P&T Committee Meeting Minutes
Commercial, Exchange, CHIP
November 19th, 2024

Present (via Teams):	**Absent:**
Bret Yarczower, MD, MBA – Chair	Alyssa Cilia, RPh
Amir Antonious, Pharm.D.	Michael Evans, RPh
Leslie Astleford, Pharm.D.	Nichole Hossler, MD
Emily Bednarz, Pharm.D.	Jason Howay, Pharm.D.
Kristen Bender, Pharm.D.	Mark Mowery, Pharm.D.
Jeremy Bennett, MD	Andrei Nemoianu, MD
Kim Castelnovo, RPh	Jonas Pearson, RPh
Kimberly Clark, Pharm.D.	Angela Scarantino
Bhargavi Degapudi, MD	William Seavey, Pharm.D.
Keri Donaldson, MD, MSCE	
Michael Dubartell, MD	
Kelly Faust, Pharm.D.	
Tricia Heitzman, Pharm.D.	
Keith Hunsicker, Pharm.D.	
Kelli Hunsicker, Pharm.D.	
Emily Jacobson, Pharm.D.	
Dennis Janozczyk, Pharm.D.	
Alexandra Kempf-Malys, MSW, BSc	
Kerry Ann Kilkenny, MD	
Philip Krebs, R.EEG T	
Briana LeBeau, Pharm.D.	
Ted Marines, Pharm.D.	
Lisa Mazonkey, RPh	
Tyreese McCrea, Pharm.D.	
Perry Meadows, MD	
Jamie Miller, RPh	
Austin Paisley, Pharm.D.	
Lauren Pheasant, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Sartori, Pharm.D.	
Kristen Scheib, Pharm.D.	
Michael Shepherd, MD	
Kirsten Smith, Pharm.D.	
Aubrielle Smith-Masri, Pharm.D.	
Michael Spishock, RPh	
Todd Sponenberg, Pharm.D.	
Jill Stone, Pharm.D.	
Luke Sullivan, DO	
Kevin Szczecina, RPh	
Amanda Taylor, MD	
Ariana Wendoloski, Pharm.D.	
Brandon Whiteash, Pharm.D.	
Margaret Whiteash, Pharm.D.	
Jeremy Garris, Pharm.D. (non-voting participant)	
Nicole Hawk, Pharmacy Student	
Edward Liu, Medical Student	
Adrienne Maximin, Pharmacy Student	

Call to Order:
Dr. Bret Yarczower called the meeting to order at 1:02 p.m., Tuesday, November 19, 2024.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the August 2024 e-vote and Sept 17, 2024 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

ENTRESTO SPRINKLE (sacubitril and valsartan)

Review: Entresto Sprinkle is a combination of sacubitril, a neprilysin inhibitor, and valsartan, an angiotensin II receptor blocker, and is indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure AND for the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older.

Entresto Sprinkle is available as film-coated oral pellets contained in a hard capsule in 6mg-6mg and 15mg-16mg strengths. Entresto Sprinkle is an alternative to Entresto tablets in patients that are unable to swallow tablets or in pediatric patients requiring lower doses than available in Entresto tablets. Entresto tablets can also be prepared as a liquid (oral) suspension in patients unable to swallow or in patients requiring a dose not available in the prescribed strength. Entresto Sprinkle contains oral pellets inside of a capsule that must be opened and sprinkled onto 1-2 teaspoons of soft food and taken right away. The complete contents of each capsule must be taken fully to achieve the dose.

The recommended starting dose of Entresto tablets in adult patients is 49/51 mg by mouth twice daily, doubling the dose after 2 to 4 weeks to the target maintenance dose of 97/103 mg twice daily as tolerated.

Approval of Entresto Sprinkle is based upon previous clinical trials of Entresto. No new clinical trials were completed for Entresto Sprinkle. Entresto (tablet) was evaluated in pediatric patients in the PANORAMA-HF trial. This multinational, randomized, double-blind trial compared the efficacy of Entresto and enalapril in patients 1 month to less than 18 years old with systemic left ventricular systolic dysfunction (LVEF < 45% or fractional shortening < 22.5%). The efficacy of Entresto was not established in patients less than 1 year old. The estimated least squares mean percent reduction at week 52 from baseline in NT-proBNP was 65% and 62% in the Entresto and enalapril groups, respectively. The between-group difference was not nominally statistically significant; however, the reductions for both Entresto and enalapril were larger than seen in adults. The effect on NT-proBNP was the basis used to infer improved cardiovascular outcomes in pediatric patients because Entresto improved outcomes and reduced NT-proBNP in adult patients (PARADIGM-HF trial showed Entresto was superior to enalapril in reducing risk cardiovascular death or hospitalization for heart failure).

Entresto, including all drugs that act on the renin-angiotensin system, can cause fetal harm when administered to a pregnant woman; consider alternative drug treatment during pregnancy and discontinue Entresto unless the drug is considered lifesaving to the mother then risk vs. benefit should be discussed. Breastfeeding is not recommended during treatment with Entresto. Safety and effectiveness have been established in pediatric heart failure patients aged 1 year to less than 18 years; however, safety and efficacy are not established in pediatric patients less than 1 year. No overall differences in safety or effectiveness have been observed in patients 65 years and older. No dose adjustment is required in patients with mild hepatic impairment; half of the starting dose is recommended in both adult and pediatric patients with moderate hepatic impairment; and the use of Entresto is not recommended in patients with severe hepatic impairment. No dose adjustment is required in patients with mild to moderate renal impairment; half the starting dose is recommended in both adult and pediatric patients with severe renal impairment.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (33 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (35 approved, 0 rejected).

Outcome: Entresto Sprinkle is a pharmacy benefit and will not be added to the Commercial, Marketplace, or GHP Kids formularies. The following prior authorization criteria should apply:

- Medical record documentation of age 1 years or older **AND**
- Medical record documentation that Entresto Sprinkle is being used for the treatment of heart failure **AND**
- Medical record documentation of weight appropriate dosing (as outlined in the policy) **AND**
- Medical record documentation of 1 of the following:
    - Weight less than 50 kg **OR**
    - Weight greater than 50 kg **AND** 1 of the following:
        - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Entresto tablets **OR**
        - Medical record documentation that member is unable to swallow tablets.

NOTE: Entresto oral suspension can be substituted at the recommended tablet dose in patients that are unable to swallow tablets. Entresto oral suspension is NOT commercially available and needs to be compounded in a pharmacy.

QUANTITY LIMIT: 8 capsules per day

AUTHORIZATION DURATION: 1 year. Subsequent approvals will be for an additional 12 months and will require:

- Medical record documentation of weight appropriate dosing **AND**
- Medical record documentation of 1 of the following:
    - Weight less than 50 kg **OR**
    - Weight greater than 50 kg **AND** 1 of the following:
        - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Entresto tablets **OR**
        - Medical record documentation that member is unable to swallow tablets

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.

CAPVAXIVE (pneumococcal 21-valent conjugate vaccine)

Review: Capvaxive was approved in June of 2024 and is a Pneumococcal 21-valent conjugate vaccine indicated for the prevention of invasive disease cause by streptococcus pneumoniae serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B in individuals 18 years of age and older. It is also indicated for prevention of pneumonia caused by S. pneumoniae serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B in individuals 18 years of age and older. The indication for the prevention of pneumonia by *S. pneumoniae* serotypes is approved under accelerated approval based on immune responses as measured by opsonophagocytic activity. Opsonophagocytic activity is a measure of antibody functional activity in vitro by how well they kill live pneumococci. Capvaxive induces

opsonophagocytic killing of *S. pneumoniae* against 22 *S. pneumoniae* serotypes. Patients who are immunocompromised may have reduced response to Capvaxive.

