documentation of clinical improvement based on signs and symptoms of seborrheic dermatitis

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: no

FORMULARY ALTERNATIVES:
Zoryve 0.3% topical cream

- calcipotriene, calcipotriene-betamethasone, tazarotene, betamethasone, betamethasone-dipropionate, clobetasol, halobetasol

Zoryve topical foam

- Low-potency topical corticosteroids: alclometasone dipropionate, desonide, fluocinolone acetonide, hydrocortisone
- Medium-potency topical corticosteroids: betamethasone valerate, fluocinolone acetonide, flurandrenolide, fluticasone propionate, hydrocortisone butyrate, hydrocortisone valerate, mometasone, prednicarbate, triamcinolone acetonide
- High-potency topical corticosteroids: amcinonide, augmented betamethasone dipropionate, betamethasone dipropionate, betamethasone valerate, desoximetasone, diflorasone, fluocinonide, fluticasone, mometasone, triamcinolone
- Topical antifungals: ciclopirox, clotrimazole, econazole, ketoconazole, selenium sulfide

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

ANKTIVA (nogapendekin alpha inbakicept-pmln)

Review: Anktiva is the first-in-class interleukin (IL)-15 superagonist consisting of an IL-15 mutant (IL-15N72D) fused with an IL-15 receptor alpha. Anktiva is administered intravesically with BCG for the treatment of adult patients with BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS), with or without papillary tumors. Anktiva was approved as both induction and maintenance therapy in combination with BCG.

Anktiva is an IL-15 receptor agonist. IL-15 signals through a heterotrimeric receptor that is composed of the common gamma chain (γc) subunit, the beta chain (βc) subunit, and the IL-15-specific alpha subunit, IL-15 receptor α. IL-15 is a trans-presented by the IL-15 receptor α to the shared IL-2/IL-15 receptor (βc and γc) on the surface of CD4+ and CD8+ T cells and NK cells.

Binding of Anktiva to its receptor results in proliferation and activation of NK, CD8+, and memory T cells without proliferation of immune-suppressive Treg cells. In vivo, intravesicular Anktiva alone or in combination with BCG showed anti-tumor activity when compared to BCG alone, in a carcinogen-induced model or bladder cancer in immunocompetent rats.

Bladder cancer is a malignancy involving the urinary system, with abnormal tissue developing in the lining of the bladder. Urothelial bladder cancer, or transitional cell carcinoma, is the most common type of bladder cancer, accounting for 90% of all bladder cancers. About 75-85% of new urothelial bladder cancers are classified as non-muscle invasive papillary tumors, often referred to as NMIBC. NMIBC includes papillary tumors classified as Ta tumors or T1 tumors (Ta, confined to the surface, and T1, invading into the lamina propria without invasion into the muscle). They are closely associated with carcinoma in situ (CIS), characterized as a flat, high-grade tumor confined to the urothelial layer. In papillary NMIBC, the occurrence of CIS raises the chances of recurrence and progression to invasive disease and metastases. The tumor-node-metastases (TNM) bladder cancer staging system categorized pure CIS (also called Tis, which is CIS without associated papillary tumors) as a separate entity from papillary tumors. Ta tumors account for an estimated 70% of NMIBC diagnoses. T1 tumors make up 20% of NMIBCs. Tis tumors make up the remaining 10%.

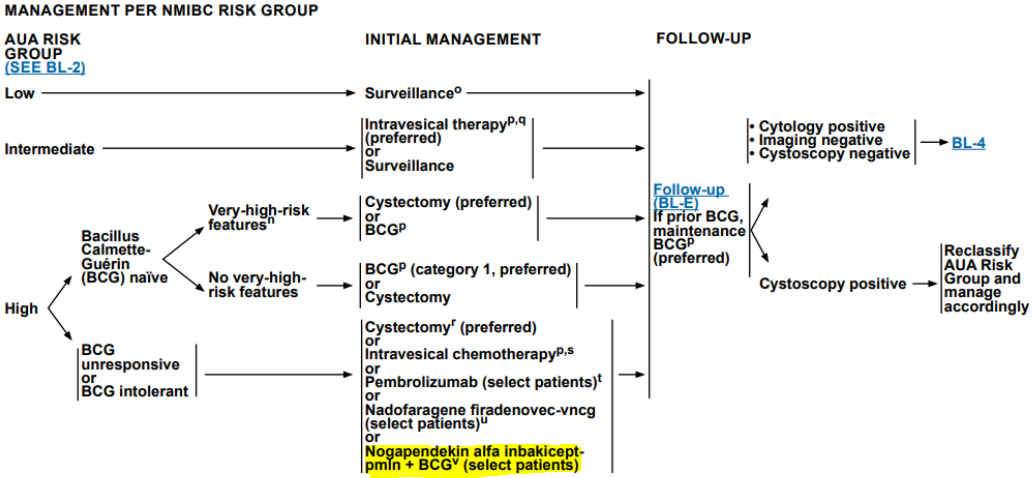
Treatment of bladder cancer depends on tumor stage, tumor size, nodal involvement, metastases, and performance status. Urothelial bladder cancer can be present as non-muscle invasive, muscle invasive, or metastatic disease. Depending on the severity of the disease, treatment options include cytotoxic chemotherapy, radiation, surgery, or immunotherapy such as PD-1 and PD-L1 checkpoint inhibitors. Patients can be treated with surgery (transurethral resection of bladder tumor, or TURBT) with or without intravesical chemotherapy. More invasive disease requires systemic therapy in addition to surgery and/or radiation. Weekly intravesical induction therapy is indicated in patients with intermediate- and high-risk disease after TURBT. This delivers high local concentrations of a therapeutic agent into the bladder, destroying remaining tumor cells.

A six-week intravesical administration of Bacillus Calmette-Guerin (BCG), a live attenuated form of Mycobacterium bovis, is the standard-of-care for patients with intermediate or high-risk disease. Alternatives to BCG include chemotherapy agents such as mitomycin, epirubicin, and gemcitabine. Patients with high-risk disease may also go on to receive maintenance treatment; however, more than 50% of patients who receive initial treatment with BCG will experience disease recurrence and progression within one year. Radical cystectomy (removal of the bladder) is considered the standard of care for any patient with BCG-unresponsive high-grade NMIBC. However, this carries a high mortality rate (up to 60%) and many patients are unfit for cystectomy.

Checkpoint inhibitors, monoclonal antibodies directed against PD-1 and PD-L1, have changed the way bladder cancer is treated. There are three checkpoint inhibitors approved for use in metastatic bladder cancer: Keytruda, Bavencio, and Opdivo. Keytruda is the only PD-L1 inhibitor indicated for use in high-risk BCG-unresponsive NMIBC with CIS with or without papillary tumors in patients who are ineligible for or have elected not to undergo cystectomy.

Another new treatment option for high-risk BCG-unresponsive NMIBC with CIS with or without papillary tumors is the gene therapy Adstiladrin, an intravesical therapy administered every 3 months.

NCCN recommendation for the use of Anktiva:



[n] Lymphovascular invasion, prostatic urethral involvement of tumor, subtype histology (eg, micropapillary, plasmacytoid, sarcomatoid).
[o] Should consider single perioperative instillation of intravesical chemotherapy at time of TURBT.
[p] See Principles of Instillation Therapy (BL-F).
[q] Options for intravesical therapy for intermediate-risk disease include BCG and chemotherapy; should consider BCG availability in decision-making.
[r] If not a cystectomy candidate, and recurrence is high-grade cTa or cT1, consider concurrent chemoradiotherapy (category 2B for cTa, category 2A for cT1) or a clinical trial. See Principles of Systemic Therapy (BL-G 5 of 7).
[s] Valrubicin is approved for BCG-refractory CIS.
[t] Pembrolizumab may be considered for the treatment of patients with BCG-unresponsive, high-risk NMIBC with Tis (with or without papillary) tumors (category 2A) or with BCG-unresponsive, high-risk NMIBC with high-grade papillary Ta/T1 only tumors without Tis (category 2B) who are ineligible for or have elected not to undergo cystectomy.
[u] Nadofaragene firadenovec-vncg may be considered for the treatment of patients with BCG-unresponsive, high-risk, NMIBC with CIS (with or without papillary) (category 2A) or with BCG-unresponsive, high-risk, NMIBC with high-grade papillary Ta/T1 only tumors without CIS (category 2B).
[v] Nogapendekin alfa inbakicept-pmln in combination with BCG may be considered for the treatment of patients with BCG-unresponsive, high-risk NMIBC with CIS (with or without papillary) tumors.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

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 (30 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (28 approvals). None were opposed.

