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

Present (via Teams):	**Absent:**
Bret Yarczower, MD, MBA – Chair Amir Antonius, Pharm.D. Emily Antosh, Pharm.D. Kristen Bender, Pharm.D. Alyssa Cilia, RPh Kimberly Clark, Pharm.D. Bhargavi Degapudi, MD Michael Dubartell, MD Kelly Faust, Pharm.D. Tricia Heitzman, Pharm.D. Nichole Hossler, MD Jason Howay, Pharm.D. Keith Hunsicker, Pharm.D. Derek Hunt, Pharm.D. Emily Jacobson, Pharm.D. Kerry Ann Kilkenny, MD Philip Krebs, R.EEG T Briana LeBeau, Pharm.D. Ted Marines, Pharm.D. Lisa Mazonkey, RPh Tyreese McCrea, Pharm.D. Jamie Miller, RPh Mark Mowery, Pharm.D. Austin Paisley, Pharm.D. Kimberly Reichard, Pharm.D. Melissa Sartori, Pharm.D. Leslie Shumlas, Pharm.D. Aubrielle Smith-Masri, Pharm.D. Kirsten Smith, Pharm.D. Michael Spishock, RPh Todd Sponenberg, Pharm.D. Jill Stone, Pharm.D. Luke Sullivan, DO Kevin Szczecina, RPh Amanda Taylor, MD Ariana Wendoloski, Pharm.D.	Jeremy Bennett, MD Kim Castelnovo, RPh Michael Evans, RPh Kelli Hunsicker, Pharm.D. Perry Meadows, MD Jonas Pearson, RPh Angela Scarantino Kristen Scheib, Pharm.D. William Seavey, Pharm.D. Michael Shepherd, MD

Brandon Whiteash, Pharm.D. Margaret Whiteash, Pharm.D. Chidubem Ifeji, Pharm.D. (Pharmacy Resident) Hailey Morgan Knittle, Pharm.D. (Pharmacy Resident) Kirsten Mascaritola, Pharm.D. (Pharmacy Resident) 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) Andrei Nemoianu, MD (non-voting participant)	

Call to Order:
Dr. Bret Yarczower called the meeting to order at 1:03 p.m., Tuesday, January 16, 2024.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the October 2023 e-vote and November 17, 2023 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

OJJAARA (momelotinib)

Review: Ojjaara is a kinase inhibitor indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary myelofibrosis or secondary MF [post-polycythemia vera (PV) and post-essential thrombocythemia (ET)] in adults with anemia. Ojjaara inhibits wild type Janus Kinase 1 and 2 (JAK1/JAK2) and mutant JAK2 which contribute to signaling of a number of cytokines and growth factors important for hematopoiesis and immune function. Additionally, Ojjaara and its major metabolite (M21) inhibit activin A receptor type 1 (ACVR1) which produces subsequent inhibition of liver hepcidin expression and increased iron availability resulting in increased red blood cell production. MF is a myeloproliferative neoplasm associated with activation and dysregulated JAK signaling that contributes to inflammation and hyperactivation of ACVR1.

The recommended dosage of Ojjaara is 200 mg orally once daily with or without food. The recommended starting dose in patients with severe hepatic impairment is 150 mg orally once daily. No dosage adjustment is recommended with mild or moderate hepatic impairment. In the case of Ojjaara-related adverse reactions, a dosage reduction of 50 mg from the last given dose may be recommended. Ojjaara is supplied as 100 mg tablets, 150 mg tablets, and 200 mg tablets.

The efficacy of Ojjaara in the treatment of adults with intermediate 1, intermediate 2, or high risk MF, including primary and secondary MF was evaluated in the MOMENTUM trial and in a subpopulation of adults with anemia in the SIMPLIFY-1 trial. Eligible patients had baseline platelet count of ≥25 × 109/L in MOMENTUM and ≥50 × 109/L in SIMPLIFY-1.

MOMENTUM was a double blind, randomized, active controlled trial in 195 symptomatic and anemic adults with MF who had previously received an approved JAK inhibitor therapy. Patients were treated with Ojjaara 200 mg once daily or danazol 300 mg twice daily for 24 weeks, then switched to open-label Ojjaara treatment. Symptoms were Myelofibrosis Symptom Assessment Form (MFSAF 4.0) diary, which captures core symptoms of MF. Efficacy was established based on a significantly higher percentage of patients treated with Ojjaara compared to danazol achieving MFSAF v4.0 Total Symptom Score reduction of 50% or more from baseline scores and Week 24.

SIMPLIFY-1 was a double-blind, randomized, active-controlled trial in 432 adults with MF who had not previously received a JAK inhibitor. Patients were treated with Ojjaara 200 mg once daily or ruxolitinib adjusted dose twice daily for 24 weeks. Patients could switch to open-label Ojjaara after 24 weeks. Efficacy results are for a subset of patients who had anemia (Hb < 10 g/dL) at baseline (n=181). Efficacy was based on spleen volume response (reduction by 35% or greater) (Table 8). A numerically lower percentage of patients treated with Ojjaara (25%) achieved a Total Symptom Score reduction of 50% or more at Week 24 compared to ruxolitinib (36%).

Warnings and precautions include risk of infections, thrombocytopenia and neutropenia, hepatotoxicity, major adverse cardiovascular events (MACE), thrombosis, and malignancies.

Serious adverse reactions occurred in 35% of patients during the MOMENTUM trial. The most common serious adverse reactions included bacterial infection, viral infection, hemorrhage, acute kidney injury, pneumonia, pyrexia, thrombosis, syncope, thrombocytopenia, and renal and urinary tract infection. Fatal adverse reactions occurred in 12% of patients who received Ojjaara, most commonly viral infection. Permanent discontinuation occurred in 18% of patients and dosage interruption or reduction occurred in 34% of patients. The most common reported adverse reactions in the MOMENTUM trial in patients treated with Ojjaara were thrombocytopenia, diarrhea, hemorrhage, and fatigue.

Serious adverse reactions occurred in 28% of the anemic patients treated with Ojjaara during randomized treatment period of the SIMPLIFY-1 trial, most commonly bacterial infection, pneumonia, heart failure, arrhythmia, and respiratory failure. A fatal adverse reaction occurred in 1 patient treated with Ojjaara. Permanent discontinuation due to adverse reaction occurred in 19% of anemic patients, dosage reductions and interruptions occurred in 21% of patients. The most common adverse reactions were dizziness, fatigue, bacterial infection, hemorrhage, thrombocytopenia, diarrhea, and nausea.

The safety and efficacy of Ojjaara in pediatric patients has not been established. In clinical trials for MF, there were 275 patients aged 65 years and older. Of the total number of Ojjaara treated patients, 163/216 (75%) were 65 years and older and 63/216 were 75 years and older. No overall differences in safety or efficacy of Ojjaara have been observed between older and younger patients.

For patients with severe hepatic impairment, a reduced dose of 150 mg orally once daily is recommended. There is no dose modification recommended for patients with mild or moderate hepatic impairment. Ojjaara exposure increased with several hepatic impairment. No clinically significant changes in Ojjaara exposure were observed in patients with mild or moderate 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: Dr. Bret Yarczower asked about the unique indication of Ojjaara compared to other myelofibrosis treatments and wanting to confirm the risk of thrombocytopenia (with Vonjo being indicated for thrombocytopenia). Would this be Carepath that we want to recommend? Kimberly Reichard, Pharm.D., responded that there is not a Carepath. Dr. Bret Yarczower stated that he thinks this would be something we should recommend for Carepath and further discussion with Keith Hunsicker, Pharm.D. Ben Andrick, Pharm.D., from Oncology stated there would be a lot of value in adding a Carepath to this treatment due to a high percentage of patients being on treatment. Dr. Yarczower will meet with Ben Andrick to discuss further. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

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

Prior Authorization Criteria:

- Medical record documentation that Ojjaara is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis **AND**
- Medical record documentation of platelet count greater than or equal to 25 x 10^9/L **AND**
- Medical record documentation of transfusion-dependent anemia associated with Myelofibrosis (not for patients with symptomatic splenomegaly only) **AND**
- Medical record documentation of splenomegaly as measured by computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound **AND**
- Medical record documentation of baseline total symptom score as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF) **AND**
- Medical record documentation that Ojjaara will not be used concurrently with other kinase inhibitors

  NOTE: Intermediate or High-Risk Myelofibrosis is defined by having at least 2 of the following factors:
  - Age > 65 years
  - WBC > 25 x 109/L
  - Hemoglobin < 10 g/dL
  - Blood Blasts ≥ 1%
  - Presence of Constitutional Symptoms (weight loss, fever, excessive sweats, etc.)
  - Transfusion dependency
  - Platelets less than 100 X 109/L
  - Unfavorable karyotype

  AUTHORIZATION DURATION: Each treatment period will be defined as six (6) months. Re-review with occur every six (6) months. Ojjaara will no longer be covered if medical record documentation does not show:
  - Medical record documentation of platelet count greater than or equal to 25 x 10^9/L **AND**
  - The member has achieved a reduction from pretreatment baseline of at least 35% in spleen volume as measured by computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound **OR**
  - The member has achieved a 50% or greater reduction in the Total Symptom Score from baseline as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF)

  QUANTITY LIMIT: 1 tablet per day, 30 day supply per fill

  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.

TRUQAP (capivasertib)

Review: Truqap is a kinase inhibitor indicated in combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced, or metastatic breast cancer with one or more PIK3CA/AKT1/PTEN-alterations as detected by an FDA-approved test following progression on at least one endocrine-based in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy. Truqap inhibits 3

isoforms of serine/threonine kinase AKT (AKT1, AKT2, and AKT3) and inhibits phosphorylation of downstream AKT substrates. AKT activation in tumors is a result of activation of upstream signaling pathways, mutations in AKT1, loss of phosphatase and tensi homolog (PTEN) function and mutations in the catalytic subunit alpha of phosphatidylinositol 3-kinase (PIK3CA). In vitro, Truqap reduced growth of breast cancer cell lines including those with relevant PIK3CA or AKT1 mutations or PTEN alteration. In vivo, Truqap alone and in combination with fulvestrant inhibited tumor growth of mouse xenograft models including estrogen receptor positive breast cancer models with alterations in PIK3CA, AKT1, and PTEN.

The recommended dosage of Truqap, in combination with fulvestrant, is 400 mg orally twice daily (approximately 12 hours apart) with or without food, for 4 days followed by 3 days off. Continue Truqap until disease progression or unacceptable toxicity. If a patient misses a dose within 4 hours of the scheduled time, the patient should take the missed dose. If a patient misses a dose more than 4 hours of the schedule time, the dose should be skipped and the next dose taken at its usual scheduled time. For premenopausal and perimenopausal women, a luteinizing hormone-releasing hormone (LHRH) agonist should be administered according to current clinical practice standards. For men, a LHRH agonist can be considered according to current clinical practice standards. Two dose reductions are recommended as needed in the event of adverse reactions. The first dose reduction is to 320 mg twice daily for 4 days followed by 3 days off, then to 200 mg twice daily for 4 days followed by 3 days off. Truqap should be permanently discontinued if the second dose reduction is not tolerated. Truqap is supplied as 160 mg and 200 mg tablets.

The efficacy of Truqap was evaluated in CAPItello-291, a randomized, double-blind, placebo-controlled trial in 708 adult patients with local advanced (inoperable) or metastatic HR-positive, HER2 negative (defined as IHC 0 or 1+, or IHC 2+/ISH-) breast cancer of which 289 had tumors eligible PIK3CA/AKT1/PTEN-alterations. All patients had progression on an aromatase inhibitor (AI) based treatment in the metastatic setting or recurrence on or within 12 months of completing neo(adjuvant) treatment with an AI. Patients could have received up to two prior lines of endocrine therapy and up to 1 line of chemotherapy for locally advanced (inoperable) or metastatic disease. Patients were excluded if they had clinically significant abnormalities of glucose metabolism.

Patients were randomized 1:1 to receive Truqap 400 mg (n=355) or placebo (n=353), given orally twice daily for 4 days followed by three days off treatment each week of a 28-day treatment cycle. Fulvestrant 500 IM injection was administered on cycle 1, days 1 and 15, and then day 1 of each subsequent 28-day cycle. Patients were treated until disease progression or unacceptable toxicity. In the patients whose tumors were PIK3CA/AKT1/PTEN-altered, seventy-six percent of patients had an alteration in PIK3CA, 13% had an alteration in AKT1, and 17% had an alteration in PTEN. All patients received prior endocrine based therapy. Seventy-one percent of patients were previously treated with a CDK4/6 inhibitor and 18% received prior chemotherapy for locally advanced (inoperable) or metastatic disease.

The major efficacy outcome was investigator-assessed progression-free survival (PFS) in the overall population, and in the population whose tumors have PIK3CA/AKT1/PTEN-alterations evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1. Additional efficacy outcomes included overall survival (OS), investigator assessed objective response rate (ORR) and duration of response (DOR). A statistically significant difference in PFS was observed in the overall population and the population of patients whose tumors have PIK3CA/AKT1/PTEN-alteration. An exploratory analysis of PFS in the 313 patients whose tumors did not have a PIK3CA/AKT1/PTEN-alterations showed a HR of 0.79, indicating the difference in the overall population was primarily attributed to the results seen in the population of patients whose tumors have PIK3CA/AKT1/PTEN-alteration.

Efficacy results from the PIK3CA/AKT1/PTEN-altered subgroup are shown in Table 4. Results from the BICR assessment were consistent with the investigator assessed PFS results. Overall survival results were immature at the time of PFS analysis (30% of patients had died).