Dosing of Capvaxive is administered as a single 0.5 mL dose. Capvaxive is a colorless, clear to opalescent solution which is administered intramuscularly. It should be kept refrigerated until use and away from light.

In a double blind study, individuals 18 years of age and older who had not previously received a pneumococcal vaccine were enrolled and randomized to receive a single dose of Capvaxive or Prevnar 20. Table below summarizes the 21 serotype-specific OPA geometric mean antibody titers (GMTs) at 30 days post vaccinations. This study demonstrated there was a noninferiority with Capvaxive compared to Prevnar 20. It also showed shared serotype polysaccharides and induces statistically significantly greater OPA GMTs compared to Prevnar 20 for 10 of 11 serotype polysaccharides unique to Capvaxive.

Also in this study, as shown below in table 5, there was a proportion of individuals who achieved a >4-fold rise from pre-vaccination to 1-month postvaccination for OPA responses. 10 of 11 serotype polysaccharides unique to Capvaxive induced statistically significance compared to Prevnar 20. Serotype 15C did not meet statistical significance. However, 64.7% of individuals 50 years of age and over, who received Capvaxive, showed a >4-fold rise in OPA titers for serotype 15B, which met prespecified success criterion.

This study compared individuals aged 18-49 to individuals aged 50-64, measuring OPA response induced by Capvaxive. Each of 22 S. pneumoniae serotypes met criteria for immunobridging. This is shown in table below. There was a cross reactive OPA GMT for serotype 15B that also showed similarities between the two groups as well (ratio 2.02 [95% CI: 1.57, 2.60]).

This was a descriptive Phase 3 study, who enrolled individuals over 50 who were previously vaccinated with other pneumococcal vaccines at least one year prior to study entry. Participants were enrolled as described below.

- Participants in cohort 1 were randomized to receive Capvaxive (n=231) or Vaxneuvance [PCV-15] (n=119)
- Participants in cohort 2 were randomized to receive Capvaxive (n=176) or Pneumovax 23 (n=85)
- Participants in cohort 3 were allocated to receive Capvaxive (n=106).

In each of the 3 cohorts serotype-specific OPA GMTs and proportion of individuals with >4 fold rise in OPA responses from baseline to 1-month postvaccination were assessed.

- Cohort 1; Capvaxive elicited OPA responses that were comparable to Vaxneuvance for 6 common serotypes and higher for 15 unique serotypes and serotype 15B.
- Cohort 2; Capvaxive elicited OPA responses to Pneumovax 23 for the 12 common serotypes and serotype 15B, and higher for the 9 unique serotypes

OPA responses to Capvaxive were similar across 3 cohorts of participants who previously received one or more pneumococcal vaccines.

This was a double-blind study where 1,080 individuals 50 years of age and older with or without prior history of prior pneumococcal vaccination were randomized in a 1:1 ratio. One group received Capvaxive and QIV flu vaccine and the second group received a QIV flu vaccine and placebo. Antibody responses were assessed 1-month postvaccination. The two groups showed non-inferiority for 20 of 21 serotypes with the only serotype that was not met was 23B. Also 3 out of 4 serotypes for influenza were also shown non-inferior between the two groups as well.

History of anaphylactic or severe systemic reactions to components of Capvaxive or diphtheria toxoid. The safety of Capvaxive was assessed in four clinical studies conducted across America, Europe, and Asia Pacific, which included individuals ranging from 18-97 years old. In all 4 studies, 4,556 individuals received Capvaxive, and 2,021 individuals received an active comparator vaccine. Adverse events were comparable between the two groups that included pain at injection site, swelling, fatigue, headache,

myalgia, and pyrexia. Safety with concomitant influenza vaccine [Fluzone Quadrivalent, (QIV)] was also measured and found similar systemic and local adverse reactions between group 1 (Capvaxive + QIV followed by placebo 30 days later) vs. group 2 (placebo followed by Capvaxive 30 days later).

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 serotypes that were not covered by this vaccine and the importance of the gaps in coverage. Ted Marines, Pharm.D., stated the CDC did not comment on the serotypes specifically but it seems this will be an add-on pneumococcal vaccine versus a replacement. The committee unanimously voted to accept the recommendations as presented. None were opposed (34 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (37 approved, 0 rejected).

Outcome: Capvaxive will be medical and pharmacy benefit for members 19 years of age and older. It should be added to the vaccine tier, covered as a preventative vaccine for 0$ copay without prior authorization. The following quantity and age limits should apply.

Quantity Limits: 0.5 mL per lifetime

Age Limit: 19 years and older

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

VORANIGO (vorasidenib)

Review: Voranigo is indicated for the treatment of adult and pediatric patients 12 years and older with Grade 2 astrocytoma or oligodendroglioma with a susceptible IDH1 or IDH2 mutation following surgery including biopsy, sub-total resection, or gross total resection.

The recommended dosage of Voranigo in adult patients is 40 mg orally once daily until disease progression or unacceptable toxicity. The recommended dosage of Voranigo in pediatric patients 12 years and older is based on body weight. For patients weighing greater than or equal to 40 kg the recommended dosage is 40 mg once daily. For patients weighing less than 40 kg the recommended dosage is 20 mg once daily. Treatment for pediatric patients is also continued until disease progression or unacceptable toxicity. Voranigo is supplied as 10 mg and 40 mg tablets.

The efficacy of Voranigo was evaluated in the INDIGO trial, a randomized, double-blind, placebo-controlled study of 221 patients with IDH1- or IDH2-mutant Grade 2 astrocytoma and oligodendroglioma with prior surgery, including biopsy, sub-total resection, or gross total resection. Included patients had measurable, non-enhancing disease; patients with centrally confirmed minimal, non-nodular, non-measurable enhancement were eligible. Patients who received prior anti-cancer treatment, including chemotherapy or radiation therapy were excluded. Patients were randomized to receive Voranigo 40 mg orally once daily or placebo until disease progression or unacceptable toxicity. IDH1 or IDH2 mutation status was prospectively determined by Life Technologies Corporation Oncomine Dx Target Test.

The major efficacy outcome was progression-free survival (PFS) as evaluated by a blinded-independent review committee (BIRC) per modified Response Assessment in Neuro-Oncology for Low Grade Glioma (RANO-LGG) criteria.

The major efficacy analyses are supported by a prospectively defined key secondary outcome measure time to next intervention (time from randomization to the initiation of first subsequent anticancer therapy

or death due to any cause). The median time to next intervention was not reached for patients in the Voranigo arm and 17.8 months for patients in the placebo arm (HR=0.26; 95% CI: [0.15, 0.43], p <0.0001).

There are no black box warnings for Voranigo. Warnings for Voranigo include hepatotoxicity including elevated hepatic transaminases which can lead to hepatic failure, hepatic necrosis, and autoimmune hepatitis; and risk of embryo-fetal toxicity. In the INDIGO trial, serious adverse reactions occurred in 7% of patients who received Voranigo. The most common adverse reactions occurring in ≥ 2% of patients was seizure (3%). Permanent discontinuation and dosage reductions of Voranigo due to adverse effects occurred in 3.6% and 11% of patients respectively, most commonly due to increased ALT. Dosage interruptions due to adverse reaction occurred in 30% of patients, most commonly due to increased ALT and AST and COVID-19. The most common adverse reactions were fatigue, COVID-19, musculoskeletal pain, diarrhea, and seizure. The most common Grade 3 or 4 laboratory abnormalities were increased ALT, AST, and GGT, and decreased neutrophils.