Outcome: Anktiva will be a medical benefit and will be added to the medical benefit cost share list. The following prior authorization criteria will apply:

- Medical record documentation of an age greater than or equal to 18 **AND**
- Medical record documentation that Anktiva is being prescribed by or in consultation with a hematologist, oncologist, or urologist b
- Medical record documentation of Bacillus Calmette-Guerin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors **AND**
- Medical record documentation that BCG will be administered with each dose of Anktiva **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: Initial approval will be for 6 months (to cover 2 potential induction courses) 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.

- Authorization of Anktiva should not exceed the approved treatment duration of 30 doses if 1 induction course **OR** 36 doses if 2 induction courses

For requests exceeding the above limits, 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

RPH SIGNOFF REQUIRED: yes

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

LIBERVANT (diazepam)

Review: Libervant is a diazepam buccal film indicated for the acute treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 2 to 5 years of age.

The recommended dosage of Libervant is dependent on patient weight (Table 1).

Table 1. Recommended Dosage for Pediatric Patients 2 to 5 Years of Age

Weight	Libervant Dose
6 kg to 10 kg	5 mg
11 kg to 15 kg	7.5 mg
16 kg to 20 kg	10 mg
21 kg to 25 kg	12.5 mg
26 kg to 30 kg	15 mg

A second dose, when required, may be administered at least 4 hours after the first dose. Do not use more than 2 doses of Libervant to treat a single episode. Do not use Libervant to treat more than one episode every five days or more than five episodes per month. Libervant is supplied as buccal films which dissolve when applied to the inside of the mouth on the top of the surface of the cheek. The entire dose should be applied and allowed to dissolve. Libervant is supplied as 5 mg, 7.5 mg, 10 mg, 12.5 mg, and 15 mg films.

The safety and efficacy of Libervant Is based on adequate and well-controlled studies of diazepam rectal gel in adult and pediatric patients, adult bioavailability studies comparing Libervant with diazepam rectal gel, adult and pediatric Libervant pharmacokinetic data, and an open-label safety study of Libervant including patients 2 years to 5 years of age.
Clinical studies to evaluate the safety and tolerability of Libervant included 197 patients, of whom 107 received Libervant for at least 6 months and 48 for at least 1 year. The adverse reactions reported were consistent with adverse reactions reported in efficacy trials of diazepam rectal gel. No new safety signals were identified and the safety profile is similar to other diazepam products.

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 (29 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Outcome: Libervant is a pharmacy benefit and will be added to the Brand Preferred tier of the Commercial, Marketplace, and GHP Kids formulary. No prior authorization will be required for patients 2 years of age to 5 years of age, operationalized by an age-safety edit. For patients under 2 years of age or over 5 years of age, the following prior authorization criteria will apply. The following quantity limits will apply to all patients:

- Medical record documentation of age greater than or equal to 2 years and less than or equal to 5 years **OR**
- Medical record documentation that the safety and effectiveness of use for the prescribed indication is supported by Food and Drug Administration (FDA) approval or adequate medical and scientific evidence in the medical literature **AND**
- Medical record documentation of why diazepam rectal gel cannot be used

QUANTITY LIMIT: 10 buccal films per 30 days

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

OJEMDA (tovorafenib)

Review: Ojemda is indicated for the treatment of patients 6 months of age and older with relapsed or refractory pediatric low-grade glioma (LDD) harboring a BRAF fusion or rearrangement, or BRAF V600 mutation. This indication was approved under accelerated approval based on response rate and duration of response.

Ojemda is administered as an immediate release tablet or as an oral suspension. Ojemda is supplied as 100 mg tablet and 25 mg/mL oral suspension. Ojemda is dosed based on body surface area (BSA) at 380 mg/m2 weekly, see Table 1 and Table 2 below. For BSA of 0.30-0.89m2, the oral suspension should be used. The maximum dose is 600 mg once weekly. The dose for patients with a BSA <0.3 m2 has not been established. Ojemda is continued until disease progression or intolerable toxicity. There are dose modifications for adverse reactions listed in the package insert. If the dose adjustment is other than 500 mg or 400 mg once weekly, the oral suspension must be used. The tablets come in boxes with blister cards: 4 blister cards (4 tablets each (total of 16 tablets, 400 mg weekly dose)) per box, 5 blister cards (4 tablets each (total of 20 tablets, 500 mg weekly dose)) per box, and 4 blister cards (6 tablets each) (total of 24 tablets, 600 mg weekly dose)) per box. The suspension must be reconstituted with exactly 14 mL of room temperature water. The reconstituted suspension is 25 mg/mL and no more than 12 mL (300 mg total) should be used from each bottle. Doses greater than 300 mg will require 2 bottles. The dose needs to be administered within 15 minutes of preparation and if not used within 15 minutes, it must be discarded.

Pediatric cancers occur infrequently (about 1% of all cancer diagnoses). Pediatric CNS cancer is the second most commonly diagnosed cancer. High-grad gliomas are the most common type of brain cancer. Pediatric LGG accounts for about one-third of estimated cases. About 75% of pLGG cases involve a BRAF alteration. The estimated U.S. incidence of pLGG with a BRAF alternation is 1,100. Surgery provides curative option if resection is possible. However, if resection is not possible, systemic therapy is generally administered. For tumors that harbor BRAF fusion/rearrangement, chemotherapy (consisting of carboplatin-based regimens) was typically utilized as treatment. Response rates were noted to be low and adverse effects were reported. For tumors that harbor BRAF V600E mutations, Mekinist plus Tafinlar is a competing treatment option with Ojemda. Ojemda has a broader label, while Mekinist and Tafinlar are approved for pediatric patients with pLGG 1 year of age and older with a BRAF V600E mutation. Ojemda is an oral, brain-penetrant, highly-selective type II RAF kinase inhibitor of mutant BRAF V600E, wild-type BRAF, and wildtype CRAF kinases.

The efficacy of Ojemda was evaluated in 76 patients enrolled in FIREFLY-1, an ongoing multicenter, open label, single -arm trial that is being conducted in collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC). Patients 6 months to 25 years of age with relapsed or refractory (R/R) pLGG harboring an activating BRAF alternation and had received at least one line of prior therapy were included in the trial. Patients were also required to have documented radiographic progression and at least one measurable lesion. The median age of patients was 8.5 years. The median number of prior systemic therapies was 3 (range: 1 to 9) and 59% received prior treatment with a MAPK pathway inhibitor. Approximately 74% of patients had KIAA1549:BRAF fusion, 16% had a V600E mutation, and 11% had a BRAF alteration, including BRAF duplication or BRAF rearrangement. Patients were excluded if they had tumors that harbored additional molecular alterations (e.g. IDH1/2 or FGFR mutations, etc.) or known/suspected diagnosis of neurofibromatosis type 1 (NF1). All patients received Ojemda 420 mg/m2 orally once weekly (range: 290-476 mg/m2) according to BSA (max dose: 600 mg) until disease progression or unacceptable toxicity. Tumor assessments were performed every 12 weeks. The major efficacy outcome measure was overall response rate (ORR), defined as the proportion of patients with complete response (CR), partial response (PR), or minor response (MR) by independent review based on RAPNO-LGG (Response Assessment in Pediatric Neuro-Oncology) criteria. Additional efficacy outcome measures were duration of response, time to response and ORR by independent review based on RANO-LGG (2011) criteria. The ORR was 51%, with 0 patients having CR, 37% had PR, and 14% had a MR. The median duration of response was 13.8 months. The median time to response was 5.3 months. The ORR was 52% for patients with BRAF fusion or rearrangement and 50% among patients with BRAF V600E mutation. The ORR was 49% among patients who received prior MAPK-targeted therapy and 55%

among patients who had not received prior MAPK-targeted therapy. Based on RANO-LGG criteria, the ORR was 53%.