Truqap has no black box warnings and has warnings and precautions for severe hyperglycemia, including ketoacidosis, diarrhea, cutaneous adverse reactions, including erythema multiforme (EM), palmar-plantar erythrodysesthesia, and drug reaction with eosinophilia and systemic symptoms (DRESS), and embryo

fetal toxicity. In the CAPItello-291, serious adverse reactions occurred in 18% of patients received Truqap with fulvestrant, most commonly cutaneous adverse reaction, diarrhea, pneumonia, vomiting, and pyrexia, hyperglycemia, hypersensitivity, fatigue, renal injury, and second malignancy. Fatal adverse reactions occurred in 1.3% and included sepsis and acute myocardial infarction. Permanent discontinuation due to adverse reactions occurred in 10% of patients. The most common adverse reaction leading to permanent discontinuation of Truqap was cutaneous adverse reactions. Dosage interruptions due to adverse reactions occurred in 39% of patients, most commonly cutaneous adverse reactions, diarrhea, pyrexia, vomiting and nausea, and fatigue. Dose reductions occurred in 21% of patients, most commonly diarrhea and cutaneous adverse reactions. The most common adverse reactions were diarrhea, increased random glucose, cutaneous adverse reactions, decreased lymphocytes, decreased hemoglobin, fatigue, increased fasting glucose, nausea and decreased leukocytes, increased triglycerides, stomatitis, decreased neutrophils, and vomiting.
The safety and efficacy of Truqap has not been established in pediatric patients. Of the 355 patients who received Truqap in CAPItello-291 115 were age 65 years or older and 24 (7%) were 75 years of age and older. No overall differences in the efficacy of Truqap were observed between older and younger patients. Safety analysis suggested a higher incidence of Grade 3 to 5 adverse reactions, dosage reductions, dosage interruptions, and permanent discontinuations. No dosage medication is recommended for patients with mild or moderate renal impairment. Truqap has not been studied in patients with severe renal impairment. No dosage modification is recommended for patients with mild hepatic impairment. Patients with moderate hepatic impairment should be monitored closely for adverse reactions due to potential increased capivasertib exposure. Truqap has not been studied in patients with 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: Dr. Bret Yarczower asked if we can ensure the FDA-approved test is covered if we are requiring it as part of the prior authorization criteria. Philip Krebs confirmed this would be covered under the medical benefit. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

Outcome: Truqap is a pharmacy benefit and will be added to the Commercial, Marketplace, and GHP Kids formularies. It will require a prior authorization for new starts only. The following prior authorization criteria will apply:

- Medical record documentation that Truqap is prescribed by an oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of locally advanced or metastatic breast cancer that is hormone receptor-positive, HER2-negative (HR+/HER2-) **AND**
- Medical record documentation of one or more PIK3CA, AKT1, or PTEN-alteration determined using a Food and Drug Administration (FDA) approved test **AND**
- Medical record documentation that Truqap is being prescribed in combination with fulvestrant **AND**
- Medical record documentation of one of the following:
    - Documentation of therapeutic failure on, intolerance to, or contraindication to prior endocrine therapy **OR**
    - Documentation of recurrence on or within 12 months of completing adjuvant therapy

NOTE:

- The FDA-approved test is the *FoundationOneCDx*

- Examples of endocrine therapy include: exemestane, letrozole, anastrozole, tamoxifen, and toremifene

AUTHORIZATION DURATION: Truqap is configured as a prior authorization for new starts only. Truqap will no longer be covered if it is identified that the member is not receiving appropriate follow-up care from the prescribing specialist or if the member has greater than or equal to a 90 day break in therapy.

- Medical record documentation that the member is receiving appropriate follow-up care from the prescribing specialist

QUANTITY LIMIT: 64 tablets 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.

NGENLA (somatrogon-ghla)

Review: Ngenla is a human growth hormone analog indicated for the treatment of pediatric patients aged 3 years and older who have growth failure due to inadequate secretion of endogenous growth hormone. Ngenla binds the growth hormone (GH) receptor and initiates a signal transduction cascade culminating in changes in growth and metabolism. Binding leads to activation of the STAT5b signaling pathway and increases in the serum concentration of Insulin-like Growth Factor (IGF-1). GH and IGF-1 stimulate metabolic changes, linear growth, and enhance growth velocity in pediatric patients with GHD.

The recommended dosage of Ngenla is 0.66 mg/kg based on actual body weight administered once weekly by subcutaneous (SC) injection. The dosage should be individualized to each patient based on growth response. When switching from daily growth hormone, once-weekly Ngenla may be initiated on the day following their last daily injection. Ngenla should be administered by subcutaneous injection on the same day each week at any time of day in the abdomen, thighs, buttocks, or upper arms. The injection site should be rotated weekly. Ngenla treatment should be supervised by a healthcare professional who is experienced in the diagnosis and management of pediatric patients aged 3 years and older with growth failure deficiency (GHD).

The efficacy of Ngenla was evaluated in randomized, open-label, active-controlled, parallel-group phase 3 study was conducted in 224 treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency (GHD). The primary efficacy endpoint was annualized height velocity at Week 52. Patients were randomized to Ngenla 0.66 mg/kg/week (n=109) or somatropin 0.034 mg/kg/day (n=115). The subjects had a mean baseline height standard deviation score (SDS) of -2.9.

Treatment with once-weekly Ngenla for 52 weeks resulted in an annualized height velocity of 10.1 cm/year. Patients treated with daily somatropin achieved an annualized height velocity of 9.8 cm/year after 52 weeks of treatment. The mean height SDS at Week 52 was -1.94 in Ngenla arm and -1.99 in the daily somatropin arm. The mean increase in height SDS from baseline at Week 52 was 0.92 in Ngenla arm and 0.87 in the daily somatropin arm.

Warnings and precautions are consistent with other growth hormones and include increased mortality in patients with acute critical illness, severe hypersensitivity, increased risk of neoplasms, glucose intolerance and diabetes mellitus, intracranial hypertension, fluid retention, hypoadrenalism, hypothyroidism, slipped capital femoral epiphysis, progression of preexisting scoliosis, pancreatitis, lipoatrophy, and sudden death in pediatric patients with Prader-Willi Syndrome. The most common adverse reactions were injection site reactions, nasopharyngitis, headache, pyrexia, anemia, cough, vomiting, hypothyroidism, abdominal pain, rash, and oropharyngeal pain.

The safety and efficacy of Ngenla have been established for the treatment of growth failure due to inadequate secretion of endogenous growth hormone (GH) in pediatric patients aged 3 years and older. The use of Ngenla for this indicated is supported by evidence from a 52-week, randomized, open-label, active-controlled, parallel-group phase 3 study in 224 treatment-naïve prepubertal pediatric subjects with growth hormone deficiency.

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

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

Financial Discussion: Dr. Bret Yarczower asked if we are synced with the health system so that they know how to get these approved. Kimberly Reichard, Pharm.D., responded that she will get in touch with pharmacists at the health system. Todd Sponenberg, Pharm.D. asked to clarify the reauthorization criteria for Medicare. Kimberly Reichard, Pharm.D., will be confirming the policy criteria and will remove the physician follow-up portion of the criteria if not appropriate. Kimberly Reichard, Pharm.D., confirmed that the language for reauthorization follows the Norditropin Part D policy. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Ngenla is a pharmacy benefit and will be added to the Specialty tier or Brand NP tier for members with a three tier Commercial, Marketplace, and GHP Kids formulary. It will require a prior authorization and will be added to the Commercial Human Growth Hormone Policy 29.0 with the following changes:

Commercial Policy 29.0 Human Growth Hormone

For Norditropin:

- Medical record documentation of use for a Food and Drug Administration (FDA) approved indication

For all other Growth Hormone Agents:

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

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

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

Adult Growth Hormone Deficiency: Norditropin, Genotropin, Humatrope, Nutropin AQ, Omnitrope, Saizen, Sogroya,

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

OPVEE (nalmefene)

Review: Opvee (nalmefene) nasal spray is an opioid antagonist indicated for the emergency treatment of known or suspected overdose induced by natural or synthetic opioids in adults and pediatric patients aged 12 years and older, as manifested by respiratory and/or central nervous system depression. The recommended initial dose of Opvee nasal spray in adults and pediatric patients aged 12 years and older is one spray delivered by intranasal administration, which delivers 2.7 mg of nalmefene. The requirement for repeat doses of Opvee (2.7 mg) depends upon the amount, type, and route of administration of the opioid being antagonized.

No clinical studies were conducted for the approval of Opvee. There have been no studies conducted to evaluate the use of Opvee in pediatric patients. Use for this indication in this age group is supported by adult studies and pharmacokinetic simulation. Opvee was evaluated in a pharmacokinetic study in 68 healthy adult subjects where the relative bioavailability of one 2.7 mg Opvee nasal spray in one nostril was compared to a single dose of nalmefene 1.0 mg administered as an intramuscular (IM) injection. In a second pharmacokinetic study in 24 healthy adult subjects, one 2.7 mg Opvee nasal spray in one nostril was compared with two 2.7 mg Opvee nasal sprays in one nostril and one 2.7 mg Opvee nasal spray in each nostril.

Opvee is contraindicated in patients known to be hypersensitive to nalmefene or to any of the other ingredients. Opvee also has warnings/precautions for risk of recurrent respiratory and central nervous system depression, risk of limited efficacy with partial agonists or mixed agonist/antagonists, precipitation of severe opioid withdrawal, and risk of opioid overdose from attempts to overcome the blockade. The most common adverse reactions (incidence at least 2%) are nasal discomfort, headache, nausea, dizziness, hot flush, vomiting, anxiety, fatigue, nasal congestion, throat irritation, rhinalgia, decreased appetite, dysgeusia, erythema, and hyperhidrosis.

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 majority voted to accept the recommendations as presented.

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

Outcome: Opvee is a pharmacy benefit and will be added to the Commercial, Exchange, and GHP Kids pharmacy formularies at the Brand Preferred Tier without prior authorization.

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

SOHONOS (palovarotene)

Review: Sohonos is a retinoid indicated for reduction in the volume of new heterotopic ossification in adults and children aged 8 years and older for females and 10 years and older for males for fibrodysplasia ossificans progressive (FOP). In patients with FOP, abnormal bone formation (including heterotrophic ossification (HO)) is caused by a mutation in the bone morphogenetic protein (BMP) type 1 receptor ALK2 (ACVR1). Sohonos is a retinoic acid receptor agonist which binds the gamma subtype RAR and decreases the BMP/ALK2 downstream signaling pathway. This in turn reduces ALK2/SMAD-dependent chondrogenesis and osteocyte differentiation resulting in reduced endochondral bone formation. Sohonos is the first FDA-approved treatment of FOP. Prior to the approval of Sohonos, standard of care (SOC) for FOP included therapy aimed at symptom relief by decreasing inflammation, and treatment of chronic pain.

The recommended dosage of Sohonos for adults and pediatric patients 14 years and older is 5 mg daily. This is a chronic daily dose, but it can be modified or increased in the event of FOP flare-up symptoms. Flare-up treatment should be initiated at the onset of the first symptoms indicative of a FOP flare-up or substantial high-risk traumatic event likely to lead to a flare-up (e.g. surgery, intramuscular immunization, mandibular blocks for dental procedures, muscle fatigue, blunt muscle trauma from bumps, bruises, falls, or influenza-like viral illnesses. Symptoms of FOP flare-up typically include but are not limited to localized pain, soft tissue swelling or inflammation, redness, warmth, decreased joint range of motion, and stiffness. The recommended dosage of Sohonos for flare-up for adults and pediatric patients 14 years and older is 20 mg daily for 4 weeks followed by 10 mg daily for 8 weeks (Total of 12 weeks of flare up treatment), even if symptoms resolve earlier, then return to daily dosing of 5 mg. During flare-up treatment, if the patient experiences worsening of the original flare-up or another flare-up in a new location, the 12-week flare-up treatment should be restarted at the 20 mg daily dosage. For flare-up symptoms that have not resolved after 12 weeks, the 10 mg daily dosage can be extended in 4 week intervals and continued based on symptom resolution.

The recommended dosage for pediatric patients aged 8 to 13 for females and 10 to 13 for males is weight based dosing of 2.5 mg to 5 mg daily (Table 2). Flare-ups follow the same guidelines noted above, but with the weight based dosing shown in Table 2. Sohonos may be swallowed whole or the capsules may be opened and contents emptied into one teaspoon (5 mL) of soft food (such as applesauce, low-fat yogurt, warm oatmeal) within 1 hour of opening. Concomitant administration of moderate CYP3A inhibitors should be avoided. If concomitant administration can't be avoided, the dosage of Sohonos should be reduced by half (Table 4) when co-administered. Sohonos is supplied as 1 mg, 1.5 mg, 2.5 mg, 5 mg, and 10 mg capsules.

The efficacy of Sohonos chronic treatment or flare up regimen was evaluated in Study 301, a single arm study in 97 patients with FOP with R206H mutation aged 4 years and older utilizing the Natural History Study as an external control (n=101). The primary efficacy endpoint was annualized volume of new heterotrophic ossification as assessed by low-dose, whole body CT (WBCT) imaging (excluding head). All WBCT images were read in a blinded manner to study origination. Patients received Sohonos at the recommended dose according to age and weight and this was adjusted accordingly at the time of a flare-up if needed.

At 12-month analysis, there were no statistically significant differences for the primary endpoint. At an 18-month post-hoc analysis, the mean annualized new HO was 9.4 cm3/year in subjects receiving the chronic/flare-up Sohonos treatment and 20.3 cm3/year in untreated patients in the NHS based on a linear mixed effect model. The treatment effect was about 10.9 cm3/year with 95% CI (-21.2 cm3/year, -0.6 cm3/year).

Sohonos has a black box warning for embryo-fetal harm and is contraindicated during pregnancy. Females of reproductive potential must obtain a negative pregnancy test within one week prior to initiating and periodically during Sohonos treatment. If pregnancy occurs, Sohonos treatment should be stopped immediately and patients should consult an obstetrician/gynecologist with experience in reproductive toxicity. Sohonos is in the retinoid class of drugs which is associated with birth defects in humans. In animal reproduction studies, Sohonos administered orally to pregnant rats during organogenesis was teratogenic and caused fetal malformations typical of retinoids, including cleft palate, misshapen skull bones, and shortening of the long bones at clinically relevant exposures. Patients should use an effective contraceptive for at least one month prior to treatment, during treatment with Sohonos, and for one month after the last dose. Patients should also be informed not to donate blood during Sohonos therapy and for one week following discontinuation to avoid exposure to Sohonos if donated blood is given to a pregnant patient.

Sohonos can also cause irreversible premature epiphyseal closure and potential adverse effects on growth. In clinical studies, premature epiphyseal closure occurred with Sohonos treatment in growing pediatric patients with FOP. Prior to starting treatment with Sohonos, all growing pediatric patients should undergo a baseline assessment of skeletal maturity, standard growth curves, and pubertal staging.

Continued monitoring is recommended every 6 to 12 months until patients reach skeletal maturity or final adult height.

There is a warning for mucocutaneous adverse reactions with Sohonos including dry skin, lips, pruritis, rash, alopecia, erythema, skin exfoliation and dry eye. These occurred in 98% of patients treated with Sohonos. It may also contribute to an increased risk of skin and soft tissue infections. Other warnings include metabolic bone disorders (reductions in bone mass and spontaneous reports of osteoporosis and fracture), psychiatric disorders (new or worsening depression, anxiety, mood alterations, and suicidal thoughts and behaviors), and night-blindness which may affect driving or operative a vehicle at night hazardous. During clinical trials, serious adverse reactions occurred in 21 patients treated with Sohonos, most commonly premature epiphyseal closure. Permanent discontinuation due to adverse reactions occurred in 11% of patients, most commonly dry skin. Mucocutaneous adverse reactions leading to dose reductions were more common during Sohonos flare-up treatment (37%) than during chronic treatment (4%). The most common adverse reactions were dry skin, dry lip, arthralgia, pruritis, pain in extremity, rash, alopecia, erythema, headache, back pain, skin exfoliation, nausea, musculoskeletal pain, myalgia, dry eye, hypersensitivity, peripheral edema, and fatigue.

Drug interactions can include moderate and strong CYP3A inducers and inhibitors, Vitamin A, tetracyclines, and systemic corticosteroids.