The safety and efficacy of Voranigo have been established in pediatric patients aged 12 years and older for the treatment of Grade 2 IDH1- or IDH2-mutant astrocytoma or oligodendroglioma. Use in this aged group is supported by evidence from an adequate and well-controlled study of Voranigo in adult and pediatric patients with additional population pharmacokinetic data demonstrating that age had no clinically meaningful effect on the pharmacokinetics of Voranigo. In addition, the course of IDH1- or IDH2-mutant astrocytoma or oligodendroglioma is sufficiently similar between adults and pediatric patients to allow extrapolation of pharmacokinetic data. The exposure of Voranigo in pediatric patients 12 years and older is predicted to be within range of exposure observed in adults at recommended dosages. The safety and efficacy of Voranigo have not been established in pediatric patients less than 12 years of age.

Of the 167 patients randomized to receive Voranigo 40 mg in the INDIGO trial, 1.2% (2 patients) were 65 years and older. Clinical studies did not include sufficient numbers of patients aged ≥ 65 years to determine if they respond differently from younger patients.

No dosage adjustment is needed for patients with creatinine clearance (CLcr) > 40 mL/min. The pharmacokinetics and efficacy of Voranigo has not been studied in patients with CLcr ≤ 40 mL/min or renal impairment requiring dialysis have not been studied. No dosage adjustment is recommended for patients with mild or moderate (Child-Pugh Class A or B) hepatic impairment. The pharmacokinetics and safety of Voranigo in patients with severe hepatic impairment (Child-Pugh Class C) have not been studied.

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 this a stand-alone treatment or if it would be used in combination with other therapies. Kim Reichard, Pharm.D., stated this would be used as stand-alone and has not been studied in combination. The committee unanimously voted to accept the recommendations as presented. None were opposed (35 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (37 approved, 0 rejected).

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

- Medical record documentation that Voranigo is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 12 years of age **AND**
- Medical record documentation of Grade 2 astrocytoma or oligodendroglioma with a susceptible isocitrate dehydrogenase-1 (IDH1) or isocitrate dehydrogenase-2 (IDH2) mutation following surgery, including biopsy, sub-total resection, or gross total resection

AUTHORIZATION DURATION: Voranigo is configured as a prior authorization for new starts only. Voranigo 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:

- **10 mg Tablets:** 2 tablets per day, 30 day supply per fill
- **40 mg Tablets:** 1 tablet per day, 30 day supply per fill

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.

SOFDRA (sofpironium)

Review: Sofdra (Sofpironium) is FDA approved for the treatment of primary axillary hyperhidrosis in patients 9 years or older. Sofdra (Sofpironium) is an anticholinergic product that works by inhibiting the acetylcholine receptors in peripheral tissue sweat glands thus decreasing the amount of sweat produced in the axilla. Current initial treatments for primary focal axillary hyperhidrosis as outlined by the International Hyperhidrosis Society (IHS) include topical antiperspirant therapy (Aluminum and Zirconium Salts) or Glycopyrronium cloths (Qbrexza). If results are not satisfactory with initial treatments, other treatments can include Botulinum Toxin A injections, microwave thermolysis or oral systemic therapies such as anticholinergics, propranolol, clonidine, and diltiazem. Currently, the IHS guidelines have not been updated to include, Sofdra (Sofpironium), but based on its mechanism of action and current recommended products by the IHS, Sofdra (Sofpironium) can be an alternative or optional product to Glycopyrronium cloths (Qbrexza).

Sofdra (Sofpironium) is supplied as a 12.45% topical gel that is to be applied as 1 pump of gel to each axilla at bedtime using the provided applicator. The underarms should be cleaned and dry before applying and, also, the gel should not be spread with hands to avoid accidental application to other skin areas. After application, the gel should be left to dry on the axillary skin for 5 mins. Washing the area for 8 hours after gel application should be avoided as well as deodorant and shaving within 8 hours of use. It should not be applied to broken skin or used within 30 minutes of exercise of showering.

The efficacy of Sofdra was determined in two randomized, vehicle-controlled multicenter trials, CARDIGAN 1 (NCT03836287) and CARDIGAN 2 (NCT03948646). Participants were randomized to receive either SOFDRA or vehicle applied once daily at bedtime to each axilla. A total of 701 participants across both studies age 10 years and older with primary axillary hyperhidrosis were included. Participants were to have symptoms of axillary hyperhidrosis for at least 6 months' duration, produce at least a Gravimetric Sweat production (GSP) of 50 mg of sweat in each axilla (underarm) with a combined total of at least 150 mg over a 5-minute period, and have a Hyperhidrosis Disease Severity Measure-Axillary, 7-item scale score (HDSM-Ax7) ≥3. The Hyperhidrosis Disease Severity Measure-Axillary, 7-item scale score measures patient reported disease severity using 7 questions with a 5-point response ranging from 0-4 where 0 is better and 4 is worst. Total scores were calculated using the average of all scores which created a final severity score at baseline. Primary endpoints in the study included a >= 2-point improvement on the Hyperhidrosis Disease Severity Measure-Axillary, 7-item scale, and a change in GSP from baseline to end of the study. The mean HDSMAx-7 scale score at Baseline was 3.5 in CARDIGAN 1, and 3.6 in CARDIGAN 2. The median (GSP) over 5 minutes at Baseline was 214.1 mg in the SOFDRA arm and 228.6 mg in the vehicle arm in CARDIGAN 1, and 207.7 mg in the SOFDRA arm and 231.1 mg in the vehicle arm in CARDIGAN 2.Contraindications can include any medical condition that can be exacerbated by anticholinergic therapy i.e., glaucoma, paralytic ileus, unstable cardiovascular status in

acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis, Sjögren's syndrome.

Warnings/Precautions to consider are using with caution in patients with a history of urinary retention, monitoring for overall lack of body sweating and using caution when operating an automobile or heavy machinery. Adverse reactions for Sofdra (Sofpironium) include, dry mouth, blurry vision, mydriasis, and urinary retention occurred in > 2% of study population. Local reactions such as pain, erythema, dermatitis, pruritic, irritation and exfoliation also occurred in > 2% of study 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 (38 approved, 0 rejected).

Financial Discussion: Dr. Bret Yarczower asked for the place in therapy compared to Botox. Tyreese McCrea, Pharm.D., stated that patients should fail all topical therapies first before resorting to Botox. The committee unanimously voted to accept the recommendations as presented. None were opposed (37 approved, 0 rejected).

Outcome: Sofdra (Sofpironium) is a pharmacy benefit and will be added to the Commercial/Exchange/CHIP formularies and will require a prior authorization. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 9 years **AND**
- Medical record documentation of a diagnosis of primary axillary hyperhidrosis **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication
- to at least 2 alternatives which must include prescription antiperspirant (aluminum chloride hexahydrate 6.25% [Xerac AC], 20% [Drysol]) and Qbrexza

QUANTITY LIMIT: 1.34 ml per day (40.2 ml per 30 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.

IQIRVO (elafibranor)

Review: Iqirvo is the first peroxisome proliferator-activated receptor (PPAR) agonist indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have had an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. PBC is a rare liver disease characterized by destruction and inflammation of the small bile ducts. It is a chronic and progressive disease varying among patients. More recently patients have been diagnosed with the disease in earlier stages and have responded well to treatment, which has led to a decrease in liver transplantation caused by the disease. If left untreated, patients can progress to liver cirrhosis, end-stage liver disease resulting in the need for a liver transplant. The prevalence of the disease is exceedingly rare and there are about 131,000 individuals with PBC in the United States affecting mainly women aged 45-65 years old. The goal of treatment for PBC is to prevent disease progression and manage symptoms related to chronic cholestasis. The most common symptoms of the disease are pruritus and fatigue. Iqirvo works by inhibiting bile acid synthesis through activation of PPAR-alpha and delta that subsequently downregulates fibroblast growth factor A21. This growth factor is a key enzyme in the synthesis of bile acids from cholesterol.