The most common adverse reactions (≥30%) were hair color changes, rash, dermatitis acneiform, fatigue, vomiting, constipation, nausea, viral infection, headache, pyrexia, hemorrhage, dry skin, and upper respiratory tract infection. Ojemda can cause hepatotoxicity. Liver tests, including ALT, AST and bilirubin should be monitored before initiation of Ojemda and during therapy. Ojemda has been reported to decrease growth velocity. Routine growth monitoring is recommended for patients while on Ojemda. Recovery of growth velocity occurred after Ojemda dose interruption. Tovorafenib may promote tumor growth in patients with NF1 tumors, so BRAF alteration should be confirmed prior to treatment initiation of Ojemda. The safety and effectiveness of Ojemda in patients younger than 6 months of age have not been established. Ojemda has not been studied in patients with moderate to severe hepatic impairment and there is no dose adjustment recommended for patients with mild hepatic impairment. There are no dose adjustments recommended for patients with mild-to-moderate renal impairment. Ojemda has not been studied in patients with severe renal impairment. Ojemda can cause fetal harm when administered to pregnant women. Pregnancy status should be verified in females of reproductive potential prior to initiating Ojemda. Nonhormonal contraception during treatment with Ojemda and 28 days after the last dose. Male patients with female partners should use nonhormonal contraception during treatment with Ojemda and 2 weeks after the last dose. Ojemda may impact fertility in males and females. The effects in female fertility were not reversible. Due to the potential for serious adverse reactions in breastfed children, lactating women should not breastfeed during treatment with Ojemda and 2 weeks following the last dose.

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 (31 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Outcome: Ojemda is a pharmacy benefit and will be added to the Commercial, Marketplace, and GHP Kids formulary at the Oral Oncology Brand Non-Preferred tier ($0 copay). The following prior authorization criteria will apply:

- Medical record documentation that Ojemda is prescribed by or in consultation with a pediatric oncologist, neuro-oncologist, or oncologist **AND**
- Medical record documentation of age greater than or equal to 6 months AND
- Medical record documentation of a diagnosis of relapsed or refractory pediatric low-grade glioma (LDD) harboring a BRAF fusion or rearrangement, or BRAF V600 mutation

AUTHORIZATION DURATION: Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

QUANTITY LIMIT:

- Ojemda 100 mg tablet (4 blister cards (4 tablets each)) (NDC 82950-001-16): 16 tablets per 28 days
- Ojemda 100 mg tablets (5 blister cards (4 tablets each)) (NDC 82950-001-20): 20 tablets per 28 days
- Ojemda 100 mg tablets (4 blister cards (6 tablets each)) (NDC 82950-001-24): 24 tablets per 28 days
- Ojemda 25 mg/mL suspension: 96 mL per 28 days

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: yes

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

IMDELLTRA (tarlatamab-dlle)

Review: Imdelltra (tarlatamab-dlle) is a bispecific delta-like ligand 3 (DLL3)-directed CD3 T-cell engager indicated for the treatment of adult patients with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy. Imdelltra is a first-in-class immunotherapy that binds to both DLL3 on tumor cells and CD3 on T cells, activating T cells to kill DLL3-expressing SCLC cells. This results in the formation of a cytolytic synapse with lysis of the cancer cell. DLL3 is a protein that is expressed on the surface of SCLC cells in approximately 85%–96% of patients with SCLC but is minimally expressed on healthy cells. Imdelltra was approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication is contingent upon verification and description of clinical benefit in confirmatory trials.

Small Cell lung cancer (SCLC) accounts for approximately 10%–15% of all lung cancers. In clinical practice, SCLC is categorized as either limited stage (LS-SCLC) or extensive stage (ES-SCLC). In LS-SCLC, the cancer may have extended to the mediastinum or to the lymph nodes above the collarbone. LS-SCLC typically warrants aggressive therapeutic approaches, aimed at potentially curing the cancer. In ES-SCLC, the cancer has metastasized beyond the lung and the mediastinum or the lymph nodes above the collarbone, spreading to other parts of the body, or the cancer may be present in only the lung but the size of the tumor may be large. Per NCCN Guidelines the two classification stages are defined as; Limited Stage: Stage I-III (T any, N any, M0) that can be safely treated with definitive radiation doses. Excludes T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan; Extensive Stage: Stage IV (T any, N any, M 1a/b/c), or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan. For extensive-stage disease, a treatment regimen combining chemotherapy with immunotherapy is typically favored to manage the cancer, although the primary goal is often disease control rather than cure. About two-thirds of patients with SCLC are diagnosed with extensive-stage disease. For those with localized SCLC, where the cancer remains confined within the lung, the overall 5-year survival rate is 30%. Approximately 94% of SCLC cases are diagnosed after the cancer has spread beyond the lung. In cases of regional SCLC, where the cancer extends to nearby regions, the 5-year survival rate is 18%. When the cancer has metastasized to distant parts of the body, the 5-year survival rate drops to 3%.

First-line treatment for patients with metastatic ES-SCLC, using etoposide and cisplatin or carboplatin, alone or in combination with Tecentriq (atezolizumab) or Imfinzi (durvalumab), is associated with high response rates, although relapse within 1-2 years is common. Reinduction chemotherapy, which involves repeating the initial chemotherapy regimen (platinum-based doublet), is a common treatment for patients with ES-SCLC who relapse after being sensitive to the initial chemotherapy. Patients with a chemotherapy-free interval (CTFI) greater than 6 months after the end of their previous chemotherapy are considered sensitive to reinduction chemotherapy. Patients with a CTFI less than or equal to 6 months are considered chemotherapy resistant and move on to other treatment options. Prior to the approval of Imdelltra, only two drugs were FDA-approved for the second-line treatment of ES-SCLC: topotecan, a topoisomerase I inhibitor, and Zepzelca (lurbinectedin), an alkylating agent. While topotecan is well established, its modest antitumor activity is short-lived, and its use is constrained due to the risk of myelosuppression and other hematological toxicities. Irinotecan, another topoisomerase I inhibitor, also has off-label support per the National Comprehensive Cancer Network (NCCN) Guidelines. Current updated NCCN Guidelines give Imdelltra a category 2A recommendation for use in extensive-stage disease as subsequent treatment (after prior platinum-based chemo regimen).

Imdelltra is supplied as a sterile, preservative-free, lyophilized powder in a single-dose vial for reconstitution with sterile water in a 1mg and 10mg vial. Imdelltra is administered as an intravenous (IV) infusion over 1 hour. To reduce the risks of cytokine release syndrome (CRS) Imdelltra should be administered using the manufacturer step-up dosing schedule. Infusions should be administered in a healthcare facility where the patient can be observed for post-infusion side effects. The initial dose is 1mg and then increases to 10mg once a week for the first two-week cycle (Cycle 1: 1mg D1, 10mg D8, 10mg D15). Subsequent 10mg doses are scheduled once every two weeks (Cycles 2-5+: 10mg D1, 10mg D15). Observation periods gradually decrease from 24 hours after the first two doses to two hours following the fourth cycle of treatment.

Imdelltra includes a Boxed Warning for cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell–associated neurotoxicity syndrome (ICANS), in addition to warnings and precautions for cytopenias, infections, hepatotoxicity, hypersensitivity, and embryo-fetal toxicity. The most common adverse reactions reported among patients were CRS (55%), fatigue (51%), pyrexia (36%), dysgeusia (36%), decreased appetite (34%), musculoskeletal pain (30%), constipation (30%), anemia (27%), and nausea (22%). Permanent discontinuations due to treatment-emergent adverse events were infrequent (7%). CRS was largely confined to the first and second dose, predominantly Grade 1 or 2, and generally managed with supportive care.