The safety and efficacy of Sohonos for the treatment of FOP have been established in pediatric patients aged 8 years and older for females and 10 years and older for males. Use of Sohonos for this indication is supported by clinical studies evidence in adult and pediatric patients. The safety and efficacy of Sohonos for the treatment of FOB in pediatric patients less than 8 years of age in females and less than 10 years of age in males has not been established. Use in this population is not recommended due to the risk of premature epiphyseal closer. Premature epiphyseal closer was observed as early as 6 months after initiating therapy with the majority occurring after 12 months. In Sohonos treated patients there was a trend of declining heigh Z-scores in adolescent subjects, potentially due to a loss of linear height and or increasing spinal deformity. The long term effects on final height in subjects with FOP treated with Sohonos has not been established.

Clinical studies did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently than younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

The effect of renal impairment on the pharmacokinetics of Sohonos has not been evaluated. Given that Sohonos is hepatically eliminated, no dose adjustment is recommended for mild or moderate renal impairment. Use is not recommended in patients with severe renal impairment.

The effect of moderate or severe hepatic impairment has not been evaluated. Sohonos undergoes extensive hepatic metabolism. No dose adjustment is recommended in patients with mild hepatic impairment. Use of Sohonos in patients with moderate or severe hepatic impairment is not recommended.

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

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

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

Outcome: Sohonos is a pharmacy benefit and will be added to the Specialty tier or Brand NP tier for members with a three tier benefit of the Commercial, Marketplace, and GHP Kids formulary. The following prior authorization criteria will be required:

- Medical record documentation that Sohonos is prescribed by or in consultation with an endocrinologist or a physician who specializes in connective tissue or bone diseases **AND**
- Medical record documentation of a diagnosis of fibrodysplasia ossificans progressive (FOP) **AND**
- Medical record documentation of confirmed Activin A Type 1 Receptor (ACVR1) R206H mutation **AND**
- Medical record documentation of age greater than or equal to 8 years for females **OR** greater than equal to 10 years for males

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

QUANTITY LIMIT:

- 1 mg tablets: 4 tablets per day, 30 days supply per fill
- 1.5 mg tablets: 2 tablets per day, 30 days supply per fill
- 2.5 mg tablets: 3 tablets per day, 30 days supply per fill
- 10 tablets: 2 tablets per day, 30 days supply per fill

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.

XACDURO (sulbactam-durlobactam)

Review: Xacduro (sulbactam and durlobactam) is indicated for patients 18 years and older for the treatment of hospital acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by susceptible isolates of Acinetobacter baumannii-calcoaceticus complex. Acinetobacter baumannii is resistant to desiccation and disinfectants, which allows it to have developed resistance to most antimicrobial agents. Carbapenem-resistant Acinetobacter baumannii (CRAB), is a gram-negative bacterium and is resistant to broad-spectrum carbapenem drugs: meropenem, imipenem, and doripenem. It can cause infections in the blood, lungs and urinary tract. At risk populations include patients who have wounds being cared for in healthcare settings, immunocompromised, or require invasive medical devices, like urinary or bloodstream catheters or ventilators. In the United States (US), the greatest source of acquiring an infection is from hospitals and other healthcare facilities. It has an estimated 7500 cases per year and in some countries its resistance to carbapenems exceeds 90% and with a mortality of 60%. In 2017 the CDC estimated 8,500 cases among U.S. hospitalized patients, which resulted in 700 deaths, and nearly 281 million dollars in excess healthcare costs.

Carbapenem-resistant A. baumannii (CRAB) possess such great US public health concern that the CDC published its summary of the impact of CRAB in 2021. Currently agents for the treatment of CRAB are limited, and the Infectious Diseases Society of America (IDSA) treatments are based on severity. For mild infection of CRAB, the IDSA recommends ampicillin-sulbactam (Unasyn) as a single agent. Alternatives include minocycline (Minocin), tigecycline (Tygacil), polymyxins (colistin), or cefiderocol (Fetroja). For moderate to severe infection of CRAB, the IDSA suggest combination therapy with at least two agents active against CRAB, ampicillin-sulbactam in addition to tetracycline derivative including minocycline followed by tigecycline polymyxin B, or cefiderocol.

The mechanisms of resistance in CRAB are due to a gene found in carbapenemase gene-positive CRAB (CP-CRAB). The antimicrobial resistance gene that allows bacteria to make carbapenemase enzymes, which allow these bacteria to degrade most β-lactam antibiotics. In addition, the carbapenemase genes are often encoded on mobile genetic elements, which can carry other resistance genes which can make these bacteria multidrug resistant. Lastly the accessibility of these genes to other bacteria can increase the risk of more multidrug resistance bacteria in different patients and different facilities. Because of this threat these organisms remain a focus of public health networks around the world.

Xacduro contains sulbactam and durlobactam. Sulbactam contains a β-lactam group which can destroy Acinetobacter baumannii-calcoaceticus complex (ABC), however due to the β-lactamase-induced resistance to sulbactam, it cannot be used as monotherapy. Durlobactam is a novel, broad-spectrum, and potent inhibitor of Class A, C, and D β-lactamases. In preclinical studies, durlobactam inhibits the β-lactamases commonly found in ABC and restores the activity of sulbactam. Xacduro is administered (1 g of sulbactam, 1 g of durlobactam) every 6 hours by intravenous (IV) infusion over 3 hours in patients with creatinine clearance (CrCl) of 45 to 129 mL/min. Dosing regimen adjustments are recommended for patients with CrCl <45 mL/min. CrCl 30 to 44 mL/minute: IV: Sulbactam 1 g/durlobactam 1 g every 8 hours. CrCl 15 to 29 mL/minute: IV: Sulbactam 1 g/durlobactam 1 g every 12 hours. CrCl <15 mL/minute: IV: Loading dose: Sulbactam 1 g/durlobactam 1 g every 12 hours for 3 doses, then sulbactam 1 g/durlobactam 1 g once daily. Administer all doses of Xacduro by IV infusion over 3 hours. Lastly the recommended duration of treatment is 7–14 days.

The effectiveness of Xacduro for the treatment of HABP/VABP, caused by susceptible isolates of ABC complex was established based on results ATTACK trial. This was a PHASE 3 multicenter, randomized, active-controlled, investigator-unblinded, independent assessor-blinded, non-inferiority trial. The key inclusion criteria were hospitalized adults ≥18 years of age with documented ABC bacterial pneumonia, VABP, ventriculoperitoneal, or bloodstream infections. The key exclusions were hypersensitivity or allergic reaction to any β-lactam, or any contraindication to the use of imipenem-cilastatin. The primary efficacy endpoint was 28-day all-cause mortality in patients with laboratory-confirmed CRAB. Primary safety endpoint was the incidence of nephrotoxicity assessed using the modified RIFLE criteria (measured by sCr or GFR) through Day 42. Patients were randomized in a 1:1 ratio to either receive Xacduro or Colistin in addition with 1 g imipenem/1 g cilastatin. 181 were randomized, 91 patients received Xacduro, and 86 patients received Colistin. For the primary efficacy endpoint, sulbactam–durlobactam was non-inferior to colistin for 28-day all-cause mortality in the carbapenem-resistant ABC microbiologically modified ITT population. In the sulbactam–durlobactam group, 28-day all-cause mortality was 12/63 (19.0%) compared with 20/62 (32.3%) in the colistin group, with the observed treatment difference of –13.2% (95% CI –30.0 to 3.5). Consistent with the differences in mortality rates, clinical cure rates at test of cure were significantly higher in patients who received sulbactam–durlobactam 39/63 [62%] versus colistin 25/62 [40%] a treatment difference of 22%. For the primary safety endpoint, the incidence of nephrotoxicity based on modified RIFLE criteria was significantly lower in the sulbactam–durlobactam group (12/91[13%]) compared with the colistin group (32/85[38%] ; p<0·001; Xacduro was well tolerated, and side effects were consistent with the pharmacologic class. Serious adverse events occurred in 40% of patients who received Xacduro and 49% of patients who received colistin. The rate of treatment emergent adverse events leading to study drug discontinuation were reported in 11% of patients who received Xacduro and 16% of patients who received colistin. The most common treatment-emergent adverse events with Xacduro were diarrhea, anemia, and hypokalemia.

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

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

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

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

- Medical record documentation of a diagnosis of Hospital-acquired Bacterial Pneumonia (HABP) or Ventilator-associated Bacterial Pneumonia (VABP) caused by susceptible isolates of *Acinetobacter baumannii-calcoaceticus complex* **AND**
- Medical record documentation that member is 18 years of age or older **AND**
- Medical record documentation that Xacduro is prescribed by or in consultation with Infectious Disease **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of a culture and sensitivity showing the patient's infection is not susceptible to preferred alternative antibiotic treatments or combination therapy depending on severity **OR**
    - Medical record documentation of history of previous intolerance to or contraindication to two (2) preferred alternative antibiotics or combination therapy depending on severity, shown to be susceptible on the culture and sensitivity.

AUTHORIZATION DURATION: 14 days

QUANTITY LIMIT: 168 vial per 14 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.

XDEMVY (lotilaner ophthalmic solution)

Review: Xdemvy is the first and only medication approved by the FDA for the treatment of *Demodex* blepharitis (DB). DB is an eyelid condition that is caused by the infestation of mites, *Demodex folliculorum or Demodex brevis,* in the eyelash follicles or meibomian glands. It is estimated that up to 25 million patients in the United States may be affected with DB. DB is characterized by eyelid redness and inflammation with the presence of collarettes or waxy debris at the base of the eyelashes. Prior to Xdemvy, treatment options for patients with DB were limited to eyelid scrubs, warm compresses, and tea tree oil.

Xdemvy is an ectoparasiticide that inhibits the gamma-aminobutyric acid (GABA)–gated chloride channel of *Demodex* mites. This inhibition results in the paralysis and death of the mites. Xdemvy is supplied as a 1.5 mL or 10 mL ophthalmic solution containing lotilaner 0.25%. It is administered as one drop in both eyes twice daily, approximately 12 hours apart, for 6 weeks.
The efficacy and safety of Xdemvy was evaluated in Saturn-1 and Saturn-2, two randomized, multicenter, double-blind vehicle-controlled trials. Patients 18 years or older were included in the study if they had all of the following signs present in the same eye: more than 10 lashes with collarettes present on the upper lid (collarette scale grade 2 or worse), at least mild erythema of the upper eyelid margin, and mite density of 1.5 mites per lash or more (upper and lower eyelids combined). A total of 833 patients with mild to severe DB were randomized 1:1 to receive Xdemvy 0.25% ophthalmic solution or vehicle solution bilaterally twice daily for 6 weeks.

The primary efficacy endpoint was the proportion of patients who achieved collarette cure at Day 43. Collarette cure was defined as a collarette grade of 0 (≤ 2 lashes with collarettes) of the upper eyelid in a scale that ranged from grade 0 to 4. Patients treated with Xdemvy had a significantly higher proportion of patients with collarette cure compared to vehicle cream (44% Xdemvy vs 7.4% vehicle) in Saturn-1 and (56% Xdemvy vs 12.5% vehicle) in Saturn-2 (P<0.0001).

The key secondary efficacy endpoints were percentage of patients with mite eradication on day 43 and composite cure of the combination of collarette and erythema grades. Mite eradication was defined as 0 mites/lash in the analysis eye and composite cure was defined as grade 0 for both collarettes and erythema on day 43. Patients treated with Xdemvy had a significantly higher percentage of patients with mite eradication compared to vehicle cream (67.9% Xdemvy vs 17.6% vehicle) in Saturn-1 and (51.8% Xdemvy vs 14.6% vehicle) in Saturn-2 (P<0.0001). In addition, composite cure was significantly higher in the patients treated with Xdemvy compared to vehicle cream (13.9% Xdemvy vs 1.0% vehicle) in Saturn-1 and (19.2% Xdemvy vs 4.0% vehicle) in Saturn-2 (P<0.0001).
There are no contraindications for Xdemvy. Warnings and precautions include risk of contamination and use with contact lenses. The most common adverse reactions seen in those taking Xdemvy was instillation site stinging and burning (10%).

Xdemvy has not been studied in pregnant or breastfeeding women, however, systemic exposure to lotilaner from ocular administration is low. The safety and efficacy of Xdemvy for the treatment of DB has not been established in pediatric patients either. Regarding geriatric use, no differences in the safety or efficacy of Xdemvy were observed in those 65 years of age or 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. None were opposed.

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

Outcome: Xdemvy will be a pharmacy benefit and should be added to the Geisinger Gold formulary at the Specialty Tier. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of chronic Demodex blepharitis (DB) evidenced by:
    - Presence of at least mild erythema of the upper eyelid margin **AND**
    - Presence of mites upon examination of eyelashes by light microscopy or presence of collarettes on slit lamp examination **AND**
- Medical record documentation that Xdemvy is prescribed by or in consultation with an ophthalmologist **AND**
- Medical record documentation of age greater than or equal to 18 years old **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

  NOTE: The clinical trials performed evaluated a 6-week treatment course only. The benefits of a longer treatment course of Xdemvy are unknown. Tarsus has stated that retreatment may be necessary in about 40% of patients at 1 year following initial treatment, so while a longer treatment course is not advisable, retreatment in some patients is likely to be necessary.

  AUTHORIZATION DURATION: 6 weeks

  QUANTITY LIMIT: 10 mL per 42 days

  GPI LEVEL: GPI-14

RPH SIGNOFF REQUIRED: No

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

YCANTH (cantharidin)

Review: Ycanth is indicated for the topical treatment of molluscum contagiosum in adults and pediatric patients 2 years of age and older. Ycanth is a topical solution containing cantharidin, a lipophilic compound, but the exact mechanism in the treated of molluscum contagiosum is unknown. Cantharidin is a blistering agent previously available through compounding pharmacies.
Ycanth is applied topically by a healthcare professional as a single application to cover each lesion. It is not for oral, mucosal, or ophthalmic use. No more than two Ycanth applicators should be used during a single treatment session. Ycanth is administered every three weeks as needed. Ycanth is supplied in a glass ampule contained within a single-use applicator and enclosed in a protective paperboard sleeve. Each ampule of Ycanth contains approximately 0.45 mL of 0.7% cantharidin solution. Each mL contains 7 mg of cantharidin. Ycanth is supplied in cartons of 6 and 12 applicators.

The efficacy of Ycanth was evaluated in two double-blind, randomized, placebo-controlled trials, Trial 1 and Trial 2, which included 528 subjects aged 2 years and older with molluscum contagiosum. Patients were randomized to receive Ycanth or vehicle only. Patients were treated at intervals of approximately 21 days until complete clearance of the lesions or for a maximum of 4 applications (Days 1, 21, 42, and 63). A healthcare professional blinded to the treatment group counted the number of lesions at each visit. The primary efficacy endpoint was the proportion of patients achieving complete clearance of all treated molluscum contagiosum lesions by Day 84. The secondary efficacy endpoints were proportion of patients achieving complete clearance of all treated molluscum contagiosum lesions at Days 63, Day 42, and Day 21.