Iqirvo is supplied as an 80mg tablet taken once daily with or without food. Currently, on the market there is one other FDA approved second-line treatment option, Ocaliva (obeticholic acid) also abbreviated as OCA. Ocaliva received accelerated approval from the FDA in 2016 for the treatment of adult patients with PBC without cirrhosis or with compensated cirrhosis who do not have evidence of portal hypertension, either in combination with UDCA for patients with an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. Iqirvo has differentiated itself from Ocaliva in that it may not worsen pruritus and dyslipidemia, which are both side effects of Ocaliva. Iqirvo also does not have any current safety concerns in compensated cirrhosis, whereas Ocaliva has a boxed warning for hepatic decompensations and failure in patients with PBC and cirrhosis. Careful monitoring on Ocaliva is required in any patient with cirrhosis. The drugs have not been studied head-to-head at this time to compare efficacy, but the treatments are similarly effective based upon reduction of ALP.

The Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases recommends UDCA at a dose of 13 to 15 mg/kg/day for first-line therapy. For second-line treatment the guidelines also mention that OCA was approved by the Food and Drug Administration in May 2016 to be used in combination with UDCA in patients with PBC who have inadequate response to at least 1 year of treatment with UDCA, or as monotherapy for those patients who are intolerant to UDCA. Patients who are inadequate responders to UDCA should be considered for treatment with OCA, starting at 5 mg/day. The guidelines were updated in 2021 with a few additional recommendations stating fibrates can be considered as off-label alternatives for patients with inadequate response to UDCA and the guidelines also added that they discouraged use of OCA patients with decompensated liver and the medication is contraindicated in patients with advanced cirrhosis and even those without advanced cirrhosis careful monitoring should be completed. Iqirvo was not on the market at the time of the current guideline publications.

The safety and efficacy of Iqirvo was studied in the ELATIVE Trial. This was a Phase 3, multinational, randomized, double-blind, placebo-controlled study to evaluate the safety and efficacy of Iqirvo 80mg in patients with PBC with inadequate response or intolerance to UDCA. This trial included 161 patients who underwent randomization in a 2:1 fashion (108 patients received Iqirvo and 53 patients received placebo). The key inclusion criteria for the trial were patients 18-75 years old with PBC who had an inadequate response to or unacceptable side effects with UDCA. Patients had to have an alkaline phosphatase level (APL) of at least 1.67 times the upper limit of the normal range (ULN) (174 U per liter for women and 215 U per liter for men) and a total bilirubin level (TBL) of no more than 2 times the ULN (41 μmol per liter). The key exclusions to the trial were any patients with autoimmune hepatitis or primary biliary cirrhosis–autoimmune hepatitis overlap and any evidence of clinically significant hepatic decompensation. For patients taking OCA prior to the trial, it had to be discontinued 3 months prior to screening.

The primary endpoint was the biochemical response defined as: (ALP <1.67 × ULN, TB ≤ULN, and ALP decrease ≥15% from baseline) at week 52. The key secondary endpoints were normalization of the ALP at Week 52, change in pruritus intensity from baseline through Week 52 and through Week 24 as measured on the Worst Itch Number Rating Scale (WI-NRS). The results showed at week 52, a biochemical response was observed in 51% of patients in the Iqirvo group compared to 4% in the placebo group (95% CI], 32 to 57; P<0.001). It was also noted a response to Iqirvo appeared to occur within 4 weeks after initiation of treatment and this response was maintained through 52 weeks. The results for the secondary endpoints showed normalization of the alkaline phosphatase level at week 52 occurred in 15% of patients in the Iqirvo group and in 0% of patients in the placebo group, (95% CI, 6 to 23; P=0.002). In patients with moderate-to-severe pruritus, the least-squares mean change in the WI-NRS score did not differ significantly between the Iqirvo group and the placebo group from baseline through week 52 (−1.93 vs. −1.15; difference, −0.78; 95% CI, −1.99 to 0.42; P=0.20) and from baseline through week 24 (−1.60 vs. −1.26; difference, −0.34; 95% CI, −1.49 to 0.80).

There are no contraindications or black box warning associated with Iqirvo. There is a warning for myalgias, myopathy, and rhabdomyolysis. In the clinical trial, one patient experience rhabdomyolysis that resulted in an acute kidney injury. Myalgia or myopathy, with or without CPK elevations, occurred in patients treated with Iqirvo alone or treated concomitantly with a stable dose of a statin also. Another warning is for fractures due to 6% of patients treated with Iqirvo in the clinical trial experienced this. Drug

induced liver injury also did occur in one patient who took the 80mg prescribed dose and this was added to the warnings as well. Hypersensitivity reactions warning was added to the labeling, but only occurred in patients who took more than the recommended dosage of the medication. The last warning is for any patient with a complete biliary obstruction, or a suspected obstruction then the medication should be stopped. The most common adverse events patients experienced compared to placebo were pruritus (20%), weight gain (19%), diarrhea (11%), abdominal pain (11%), nausea (11%), vomiting (11%), UTI (11%), fatigue (9%), and headache (8%). The most common side effect that led to discontinuation of the medication is the clinical trial was increased creatine phosphokinase (CPK) (4%).

Iqirvo may cause fetal harm during pregnancy based upon animal data. It is recommended that women of reproductive potential have pregnancy testing prior to initiating therapy. Females of reproductive potential are advised to use non hormonal contraception or a barrier method and hormonal contraceptive during treatment and for 3 weeks after the last dose of the medication. There is no data available on the presence of Iqirvo or its metabolites in human or animal milk, or on effects of the drug on the breastfed infant or the effects on milk production. The safety and effectiveness of Iqirvo have not been established in pediatric patients. 23% of patients in the clinical trial treated with Iqirvo were 65 years and older and during the trial experienced no differences in effectiveness. However, because of limited clinical experience with Iqirvo in patients older than 75 years old, closer monitoring of adverse events in patients older than 75 years is recommended. There are no renal dose adjustments needed. The safety and efficacy of Iqirvo in patients with decompensated cirrhosis have not been established and it is not recommended in patients who have or develop decompensated cirrhosis. It is recommended to monitor patients with cirrhosis for evidence of decompensation (e.g., ascites, variceal bleeding, hepatic encephalopathy) and recommended to consider discontinuing Iqirvo if the patient progresses to moderate or 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 (33 approved, 0 rejected).

Financial Discussion: Dr. Bret Yarczower asked how many members we had with this. Lauren Pheasant, Pharm.D., stated there were 6 overall members on Ocaliva that would indicate they share the same disease state and no members on Iqirvo. The committee unanimously voted to accept the recommendations as presented. None were opposed (33 approved, 0 rejected).

Outcome: Iqirvo is a pharmacy benefit and will not be added to the Commercial, Exchange, and GHP Kids Formulary. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of primary biliary cholangitis (primary biliary cirrhosis) **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Iqirvo is prescribed by a board-certified gastroenterologist, hepatologist, or liver transplant specialist **AND**
- Medical record documentation that Iqirvo is not being used in members with complete biliary obstruction **AND**
- Medical record documentation that Iqirvo is not being used in members with decompensated cirrhosis **AND**
- Medical record documentation that Iqirvo is not being used in combination with Ocaliva AND
- Medical record documentation of contraindication or intolerance to UDCA (ursodiol tablets, Urso Forte, or Reltone) **OR**
- Medical record documentation of inadequate biochemical response to an appropriate dose of UDCA (ursodiol tablets, Urso Forte, or Reltone) for at least 12 months AND that UDCA product will be continued in combination with Iqirvo

AUTHORIZATION DURATION: 12 months. Subsequent approvals will be for an additional 12 months.

The medication will no longer be covered if medial record documentation does not show:

- Medical record documentation of a positive clinical response based on biochemical response (defined as: ALP <1.67 × ULN **OR** TB ≤ULN O**R** ALP decrease ≥15% from baseline) **OR** clinical symptom improvement (ex: reduction of itch, fatigue) **AND**
- Medial record documentation that the patient does NOT have decompensated cirrhosis **OR** a complete biliary obstruction

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

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.