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 (31 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Outcome: Imdelltra is a medical benefit and will require a prior authorization for Commercial, Marketplace, and GHP Kids. Imdelltra will be added to the medical benefit cost share list. When processed at a specialty pharmacy, Imdelltra will process at the Specialty tier or Brand NP 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 Imdelltra is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of extensive-stage small cell lung cancer (ES-SCLC) (ES-SCLC is classified as SCLC that is Stage IV (T any, N any, M 1a/b/c), or Stages 1-3 with T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan) **AND**
- Medical record documentation of disease progression on or after treatment with platinum-based chemotherapy

GPI LEVEL: GPI-12

AUTHORIZATION DURATION: Initial approval will be for 6 months. Subsequent approvals will be for an additional 6 months and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if the member experiences unacceptable toxicity or worsening of disease.

RPH SIGNOFF REQUIRED: yes

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

LANTIDRA (donislecel-jujn)

Review: Lantidra is an allogeneic pancreatic islet cellular therapy indicated for the treatment of adults with Type 1 diabetes who are unable to approach target HbA1c because of current repeated episodes of severe hypoglycemia despite intensive diabetes management and education. It is used in conjunction with concomitant immunosuppression. When considering the risks associated with the infusion procedure and long-term immunosuppression, there is no evidence to show a benefit of administration of Lantidra patients whose diabetes is well-controlled with insulin therapy or patients with hypoglycemic unawareness who are able to prevent current repeated severe hypoglycemic events (neuroglycopenia requiring active intervention from a third party) using intensive diabetes management (including insulin, devices, and education). Repeated intraportal islet infusions are not recommended in patients who have experienced prior portal thrombosis unless the thrombosis was limited to second- or third-order portal vein branches. There is no evidence to support the safe and effective use of Lantidra in patients with liver disease, renal failure, or who have received a renal transplant.

Pancreatic islets regulate blood glucose levels through secretion of multiple hormones in response to increases and decreases in blood glucose. The active ingredient in Lantidra is allogeneic islets of Langerhans derived from a deceased donor pancreas. Islets contain several types of endocrine (hormone-secreting) cells, including β-, α-, pancreatic peptide- (PP-), δ-, and ε-cells. The primary mechanism of action of Lantidra is believed to be secretion of insulin by infused (transplanted) β-cells. Lantidra is administered through intravenous infusion into the hepatic portal vein only. The recommended dosage of Lantidra is 5,000 EIN/kg for initial infusion and 4,500 EIN/kg for subsequent infusion in the same recipient. The maximum dose per infusion is dictated by the estimated tissue volume, which should not exceed 10 cc per infusion, and the total EIN present in the infusion bag (up to a maximum of 1 x 106 EIN per bag). A second infusion may be performed if the patient does not achieve independence from exogenous insulin or within one year after losing independence from exogenous insulin after a previous infusion. If needed, a third infusion may be performed using the same criteria. There is no data regarding the effectiveness or safety for patients receiving more than three infusions. Currently all infusions will occur at the University of Illinois Hospital/CellTrans facilities.

Pre-procedure induction immunosuppression should be started 30-360 minutes prior to Lantidra infusion and can include the following: non-depleting monoclonal anti-interleukin-2 (anti-IL-2) receptor antibody, calcineurin inhibitor, mammalian target of rapamycin (mTOR) inhibitor, and/or tumor necrosis factor blocker. Periprocedural antibiotic prophylaxis is also recommended.

Post-infusion, patients should be monitored in the hospital for a minimum of 24 hours. Post-infusion medications include anti-infective medications, including Pneumocystis jirovecii pneumonia (PCP) and cytomegalovirus (CMV) prophylaxis; a non-depleting monoclonal anti-IL-2 receptor antibody (or a polyclonal T-cell-depleting antibody for sensitized patients), and tumor necrosis factor (TNF) blocker. Long term immunosuppression should be continued permanently to prevent islet graft rejection. Systemic steroids should be avoided. A combination of a calcineurin inhibitor and an mTOR inhibitor or appropriate alternatives are recommended at the discretion of the physician.

Lantidra is supplied as a cellular suspension of allogenic pancreatic islets (islets of Langerhans) in buffered transplant media. Each infusion uses one lot of Lantidra which consists of islets manufactured from the pancreas of a single deceased donor. Each dose is provided as two infusion bags connected via sterile connector. One bag contains Lantidra up to a maximum of 1 x106 EIN in 400 mL of transplant media and the second bag contains transplant media used to rinse the Lantidra bag and the infusion line.

Warnings for Lantidra include risks from concomitant immunosuppression, procedural complications, including liver laceration, hemorrhage, and intra-abdominal bleeding; increased risk of islet graft rejection, transmission of donor-derived infections, panel reactive antibodies (PRA) which may impact candidacy for renal transplant.

Ninety percent of patients had at least one serious adverse reactions. The major causes were attributed to infusion procedure (liver laceration/hematoma, hemorrhage, and intra-abdominal bleeding [13%] and

elevation of portal pressure [7]) and immunosuppression (infection [87%] and malignancy [37%]). Serious reactions were reported in 27 (90%) of subjects. There were two (7%) deaths; one death from multi-organ failure with sepsis (1.6 years after the first infusion), and one from progressive confusion, global atrophy and micro-ischemic disease (9.7 years after the first infusion). Both subjects were using immunosuppression at the time of the event. Additionally, 8 (27%) subjects experienced at least one life-threatening adverse reaction and 26 (87%) subjects experienced at least one severe reaction before their last follow-up. Table 6 shows the adverse reactions occurring in ≥ 20% of patients.

The safety and efficacy on Lantidra has not been established in pediatric patients with type 1 diabetes.

The safety and efficacy of Lantidra had not been established in geriatric patients with type 1 diabetes and hypoglycemic awareness. Clinical studies of Lantidra did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently than 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: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (28 approvals). None were opposed.

Outcome: Lantidra is a medical benefit and will require a prior authorization. It will be added to the medical benefit cost share list. Lantidra will not be dispensed by specialty pharmacies. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Lantidra is prescribed by or in consultation with an endocrinologist **AND**
- Medical record documentation of a diagnosis of Type I diabetes mellitus for at least 5 years **AND**
- Medical record documentation of failure to achieve target HbA1c with current treatment regimens **AND**
- Medical record documentation of intensive diabetes management and education, including all of the following
    - Documentation of use of greater than or equal to three daily injections of prandial and/or basal insulin or continuous subcutaneous insulin through an insulin pump **AND**
    - Documentation of use of a continuous glucose monitor **OR** both of the following:
        - Documentation of reason why a continuous glucose monitor cannot be used **AND**
        - Documentation of daily monitoring of blood glucose levels

    AND
    - Documentation that member has received education on insulin administration and dosing and dietary management **AND**
- Medical record documentation of repeated severe uncontrolled hypoglycemia including BOTH of the following:
    - At least one episode of severe hypoglycemia in the past 3 years defined as an event with symptoms compatible with hypoglycemia in which the subject required the assistance of another person, and which was associated with either a blood glucose level < 50 mg/dL (2.8 mmol/L) or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration **AND**
    - Reduced awareness of hypoglycemia, as defined by the absence of adequate autonomic symptoms at capillary glucose levels of < 54 mg/dL (3 mmol/L) as reported by the subject **AND**
- Medical record documentation that Lantidra will be used in conjunction with concomitant immunosuppression

AUTHORIZATION DURATION: Initial authorization will be for one (1) infusion of Lantidra. Re-authorization for Lantidra will be for one(1) additional infusion up to three (3) infusions per lifetime and will require all of the following:

- Medical record documentation that member has not achieved exogenous insulin independence within one year following the first or second Lantidra infusion (islet transplantation) **OR** within one year after losing independence from exogenous insulin after a previous infusion **AND**
- Medical record documentation that member has not exceeded the maximum of three (3) infusion per lifetime