Warnings and Precautions for Ycanth included the risk of toxicities associated with inappropriate administration. Ycanth is for topical use only, not for oral, mucosal, or ophthalmic use. Life threatening or fatal toxicities can occur if Ycanth is administered orally, including renal failure, blistering and severe damage to the gastrointestinal tract, coagulopathy, seizures, and flaccid paralysis. Ocular toxicity can occur if Ycanth comes in contact with eyes, including corneal necrosis, ocular perforation, and deep ocular injuries.

Local skin reactions can occur, including vesiculation, pruritis, pain, discoloration, and erythema. Local skin reactions at the application site occurred in 97% of patients treated with Ycanth in clinical trials. Administration of other topical products should be avoided until 24 hours after Ycanth treatment or until washing since application of other topical products may spread Ycanth and cause blistering or other adverse reactions to healthy skin. Ycanth is a flammable liquid, even after drying and contact with fire or flame and smoking near lesion(s) should be avoided during treatment and after application until removed. Adverse reactions observed during clinical trials were primarily local skin reactions at the application site. There were no serious adverse reactions reported in the two clinical trials. The discontinuation rate due to adverse reaction was 2.3% in Ycanth treated patients compared to 0.5% in patients treated with vehicle.

The safety and efficacy of Ycanth for the treatment of molluscum contagiosum has been established in pediatric patients aged 2 years and older. The use of Ycanth in pediatric patients is supported by results from adequate and well controlled trials in patients 2 years of age and older, although safety and efficacy of drug use for longer than 12 weeks has not been established. The safety and efficacy in pediatric patients less than 2 years of age has not been established. Ycanth has not been studied in geriatric patients.

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

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

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

Outcome: Ycanth is a medical benefit that will require a prior authorization. Ycanth will be added to the medical benefit cost share list. When processed at a Specialty pharmacy, Ycanth will process on 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 2 years **AND**
- Medical record documentation that Ycanth is prescribed by a dermatologist **AND**
- Medical record documentation of a diagnosis of molluscum contagiosum (MC)

AUTHORIZATION DURATION: 3 months

QUANTITY LIMIT: 2 applicators per 21 days

GPI LEVEL: GPI-12

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

FRUZAQLA (fruquintinib)

Review: Fruzaqla is a kinase inhibitor indicated for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and if RAS wild-type and medically appropriate, an anti-EGFR therapy. Fruzaqla is a small molecule kinase inhibitor of vascular endothelial growth factors receptors (VEGFR)-1, -2, and -3. In vitro and in vivo studies show that Fruzaqla inhibited VEGF-induced VEGFR-2 phosphorylation. In vivo studies showed Fruzaqla inhibited tumor growth in a tumor xenograft mouse model of colon cancer.

The recommended dosage of Fruzaqla is 5 mg orally once daily for the first 21 days of each 28-day cycle until disease progression or unacceptable toxicity. In the event of adverse reactions, the dose can be reduced to 4 mg orally once daily, then 3 mg orally once daily. Patients unable to tolerate 3 mg orally once daily should permanently discontinue Fruzaqla. Fruzaqla is supplied as 1 mg and 5 mg capsules.

The efficacy of Fruzaqla was evaluated in FRESCO-2, an international, randomized, double-blind, placebo-controlled study in 691 patients with metastatic colorectal cancer who had disease progression during or after prior treatment with fluoropyrimidine-, oxaliplatin-, irinotecan-based chemotherapy, an anti-VEGF biological therapy, if RAS wild type, an anti-EGFR biological therapy, and trifluridine/tipiracil, regorafenib, or both. Patients with left ventricular fraction ≤ 50%, systolic blood pressure > 140 mm Hg or diastolic blood pressure >90 mm Hg, urine protein ≥1 g/24 hours, or untreated brain metastases were ineligible. Patients were randomized 2:1 to receive Fruzaqla 5 mg orally once daily (n=461) for the first 21 days of each 28-day cycle plus BSC or placebo (n=230) plus BSC. Treatment was continued until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall survival (OS) and additional outcomes measure was progression-free survival (PFS) as determined by RECIST v1.1.

All patients received prior treatment with fluoropyrimidine, oxaliplatin, and irinotecan-based chemotherapy; 96% received prior anti-VEGF therapy, 39% received prior anti-EGFR therapy, 91%

received trifluridine/tipiracil, 48% received regorafenib, and 39% received both trifluridine/tipiracil and regorafenib.

Fruzaqla plus BSC resulted in a statistically significant improvement in OS and PFS compared to placebo (Table 4) in FRESCO-2.

The FRESCO study conducted in China was a randomized, double-blind, placebo-controlled trial in 416 patients with metastatic colorectal cancer with who had disease progression during or after prior treatment with fluoropyrimidine-, oxaliplatin-, or irinotecan-based chemotherapy. Patients older than 75 years of aged, left ventricular ejection fraction ≤ 50 systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, urine protein ≥ 1 g/24h, or brain metastases were excluded. Patients were randomized 2:1 to received Fruzaqla 5 mg (n=278) once daily for 21 days of each 28 day cycle plus BSC or placebo (n=138) plus BSC. Treatment was continued until disease progression or unacceptable toxicity. The major efficacy outcome was overall survival and an additional efficacy outcome was PFS determined by investigators according to RECIST v1.1.

All patients received prior treatment with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy; 30% of patients received prior anti-VEGF therapy, and 14% received prior anti-EGFR therapy. Fruzaqla plus BSC resulted in a statistically significant improvement in OS compared to placebo plus BSC.

There are no black box warnings for Fruzaqla Warnings and Precautions for Fruzaqla include hypertension, risk of hemorrhagic events, increased risk of infections, gastrointestinal perforation, hepatotoxicity, proteinuria, palmar-planter erythrodysesthesia (PPE), posterior reversible encephalopathy syndrome (PRES), impaired wound healing, arterial thromboembolic events, allergic reactions to FD&C Yellow No 5 and No 6, and embryo-fetal toxicity. In FRESCO-2, serious adverse reactions occurred in 38% of patients treated with Fruzaqla, most frequently hemorrhage and gastrointestinal perforation. Fatal adverse reactions occurred in 14 patients (3.1%) who received Fruzaqla, including pneumonia, sepsis/septic shock, and hepatic failure/encephalopathy. Treatment discontinuation occurred in 20% of patients, most commonly asthenia and gastrointestinal perforation. Dose interruptions and dose reductions occurred in 47% and 24% of patients, respectively. In the FRESCO study, serious adverse reactions occurred in 15% of patients and included intestinal obstruction and hemorrhage. Fatal adverse reactions occurred in 7 patients (2.5%) including cerebral infarction, gastrointestinal hemorrhage, hemoptysis, bacterial infection, lung/lower respiratory infection, and multiple organ dysfunction. Treatment discontinuation occurred in 15% of patients due to adverse reactions, including intestinal obstruction, proteinuria, and hepatic function abnormalities. Dose interruptions and dose reductions occurred in 35% and 24%, respectively. The most common reactions were hypertension, palmar-plantar erythrodysesthesia, proteinuria, dysphonia, abdominal pain, diarrhea, and asthenia.

The safety and efficacy of Fruzaqla has not been established in pediatric patients. In FRESCO-2, 212 (46%) of patients who received Fruzaqla were 65 years of age and older and 43 were 75 years and older. In FRESCO, 50 patients (18%) were 65 years and older and 1 patient was 75 years or older. There were no observed overall differences in safety and efficacy in geriatric patients compared to younger patients. No dosage adjustment is recommended for patients with mild hepatic impairment. Fruzaqla has not been sufficiently studied in patients with moderate hepatic impairment. Fruzaqla is not recommended for use in patients with 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. None were opposed.

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

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

- Medical record documentation that Fruzaqla is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of metastatic colorectal cancer (mCRC) **AND**
- Medical record documentation of previous treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy

AUTHORIZATION DURATION: Fruzaqla is configured as a prior authorization for new starts only. Fruzaqla will no longer be covered if it is identified that the member is not receiving appropriate follow-up care from the prescribing specialist or if the member has greater than or equal to a 90 day break in therapy.

- Medical record documentation that the member is receiving appropriate follow-up care from the prescribing specialist

QUANTITY LIMIT:

- **1 mg capsules:** 84 capsules per 28 days
- **5 mg capsules:** 21 capsules per 28 days

GPI LEVEL: GPI-12

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

REZZAYO (rezafungin)

Review: Rezzayo is indicated for adult patients who have limited or no alternative options for the treatment of candidemia and invasive candidiasis. Approval of this indication is based on limited clinical safety and efficacy data for Rezzayo. Rezzayo has not been studied in patients with endocarditis, osteomyelitis, and meningitis due to Candida. Rezzayo is an echinocandin antifungal drug that inhibits the synthesis of 1,3-β-D-glucan, an essential component of fungal cell walls.

The recommended dosage of Rezzayo is a once-weekly intravenous infusion, with an initial loading dose of 400 mg followed by a 200 mg dose once weekly thereafter. The safety of Rezzayo has not been established beyond 4 weekly doses. Rezzayo is supplied as a single-dose vial containing 200 mg of rezafungin.

The safety and efficacy of Rezzayo in the treatment of patients with candidemia and/or invasive candidiasis (IC) were evaluated in a randomized, double-blind study (Trial 1). Patients were randomized 1:1 to receive Rezzayo or caspofungin. Patients with septic arthritis in a prosthetic joint, osteomyelitis, endocarditis or myocarditis, meningitis, endophthalmitis, chorioretinitis, or any central nervous system infection, chronic disseminated candidiasis, or urinary tract candidiasis due to ascending Candida infection secondary to obstruction or surgical instrumentation of the urinary tract were excluded.

Patients in the Rezzayo treatment arm received a single 400 mg loading dose on Day 1 of Week 1, followed by 200 mg once weekly, for a total of two to four doses. Patients in the caspofungin arm received a single 70 mg IV loading dose followed by caspofungin 50 mg IV once daily for a total of 2 to 4 weeks. After ≥ 3 days of IV therapy, patients in the caspofungin group could be switched to oral step-down therapy (fluconazole), if the patient met the criteria for cure and was preparing to be discharged. Efficacy was assessed by all-cause mortality at Day 30. Additional efficacy outcomes were global cure (mycological eradication/presumed eradication, clinical cure, and radiological cure [for patients with

documented IC by radiologic or other imaging findings at baseline]), mycological eradication/presumed eradication, and investigator's assessment of clinical cure.

Warnings and Precautions for Rezzayo includes infusion related reactions, photosensitivity, and hepatic adverse reactions. The most common adverse reactions were hypokalemia, pyrexia, diarrhea, anemia, vomiting, nausea, hypomagnesemia, abdominal pain, constipation, and hypophosphatemia. Adverse reactions led to discontinuation of study medication in 9.3% of patients in the Rezzayo arm and 9.0% in the caspofungin arm.

Less common adverse reactions occurring in less than 5% of patients included infusion related reactions, tremor, disseminated intravascular coagulation, dysphagia, gastrointestinal hemorrhage, fluid overload, insomnia, erythema, headache, dizziness, acute kidney injury, abnormal liver tests, and peripheral neuropathy.
The safety and efficacy of Rezzayo have not been established in pediatric patients. Of the 151 Rezzayo treated patients, 64 patients (42%) were 65 years of age and older while 26 patients (17%) were 75 years of age and older. Clinical studies did not include sufficient numbers of older adult patients to determine if patients 65 years and older respond differently from 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. None were opposed.

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

Outcome: Rezzayo is a medical benefit and will require a prior authorization for Commercial, Marketplace, and GHP Kids. Rezzayo will be added to the medical benefit cost share list. When processed at a specialty pharmacy, it will process on the Specialty tier or the Brand Non-Preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a non-neutropenic patient with a diagnosis of candidemia or invasive candidiasis (other than endocarditis, osteomyelitis, or meningitis) **AND**
- Medical record documentation that Rezzayo is prescribed by an infectious disease specialist **AND**
- Medical record documentation that member has limited or no alternative treatment options.

  AUTHORIZATION DURATION: 4 weeks (one course of therapy)

  GPI LEVEL: GPI-12

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

VEOPOZ (pozelimab-bbfg)

Review: Veopoz is a complement inhibitor indicated for the treatment of adult and pediatric patients 1 year of age and older with CD55-deficient protein losing enteropathy (PLE), also known as CHAPLE disease. Veopoz is the first FDA-approved treatment for CHAPLE disease.

Veopoz is supplied as a 400 mg/2 ml (200 mg/ml) single-dose vial. The recommended dosage for Veopoz is as follows:

- Day 1 (loading dose): Administer a single 30 mg/kg dose by intravenous infusion after dilution
- Day 8 and thereafter (maintenance dosage): Inject 10 mg/kg as a subcutaneous injection once weekly starting on Day 8
- The maintenance dosage may be increased to 12 mg/kg once weekly if there is an inadequate clinical response after at least 3 weekly doses

The maximum maintenance dosage is 800 mg once weekly. IV and SC dosing should be administered by a healthcare professional.

The efficacy and safety of Veopoz were evaluated in a Phase 2/3, single-arm study (NCT04209634) where outcomes were compared to pre-treatment data in patients with active CHAPLE disease who had hypoalbuminemia. Diagnosis was based on a clinical history of PLE and with a confirmed genotype of biallelic CD55 loss-of-function mutation. Active CD55-deficient PLE was defined as hypoalbuminemia (serum albumin concentration of ≤ 3.2 g/dL) with one or more of the following signs or symptoms within the last 6 months: abdominal pain, diarrhea, peripheral edema, or facial edema.

Patients received a single 30 mg/kg loading dose of Veopoz administered by intravenous infusion over approximately one hour, followed by a once weekly weight-tiered maintenance dosage, administered as a subcutaneous injection starting one week after the loading dose. All patients received meningococcal vaccination prior to treatment and antibacterials for prophylaxis of meningococcal infection. Patients were permitted to receive additional therapies as part of standard of care. Use of other complement inhibitors was prohibited. Key exclusion criteria included history of meningococcal infection, no documented meningococcal vaccination within 3 years prior to screening and patient unwilling to undergo vaccination during the study, no documented vaccination for *Haemophilus influenzae* and *Streptococcus pneumoniae* if applicable based on local practice or guidelines, and presence of concomitant disease that leads to hypoproteinemia.

Ten patients ranging from 3 to 19 years of age (median 8.5 years) were assessed for efficacy. The results are based off of an interim report and additional safety and efficacy will be collected at the 2 and 3 year marks. Primary endpoints were both normalization of serum albumin and improvement of clinical outcomes at Week 24. Key secondary outcomes included incidence and severity of adverse events, albumin transfusions, serum IgG concentrations, and hospitalizations. The mean baseline serum albumin concentration was 2.2 g/dL (normal range 3.4-5.4 g/dL) with a range of 1.1 to 2.9 g/dL. The median time for serum albumin to reach at least 3.5 g/dL was 15.5 days (N=10; 95% CI: 8 to 28). All 10 patients achieved normalization by Week 12 and maintained serum albumin concentrations within the normal range through at least 72 weeks of treatment. Five of the ten patients received a total of 60 albumin transfusions in the 48 weeks prior to treatment. In the 48 weeks after starting treatment, one patient received one albumin transfusion. Nine of the ten patients were hospitalized for a total of 268 days in the 48 weeks prior to treatment. In the 48 weeks after starting treatment, two patients were hospitalized for a total of 7 days. Serum IgG concentrations reached normal values for age in all patients within the first 12 weeks of treatment and improvement was maintained through at least 72 weeks of treatment.