TEVIMBRA (tislelizumab-jsgr)

Review: Tevimbra (tislelizumab-jsgr) is a humanized immunoglobulin G4 (IgG4), monoclonal antibody, programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of adult patients with unresectable or metastatic esophageal squamous cell carcinoma (ESCC) after prior systemic chemotherapy that did not include a PD-(L)1 inhibitor. Tevimbra is designed to minimize binding to Fc-gamma receptors on macrophages, aiding the body's immune cells in detecting and fighting tumors.

Tevimbra is the third PD-1/PD-L1 approved for use in second-line ESCC in the United States, joining Keytruda and Opdivo. Current NCCN Guidelines for the treatment of second-line ESCC have been updated to include Tevimbra as a category 1 recommendation preferred regimen, aligning its place in therapy with Keytruda and Opdivo.

Tevimbra is supplied as a sterile, preservative-free, single-dose vial containing 100mg/10ml solution for intravenous use. Prior to infusion the recommended dosage should be diluted in an intravenous infusion bag containing 0.9% sodium chloride for injection to prepare an infusion with a final concentration between 2mg/ml to 5mg/ml. The recommended dose of Tevimbra is 200mg given intravenously once every 3 weeks until disease progression or unacceptable toxicity. The first infusion should be infused over 60 minutes, and subsequent infusions if tolerated may be administered over 30 minutes.

The approval of Tevimbra is based on results from the Phase 3, randomized, controlled, open-label RATIONALE 302 trial, which included 512 patients from Europe, Asia, and North America with unresectable advanced or metastatic ESCC who progressed on or after prior systemic chemotherapy. Patients were enrolled regardless of their tumor PD-L1 expression level. Eligible patients had to be ≥18 years of age with histologically confirmed ESCC and advanced or metastatic disease that progressed after first-line systemic treatment; tumor progression within 6 months after definitive chemoradiotherapy, neoadjuvant, or adjuvant therapy; ECOG performance status of 0 or 1, ≥1 measurable/evaluable lesion by RECIST v1.1, and adequate hematologic, hepatic, renal, and coagulation function. The trial excluded patients who received a prior immune checkpoint inhibitor, had brain or leptomeningeal metastases that were symptomatic or required treatment, active autoimmune disease, a medical condition requiring systemic corticosteroids or immunosuppressants, or apparent tumor invasion of organs adjacent to the esophageal tumor. The major efficacy outcome measure was overall survival (OS) in the Intent-to-Treat (ITT) population. Additional efficacy outcome measures were investigator-assessed progression-free survival (PFS), overall response rate (ORR), and duration of response (DOR) per RECIST v1.1

The study met its primary endpoint of overall survival (OS) in the intention-to-treat population, with a statistically significant and clinically meaningful survival benefit for Tevimbra compared with chemotherapy. At final analysis, conducted after 410 death events occurred, OS was significantly longer with Tevimbra versus chemotherapy in all patients (median, 8.6 versus 6.3 months) and in patients with tumor area positivity (TAP) score ≥10% (median, 10.3 months versus 6.8 months).Survival benefit was consistently observed across all predefined subgroups, including those defined by baseline TAP score,

region, and race. Treatment with Tevimbra was associated with higher objective response rate (ORR) (20.3% versus 9.8%) and a more durable antitumor response (median, 7.1 months versus. 4.0 months) versus chemotherapy in all patients.

There are no black box warnings for Tevimbra. Warnings and precautions include Immune-mediated Adverse Reactions, Infusion-related reactions, Complications of Allogenic Hematopoietic Stem Cell Transplantation, and Embryo-Fetal toxicity. Side effects among PD-1 inhibitors tend to be similar, with the most common adverse effects including fatigue, fever/chills, infusion reactions, and hypothyroidism. In RATIONALE-302, the most common (≥20%) adverse reactions for Tevimbra, including laboratory abnormalities, were increased glucose, decreased hemoglobin, decreased lymphocytes, decreased sodium, decreased albumin, increased alkaline phosphatase, anemia, fatigue, increased aspartate aminotransferase (AST), musculoskeletal pain, decreased weight, increased alanine aminotransferase (ALT), and cough.

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 (34 approved, 0 rejected).

Financial Discussion: Dr. Yarczower asked how far along we were with medical rebates and if there was any advantage in preferring any of the agents in this class. Keith Hunsicker, Pharm.D., responded that there are not any rebates in this class and the agents are priced similarly at this time. The committee unanimously voted to accept the recommendations as presented. None were opposed (35 approved, 0 rejected).

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

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Tevimbra is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of a diagnosis of unresectable or metastatic esophageal squamous cell carcinoma (ESCC) **AND**
- Medical record documentation of disease progression after one or more prior lines of systemic chemotherapy that did not include a PD-(L) 1 inhibitor

AUTHORIZATION DURATION: Initial approval will be for **6 months** or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional **12 months** or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

GPI LEVEL: GPI-12

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.

OHTUVAYRE (ensifentrine)

Review: Ohtuvayre or ensifentrine is an inhalation suspension indicated for the maintenance treatment of chronic obstructive pulmonary disease (COPD) in adult patients. It is a selective phosphodiesterase

(PDE)3 and PDE4 inhibitor. PDE3 hydrolyzes the second-messenger molecule cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP). PDE4 hydrolyzes cAMP only. Inhibitors of PDE3 and PDE4 target cAMP and cGMP concentrations expressed on airway smooth muscle, bronchial epithelial cells and inflammatory cells. The combination of PDE3 and PDE4 may have a synergistic effect resulting in enhanced effect on bronchodilation, airway inflammation, and mucociliary clearance.

The only other PDE4 inhibitor indicated for treatment of COPD is roflumilast (Daliresp). It is used to reduce the risk of COPD exacerbation in patients with severe COPD association with chronic bronchitis and history of exacerbation. Roflumilast is a once daily oral medication with no direct bronchodilator activity.

One ampule (3 mg) of inhalation suspension is administered twice a day by oral inhalation with a standard jet nebulizer and mouthpiece. The inhalation suspension is dispensed in 3 mg/2.5 mL yellow to pale yellow aqueous suspension in unit-dose low-density polyethylene ampule. The ampule is overwrapped in a sealed foil pouch and the ampule should only be removed immediately before use. Ohuvayre should be stored at room temperature, protected from direct sunlight and excessive heat.

Two 24-week Phase 3, randomized, double-blind, placebo-controlled, parallel-group clinical trials - ENHANCE-1 [NCT04535986] and ENHANCE-2 [NCT04542057] evaluated the efficacy of Ohtuvayre. The trials enrolled a total of 1553 adults with moderate to severe COPD. Inclusion criteria for both trials includes patients 40-80 years old; moderate to severe COPD; with or without background therapy. Background therapies included: long-acting beta-2 agonist (LABA) ± inhaled corticosteroid (ICS) or long-acting muscarinic antagonist (LAMA) ± ICS maintenance COPD therapy); ≥ 10 pack-year current or former smoking history; post-bronchodilator FEV1 ≥ 30 and ≤ 70% of predicted; FEV1/FVC <0.7; symptomatic (Modified Medical Research Council (mMRC) Dyspnea Scale ≥ 2) at screening. Patients were randomized 5:3 to receive 3 mg of Ohtuvayre administered by oral inhalation via standard jet nebulizer twice daily. The primary endpoint for both trials was the change from baseline in FEV1 area under the curve over 12 hours post dose at week 12. Ohtuvayre demonstrated statistically significant improvement for the primary endpoint vs placebo in both trials – ENHANCE-1, 87 mL [95% confidence interval, 55, 118]; ENHANCE-2, 94 ml [65, 124]; both P < 0.001).