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: Yes

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

CLASS REVIEWS

INJECTABLE ANTIPSYCHOTIC CLASS REVIEW

Agents for Disease State		
Brand Name	**Generic Available?**	**Manufacturer**
Aripiprazole		
Abilify Maintena	No	Otsuka America Pharmaceutical
Aristada	No	Alkermes
Aristada Initio	No	Alkermes
Abilify Asimtufii	No	Otsuka America Pharmaceutical
Olanzapine pamoate		
Zyprexa Relprevv	No	Eli Lilly
Paliperidone palmitate		
Invega Sustenna	No	Janssen Pharmaceuticals
Invega Trinza	No	Janssen Pharmaceuticals
Invega Hafyera	No	Janssen Pharmaceuticals
Risperidone microsphere		
Risperdal Consta	Yes	Ortho-McNeil-Janssen Pharmaceuticals
Rykindo	No	Shandong Luye Pharmaceutical
Risperidone ER		
Perseris	No	Indivior
Uzedy	No	Teva Neuroscience

Background of Disease State:

- Schizophrenia: psychiatric disorder that affects how a person thinks, feels, and behaves
- DSM-5 Diagnostic Criteria:
    - At least two of the following, each present for a significant portion of time during a one-month period.
        - Delusions*
        - Hallucinations*
        - Disorganized speech*
        - Grossly disorganized or catatonic behavior
        - Negative symptoms (diminished emotional expression or avolition)
    - Patient must have at least one of the symptoms annotated with (*)
- First and second-generation antipsychotics are the mainstay of therapy for schizophrenia
    - Oral and long-acting injectable antipsychotics are available for the treatment of this disease state

Pharmacology/Place in Therapy: European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

- Long-acting antipsychotics may be considered in many circumstances in the context of treating psychiatric disorders. Patients may benefit if they are at risk of poor adherence to an oral regimen, or if they did not have an adequate response to an oral regimen previously. They may also be beneficial for patients transitioning between care settings.
- Long-acting injectable antipsychotics have dosing guidelines that vary in frequency of injection and requirements for lead-in oral therapy. This should be considered when considering therapy with long-acting injectables for patients with schizophrenia.

- Long-acting injectable antipsychotics are used for the treatment of schizophrenia; however, some LAI are indicated for additional psychiatric disease states.
- Indications:
    - Abilify Maintena
        - Schizophrenia
    - Aristada
        - Schizophrenia in adults
    - Abilify Asimtufii
        - Schizophrenia in adults
        - *Maintenance monotherapy treatment of bipolar I disorder in adults*
    - Zyprexa Relprevv
        - Schizophrenia
    - Invega Sustenna
        - Schizophrenia
        - *Shizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants*
    - Invega Trinza
        - Schizophrenia in patients after they have been adequately treated with Invega Sustenna for at least four months
    - Invega Hafyera
        - Schizophrenia in patients after they have been adequately treated with Invega Sustenna for at least four months, followed by Invega Trinza for at least one 3-month cycle
    - Risperdal Consta
        - Schizophrenia
        - *Monotherapy or adjunctive therapy to lithium or valproate for the maintenance treatment of Bipolar I Disorder*
    - Rykindo
        - Schizophrenia
        - *Monotherapy or adjunctive therapy to lithium or valproate for the maintenance treatment of Bipolar I Disorder*
    - Perseris
        - Schizophrenia in adults
    - Uzedy
        - Schizophrenia in adults
- The American Psychiatric Association Practice Guideline for the Treatment of Patients With Schizophrenia
    - The American Psychiatric Association Guidelines for the treatment of Schizophrenia state, “APA suggests that patients receive treatment with a long-acting injectable antipsychotic medication if they prefer such treatment or if they have a history of poor or uncertain adherence.”
    - Improved adherence - fewer opportunities to miss a medication dose
        - Clinicians immediately aware of a missed visit or injection --> greater time for intervention before symptoms recur
    - LAI demonstrate decreased risk of mortality, reduced risk of hospitalization, and decreased rates of treatment discontinuation
    - Do not indicate preference for one long-acting injectable antipsychotic compared to another
        - Patients may have preference based on frequency of injections or location of injection
    - Consider LAI in patients that failed to respond to oral regimens
    - Product labeling for each medication describes approximate conversion ratios and whether a period of concomitant oral and LAI medication is needed
    - Barriers:
        - Transportation to clinic for administration
        - Lack of resources, space, or trained personnel to administer injections

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (31 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (29 approvals). None were opposed.

Outcome:

Commercial/ Exchange/ CHIP Medical		
Medication	**Current Policy**	**Recommendations**
Abilify Maintena Aristada Abilify Asimtufii Zyprexa Relprevv Invega Sustenna Invega Trinza Invega Hafyera Risperdal Consta Perseris Uzedy	• Medical record documentation that the patient is 18 years of age or older **AND** • Medical record documentation of a history of poor adherence to oral medications and documentation that education to improve adherence has been attempted **AND** • Medical record documentation of use for an FDA approved indication. ○ Abilify Asimtufii – Schizophrenia or maintenance monotherapy treatment of Bipolar I Disorder ○ Abilify Maintena – Schizophrenia or maintenance monotherapy treatment of Bipolar I Disorder ○ Aristada – Schizophrenia ○ Aristada Initio – Initiation of Aristada (in combination with oral aripiprazole) to treat schizophrenia ○ Invega Hafyera – Schizophrenia ○ Invega Sustenna – Schizophrenia or Schizoaffective disorders as monotherapy and as an adjunct to mood stabilizers or antidepressants ○ Invega Trinza – Schizophrenia ○ Perseris- Schizophrenia ○ Risperdal Consta – Schizophrenia or Bipolar I Disorder as monotherapy or as adjunctive therapy to lithium or valproate ○ Uzedy – Schizophrenia ○ Zyprexa Relprevv – Schizophrenia • In addition: The following criteria should apply to Invega Trinza: ○ Medical record documentation that the patient has been adequately treated with Invega Sustenna for at least 4 months. • In addition: The following criteria should apply to Invega Hafyera: ○ Medical record documentation that the patient has been adequately treated with Invega Sustenna for at least 4 months OR Invega Trinza for at least 3 months.	No changes recommended.
Rykindo	Non-preferred medication, no drug-specific policy	No changes recommended.

There are no changes recommended to formulary placement at this time.

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

OPHTHALMIC VEGF INHIBITOR CLASS REVIEW

VEGF Inhibitors				
Brand Name	**Generic**	**Generic/Biosimilar Available?**	**Date of Approval**	**Manufacturer**
Visudyne	Verteporfin	N	4/12/2000	Valeant Bausch Health
Avastin	Bevacizumab	Y	2/26/2004	Genentech Roche
Lucentis	Ranibizumab	Y	6/30/2006	Genentech Roche
Eylea	Aflibercept	N	11/18/2011	Regeneron
Beovu	Brolucizumab-dbll	N	10/7/2019	Novartis
Byooviz	Ranibizumab-nuna	-	9/17/2021	Samsung Bioepis Biogen
Cimerli	Ranibizumab-eqrn	-	9/17/2021	Coherus BioSciences
Susvimo	Ranibizumab	N	10/22/2021	Genentech Roche
Vabysmo	Faricimab-avoa	N	1/28/2022	Genentech Roche
Eylea HD	Aflibercept	N	8/18/2023	Regeneron

Vabysmo Fast Fact:
Vabysmo was previously indicated for:

- Neovascular (Wet) Age-Related Macular Degeneration (nAMD)
- Diabetic Macular Edema (DME)

Vabysmo is now indicated for:

- Neovascular (Wet) Age-Related Macular Degeneration (nAMD)
- Diabetic Macular Edema (DME)
- Macular Edema Following Retinal Vein Occlusion (RVO)

The dosing for Vabysmo for the indications of nAMD and DME remain the same as previous. For nAMD, the dose is 6 mg by intravitreal injection every 4 weeks for the first 4 doses, followed by either: 1) every 16 week dosing; 2) every 12 week dosing; or 3) every 8 week dosing [some patients may require every 4 week dosing]. For DME, the dose is either: 1) 6 mg by intravitreal injection every 4 weeks for 4 doses followed by extensions of intervals by 4 weeks or reductions of intervals by 8 weeks; or 2) 6 mg by intravitreal injection every 4 weeks for 6 doses followed by every 8 week dosing [some patients may require every 4 week dosing]. The dosing for the new indication of RVO is 6 mg every 4 weeks (approximately every 28 ± 7 days, monthly) for 6 months.