Veopoz is contraindicated in patients with unresolved *Neisseria meningiditis* infection (Black Box Warning). Veopoz has warnings and precautions for other bacterial infections, systemic hypersensitivity reactions, and immune complex formation. The most common adverse reactions (in two or more patients) are: upper respiratory tract infection, fracture, urticaria, and alopecia. CHAPLE disease is largely a disease of pediatric patients. Veopoz has not been studies in the geriatric population.

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

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

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

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

- Medical record documentation of CD55-deficient protein losing enteropathy (CHAPLE disease) with a confirmed genotype of biallelic CD55 loss-of-function mutation **AND**
- Medical record documentation of age greater than or equal to 1 year **AND**
- Prescribed by or in consultation with a hematologist, gastroenterologist, or a provider specialized in rare genetic hematologic diseases **AND**
- Medical record documentation that the patient is vaccinated with the meningococcal vaccine **AND**
- Medical record documentation that Veopoz will not be used in combination with Soliris (eculizumab) **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 or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for 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 (i.e., improvement or no worsening of clinical symptoms, increase in or stabilization of albumin and IgG concentration).

  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.

ZURZUVAE (zuranolone)

Review: Zurzuvae is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator indicated for the treatment of postpartum depression (PPD) in adults. The mechanism of action of Zurzuvae in the treatment of PPD is not fully understood but it is thought to be related to positive allosteric modulation of GABAA receptors.

The recommended dosage of Zurzuvae is 50 mg orally once daily in the evening for 14 days. Administer Zurzuvae with fat-containing food (25% to 50% fat). If patients experiencing CNS depressant effects within the 14-day period, consider reducing the dose to 40 mg once daily in the evening within the 14- day period. When used in combination with a strong CYP3A4 inhibitor, the dosage of Zurzuvae should be reduced to 30 mg once daily. No dosage adjustments are needed for moderate CYP3A4 inhibitors. The recommended dosage in patients with severe hepatic impairment is 30 mg orally once daily in the evening for 14 days. No changes are recommended in patients with mild or moderate hepatic impairment. The recommended dosage for Zurzuvae in patients with moderate or severe renal impairment (eGFR < 60 mL/min/1.73 m2) is 30 mg once daily for 14 days. There is no change to the recommended dosage for patients with mild renal impairment. Zurzuvae can be used alone or as an adjunct to oral antidepressant therapy. The safety and effectiveness of Zurzuvae use beyond 14 days in a single treatment course have not been established. Zurzuvae is supplied as 20 mg, 25 mg, and 30 mg capsules.

The efficacy of Zurzuvae for the treatment of PPD in adults was evaluated in two randomized, placebo-controlled, double-blind studies in women with PPD who met the Diagnostic and Statistical Manual of Mental Disorders criteria for a major depressive episode (DSM-5 for Study 1, and DSM-IV for Study 2) with onset of symptoms in the third trimester or within 4 weeks of delivery. Concomitant use of existing oral antidepressants was allowed for patients taking a stable dose of oral antidepressants for at least 30 days from baseline. These studies included patients with HAMD-17 scores ≥ 26 at baseline.

In Study 1, patients received 50 mg of Zurzuvae (n=98) or placebo (n=97) once daily in the evening. The patients were followed for a minimum of 4 weeks after the 14-day treatment course. In Study 2, patients received another zuranolone capsule formulation (approximately equivalent to 40 mg of Zurzuvae) (n=76) once daily for 14 days. The patients were followed for a minimum of 4 weeks after the 14-day treatment course.

The primary endpoint for Studies 1 and 2 was the change from baseline in depressive symptoms as measured by the HAMD-17 total score at Day 15. In both studies, Zurzuvae demonstrated a statistically significant improvement over placebo for the primary endpoint.

The effects of Zurzuvae on driving was evaluated in two randomized, double-blind, placebo- and active-controlled four way crossover studies (Study 3 and Study 4) which evaluated the effects of nighttime Zurzuvae administration on next-morning driving performance, 9 hours after dosing, using a computer-based driving simulation. Study 3 evaluated the effect of 50 mg of Zurzuvae x 6 nights, then 50 mg or 100 mg on the seventh night in 67 healthy individuals. A single 50 mg dose of Zurzuvae caused statistically significant impairment in next-morning driving performance compared to placebo. Statistically significant effects on driving were also observed on Day 8 following daily administration of 50 mg of Zurzuvae. Administration of 100 mg of Zurzuvae (twice the maximum recommended dose) on the final night increased impairment in driving ability.

Study 4 included 60 healthy participants who received Zurzuvae 30 mg x 4 nights, then 30 mg or 60 mg on the fifth night. A single 30 mg dose of Zurzuvae caused a statistically significant impairment in next-morning driving performance compared to placebo. The mean effect on driving performance was not statistically significantly different following 30 mg of Zurzuvae compared to placebo on Day 6; however, driving ability was impaired in some participants taking Zurzuvae. Administration of 60 mg of Zurzuvae on the final night caused statistically significant impairment in next-morning driving performance compared to placebo.

Zurzuvae includes a black box warning for the impaired ability to drive or engage in other potentially hazardous activities. Other warnings and precautions for Zurzuvae include CNS depressant effects, suicidal thoughts and behaviors, and embryo-fetal toxicity. CNS depressant effects include impaired ability to drive or engage in other hazardous activities, somnolence, confusion, and respiratory depression. Other CNS depressants such as alcohol, benzodiazepines, opioids, tricyclic antidepressants or drugs that increase Zurzuvae concentration may increase impairment of psychomotor performance or CNS depressant effects. The most common adverse reactions included somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection. Serious adverse reactions in Studies 1 and 2 occurred in 1% of patients (confusional state). In study 1, the incidence of adverse reactions led to discontinuation in patients treated with Zurzuvae was 2% compared to 1% of patients treated with placebo, most commonly somnolence. Dosage reduction due to adverse reaction occurred in 14% of patients, most commonly somnolence and dizziness. In Study 2, the incidence of adverse reactions leading to discontinuation was 1% in zuranolone treated patients compared to 0% of placebo treated patients. Dosage reduction occurred in 4% of zuranolone-treated patients (somnolence and confusional state).

The safety and efficacy of Zurzuvae in pediatric patients has not been established. There is no geriatric experience with Zurzuvae in patients with postpartum depression. Exposure to zuranolone was increased in patients with severe hepatic impairment and the recommended dosage is lower in these patients. There are no changes recommended to the dosage in patients with mild or moderate hepatic impairment. Exposure to zuranolone was increased in patients with moderate and severe renal impairment. The recommended dosage of Zurzuvae is lower in patients with moderated and severe renal impairment compared to those with normal renal function. Zurzuvae has not been studied in patients with eGFR <15 mL/min/1.73 m^2 or patients requiring dialysis.

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

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

Financial Discussion: Keith Hunsicker, Pharm.D., stated that it's worth mentioning Zulresso is usually given inpatient so there is the added cost of the inpatient stay associated with its administration. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Zurzuvae is a pharmacy benefit and will be added to the Specialty tier or Brand non-preferred tier for members with a three tier benefit on the Commercial, Marketplace, and GHP Kids formulary. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of postpartum depression (PPD) as defined by both of the following:
    - Medical record documentation that member is experiencing a major depressive episode **AND**
    - Medical record documentation that member experienced onset of symptoms within the third trimester or within 4 weeks of delivery **AND**
- Medical record documentation that member is less than or equal to 12 months postpartum **AND**
- Medical record documentation that the current depressive episode is moderate to severe based on a standardized and validated questionnaire/scale [e.g., a score of greater than 10 on the Patient Health Questionnaire (PHQ-9), a score of greater than 20 on the Hamilton Depression Rating Scale (HAM-D), etc.]

  AUTHORIZATION DURATION: One 14 day course of therapy. Additional course of Zurzuvae for future cases of PPD associated with additional pregnancies will be reviewed for medical necessity based on the above criteria. More than one administration of Zurzuvae per pregnancy/birth is considered investigational and not covered.

  QUANTITY LIMIT:
    - **Zurzuvae 20 and 25 mg tablets:** 2 tablets per day
    - **Zurzuvae 30 mg tablets:** 1 tablet per day

  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.

IZERVAY (avacincaptad pegol intravitreal solution)

Review: Izervay is a complement inhibitor indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD). Izervay is an RNA aptamer, a PEGylated oligonucleotide that binds to and inhibits complement protein C5. By inhibiting C5, avacincaptad pegol may prevent its cleavage to C5a an C5b thus decreasing membrane attack complex (MAC) formation.

Izervay must be administered by a qualified physician. The recommended dosage for Izervay is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately every 28 ± 7 days) for up to 12 months. Only 0.1 mL (2 mg) should be administered to deliver a single dose. Any excess volume should be disposed. Izervay is supplied as a 20 mg/mL solution in a single dose vial.

The safety and efficacy of Izervay were demonstrated in GATHER-1 and GATHER-2 two randomized, double-masked, sham-controlled 18- and 12-month studies. Patients were randomized to receive Izervay 2 mg (n=292) or sham (n=332). In both trials, the mean rate of GA growth measure by Fundus Autofluorescence (FAF) was evaluated at three time points (baseline, Month 6, Month 12). For GATHER1, data was available through Month 18. At any time during the GATHER2 study, patients that developed choroidal neovascularization were concomitantly treated with anti-VEGF therapy. In both studies, over the 12-month period, there was a statistically significant reduction of the rate of GA growth in patients treated with Izervay compared to sham (Table 5). Treatment in all pre-specified subgroups (e.g., age, gender, baseline GA disc area) were consistent with the results in the overall population.

Izervay is contraindicated with patients with ocular or periocular infections or with active intraocular inflammation. Warnings and precautions include endophthalmitis and retinal detachments, neovascular (wet) AMD, and increases in intraocular pressure. The most common adverse reactions included conjunctival hemorrhage, increased IOP, blurred vision, and neovascular age-related macular degeneration. The safety and efficacy of Izervay in pediatric patients has not been established. Of the total number of patients who received Izervay in clinical trials, 90% were ≥ 65 years and 61% were ≥ 75 years. No significant differences in efficacy and safety were seen with increasing age in these studies. No dose adjustment is required in patients 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: Dr. Michael Dubartell, stated that he struggles with “mixed picture” patients where one eye has wet AMD and one eye has dry AMD, so he wants to know if the Izervay will increase the risk of wet AMD in the eye not being treated. Kimberly Reichard, Pharm.D., stated there is increased risk of wet AMD associated with use of the drug in the treated eye, but not sure of how it affects the non-treated eye. Dr. Bret Yarczower asked if we can forward this to Geisinger ophthalmology for input on the drug and “mixed patients”. Austin Paisley, Pharm.D., stated he reached out to them during the Syfovre drug review and they feel it should be left up to the prescribing physician. Further meetings will be had with ophthalmology to clarify the criteria appropriateness. Austin Paisley, Pharm.D., asked if we can take an update on Syfovre policy to include criteria surrounding concomitant use with Izervay. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

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

- Medical record documentation of the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) **AND**
- Medical record documentation of a confirmed diagnosis of GA using imagining modalities, including but not limited to fundus autofluorescence (FAF), fundus photography, or optical coherence tomography (OCT) **AND**
- Medical record documentation that Izervay will not be administered concurrently with other complement inhibitors for the treatment of geographic atrophy secondary to age-related macular degeneration (AMD) (i.e., Syfovre) **AND**
- For new starts only: Medical record documentation of the absence of active, or history of, choroidal neovascularization* (CNV) in the eye(s) to be treated with Izervay

  ***NOTE:** Age-related macular degeneration (AMD) with CNV is often referred to as exudative AMD (eAMD), neovascular AMD (nAMD), or wet AMD (wAMD).

  AUTHORIZATION DURATION: 12 months

QUANTITY LIMIT: 0.2 mL (4 mg) per 28 days (2 mg per eye 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.

CLASS REVIEWS

BEVACIZUMAB CLASS REVIEW

Review:

Bevacizumab Agents			
Brand Name	**Generic**	**Date Approved**	**Manufacturer**
Avastin	bevacizumab	02/26/2004	Genentech
Mvasi	bevacizumab-awwb	09/14/2017	Amgen
Zirabev	bevacizumab-bvzr	06/27/2019	Pfizer
Alymsys	bevacizumab-maly	04/13/2022	Amneal
Vegzelma	bevacizumab-adcd	09/27/2022	Celltrion

Bevacizumab binds to and prevents the interaction of VEGF to its receptors Flt-1 and KDR on endothelial cells. By preventing VEGF from binding to its receptors, endothelial cell proliferation and new blood vessel formation is prevented. Administration of bevacizumab to xenotransplant models of colon cancer in athymic mice caused reduction of microvascular growth and inhibition of metastatic disease progression.

Zirabev (bevacizumab-bvzr), Alymsys (bevacizumab-maly), and Vegzelma (bevacizumab-adcd) are the second, third, and fourth biosimilars of bevacizumab approved, respectively. All products do not have interchangeability with the reference product, Avastin. Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved reference product, and that there are no clinically meaningful differences between the biosimilar and reference product. Mvasi was approved on 9/14/2017, Zirabev on 6/27/2019, Alymsys on 4/13/2022, and Vegzelma on 9/27/2022.

Zirabev, Vegzelma and Mvasi all have identical indications. Alymsys has similar indications to other biosimilars except does not contain the indications of: 1) Epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel, followed by bevacizumab as a single agent, for stage III or IV disease following initial surgical resection and 2) Epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by bevacizumab as a single agent, for platinum sensitive recurrent disease. Avastin, the reference product, has an indication for hepatocellular carcinoma in combination with atezolizumab for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy. None of the biosimilars carry this indication however NCCN compendium for hepatocellular carcinoma states the biosimilars may be a substitute for bevacizumab.

No new clinical trials were included in the Zirabev prescribing information. The clinical trials in the Zirabev prescribing information are consistent with those presented in the Avastin prescribing information for the approved indications. Zirabev's clinical trial program included two trials to support its biosimilarity in healthy subjects and in patients with newly diagnosed stage IIIB or IV NSCLC or recurrent NSCLC. The totality of evidence submitted indicated there are similar efficacy, PK, immunogenicity, and safety profiles between Zirabev and Avastin. The safety considerations outlined in the Zirabev prescribing information are consistent with those presented in the Avastin prescribing information.