A secondary endpoint of health-related quality of life was assessed using the St. George's Respiratory Questionnaire in both trials. It showed statistically significant improvement in the EHANCE-1 trial only. An exploratory analysis was done on the annual rate of moderate to severe COPD exacerbation. The rate was shown to be reduced in both trials however, ENHANCE-1 trial was not statistically significant.

Ensifentrine was well tolerated in the phase 3 ENHANCE-1 and ENHANCE 2 trials. Patients who discontinued treatment due to adverse reactions were 7.6% for the Ohtuvayre-treated patients and 8.2% for placebo-treated patients.

- Drug interactions: There are no significant drug interactions.
- Contraindications: patients with hypersensitivity to ensifentrine or any component of this product
- Warnings/Precautions: acute episodes of bronchospasms, paradoxical bronchospasms, psychiatric adverse reactions including suicidality.
- Adverse events: back pain (Ohtuvayre 1.8% vs placebo 1.0%), hypertension (Ohtuvayre 1.7% vs placebo 0.9%), urinary tract infection (Ohtuvayre 1.3% vs placebo 1.0%) and diarrhea (Ohtuvayre 1.0% vs placebo 0.7%).

Based on the existing evidence, pulmonologist Dr. Paul Simonelli, found the trial's selection criteria and primary goals to be lacking. The selection criteria did not stratify study participants based on ABE criteria per current GOLD guidelines. The selection criteria included patients with no background therapy for COPD indicating unclear intention of the medication for frontline or add-on therapy. The primary goals did not align with COPD pharmaceutical management to show reduction of exacerbation or improved functional status. The primary goals were relied on improvement of lung function using area over the curve over 12-hour intervals, instead of standard trough or peak FEV1. In addition, there are no

specification on whether their primary goals have surpassed the minimal important difference, and the patients failed to reproduce quality of life improvement.

A possible advantage of Ohtuvayre would be in Medicare patient's as it provides a nebulized therapy included in Medicare part B as many Medicare patients are unable to afford inhalers recommended by GOLD guidelines. However, due to the cost of the medication, it would preclude this benefit. Another possible advantage would be in patients with dexterity issues that are unable to use meter-dose-inhalers or dry-powder inhalers. However, there is no confidence Ohtuvayre "offers more than currently available nebulized medications, such as ipratropium, albuterol, arformoterol or glycopyrrolate." Ohtuvayre's place in therapy would need to be revisited once the updated GOLD guidelines are released in November.

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 there was any data of how many members do not fill the drug at all after an initial prior authorization approval. Aubrielle Smith-Masri, Pharm.D., stated that she did not have that data available but would look into trying to pull it. The committee unanimously voted to accept the recommendations as presented. None were opposed (32 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (34 approved, 0 rejected).

Outcome: Ohtuvayre is a pharmacy benefit and will not be added to the Commercial, Marketplace, or GHP Kids formularies. The following prior authorization criteria will apply:

- Medical record documentation of diagnosis of moderate to severe COPD **AND**
- Medical documentation of age greater than 18 years **AND**
- Medical record documentation of therapeutic failure on, intolerance or contraindication to two formulary long-acting beta-2 agonists (LABAs) used in combination with long-acting muscarinic antagonists (LAMA) and/or inhaled corticosteroids (ICS)

QUANTITY LIMIT: 5 mL (2 ampules) per day

AUTHORIZATION DURATION: Initial approval will be for **6 months**. Subsequent approvals will be for **12 months** and will require medical record documentation of continued disease improvement or lack of disease progression.

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.

BEQVEZ (fidanacogene elaparvovec-dzkt)

Review: Beqvez is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with moderate to severe hemophilia B (congenital factor IX deficiency) who:

- Currently use factor IX prophylaxis therapy or
- Have current or historical life-threatening hemorrhage or
- Have repeated serious spontaneous bleeding episodes and
- Do not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA approved test

Beqvez introduces transduced cells with a functional copy of the factor IX gene encoding a high-activity FIX variant. Beqvez is developed with recombinant DNA technology that consists of a recombinant viral capsid (AAVRh74var) derived from a naturally occurring AAV serotype (Rh74) vector containing the human coagulation factor IX (FIX) transgene modified to a high-specific factor IX activity variant known as FIX-R338L. Single intravenous infusion of Beqvez results in cell transduction and increase in circulating factor IX activity in patients with hemophilia B.

Beqvez is the second gene therapy approved for the treatment of hemophilia B, following CSL Behring's Hemgenix (etranacogene dezaparvovec-drlb), which was approved in November 2022.

Beqvez is administered as a one-time single-dose intravenous infusion. Prior to administering Beqvez, factor IX inhibitor testing, HIV testing, and liver health assessments should be performed. Beqvez should not be administered in patients with ≥ 0.6 Bethesda Units (BU) or a prior history of factor IX inhibitor. Beqvez should not be administered to patients with either CD4+ cell count < 200 mm3 or viral load ≥20 copies/mL in case of serological evidence of HIV-1 or HIV-2 infection. Beqvez should not be administered to patients with current liver-related coagulopathy, hypoalbuminemia, persistent jaundice, or cirrhosis), portal hypertension, splenomegaly, hepatic encephalopathy, hepatic fibrosis, or active viral hepatitis.

The recommended dosage of Beqvez is a single-dose intravenous infusion of 5 x 1011 vector genomes per kg (vg/kg) of body weight. To determine the required dose, dose weight is calculated from the patient's body mass index (BMI) in kg/m2. Calculate dose volume in milliliters by dividing the dose weight by 20 (the amount of vector genomes per mL of Beqvez suspension divided by per kilogram dose). Beqvez is then administered to the patient as a peripheral IV infusion over 60 minutes. In the event of infusion reaction, the rate of infusion can be reduced or stopped and treatment can be administered to manage infusion reaction. If stopped, the infusion can be resumed at a lower rate once the infusion reaction has resolved. Beqvez should be infused within 24 hours of dose preparation. After Beqvez administration, AST, ALT, and factor IX activity should be monitored.

A course of corticosteroids should be considered for AST or ALT ≥ 1.5 fold from baseline after screening, consecutive increases in AST, ALT, or both on 2 subsequent blood tests, or a Factor IX activity decrease (a decrease that could trigger the risk of bleeding or a decrease in factor IX activity on 2 consecutive blood tests [especially during the first 4 months post-infusion]).

Beqvez is supplied as a suspension for intravenous infusions with each mL containing 1 x 1013 vector genomes (vg). Each vial of Beqvez contains 1 mL of extractable volume. The total number of vials is customized to meet the individual dosing requirements based on body weight as outlined above. It is shipped frozen in a customized kit containing the number of vials required to meet dosing requirements for each patient.

The efficacy of Beqvez was evaluated in BENEGENE-2, an ongoing, prospective, open-label, single-arm, in 45 adult male patients with moderately severe to severe hemophilia B (factor IX activity ≤ 2 IU/dL). All patients completed a prospective, lead-in study of at least six months for baseline data collection while receiving factor IX prophylaxis in the usual care setting. Patients enrolled received a single infusion dose of Beqvez and entered a follow-up (FU) period of 6 years. Of the 45 patients, 41 completed at least 15 months of FU. The median FU of the 45 treated patient was 2.0 years from the time of infusion.

The trial only included patients who were negative for pre-existing neutralizing antibodies to AAVRh74var capsid. The trial excluded patients with a history of or current inhibitor to factor IX (≥ 0.6 Bethesda units), active hepatis B or C infection, HIV infection with CD4 cell count ≤ 200 mm3 or viral load > 20 copies/mL, hypersensitivity to factor IX product, ALT/AST/ALP > 2 times ULN, bilirubin > >1.5 times ULN, unstable liver or biliary disease, and significant liver fibrosis.