With the addition of the newly approved indication, a warning and precaution was also added for retinal vasculitis and/or retinal vascular occlusion. These typically occur in the presence of intraocular inflammation and have been reported with Vabysmo use. The prescribing information recommends to discontinue treatment in these patients. There are no changes to the contraindications of ocular or periocular infections and active intraocular inflammation. Other than the change mentioned above, there were no additional changes to the warnings and precautions of endophthalmitis and retinal detachments, increase in intraocular pressure, and thromboembolic events. In the RVO trials, of the patients treated with Vabysmo the following adverse events occurred in greater than 1% of the population: conjunctival hemorrhage (3%), vitreous detachment (2%), and vitreous floaters (2%).

Background of Disease State

- Age-related macular degeneration (AMD): AMD is the leading cause of severe vision impairment in the United States, with an estimated prevalence of 22 million for AMD in the United States by the year 2050. AMD damages the macula which is a small spot of the retina near the center of the eye that is needed for sharp, central vision. The disease is a spectrum consisting of early and late stages, and non-neovascular and neovascular, or wet, (nAMD) disease. Neovascular or wet disease is associated with subretinal serous fluid, exudates and/or blood. About 80% of patients have non-neovascular disease or atrophic AMD, however about 90% of severe vision loss from any AMD comes from neovascular, or wet, AMD.

- Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME): DR is a common complication of type 1 and type 2 diabetes, with retinal neurodegeneration occurring early in the progression of diabetic retinopathy. Microvascular damage leads to increased vascular permeability which can result in edema (retinal thickening) and or exudates, which can then lead to loss in central visual acuity. DR is a leading cause of blindness in working-age Americans, with a prevalence of 4.2 million (28.5%) for adults aged 40 or older and with diabetes in the United States. The prevalence is expected to increase as the incidence of diabetes and duration of diabetes increases in the United States.
- Retinal Vein Occlusion (RVO): RVO results from a partial or complete obstruction of the retinal vein, which can occur at the retinal vein itself, posterior to the optic nerve (central RVO [CRVO]) or at a branch or tributary of the central retinal vein (branch RVO [BRVO]). The leaking retinal vasculature leads to macular edema and an increase in intravenous pressure which then leads to intraretinal hemorrhage. Macular ischemia, macular edema, retinal hemorrhage, vitreous hemorrhage and epiretinal membrane formation leads to vision loss in this disease. RVO is the second most common retinal vascular disorder next to DR, with a prevalence of 1.12 per 1000 people for BRVO and 0.8 per 1000 people for CRVO worldwide.
- Myopic Choroidal Neovascularization (mCNV): mCNV is one of the most serious complications of pathologic myopia (PM), resulting in a sudden and progressive decline in central vision. CNV can be seen in both myopia patients and in AMD patients. The exact mechanism for mCNV is unknown, however the gradual decline in vision is thought to be from development and progression of patchy retinal atrophy around regressed CNV tissue. Prevalence for PM is 3% in the global population, with approximately 5-11% of these diseases developing into mCNV, although this is considered to be a possible underestimation for mCNV. PM is a frequent cause of vision loss in the young, working-age population.

Pharmacology/Place in Therapy: Vascular endothelial growth factor (VEGF) inhibitors all generally bind to the receptor binding site of active forms of VEGF-A, which prevents interaction of VEGF-A with the receptors VEGFR1 and VEGFR2. The inhibition of VEGF-A suppresses endothelial cell proliferation, vascular leakage, and new blood vessel formation. VEGF-A is thought to contribute to the pathophysiology of neovascular AMD, mCNV, DR, DME and macular edema following RVO. In addition to inhibiting VEGF-A, Vabysmo also inhibits Ang-2. Ang-2 inhibition is thought to promote vascular stability and desensitize blood vessels to the effects of VEGF-A, however the treatment effect and clinical response of Ang-2 inhibition has yet to be established. Eylea also inhibits placental growth factor (PlGF), which binds to only VEGFR1.

The FDA-approved indications for each VEGF inhibitor and the FDA-approved dosages of each VEGF inhibitor is summarized in Table 3 and Table 4 below. Vabysmo and Eylea HD are the extended interval formulations approved to date, allowing for intervals of up to 16 weeks per the prescribing information.

IPD Analytics states one of three treatment schedules are followed by most doctors when using anti-VEGF therapy. Option one includes injecting the first three doses monthly, then following with treatment on an as needed basis (“treat and observe”). Option two includes injecting the first three doses monthly, then gradually increasing time between treatments until wet AMD is stabilized (“treat and extend”). Option three includes injecting at intervals ranging from 4 to 16 weeks. IPD goes on to state that prescribers frequently use the “treat and extend” protocol for all VEGF inhibitors.

Byooviz and Cimerli were the first and second FDA-approved biosimilars in the ophthalmic VEGF space, respectively. Per Byooviz prescribing information, biosimilar means that the new product is highly similar to the reference product (RP), with no clinically meaningful differences between the two. In addition, Cimerli is the first interchangeable biosimilar approved in the ophthalmic VEGF inhibitor space. Per Cimerli prescribing information, interchangeable product (IP) means that the new product is highly similar to the RP, with no clinically meaningful differences between the two. The IP is expected to produce the same clinical result as the RP in any given patient, and the safety or diminishing efficacy risk when switching from an IP to an RP is not any greater than that from the RP alone. Eylea biosimilars are in the pipeline, currently in Phase 3 clinical trials.

Table 3. FDA-approved indications of intravitreal VEGF inhibitors

Medication	Indication					
	nAMD	DR	DME	RVO	mCNV	ROP
Avastin (bevacizumab)						
Eylea (aflibercept)	X	X	X	X		X
Lucentis (ranibizumab)	X	X	X	X	X	
Cimerli (ranibizumab-eqrn)	X	X	X	X	X	
Byooviz (ranibizumab-nuna)	X			X	X	
Beovu (brolucizumab)	X		X			
Vabysmo (faricimab)	X		X	X		
Eylea HD (aflibercept)	X	X	X			
Susvimo (ranibizumab)	X					
Visudyne (Verteporfin)	X				X	

Table 4. FDA-approved dosages of intravitreal VEGF Inhibitors

Medication	nAMD	DR	DME	RVO	mCNV	ROP
Avastin (bevacizumab)	-	-	-	-	-	-
Eylea (aflibercept)	2 mg q4w for 3 doses, then q8w (or q4w or q12w)	2mg q4w for 5 doses, then q8w (or q4w)	2mg q4w for 5 doses, then q8w (or q4w)	2mg q4w	-	0.4mg at least 10 days apart
Lucentis (ranibizumab)	0.5mg q4w OR q4w for 3 doses, then less frequently OR q4w for 4 doses, then q12w	0.3mg q4w	0.3mg q4w	0.5mg q4w	0.5mg q4w for up to 3 doses	-
Cimerli (ranibizumab-eqrn)	0.5mg q4w OR q4w for 3 doses, then less frequently OR q4w for 4 doses, then q12w	0.3mg q4w	0.3mg q4w	0.5mg q4w	0.5mg q4w for up to 3 doses	-
Byooviz (ranibizumab-nuna)	0.5mg q4w OR q4w for 3 doses, then less frequently OR q4w for 4 doses, then q12w	-	-	0.5mg q4w	0.5mg q4w for up to 3 doses	-

Beovu (brolucizumab)	**6mg q4w for 3 doses, then q8-12w**	**-**	**6mg q6w for 5 doses, then q8-12w**	**-**	**-**	**-**
Vabysmo (faricimab)	**6mg q4w for 4 doses, then either q16w OR q12w OR q8w (or q4w)**	**-**	**6mg q4w for 4 doses, then less frequently OR q4w for 6 doses, then q8w (or q4w)**	**6mg q4w**	**-**	**-**
Eylea HD (aflibercept)	**8mg q4w for 3 doses, then q8-16w**	**8mg q4w for 3 doses, then q8-12w**	**8mg q4w for 3 doses, then q8-16w**	**-**	**-**	**-**
Susvimo (ranibizumab)	**2mg via implant q24w**	**-**	**-**	**-**	**-**	**-**
Visudyne (Verteporfin)	**6mg/m^2, then light therapy every 3 months**	**-**	**-**	**-**	**-**	**-**

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (30 approvals). None were opposed.