No new clinical trials were included in the Alymsys prescribing information. The clinical trials in the Alymsys prescribing information are consistent with those presented in the Avastin prescribing information for the approved indications. Alymsys's clinical trial program included three trials to support its biosimilarity in healthy subjects and in patients with metastatic NSCLC and no prior chemotherapy for metastatic disease. The totality of evidence submitted indicated there are no clinically meaningful differences between Alymsys and Avastin in terms of the safety, purity, and potency of the product. The safety considerations outlined in the Alymsys prescribing information are consistent with those presented in the Avastin prescribing information.

No new clinical trials were included in the Vegzelma prescribing information. The clinical trials in the Vegzelma prescribing information are consistent with those presented in the Avastin prescribing information for the approved indications. The totality of evidence submitted indicated there are no clinically meaningful differences between Vegzelma and Avastin in terms of the safety, purity, and potency of the product. The safety considerations outlined in the Vegzelma prescribing information are consistent with those presented in the Avastin prescribing information.

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

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

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

Outcome: Mvasi, Zirabev, Alymsys, and Vegzelma are medical benefits and will not require prior authorization. Avastin is a medical benefit and will require prior authorization. All medications should be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, all medications will process at the Specialty tier or the Brand Non-preferred tier for members with a three tier benefit. The following prior authorization criteria will apply to Avastin:

- Medical record documentation of a therapeutic failure of, intolerance to, or contraindication to all of the following: Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr), Alymsys (bevacizumab-maly), Vegzelma (bevacizumab-adcd).

  AUTHORIZATION DURATION:
  For adjuvant treatment of Stage III or IV Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer following initial surgical resection:
  Authorization will be for one (1) 21 month approval. Authorization of Avastin for adjuvant treatment should not exceed the FDA-approved treatment duration of 21 months (28 cycles). For requests exceeding the above limit, medical record documentation of the following is required:
  - Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration

  For all other indications: Authorization will be open-ended

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

HEREDITARY ANGIOEDEMA CLASS REVIEW

Review:

Name	Generic	Generic Available?	Manufacturer
C1 Esterase Inhibitor			
Cinryze	Plasma-derived nanofiltered C1INH (IV)	No	Takeda Pharmaceuticals
Haegarda	Plasma-derived nanofiltered C1INH (SQ)	No	CSL Behring LLC
Kallikrein Inhibitor			

Takhzyro	lanadelumab-flyo	No	Takeda Pharmaceuticals
Orladeyo	berotralstat	No	Biocryst
Androgen			
Danocrine	danazol	Yes	Sanofi

Hereditary angioedema (HAE) is a rare autosomal dominant disease characterized by episodic unpredictable swelling. There are two main types of HAE: HAEC1INH or HAE-nl-C1INH. HAE-C1INH is further broken down into Type 1 HAE (deficient levels of C1INH protein and function) and Type 2 HAE (normal level of C1INH protein that is dysfunctional). There are 6 subtypes of NAE-nl-C1INH.

According to the 2020 US HAEA Medical Advisory Board, it is recommended to have access to effective on-demand treatment for attacks. For HAE-C1INH, short term prophylaxis can be either a single dose of pdC1INH or a course of anabolic androgen. Long-term prophylaxis is dependent on the needs of the patient, but first line recommendations are Cinryze, Haegarda, and Takhzyro. Second-line options would be anabolic androgens (Danocrine).

According to the 2021 Revision and Update of the International WAO/EAACI Guidelines for the Management of HAE, long-term prophylactic first-line agents for HAE are plasma-derived C1-INH (Cinryze, Haegarda), lanadelumab (Takhzyro), and berotralstat (Orladeyo). Androgens (danazol) are considered second-line agents due to increased risk of side effects and drug interactions.

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

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

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

Outcome: The following changes are recommended to existing policies:

Cinryze, MBP 85.0

Cinryze (C1 esterase inhibitor, human) will be considered medically necessary for the commercial, exchange and CHIP lines of business for prophylaxis against attacks of hereditary angioedema when the following criteria are met:

- Member is 6 years of age or older; **AND**
- Prescription is written by an allergist, immunologist, hematologist, or dermatologist; **AND**
- Medication is being used as prophylactic therapy for HAE attacks; **AND**
- Diagnosis of hereditary angioedema has been established and supported by physician provided documentation of:
    - Recurrent, self-limiting non-inflammatory subcutaneous angioedema without urticaria, lasting more than 12 hours; **OR**
    - Laryngeal edema; **OR**
    - Recurrent, self-remitting abdominal pain lasting more than 6 hours, without clear organic etiology

      AND
- the presence of specific abnormalities in complement proteins, in the setting of a suggestive clinical history of episodic angioedema without urticaria; supported by
    - Medical record documentation of 2 or more sets of complement studies, separated by one month or more, showing consistent results of
        - Low C4 levels **AND**
        - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
        - Less than 50% of the lower limit of normal C1-INH function levels **AND**

- ~~Physician provided documentation of failure on, intolerance to, or contraindication to danazol; **AND**~~
- Physician provided documentation of history of more than one (1) severe event per month OR a history of laryngeal attacks

Haegarda, Commercial Policy 471.0

A formulary exception for coverage of Haegarda may be made for members who meet the following criteria:

- Medical record documentation of age greater than or equal to ~~12~~ 6 years **AND**
- Medical record documentation that Haegarda is prescribed by an allergist, immunologist, hematologist, or dermatologist **AND**
- Medical record documentation of a diagnosis of hereditary angioedema (HAE) established and supported by documentation of:
    - Recurrent, self-limiting, non-inflammatory subcutaneous angioedema without urticaria which lasts more than 12 hours **OR**
    - Laryngeal edema **OR**
    - Recurrent, self-remitting abdominal pain which lasts more than 6 hours, without clear organic etiology **AND**
- Medical record documentation of specific abnormalities in complement proteins, in the setting of a suggestive clinical history or episodic angioedema without urticaria; supported by:
    - Medical record documentation of two (2) or more sets of complement studies, separated by one month or more, showing consistent results of:
        - Low C4 levels **AND**
        - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
        - Less than 50% of the lower limit of normal C1-INH function levels **AND**
- Medical record documentation of history of more than one (1) severe event per month **OR** a history of laryngeal attacks **AND**
- Medical record documentation that Haegarda is being used as prophylactic therapy for hereditary angioedema (HAE) attacks ~~**AND**~~
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to danazol~~

Takhzyro, Commercial Policy 543.0

An exception for coverage of Takhzyro may be made for members who meet the following criteria:

- Medical record documentation of age greater than or equal to ~~12~~ 2 years **AND**
- Medical record documentation that Takhzyro is prescribed by an allergist, immunologist, hematologist, or dermatologist **AND**
- Medical record documentation of a diagnosis of hereditary angioedema (HAE) established and supported by documentation of:
    - Recurrent, self-limiting, non-inflammatory subcutaneous angioedema without urticaria which lasts more than 12 hours **OR**
    - Laryngeal edema **OR**
    - Recurrent, self-remitting abdominal pain which lasts more than 6 hours, without clear organic etiology **AND**
- Medical record documentation of specific abnormalities in complement proteins, in the setting of a suggestive clinical history or episodic angioedema without urticaria; supported by:
    - Medical record documentation of two (2) or more sets of complement studies, separated by one month or more, showing consistent results of:
        - Low C4 levels **AND**
        - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
        - Less than 50% of the lower limit of normal C1-INH functions levels **AND**
- Medical record documentation of history of more than one (1) severe event per month **OR** a history of laryngeal attacks **AND**

- Medical record documentation that Takhzyro is being used as prophylactic therapy for hereditary angioedema (HAE) attacks
- Medical record documentation that the member is receiving an appropriate dose* based on patient's age **AND**
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to danazol~~

Orladeyo, Commercial Policy 660.0

An exception for coverage of Orladeyo may be made for members who meet the following criteria:

- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation that Orladeyo is prescribed by an allergist, immunologist, hematologist, or dermatologist **AND**
- Medical record documentation of a diagnosis of hereditary angioedema (HAE) established and supported by documentation of:
    - Recurrent, self-limiting, non-inflammatory subcutaneous angioedema without urticaria which lasts more than 12 hours **OR**
    - Laryngeal edema **OR**
    - Recurrent, self-remitting abdominal pain which lasts more than 6 hours, without clear organic etiology **AND**
- Medical record documentation of specific abnormalities in complement proteins, in the setting of a suggestive clinical history or episodic angioedema without urticaria; supported by:
    - Medical record documentation of two (2) or more sets of complement studies, separated by one month or more, showing consistent results of:
        - Low C4 levels **AND**
        - Less than 50% of the lower limit of normal C1-INH antigenic protein levels **OR**
        - Less than 50% of the lower limit of normal C1-INH functions levels **AND**
- Medical record documentation of history of more than one (1) severe event per month **OR** a history of laryngeal attacks **AND**
- Medical record documentation that Orladeyo is being used as prophylactic therapy for hereditary angioedema (HAE) attacks **AND**
- Medical record documentation that Orladeyo is not being used in combination with another prophylactic human C1 esterase inhibitor (Cinryze or Haegarda) or lanadelumab (Takhzyro) therapy for hereditary angioedema ~~**AND**~~
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to danazol~~

Danocrine

No Change

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

FAST FACTS

XTANDI (generic name)

Clinical Summary: Xtandi is now indicated for the treatment of adult patients with nonmetastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR). Previously, this was only indicated for the treatment of metastatic castration-sensitive prostate cancer (mCSPC) or castration-resistant prostate cancer (CRPC).

The recommended dosage of Xtandi remains the same at 160mg administered orally once daily. Patients receiving Xtandi for nmCSPC may be treated with or without receiving concurrent gonadotropin-releasing hormone (GnRH) analog, whereas patients receiving Xtandi for CRPC or mCSPC should receive a gonadotropin-releasing hormone (GnRH) analog concurrently or should have had a bilateral orchiectomy.

The safety and efficacy of Xtandi in patients with nonmetastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR) were assessed in the EMBARK trial (NCT02319837). The trial included 1068 patients with nmCSPC with high-risk BCR and ranged in age from 49-93 years. All patients had prior radical prostatectomy and/or radiotherapy with curative intent, confirmation of non-metastatic disease by BICR, and a prostate-specific antigen (PSA) doubling time less than or equal to 9 months. Patients were not candidates for salvage radiotherapy at the time of enrollment. Patients were randomized 1:1:1 to receive Xtandi at a dose of 160mg daily concurrently with leuprolide, Xtandi at a dose of 160mg once daily as a single agent, or placebo once daily concurrently with leuprolide. Patients were treated until radiographic disease progression, initiation of new treatment, unacceptable toxicity, or withdrawal. The primary efficacy outcome was metastasis-free survival (MFS) with statistically significant improvement in patients who received Xtandi plus leuprolide compared to patients who received placebo plus leuprolide. And the secondary efficacy outcome was MFS with statistically significant improvement in patients who received Xtandi as a single agent compared to patients who received placebo plus leuprolide.

Common adverse reactions included fatigue, hot flush, nausea, and cognitive disorder. No new warnings, contraindications or black box warnings were identified.

Current Formulary Status: Pharmacy Benefit on the Specialty tier, requiring a prior authorization.

Recommendation: No changes are recommended to the formulary placement of Xtandi. The following formatting changes and criteria will be added to Commercial Policy 262.0 Policy for Xtandi to include the new indication:

- Medical record documentation that Xtandi is prescribed by a hematologist, oncologist, or urologist **AND**
- Medical record documentation of a diagnosis of prostate cancer **AND**
- Medical record documentation of one of the following:
  - That the member has nonmetastatic castration-sensitive prostate cancer (nmCSPC) with biochemical recurrence at high risk for metastasis (high-risk BCR)†

  OR
  - That the member is no longer responding to castration or is hormone resistant (CRPC) **AND**
  - Medical record documentation that a gonadotropin-releasing hormone (GnRH) analog will be used concurrently **OR** member has had bilateral orchiectomy

  OR
  - That the member has metastatic castration-sensitive prostate cancer (mCSPC) **AND**
  - Medical record documentation that a gonadotropin-releasing hormone (GnRH) analog will be used concurrently **OR** member has had bilateral orchiectomy

†**NOTE**: In clinical trials, high-risk BCR patients were defined by a PSA doubling time ≤ 9 months

Discussion: No comments or questions.

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

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

UPDATES

AMVUTTRA UPDATE

Background: As part of the annual review process, it was discovered an "AND" needed to be added to the Amvuttra commercial, exchange, and CHIP policy.

Recommendations: It is recommended to update the prior authorization criteria for Amvuttra medical commercial/exchange/CHIP policy to represent the correct transition between criteria points.
MBP 268.0 Amvuttra (vutrisiran)

Amvuttra (vutrisiran) will be considered medically necessary for the commercial, exchange, and CHIP lines of business when all of the following criteria are met:

- Prescription written by or in consultation with a neurologist, board-certified medical geneticist, or specialist with experience in the treatment of hereditary transthyretin-mediated amyloidosis (hATTR) **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of hereditary transthyretin-mediated amyloidosis as confirmed by genetic testing to confirm a pathogenic mutation in TTR AND one of the following:
    - Biopsy of tissue/organ to confirm amyloid presence **OR**
    - A clinical manifestation typical of hATTR (Neuropathy and/or CHF) without a better alternative explanation **AND**
- Medical record documentation of Amvuttra being used to treat polyneuropathy **AND**
- Medical record documentation of familial amyloid polyneuropathy (FAP) stage 1-2 and/or polyneuropathy disability score (PND) indicating the patient is not wheelchair bound or bedridden **AND**
- Medical record documentation of a dose and duration of therapy that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature **AND**
- Medical record documentation that Amvuttra will not be used in combination with other RNA interference treatment **AND**
- Medical record documentation that the member has been evaluated and treated by a contracted Center of Excellence in amyloidosis management

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

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. None were opposed.

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

DURYSTA UPDATE

Background: Currently on the Geisinger Commercial line of business, tier 1 formulary alternatives in the prostaglandin category include latanoprost, bimatoprost, tafluprost and travoprost. Tier 2 formulary alternative is Xelpros. Tier 3 formulary alternatives include Lumigan and Vyzulta.

Recommendations: It is recommended to update the Durysta prior authorization criteria to include all available formulary alternatives.

MBP 243.0 Durysta (bimatoprost intraocular implant)

Durysta (bimatoprost intraocular implant) will be considered medically necessary for the commercial, exchange, and CHIP lines of business when all of the following criteria are met:

- Prescription written by or in consultation with an ophthalmologist **AND**
- Medical Record documentation of a diagnosis of open-angle glaucoma (OAG) or ocular hypertension (OHT) **AND**
- Medical record documentation that patient has not received a previous administration of Durysta to the requested eye **AND**
- Medical record documentation of intolerance to, contraindication to, or therapeutic failure on ~~latanoprost AND travoprost AND bimatoprost ophthalmic solutions~~. three ophthalmic prostaglandin analogs, one of which must be bimatoprost*

*step therapy required

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. None were opposed.