The main efficacy outcome was non-inferiority (NI) test of annualized bleeding rate (ABR) during the efficacy evaluation period (EEP), Week 12 (Day 82) to data cutoff following Beqvez treatment, compared with baseline ABR during the lead-in period. The ABR included treated and untreated blead and excluded

procedural bleeds. The NI margin on the difference between the mean EEP ABR and mean baseline ABR was 3.0 bleeds/year.

The model derived mean ABR was 4.5 bleeds/year during the baseline period and 2.5 bleeds/year during post-BEQVEZ EEP, resulting in a difference between mean post-Beqvez EEP ABR and baseline ABR of -2.1 bleed/year, which met NI study success criterion (Table 7). Six of 45 patients resumed routine factor IX prophylaxis after Beqvez treatment, starting from 0.4 years to 1.7 years after Beqvez infusion. An additional patient had intermittent exogenous factor IX use and had a higher ABR post Beqvez (5.0 bleeds/year) compared to baseline (1.2 bleeds/year) with a factor IX activity <5% starting at 0.4 years.

Warnings and precautions for Beqvez include hepatotoxicity due to the liver-directed AAV vector; infusion reactions, including hypersensitivity reactions and anaphylaxis; and risk of hepatocellular carcinoma. In clinical trials, elevated transaminase occurred in 29 of 45 and 7 of 15 patients in study 1 and study 2 respectively. In Study 1, 62% of patients received corticosteroids for elevated transaminases and/or decline in factor IX activity, mean time to corticosteroid initiation was 45 days, and mean duration of corticosteroid treatment was 113 days.

During clinical trials, the most common adverse reaction reported was increased transaminases. No serious adverse reactions were reported in patients treated with Beqvez.

The safety and efficacy of Beqvez has not been established in pediatric patients. The clinical study of Beqvez did not include patients ≥ 65 years of age. The safety and efficacy of Beqvez have not been established in geriatric patients. Beqvez has not been studied in patients with hepatic or renal impairment. Clinical studies included a limited number of HI patients which precludes a determination of whether the safety and efficacy data differs when compared to patients without HIV infection. The safety and efficacy of Beqvez in patients with prior or active factor IX inhibitors have not been established. Patients with a history of or active factor IX inhibitors should not take Beqvez. After administration of Beqvez, patients should be monitored for the development of factor IX inhibitors.

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 (34 approved, 0 rejected).

Financial Discussion: Dr. Bret Yarczower asked if this drug is part of the non-risk agreement with Medicaid. Kevin Szczecina, RPh, stated he is not sure but will check. Aubrielle Smith-Masri, Pharm.D., stated that this medication is not included on the specialty list for Navitus, so would recommend making this a medical benefit only for Commercial/Exchange/CHIP. Kimberly Clark, Pharm.D., stated that CHIP does not cover gene therapies and if members qualify for these drugs, then they would be referred to Medicaid. The committee unanimously voted to accept the recommendations as presented. None were opposed (31 approved, 0 rejected).

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

- Prescription written by or in consultation with a hematologist **AND**
- Medical record documentation that the member is a male based on assigned sex at birth and age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of moderate or severe hemophilia B with Factor IX level < 2 IU/dL or ≤ 2% of normal **AND**
- Medical record documentation of one of the following:
    - Member has current use of Factor IX prophylaxis therapy for at least 6 months with ≥ 50 exposure days^ of treatment with Factor IX protein
    - Member has current or historical life-threatening hemorrhage
    - Member has repeated, serious spontaneous bleeding episodes **AND**

- Medical record documentation that member does not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid as detected by an FDA-approved test* **AND**
- Medical record documentation that the member has a recent negative inhibitor status to Factor IX prior to administration of Beqvez **AND**
- Medical record documentation that the member does not have an active hepatitis B or hepatitis C infection** assessed within the last 6 months **AND**
- Medical record documentation that the member does not have uncontrolled HIV*** assessed within the last 6 months **AND**
- Medical record documentation that the member does not have evidence of advanced cirrhosis**** assessed within the last 6 months **AND**
- Medical record documentation that the member has not received any previous gene therapy for hemophilia B **AND**
- Medical record documentation that Beqvez is being dosed according to the Food and Drug Administration approved labeling***** **AND**
- Medical record documentation of the frequency of bleeds within the previous 12 months

NOTES:

- *The FDA approved test for AAVRh74var capsid neutralizing antibodies is nAbCyte Anti-AAVRh74var HB-FE Assay (Labcorp Drug Development)
- **The BENEGENE-2 trial excluded patients currently on antiviral therapy for hepatitis B or C, hepatitis B surface antigen, hepatitis B virus deoxyribonucleic acid positivity, or hepatitis C ribonucleic positivity
- ***The BENEGENE-2 trial excluded patients with serological evidence of HIV1 or HIV2 infection with either CD4+ cell count <=200 mm3 and/or a viral load >20 copies/mL.
- ****The BENEGENE-2 trial excluded patients with history of chronic infection or other chronic disease, clinically significant major disease or condition unsuitable for participation and/or may interfere with the interpretation of study results, current unstable liver or biliary disease, or significant liver fibrosis and disease.
- *****Beqvez is a single IV infusion. The recommended dosage is based on body weight in kg/m2

Patient's BMI	Patient's Dose Weight
≤ 30 kg/m^2	Dose Weight = Actual body weight
>30 kg/m^2	Determine using the following calculation: Dose Weight (kg) = 30 kg/m^2 × [Height (m)]^2

Beqvez dose (mL)= Beqvez dose weight (kg) / 20 = dose in mL

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

RPH SIGNOFF REQUIRED: yes

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

MRESVIA (respiratory syncytial virus vaccine)

Review: Mresvia is indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older.

Mresvia induces an immune response against RSV pre-F protein that protects against LRTD caused by RSV. Each 0.5 ml dose of Mresvia contains 50 mcg of nucleoside modified mRNA encoding the RSV F glycoprotein stabilized in the prefusion conformation (pre-F protein). Mresvia is the first mRNA vaccine for the prevention of RSV.
The CDC and ACIP currently recommend only a single dose of RSV vaccine for all adults aged 75 years and older and for adults ages 60-74 with increased risk of severe RSV disease. Individuals at increased risk include persons with certain chronic medical conditions (chronic cardiovascular disease, chronic lung disease or respiratory disease, end-stage renal disease, diabetes, neurologic or neuromuscular conditions causing impaired airway clearance or respiratory muscle weakness, chronic liver disease, chronic hematologic conditions, and severe obesity), persons with moderate or severe immune compromise, and persons living in nursing homes. Adults who have previously received the RSV vaccine should not receive another dose.

Mresvia is administered as a single 0.5 ml dose as an intramuscular injection. Mresvia is supplied as a pre-filled syringe that contains frozen suspension that must be thawed prior to administration.

Study 1 (NCT05127434) is a randomized, placebo-controlled, observer-blind, case-driven clinical study to evaluate the safety and efficacy of Mresvia to prevent RSV-LRTD in individuals 60 years of age and older with or without underlying medical conditions after receipt of a single dose of Mresvia. Study 1 is being conducted in 22 countries and includes participants from North America/Europe, Central/Latin America, Africa, and Asian/Pacific regions and is designed to follow participants for up to 24 months after vaccination.

Participants were randomized to a single dose of Mresvia or placebo (in a 1:1 ratio). Randomization was stratified by age (60 to 74 years; ≥ 75 years) and risk factors for LRTD, which were defined as congestive heart failure and/or chronic obstructive pulmonary disease at screening. The primary efficacy analysis population (Per-Protocol Efficacy Set) included 34,064 participants who received either Mresvia (n=17,561) or placebo (n=17,503).

Study exclusion criteria included history of myocarditis, pericarditis, or myopericarditis within 2 months prior to screening; autoimmune conditions requiring systemic immunosuppressants; history of serious reaction to any prior vaccination. Individuals were not eligible for inclusion in the Per-Protocol Efficacy Set if they received any other vaccine within 28 days before or after administration of the study injection.