Outcome:

Commercial (Traditional)/ Exchange (Marketplace)/ CHIP (Kids)		
Medication	**Current Policy**	**Recommendations**
Avastin (bevacizumab)	**No prior authorization required**	No changes recommended
Eylea – Eylea HD (aflibercept)	MBP 94.0 Eylea – Eylea HD **Eylea** • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin). **OR** • Medical record documentation of a diagnosis of diabetic retinopathy with or without macular edema **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) OR medical record documentation of baseline best-corrected visual acuity 20/50 or worse. **OR** • Medical record documentation of a diagnosis of macular edema following retinal vein occlusion **OR** • Medical record documentation of a diagnosis of retinopathy of prematurity	MBP 94.0 Eylea – Eylea HD • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin). **OR** • Medical record documentation of a diagnosis of diabetic retinopathy with or without macular edema **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) OR medical record documentation of baseline best-corrected visual acuity 20/50 or worse. **OR** • Medical record documentation of a diagnosis of macular edema following retinal vein occlusion **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin).
Lucentis (ranibizumab), Byooviz (ranibizumab-nuna), Cimerli (ranibizumab-eqrn)	MBP 47.0 Lucentis (ranibizumab), Byooviz (ranibizumab-nuna), and Cimerli (ranibizumab-eqrn) • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND**	MBP 47.0 Lucentis (ranibizumab), Byooviz (ranibizumab-nuna), and Cimerli (ranibizumab-eqrn) • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND**

	• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **OR** • Medical record documentation of a diagnosis of diabetic retinopathy with or without macular edema **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **OR** • Medical record documentation of a diagnosis of macular edema following retinal vein occlusion OR myopic choroidal neovascularization	• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **OR** • Medical record documentation of a diagnosis of diabetic retinopathy with or without macular edema **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **OR** • Medical record documentation of a diagnosis of macular edema following retinal vein occlusion OR myopic choroidal neovascularization **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin)
Vabysmo (faricimab)	MBP 253.0 Vabysmo • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) additional intravitreal VEGF inhibitors (e.g. Eylea, Beovu, or Lucentis) **OR** • Medical record documentation of a diagnosis of diabetic macular edema **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) additional intravitreal VEGF inhibitors (e.g. Eylea and Lucentis)	MBP 253.0 Vabysmo • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ~~two (2)~~ one (1) additional intravitreal VEGF inhibitor~~s~~ (e.g. Eylea, Beovu, or Lucentis) **OR** • Medical record documentation of a diagnosis of diabetic macular edema **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ~~two (2)~~ one (1) additional intravitreal VEGF inhibitor~~s~~ (e.g. Eylea ~~and~~ or Lucentis) **OR**

		• Medical record documentation of a diagnosis of macular edema following retinal vein occlusion **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to one (1) additional intravitreal VEGF inhibitor (e.g. Eylea or Lucentis)
Beovu (brolucizumab-dbll)	MBP 251.0 Beovu • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **OR** • Medical record documentation of a diagnosis of diabetic macular edema **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin).	No changes recommended
Susvimo (ranibizumab)	MBP 252.0 Susvimo • Medical record documentation of a diagnosis of neovascular age-related macular degeneration **AND** • Medical record documentation patient has previously responded to at least two (2) intravitreal doses of a Vascular Endothelial Growth Factor (VEGF) inhibitor medication **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to intravitreal bevacizumab (Avastin) **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) additional intravitreal VEGF inhibitors (e.g. Eylea, Beovu, or Lucentis) **AND** • Medical record documentation that Susvimo (ranibizumab) will not be given in combination with an intravitreal Vascular Endothelial Growth Factor (VGEF) inhibitor administration to the same eye **OR**	No changes recommended

	• If the request is for use in combination with an intravitreal VEGF inhibitor administration to the same eye, all of the following must be met: ○ Medical record documentation Susvimo (ranibizumab) will be given in combination with intravitreal ranibizumab injection (Lucentis) **AND** ○ Medical record documentation intravitreal ranibizumab injection will be administered on an as needed basis, as determined by the prescriber	
Visudyne (Verteporfin)	**No prior auth required**	No changes recommended

There are no changes recommended to formulary placement at this time.

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

UPDATES

HUMIRA COVERAGE UPDATE

Background: The introduction of adalimumab biosimilars has presented a significant financial opportunity to the Health Plan while keeping member costs the same or lower. All adalimumab biosimilars have shown pharmacokinetic similarities and no clinically meaningful differences have been identified between any of the biosimilars and US-Humira in terms of efficacy, safety, and immunogenicity.

Currently, all plans prefer brand Humira alongside biosimilars adalimumab-FKJP, Hadlima, and Yusimry. All products are currently reviewed utilizing Commercial Policy 84.0 Humira, Adalimumab-FKJP, Hadlima, and Yusimry.

Recommendations: In order to promote utilization of adalimumab biosimilars it is recommended that brand Humira is removed from the Commercial formulary effective 10/1/2024. It is recommended that brand Humira is removed from the Marketplace and CHIP effective 1/1/2025.

Commercial Policy 84.0 should continue to be utilized for adalimumab-FKJP, Hadlima, and Yusimry requests. It is recommended Commercial Policy 788.0 Non-Preferred Adalimumab Biosimilars is updated to include brand Humira. Changes to both policies are summarized below. Additionally, a adalimumab quantity limit reference chart has been created and will be cited as a reference within the policy.

Summary of Changes:

- Created quantity limit reference document based on formulation, strength, and indication
- Commercial Policy 84.0 Adalimumab-FKJP, Hadlima, & Yusimry
    - Removed references to brand Humira
    - Updated criteria to remove pediatric ulcerative colitis, pediatric uveitis, and adolescent hidradenitis suppurativa
    - Added reference to quantity limit spreadsheet
- Commercial Policy 788.0 Non-Preferred Adalimumab Biosimilars and Humira
    - Added brand Humira to policy
    - Removed failure of brand Humira
    - Add authorization duration
    - Added reference to quantity limit spreadsheet
    - Added criteria for coverage of Brand Humira for pediatric ulcerative colitis, pediatric uveitis, and adolescent hidradenitis suppurativa

Discussion: Dr. Denio stated that both patients and prescribing rheumatologists will be displeased with the removal of brand Humira from the formulary. Dr. Denio asked if members already on Humira would be grandfathered to which Kim Clark responded that members would not be grandfathered. He is particularly concerned in disease states where the biosimilars have not been as studied. Dr. Denio asked if there would be an exceptions process for members to continue on brand Humira to which Kim Clark responded yes. Kim Clark went on to clarify that this change will impact Commercial members effective 10/1/2024 and Exchange/CHIP/Medicare members on 1/1/2024. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: The committee unanimously voted to accept the recommendations as presented (30 approvals). 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

Recommendations:
The following policies were modified following PARP review:

Policy	DHS Identified Issue	Changes to Policy
MBP 234.0 Oxlumo (lumasiran)	Labeling updated to include dosing recommendations for patients on hemodialysis.	Removed kidney function criteria.