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

2024 FORMULARIES FOR APPROVAL

Background: Copies of the following 2024 formularies were provided to the P&T committee for review and approval:

- AON Exchange Formulary
- Commercial 4 Tier Formulary
- Commercial Traditional Formulary
- Commercial Triple Choice Formulary
- GHP Kids Formulary
- Marketplace Formulary
- Northern Light Employee Formulary

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. None were opposed.

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

DUR Update

Background:

Commercial/Exchange/TPAs (COMM, D6)

Drug Use Evaluations (DUEs)

- Overutilization of albuterol and levalbuterol
  - This is our 2022 3rd quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, Chip
  - For this report, we identified members who had greater than a 180-day cumulative day supply of Albuterol and/or levalbuterol (based on pharmacy claims from 1/1/2022-12/23/22) with a diagnosis of Asthma (based on medical claims from 4/1/2021 through 12/23/22)
    - See below for the number of members identified:
      - For COMM: **61**
      - For D6: **66**
    - Letters were sent to the MI attributed PCP of each member with their medication fill history of both their controller and rescue inhalers to help providers identify members that may be overutilizing their rescue inhalers and to identify potential compliance concerns with their controller inhaler.
    - Adam K. re-ran this data on 8/4/23 to analyze the effectiveness of the letter. Of the original 150 Commercial/Exchange members 114 members were still active and only 28 of those members still have 180+ days with a rescue inhaler. This is 24.6% of members and included data from 1/1/23 to 7/27/23.
- Use of Opioids at High Dosage
  - This is our 2022 2nd quarter Geisinger Health Plan DUE for Commercial, Exchange, TPA, Medicaid, Medicare
  - From this report, we identified members 18 years and older with 15+ opioid covered days and had an MME of 90 or greater per day based on claims from 1/1/2022 through 7/27/2022
    - See below for the number of members that were identified with an MME of 90 or greater per day:
      - For COMM: **13**
      - For D6: **19**
      - For TP45: **2**
      - For TPE0: **1**
      - For SASN: **1**
      - For TG48/TG51: **18**
    - Letters were sent to the MI attributed PCP of each member with the respective medication fill history for providers to evaluate their patients current pain regimen and ensure lowest effective doses are utilized.
    - Letters were mailed out on 9/15/2023
    - Adam K. re-ran this data on 5/5/2023 to analyze the effectiveness of the letter. The following number of members had not filled an opioid within the past 60 days, had an MME less than 90, and/or had an average MME decrease:
      - For COMM: Of the 13 members originally identified, 7 were still active. Of those members, **2 members** did not fill an opioid in the past 60 days, **4 members** had an average MME decrease
      - For D6: Of the 19 members originally identified, 15 were still active. Of those members, **1 member** did not fill an opioid in the

past 60 days, **1 member** had an average MME less than 90, **8 members** had an average MME decrease
    - For TG48: Of the 18 members originally identified, 15 were still active. Of those members, **1 member** did not fill an opioid in the past 60 days, **1 member** had an average MME less than 90, **8 members** had an average MME decrease
    - For TG45: Of the 2 members originally identified, 2 were still active. Of those members, **1 member** had an average MME decrease
    - For TPE0: Of the 1 member originally identified, 1 was still active. Of those members, **1 member** had an average MME decrease
    - For SASN: Of the 1 member originally identified, 1 was still active. Of those members, **1 member** had an average MME decrease

In Progress

- Pharmacotherapy for Opioid Use Disorder (POD) HEDIS measure report

Ongoing

- DPP-4/GLP-1 Diabetes Duplicate Therapy Report
    - We receive this report monthly for all LOBs (Star team addresses Medicare) from Adam Kelchner. This report identifies members who potentially have duplicate therapy on a DPP-4/GLP-1 combination. Calls are made to the prescribers to discuss the lack of clinical evidence of this combination and/or duplicate therapy. Recommendations are made to discontinue one agent (ex. the DPP-4 if member on both a GLP-1 and DPP-4).
        - For 2023 we have resolved the following number of **c**ases of therapeutic duplication:
        - **COMM: 17 cases** of therapeutic duplication resulting in a projected savings of **$9,626.47 per script** (this is savings to both member and the health plan)
        - **D6: 5 cases** of therapeutic duplication resulting in a projected savings of **$2,907.61 per script** (this is savings to both member and the health plan)
        - **TG48: 6 cases** of therapeutic duplication resulting in a projected savings of **$3,684.72 per script** (this is savings to both member and the health plan)
        - **EMYD: 4 cases** of therapeutic duplication resulting in a projected savings of **$2,849.14 per script** (this is savings to both member and the health plan)
        - **TPN2: 1 case** of therapeutic duplication resulting in a projected savings of **$529.60 per script** (this is savings to both member and the health plan)
        - **TPM2: 1 case** of therapeutic duplication resulting in a projected savings of **$488.33 per script** (this is savings to both member and the health plan)
- TNF and Oral Oncology Agent Report
    - We get this report monthly for the Commercial/Exchange, TPA, and CHIP LOBs from Adam Kelchner.
    - This report was generated in response to removing the renewal prior authorization requirement for these agents.
    - This report identifies members who are on a TNF or Oral Oncology agent and may not have been seen by their applicable specialist in the last 15 months.

- We research these members and reach out to the offices/members as necessary to ensure the member has been seen within the last 15 months, an appointment has been scheduled or will be scheduled with the member to ensure the member continues to be able to receive their medication.
- For 2023:
  - For COMM
    - Members Reviewed: **45**
    - Outreaches Made: **11**
    - Letters Sent: **3**
    - Negative Overrides Entered: **0**
  - For D6
    - Members Reviewed: **61**
    - Outreaches Made: **14**
    - Letters Sent: **5**
    - Negative Overrides Entered: **1**
  - For TG48
    - Members Reviewed: **44**
    - Outreaches Made: **11**
    - Letters Sent: **4**
    - Negative Overrides Entered: **0**
  - For TG51
    - Members Reviewed: **12**
    - Outreaches Made: **2**
    - Letters Sent: **1**
    - Negative Overrides Entered: **1**
  - For TGW2
    - Members Reviewed: **5**
    - Outreaches Made: **0**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TP23
    - Members Reviewed: **2**
    - Outreaches Made: **0**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TP45
    - Members Reviewed: **1**
    - Outreaches Made: **0**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TP50
    - Members Reviewed: **1**
    - Outreaches Made: **0**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TPH0
    - Members Reviewed: **4**
    - Outreaches Made: **1**
    - Letters Sent: **0**
    - Negative Overrides Entered: **0**
  - For TPT2

        - Members Reviewed: **1**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
    - For WF89
        - Members Reviewed: **1**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
    - For SASE
        - Members Reviewed: **1**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
    - For SASN
        - Members Reviewed: **3**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
    - For SASX
        - Members Reviewed: **1**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
- Cystic Fibrosis Adherence Report
    - We get this report monthly for all LOBs from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.
        - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence
        - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
        - And for all members we send a letter discussing the importance of medication adherence
        - For 2023, please see below for the number of **members** an adherence letter was sent to:
            - Letters are only sent to members every 6 months
                - For COMM: 6
                - For D6: 5
                - For TG48: 4
                - For WF89: 3
        - Please see below for the number of letters sent to non-GHS pulmonologists
            - For D6: **0**
        - Please see below for the number of members referred to the CF coordinators:
            - For COMM: **14**
            - For D6: **14**
            - For TG48: **13**
            - For WF89: 6

- Duplicate Anticoagulant Report
    - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
    - For 2023:
        - For COMM (Commercial): **8 members** reviewed and **0 interventions** made
        - For D6 (Exchange): **9 members** reviewed and **0 interventions** made
        - For TG48/GH51: **10 members** reviewed and **1 intervention** made
        - For TP23: **0 members** reviewed and **0 interventions** made
        - For TP45: **0 members** reviewed and **0 interventions** made
        - For TP56: **0 members** reviewed and **0 interventions** made
        - For EMYD: **2 members** reviewed and **0 interventions** made
        - For MT38: **0 members** reviewed and **0 interventions** made
        - For TP74: **0 members** reviewed and **0 interventions** made
        - For SASN: 0 **member** reviewed and **0 interventions** made
        - For SASF: 0 **member** reviewed and **0 interventions** made
        - For TPH3: **2 memberd** reviewed and **0 interventions** made
- Duplicate Specialty Therapy
    - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Smith. These members are identified and written up and sent to a medical director if follow up is needed.
        - For Commercial/Exchange/TPA for, **0 members** were referred to Dr. Yarczower for additional follow-up.
- Duplicate Buprenorphine Therapy
    - We get this report **quarterly** with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows and Dr. Hossler for further outreach.
        - For Commercial/Exchange, TPAs for 2023, we have reviewed **0 members** and **0 members** were referred to Dr. Meadows
- Suboxone with an Opioid Report
    - We get this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each new member that flags on the report. These members are being discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both medical directors look into whether it is appropriate to end the opioid authorizations still in place or if further intervention is required.
    - For Commercial/Exchange/TPA for 2023, see below for the new members reviewed and those referred to the MDs:
        - For COMM: we have reviewed **0 new members** and **0 members** were referred to MDs
        - For D6: we have reviewed **3 new members** and **0 members** were referred to MDs
        - For EMYD: we have reviewed **0 new members** and **0 members** were referred to MDs
        - For TG48: we have reviewed **4 new members** and **0 members** was referred to MDs

        - For SASE: we have reviewed **0 new members** and **0 members** was referred to MDs
        - For SASN: we have reviewed **0 new members** and **0 members** was referred to MDs
        - For TPI2: we have reviewed **0 new members** and **0 members** was referred to MDs
- Ending Opioid Authorizations
    - We are working on identifying members who have active opioid authorizations in place but have since started Buprenorphine therapy. The letter is sent to the members notifying them the opioid authorization has been ended due to the start of buprenorphine therapy.
    - For Commercial/Exchange/TPA for 2023, see below for the number of letters we sent to members notifying them that we are ending their opioid authorization(s):
        - For D6: **0**
        - For COMM: **0**
        - For TG48/TG51: **0**
        - For SASN: **0**
- Opioid Overutilization Report
    - We get this report **monthly** from PerformRx and we write up each member that flags on the report. We have been monitoring the members that are continuously showing up on the report by any change in their MED. For those members we deem appropriate we will send a letter to their PCP.
    - For Commercial/Exchange/TPA for 2023, see below for the number of reviewed cases.
        - For COMM: we have reviewed **0 members** and sent **0 cases** to MDs for review
        - For EMYD: we have reviewed **0 members** and sent **0 cases** to MDs for review
        - For TG48: we have reviewed **1 members** and sent **0 cases** to MDs for review
- FWA Reports
    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For COMM for 2023, we have reviewed **50** cases and corrected claims, resulting in a potential **cost savings/avoidance of $5,831.86**
        - For D6 for 2023, we have reviewed **30** cases and corrected claims, resulting in a potential **cost savings/avoidance of $6,777.08**
        - For TPN2 for 2023, we have reviewed **1** cases and corrected claims, resulting in a potential **cost savings/avoidance of $297.44**
        - For EMYD for 2023, we have reviewed **27** cases and corrected claims, resulting in a potential **cost savings/avoidance of $4,561.05**
        - For TG48, TG51 for 2023, we reviewed **35** cases and corrected claims, resulting in a potential **cost savings/avoidance of $13,357.05**
        - For SASE for 2023, we reviewed **1** cases and corrected claims, resulting in a potential **cost savings/avoidance of $1.00**
        - For SASN for 2023, we reviewed **4** cases and corrected claims, resulting in a potential **cost savings/avoidance of $1,072.28**
        - For TP23 for 2023, we reviewed **2** cases and corrected claims, resulting in a potential **cost savings/avoidance of $83.24**

        - For TP45 for 2023, we reviewed **3** cases and corrected claims, resulting in a potential **cost savings/avoidance of $4.45**
        - For WF89 for 2023, we reviewed **3** cases and corrected claims, resulting in a potential **cost savings/avoidance of $321.02**
        - For TPD2 for 2023, we reviewed **1** cases and corrected claims, resulting in a potential **cost savings/avoidance of $286.50**
        - For TPJ0 for 2023, we reviewed **1** cases and corrected claims, resulting in a potential cost savings/avoidance of **$21.78**
        - For TP49 for 2023, we reviewed **1** cases and corrected claims, resulting in a potential **cost savings/avoidance of $27.91**
        - For TP56 for 2023, we reviewed **1** cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
        - For TGW2 for 2023, we reviewed **1** cases and corrected claims, resulting in a potential **cost savings/avoidance of $0**
- Duplicate Antipsychotics
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - We have sent the following provider letters in 2023
            - For COMM: **30**
            - FOR D6: **31**
            - FOR TG48, TG51: **29**
            - For TP45: **2**
            - For TP50: **1**
            - For TP56: **0**
            - For EMYD: **0**
            - For MT38: **0**
            - For TP74: **0**
            - For SASN: **0**
            - For SASF: **0**
            - For SASX: **1**
            - For TGW2: **2**

- Severity Report
    - We get this report **monthly** for **all LOBs** on members who have filled a medication that has a level one interaction with another medication they have a claim for
        - For Commercial/Exchange/TPA for 2023 see below for the number of members identified and had sent letters to their MI attributed PCP:
            - For COMM: **41**
            - For D6: **38**
            - For EMYD: **1**
            - For SASF: **1**
            - For SASN: **6**
            - For SASE: **1**
            - For TG48: **47**
            - For TG51: **7**
            - For TGW2: **4**
            - For TPB3: **0**
            - For TPE0: **0**
            - For TPF3: **1**
            - For TPH2: **0**

        - For TPH3: **1**
        - For TPJ3: **1**
        - For TPM2: **0**
        - For TP23: **0**
        - For TP41: **1**
        - For TP45: **5**
        - For TP46: **1**
        - For TP50: **3**
        - For TP56: **1**
        - For TP64: **1**
        - For TP88: **0**
        - For TPU1: **1**
        - For TPU2: **1**
        - For TPZ2: **1**
        - For TPA6: **0**
        - For WF89: **0**
- Tobacco Cessation Program
    - We get this report **monthly** to identify members on prolonged tobacco cessation treatment. We send a letter and resource pamphlet to provide additional behavioral health support through Geisinger Health and Wellness.
    - For Commercial/Exchange/TPA for 2023, we sent letters to the below number of members:
        - For COMM: **21**
        - For D6: **18**
        - For EMYD: **11**
        - For SASN: **2**
        - For SASE: **3**
        - For SASK: **1**
        - For TG48, TG51: **12**
        - For TGW2: **1**
        - For TPB3: **0**
        - For TP23: **0**
        - For TP33: **0**
        - For TP41: **1**
        - For TP45: **3**
        - For TP46: **0**
        - For TP50: **0**
        - For TP56: **0**
        - For TP64: **0**
        - For TP88: **1**
        - For TPA6: **0**
        - For TPI3: **1**
        - For TPM2: **1**
        - For TPT2: **0**
        - For WF89: **0**
- STENT Adherence Report
    - We get this report **monthly** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
    - In 2023, we have sent letters encouraging adherence to the below number of members:
        - **Members for Antiplatelet:**