MBP 234.0 was updated to reflect the following changes (All LOB):

- Prescription written by or in consultation with an appropriate specialist (including but not limited to a nephrologist, urologist, geneticist, or hepatologist) **AND**
- Medical Record documentation of primary hyperoxaluria type 1 (PH1) as confirmed by ONE of the following:
    - Molecular genetic testing that confirms a mutation of alanin:glyoxylate aminotransferase (AGXT) gene* **OR**
    - A liver biopsy to confirm absent or significantly reduced alanin:glyoxylate aminotransferase (AGT)

AND

- Medical record documentation of metabolic screening that demonstrates ONE of the following:
    - Markedly increased urinary oxalate excretion (i.e. generally greater than 0.7 mmol/1.73 m^2 per day or greater than the upper limit of normal) **OR**
    - Increased urinary oxalate to creatinine ratio (i.e. greater than the age-specific upper limit of normal)

~~**AND**~~

- ~~Medical record documentation of sufficient kidney function as defined by ONE of the following:~~
    - ~~Medical record documentation patient has an eGFR ≥30 mL/min/1.73m^2 **OR**~~
    - ~~If eGFR is not calculated due to age limitations, a serum creatine within the normal age-specific reference range~~

AND

- Medical record documentation that the patient does not have a history of liver transplant.

*Note: AGXT genotypes include but are not limited to: PR/RR, PR/M, PR/N, M/M, M/N, N/N

AUTHORIZATION DURATION: Approval will be given for an **initial duration of six (6) months** or less if the reviewing provider feels it is medically appropriate. After the initial six (6) month approval, subsequent approvals will be for a **duration of twelve (12) months** or less if the reviewing provider feels it is medically appropriate, requiring medical record documentation of:

- ~~Sufficient kidney function as defined by ONE of the following:~~
    - ~~Medical record documentation patient has an eGFR ≥30 mL/min/1.73m^2 **OR**~~
    - ~~If eGFR is not calculated due to age limitations, a serum creatine within the normal age-specific reference range~~

~~**AND**~~

- Medical record documentation that the patient does not have a history of liver transplant.

Ongoing subsequent approvals will be for a **duration of twelve (12) months** or less if the reviewing provider feels it is medically appropriate, requiring medical record documentation of:

- ~~Sufficient kidney function as defined by ONE of the following:~~
    - ~~Medical record documentation patient has an eGFR ≥30 mL/min/1.73m^2 **OR**~~
    - ~~If eGFR is not calculated due to age limitations, a serum creatine within the normal age-specific reference range~~

~~**AND**~~

- Medical record documentation that the patient does not have a history of liver transplant.

MBP 300.0 Medical Benefit Drug Optimization Program (Commercial, Exchange, CHIP, Medicaid)

I. Policy:

Medical Benefit Drug Optimization Program

II. Purpose/Objective:

To provide a policy of coverage regarding certain complex, rare disease, and specialty drugs, which are required to be obtained from and billed by a Specialty Pharmacy and are not eligible for direct reimbursement to a provider or facility. This policy applies to these medications:

1. Atezolizumab (Tecentriq) [effective 8/12/24]
2. Avelumab (Bavencio) [effective 8/12/24]
3. Cemiplimab (Libtayo) [effective 8/12/24]
4. Dostarlimab (Jemperli) [effective 8/12/24]
5. Durvalumab (Imfinzi) [effective 8/12/24]
6. Enfortumab Vedotin (Padcev) [effective 8/12/24]
7. Ipilimumab (Yervoy) [effective 8/12/24]
8. Nivolumab (Opdivo) [effective 8/12/24]
9. Pembrolizumab (Keytruda)
10. Relatlimab and nivolumab (Opdualag) [effective 8/12/24]
11. Retifanlimab (Zynyz) [effective 8/12/24]
12. Tislelizumab (Tevimbra) [effective 8/12/24]
13. Toripalimab (Loqtorzi) [effective 8/12/24]
14. Tremelimumab (Imjudo) [effective 8/12/24

III. Responsibility:

A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Health Plan – Shall refer to Geisinger Health Plan and Geisinger Indemnity Insurance Company collectively.
6. Revised – the date of every revision to the policy, including typographical and grammatical changes.
7. Reviewed – the date documenting the annual review if the policy has no revisions necessary.
8. Specialty Medication – high-cost prescriptions used to treat and manage complex and chronic conditions. Specialty medications sometimes require special handling and administration, typically injection or infusion.
9. Specialty Pharmacy – a closed door pharmacy that is trained to dispense specialty medications.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;

b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;

c. in accordance with current standards good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and
e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

DESCRIPTION:
Specific intravenous and injectable drugs must meet applicable medical necessity criteria for coverage. If these criteria are met, this coverage policy will be used to define which medications must be obtained through a Specialty Pharmacy. The Specialty Pharmacy will distribute the patient specific medication directly to the providers office or facility where the medication will be prepared and administered to the patient. This policy is effective for the ~~Medicaid~~, exchange, commercial, and ASO lines of business, excluding PEBTF and medical benefit only ASOs.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

This policy lists medications that are suitable for distribution from a specialty pharmacy to a prescribing provider or facility to administer.

Prescribing providers or facilities

The prescribing provider must order a specialty medication from a contracted preferred Specialty pharmacy. The prescribing provider or facility will be responsible for a well-trained staff to admix and administer the medication safely to the patient. The specialty pharmacy will be able to answer any questions they may have regarding the specialty medication. The prescribing provider or facility can bill for the administration of the medication only. The prescribing provider or facility may not bill for the full cost of the medication because they did not purchase it or dispense from their own supply (as would be the practice of buy and bill).

If prior authorization is needed, the prescribing provider must submit the prior authorization request including relevant chart information to the health plan for review.

Specialty Pharmacy

The specialty pharmacy will dispense the member specific medication and bill Geisinger Health Plan. The specialty pharmacy will then dispense (ship out/deliver) the medication directly to the provider's office or facility for administration.

Medications are subject to cost-sharing and utilization management, as outlined in formulary and/or benefit documentation.

The specialty pharmacy will dispense (ship out/deliver) the prescribed medication to the administering provider or facility with patient-specific labeling (after prior authorization is approved, if applicable). The specialty pharmacy must package the drug for delivery to ensure product integrity and temperature control of the medications in transit. The drug shipment will not include the IV bags, lines, and other administrative supplies. These will need to be issued/supplied by the administering provider or facility.

To mitigate wastage, the specialty pharmacy will need to do the following two steps when dispensing:

1. If the drug is to be admixed or compounded, it is their responsibility to send out a dosage that is the smallest amount possible above the prescribed amount. This will be monitored and addressed with the specialty pharmacies if wastage discrepancies are noticed.
2. Verify the date of administration with the member and provider or facility, as the claim will be processed at the time of dispense (not the date of administration). The drug will not be able to be

returned after it is dispensed, if not used for that specific member.

The specialty pharmacy is responsible for delivering the medication to the administering facility or provider's office in time for the patient's administration appointment. In the case of same day treatment changes, a provider's office or facility may request a one-time emergency reimbursement from the health plan by contacting the customer call center so that the member may obtain their infusion and there is no delay in therapy. The one-time authorization is only valid the same day as the treatment change and the request for the emergency authorization. If approved, the drug would be reimbursed to the office or facility at the contracted rate of the specialty pharmacy.

LIMITATIONS:

- If the above conditions are not met, but the administration location is determined by the Health Plan to be a least costly administration site, the provider may be approved for direct reimbursement of the administered medication.
- Home infusion companies administering the intravenous or injectable drug in a home or suite setting may opt, but are not required, to supply the administered drug via specialty pharmacy.

LINE OF BUSINESS:
This policy does not apply to the Medicare, Medicaid, CHIP, PEBTF, or medical benefit only ASO lines of business. Eligibility and contract specific benefit limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy.

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

Outcome: The committee unanimously voted to accept the recommendations as presented (29 approvals). None were opposed.

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

QUARTERLY CASE AUDIT

The Quarterly Case Audit for 1st quarter 2024 was held on June 3, 2024. There were no formulary changes proposed at this meeting. We will continue to look for opportunities to create more drug specific policies at future quarterly case audit meetings.

Meeting adjourned at 3:37 pm.

The next bi-monthly scheduled meeting will be held on September 17th, 2024 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.