- COMM: **81**
- D6: **61**
- EMYD: **9**
- SASN: **11**
- TG48, TG51: **32**
- TGW2: **1**
- TP41: **0**
- TP23: **0**
- TP33: **1**
- TP45: **1**
- TP46: **1**
- TP50: **0**
- TP56: **3**
- TP64: **0**
- TP74: **0**
- PM71: **0**
- TP88: **0**
- TPA6: **0**
- WF89: **5**
- TPD2: **0**
- SASE: **4**
- SASF: **0**
- SASK: **0**
- SASX: **2**
- TPB3: **0**
- TPF2: **0**
- TPH2: **2**
- TPI0: **0**
- TPL0: **0**
- TPM2: **0**
- TPT2: **2**
- TPU2: **1**
- **P**M70: **0**
- PM71: **0**

- **Members for Beta-Blocker:**
  - COMM: **100**
  - D6: **91**
  - EMYD: **12**
  - SASN: **13**
  - TG48, TG51: **47**
  - TP23: **0**
  - TP33: **1**
  - TP41: **2**
  - TP45: **4**
  - TP46: **1**
  - TP50: **0**
  - TP56: **1**
  - TP88: **1**
  - TPA6: **0**
  - WF89: **4**
  - TPI0: **0**
  - SASK: **1**
  - TPB3: **0**
  - TPI3: **2**
  - TPR1: **0**
  - TPT2: **0**
  - TPU1: **2**
  - TGW2: **3**
  - SASE: **4**
- **Members for Statin:**
  - COMM: **103**
  - D6: **81**
  - EMYD: **15**
  - SASN: **8**
  - SASF: **0**
  - TG48, TG51: **52**
  - TGW2: **1**
  - TP23: **0**
  - TP41: **2**
  - TP45: **3**
  - TP46: **2**
  - TP56: **0**
  - PM71: **0**
  - SASK: **0**
  - SAQ2: **0**
  - TPI0: **0**
  - TPM2: **0**
  - TPR1: **0**
  - TP88: **0**
  - TPA6: **0**
  - TPA7: **1**
  - TPU1: **0**
  - WF89: **6**
  - TP33: **2**
  - TP50: **0**
  - TP64: **0**
  - PM70: **0**
  - TP74: **0**
  - SASE: **1**
  - SASX: **1**
  - TPB3: **0**
  - TPH2: **2**
  - TPT2: **1**
  - TP41: **0**
- *member may flag for more than one measure and are included in the count for each measure

- In 2023, we have attempted telephonic outreach to the below number of members non-adherent in all 3 measures and reached the below members to encourage adherence.
  - COMM:
    - Attempted: **1**
    - Reached: **0**
  - D6:
    - Attempted: **0**
    - Reached:**0**
  - EMYD:
    - Attempted: **1**
    - Reached: **1**
  - SASN:
    - Attempted: **0**
    - Reached: **0**

- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR)
  - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
    - For Commercial/Exchange for 2023, see below for the number of letters sent to members:
      - COMM: **45**
      - D6: **27**
- Asthma Medication Ratio (AMR) Member Calls
  - Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. The RPHs call Commercial/Exchange members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication.
  - For Commercial/Exchange for 2023, see below for the number of members we have outreached to and the number of members that have been reached:
    - COMM:
      - Outreached to: **42**
      - Reached: **23**
    - D6:
      - Outreached to: **53**
      - Reached: **38**
- Antidepressant Medication Management (AMM)
  - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
    - For Commercial/Exchange for 2023, see below for the number of letters sent to members:
      - Effective Acute Phase:
        - COMM: **0**
        - D6: **1**
      - Effective Continuation Phase:
        - COMM: **34**
        - D6: **16**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
  - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.

        - For Commercial/Exchange for 2023, see below for the number of letters sent to members:
            - COMM: **3**
            - D6: **0**
- Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange in 2023, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **31**
            - D6: **20**
        - For Commercial/Exchange in 2023, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **33**
            - D6: **12**
- Statin Therapy for Patients with Diabetes (SPD)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange for 2023, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **342**
            - D6: **171**
        - For Commercial/Exchange for 2023, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **47**
            - D6: **13**
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)
    - We get this report **monthly** to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For Commercial/Exchange for 2023, see below for the number of letters sent to **members:**
            - COMM: **0**
            - D6: **0**
- Use of Opioids from Multiple Providers (UOP)
    - We get this report quarterly to identify members 18 years of age and older with a total day supply of all opioid claims to be 15 days or greater
        - See below for the number of members that were identified who were seeing 4 or more providers from different offices for their opioid prescriptions for 2023
            - **COMM: 27**
            - **D6: 14**
        - See below for the number of members that were identified who were seeing 4 or more providers within the same office for their opioid prescriptions for 2023
            - **COMM: 1**
            - **D6: 2**

        - We sent letters to the MI attributed PCP of each member with the respective medication fill history to encourage medication evaluation of the opioid medications
- **HEDIS PQA Initiatives:**
- HEDIS PQA- INR Report
    - We get this report **weekly** for the Exchange population from Adam Kelchner
    - This report looks at the percentage of members 18 years of age and older who had at least one 56-day interval of warfarin therapy and who received at least one international normalized ratio (INR) monitoring test during each 56-day interval with active warfarin therapy.
        - For Exchange for 2023, we have performed telephonic outreach to providers for **9 members** that had not had an INR level drawn.
- HEDIS PQA-AMO Report
    - We get this report **monthly** for the Exchange population from Adam Kelchner
    - This report looks at the percentage of members 18 years of age and older who are prescribed long-term opioid therapy and have not received a drug test at least once during the measurement year.
        - For Exchange for 2023, we have reviewed **110 members** that had not had a drug test completed and completed outreach to those without a drug test.
- HEDIS PQA-PDC Letters
    - We get this report **monthly** for the Exchange population from Adam Kelchner
    - This report looks at the percentage of members 18 years of age and older who have a PDC of less than 80% during the measurement year for the below medication classes who are past due for a medication refill:
        - Renin Angiotensin System Antagonists (PDC-RASA)
        - Diabetes All Class (PDC-DR)
        - Statins (PDC-STA)
        - For Exchange for 2023, we have identified the following number of members and sent letters:
            - Renin Angiotensin System Antagonists (PDC-RASA): **527**
            - Diabetes All Class (PDC-DR): **261**
            - Statins (PDC-STA): **518**

Fliers/Letters

- Commercial/Exchange DUR/FWA Program internal Fliers
    - Last updated 6/2023 next update 11/2023
- Current Provider Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Statin Use in Persons with Diabetes DUE
        - Opioid Overutilization
        - Duplicate Antipsychotic medication
        - Severity Report
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - SUPD/SPD Provider Letter
        - HEDIS: Asthma Medication Ratio (AMR)
        - HEDIS: Use of Opioids from multiple providers (UOP)
        - HEDIS: Use of Opioids at High Dosage (HDO)

- Current Member Letters
    - Exchange PQA Adherence Letters
    - Cystic Fibrosis Adherence Letter
    - TNF/Oral Oncology Letter
    - Ending Opioid Authorizations
    - Tobacco Cessation Letter
    - STENT Adherence Report
    - HEDIS: Asthma Medication Ratio (AMR)
    - HEDIS: Antidepressant Medication Management (AMM)
    - HEDIS: Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - HEDIS: Statin Therapy for Patients with Diabetes (SPD)
    - HEDIS: Persistence of eta-Blocker Treatment After a Heart Attack (PBH)

CHIP (CHBQ)

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

Drug Use Evaluations (DUEs)

- Overutilization of albuterol and levalbuterol
  - This is our 2022 3rd quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, Chip
  - For this report, we identified members who had greater than a 180-day cumulative day supply of Albuterol and/or levalbuterol (based on pharmacy claims from 1/1/2022-12/23/22) with a diagnosis of Asthma (based on medical claims from 4/1/2021 through 12/23/22)
    - **5 members** were identified with overutilization of their inhalers
    - Letters were sent to the MI attributed PCP of each member with their medication fill history of both their controller and rescue inhalers to help providers identify members that may be overutilizing their rescue inhalers and to identify potential compliance concerns with their controller inhaler.
    - Adam K. re-ran this data on 8/4/23 to analyze the effectiveness of the letter. Of the original 5 CHIP members 5 members were still active and only 1 of those members still have 180+ days with a rescue inhaler. This is 20% of members and included data from 1/1/23 to 7/27/23.

In Progress

- Pharmacotherapy for Opioid Use Disorder (POD) HEDIS measure report

Ongoing

- DPP-4/GLP-1 Diabetes Duplicate Therapy Report
  - We receive this report monthly for all LOBs (Star team addresses Medicare) from Adam Kelchner. This report identifies members who potentially have duplicate therapy on a DPP-4/GLP-1 combination. Calls are made to the prescribers to discuss the lack of clinical evidence of this combination and/or duplicate therapy. Recommendations are made to discontinue one agent (ex. the DPP-4 if member on both a GLP-1 and DPP-4).
    - For 2023 we have resolved **0 cases** of therapeutic duplication.
- Cystic Fibrosis Adherence Report
  - We get this report **monthly** for **all LOBs** from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.
    - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence with the member
    - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
    - And for all members we send a letter discussing the importance of medication adherence
    - For CHBQ for 2023, we sent **0 members** an adherence letter
      - Letters are only sent to members every 6 months
      - There were **0 members** who saw a non-GHS pulmonologist and a letter was sent to that pulmonologist
      - There were **0 members** who saw GHS pulmonologists and were sent to the CF coordinators for follow up
- Duplicate Anticoagulant Report

    - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
        - For CHBQ in 2023, we have reviewed **0 members** and have made interventions for **0 members**
- Duplicate Specialty Therapy
    - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Smith. These members are identified and written up and sent to a medical director if follow up is needed.
        - For CHBQ for 2023, **0 members** were referred to Dr. Yarczower for additional follow-up.
- Duplicate Buprenorphine Therapy
    - We get this report **quarterly** with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows and Dr. Hossler for further outreach.
        - For CHBQ for 2023, we have reviewed **0 members** and **0 members** were referred to MDs
- Suboxone with an Opioid Report
    - We get this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each member that flags on the report. These members are being discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both MDs look into whether it is appropriate to end the opioid authorizations still in place or if further intervention is required.
        - For CHBQ for 2023, we have reviewed **0 new members**, and **0 members** were referred to MDs
- Ending Opioid Authorizations
    - We are working on identifying members who have active opioid authorizations in place but have since started Buprenorphine therapy. The letter is sent to the members notifying them the opioid authorization has been ended due to the start of buprenorphine therapy.
        - For CHBQ for 2023, we sent **0 members** a letter notifying them of the end of their opioid authorization(s).
- Severity Report
    - This is a **monthly** report for **all LOBs** on members who have filled a medication that has a level one interaction with another medication they have a claim for
        - For CHBQ for 2023, letters have been sent to MI attributed providers of **3 CHIP members**
- FWA Reports
    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For CHBQ for 2023, we have reviewed **11** cases and corrected claims, resulting in a potential **cost savings/avoidance of $1,510.01**
- TNF and Oral Oncology Agent Report
    - We get this report monthly for the Commercial/Exchange, TPA, and CHIP LOBs from Adam Kelchner.

    - This report was generated in response to removing the renewal prior authorization requirement for these agents.
    - This report identifies members who are on a TNF or Oral Oncology agent and may not have been seen by their applicable specialist in the last 15 months.
    - We research these members and reach out to the offices/members as necessary to ensure the member has been seen within the last 15 months, an appointment has been scheduled or will be scheduled with the member to ensure the member continues to be able to receive their medication.
    - For 2023:
        - For CHBQ
            - Members Reviewed: **2**
            - Outreaches Made: **0**
            - Letters Sent: **0**
            - Negative Overrides Entered: **0**
- Tobacco Cessation Program
    - We get this report **monthly** to identify members on prolonged tobacco cessation treatment. We send a letter and resource pamphlet to provide additional behavioral health support through Geisinger Health and Wellness.
        - For CHBQ for 2023, we have not sent any letters
- STENT Adherence Report
    - We get this report **monthly** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
    - For CHBQ for 2023, we have sent letters encouraging adherence to:
        - Members for Antiplatelet:
            - CHBQ: **0**
        - Members for Beta-blocker:
            - CHBQ: **0**
        - Members for Statin:
            - CHBQ: **0**
        - *member may flag for more than one measure and are included in the count for each measure
- Antipsychotic with Opioid Report
    - We get this report **quarterly** to identify **CHIP** members with an overlap of 8 or more days between an opioid and antipsychotic medication.
    - We send a letter with claims data to both the opioid prescriber and the antipsychotic prescriber to encourage collaboration in medication management.
        - For CHBQ for 2023, we sent **0 letters** to **opioid and antipsychotic prescribers**
- Duplicate Antipsychotics
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - For CHBQ in 2023, we have sent letters to **4 providers**
- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR)
    - Jesse Barsh runs this proactive HEDIS report **monthly,** and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
        - For CHBQ for 2023, we sent **3 letters** to members
- Asthma Medication Ratio (AMR) Member Calls

- Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. we send CHIP members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication to the Respiratory Therapists for direct telephonic outreach.
    - For CHBQ for 2023, we have referred **10 members** to the Respiratory Therapists for outreach.
    - For CHBQ for 2023, our pharmacy technician and the STAR reps have outreached to **8 members** and reached **7 members**
- Antidepressant Medication Management (AMM)
    - Jesse Barsh runs this proactive HEDIS report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
        - For CHBQ for 2023, we sent **0 letters** to members in the **Effective Acute Phase**, and **1 letter** to members in the **Effective Continuation Phase**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
        - For CHBQ for 2023, we have sent **0 letters** to members
- Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ for 2023, we have sent **0 letters** to providers
        - For CHBQ for 2023, we have sent **0 letters** to members
- Statin Therapy for Patients with Diabetes (SPD)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ for 2023, we have sent **0 letters** to providers
        - For CHBQ for 2023, we have sent **0 letters** to members
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)
    - This is a **monthly** report to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For CHBQ for 2023, we have sent **0 letters** to members

Fliers/Letters

- Chip DUR/FWA Program internal Fliers
    - Last updated 6/2023 next update 11/2023
- Current Provider Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Duplicate Antipsychotic medication
        - Severity Report
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - SUPD/SPD Provider Letter
        - HEDIS: Asthma Medication Ratio (AMR)
- Current Member Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Ending Opioid Authorizations

- Tobacco Cessation Letter
- STENT Adherence Report
- HEDIS: Asthma Medication Ratio (AMR)
- HEDIS: Antidepressant Medication Management (AMM)
- HEDIS: Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
- HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
- HEDIS: Statin Therapy for Patients with Diabetes (SPD)

Discussion: No comments or questions.

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

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

Meeting adjourned at 3:40 pm.

The next bi-monthly scheduled meeting will be held on March 19th, 2024 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.