The primary efficacy endpoints were the prevention of a first episode of RSV-LRTD with either ≥ 2 signs/symptoms or ≥ 3 signs/symptoms starting 14 days after vaccination. The primary efficacy analyses were performed when at least 50% of targeted RSV-LRTD cases had accrued, which occurred after a median of 3.7 months of follow-up when 20.2% of participants had reached 6 months of follow-up. Both primary efficacy analyses met the predefined success criterion. Additional analyses of efficacy were performed after a median of 8.6 months of follow-up when 94.2% of participants had reached 6 months of follow-up after vaccination and met the same success criterion.

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 (27 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (32 approved, 0 rejected).

Outcome: Mresvia will be medical or pharmacy benefit and should be added to the Commercial, Exchange, and GHP Kids formulary as preventive vaccines ($0 copay). Mresvia will not require a prior authorization for members 60 years of age and older. For members under 60 years of age, the following prior authorization criteria will apply:

- Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by administering to an individual with an age under the FDA-approved age

QUANTITY LIMIT: 0.5 mL per lifetime
GPI LEVEL: GPI-12

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.

MYHIBBIN (mycophenolate mofetil suspension)

Review: Myhibbin is an immunosuppressive agent indicated for the prophylaxis of organ rejection in patients 3 months of age or greater receiving allogeneic kidney, heart, or liver transplants, in combination with other immunosuppressants. Myhibbin is available as a 200mg/ml oral suspension and may be administered orally or via a nasogastric tube. The recommended dosing of Myhibbin is 1g twice daily for adult kidney transplant patients and 1.5g twice daily in adult heart and liver transplant patients. Dosing is based off body surface area (BSA) for pediatric patients, with the recommended dosing being 600mg/m2 twice daily (with a maximum daily dose of 2g) for pediatric kidney transplant patients and initial dosing of 600mg/m2 twice daily with an increase if well tolerated to 900mg/m2 twice daily (with a maximum daily dose of 3g) for pediatric heart and liver transplant patients. Myhibbin is recommended to be taken on an empty stomach, but in stable transplant patients, it may be taken with food if necessary. It is recommended for the liquid to avoid direct contact of the skin or mucous membranes due to its teratogenic effects. Myhibbin must be discarded after 60 days from first opening the bottle and should not be mixed with other liquids prior to administration. Patients should take missed doses as soon as they remember unless it is closer than 2 hours to the next scheduled dose.

Maintenance immunosuppression for transplant recipients is usually initiated at the time of transplantation and continued long-term. Regimens can include glucocorticoids, calcineurin inhibitors (tacrolimus or cyclosporine), antiproliferative agents (mycophenolate mofetil, mycophenolic acid, or azathioprine), mTOR inhibitors (sirolimus or everolimus), or costimulatory blockade agents (Nulojix). The most recent Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines for care of kidney transplant recipients recommend mycophenolate as a first-line antiproliferative agent and azathioprine (AZA) as second-line. Per UpToDate, in the United States, over 90 percent of transplant recipients were on mycophenolate and tacrolimus at one year posttransplant. Mycophenolate mofetil (MMF) is also used for many off-label uses, including rhematic diseases, such as SLE.

The efficacy of Myhibbin has been established in clinical trials of mycophenolate mofetil (MMF). The study included 5 randomized, active controlled double-blind 12-month trials in 1,557 patients with *de novo* kidney (3), heart (1), and liver (1) transplants. Patients in all trials also received cyclosporine and corticosteroids. In the kidney transplant trials, patients received MMF, AZA, or placebo. The primary efficacy endpoint was the proportion of patients in each treatment group who experienced treatment failure within the first 6 months after transplantation, with MMF significantly reducing the incidence of treatment failure. In the heart transplant trial, patients received MMF or AZA. The two primary efficacy endpoints were the proportion of patients who experienced biopsy-proven rejection within the first 6 months after transplantation, with MMF showing no difference to AZA, and the proportion of patients who died or were re-transplanted during the first 12 months after transplantation, with MMF showing to be at least as effective as AZA. In the liver transplant trial, patients received MMF or AZA. The two primary efficacy endpoints were the proportion of patients who experienced biopsy-proven rejection within the first 6 months after transplantation, with MMF showing a lower rate of acute rejection compared to AZA, and the proportion of patients who died or were re-transplanted during the first 12 months after transplantation, with MMF showing to have a similar rate compared to AZA. There were no other direct clinical trials completed for Myhibbin.

The safety profile of Myhibbin is similar to other mycophenolate products. Myhibbin is contraindicated in patients with a hypersensitivity to MMF, mycophenolic acid, and polysorbate 80 (TWEEN) or any other components of the drug. There are boxed warnings for increased risk of developing lymphomas and other malignancies (particularly of the skin), increased risk of developing serious infections, and embryofetal toxicity. While taking Myhibbin, it is recommended to decrease sunlight and UV light exposure by wearing protective clothing and sunscreen, to avoid use of Myhibbin during pregnancy, and to counsel women of reproductive potential regarding pregnancy prevention and planning. There is also a REMS program to help mitigate the embryofetal risk. Other warnings include bone marrow suppression, pure red cell aplasia (PRCA), gastrointestinal complications, and acute inflammatory syndrome (AIS). Patients with hereditary deficiencies of HGPRT should avoid use of Myhibbin and immunization of live attenuated vaccines, blood donations, semen donation, and driving or using machines (if experiencing adverse reactions) should be avoided while using Myhibbin. There are many common adverse reactions including cardiovascular, dermatologic, endocrine and metabolic, gastrointestinal, genitourinary, hematologic and oncologic, hepatic, infection, nervous system, neuromuscular and skeletal, renal, and respiratory effects.

There was an insufficient number of patients aged 65 years and older in clinical studies to establish if geriatric patients respond differently than younger patients. No dosage adjustments are needed in kidney transplant patients with severe chronic impairment of the graft, however doses greater than 1g administered twice daily should be avoided. No dosage adjustments are needed in kidney transplant patients with severe liver disease. No studies were completed in heart and liver transplant patients with renal impairment, or in heart transplant patients with hepatic impairment.

Generic MMF has been available in multiple product formulations, including oral capsules, oral tablets, oral suspension reconstituted, and intravenous solution reconstituted. Myhibbin offers a new “ready-to-use” oral suspension that does not need to be reconstituted or refrigerated. Myhibbin does not appear to have any clinical advantages over other generic formulations of MMF.

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 (30 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (30 approved, 0 rejected).

Outcome: Myhibbin will be a pharmacy benefit and will not be added to the Commercial, Exchange, and CHIP formularies. Myhibbin will require a prior authorization and will be reviewed under the existing Policy 3.0 Formulary Exception

- Medical record documentation of <u>one</u> of the following:
  - Medical record documentation of use for prophylaxis of organ rejection in patients receiving allogeneic kidney, heart, or liver transplants, in combination with other immunosuppressants **OR**
  - Medical record documentation of use for a medically accepted indication

  AND
- Medical record documentation of therapeutic failure on or intolerance to two formulary mycophenolate products **OR**
- If member has difficulty swallowing or has a nasogastric (NG) tube, medical record documentation of therapeutic failure on or intolerance to mycophenolate mofetil reconstituted suspension.

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

DUVYZAT (givinostat)

Review: Duvyzat is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older. Although the exact mechanism of Duvyzat in the treatment of DMD is unknown, Duvyzat contains a histone deacetylase inhibitor which activate repair mechanisms and may aid in prevention of muscle degeneration and reduction of inflammation. Other treatment options for improvement of muscle function in DMD include corticosteroids, such as prednisone, Emflaza, or Agamree. Other therapies focus on restoring dystrophin function and include gene-based therapies, such as Exondys 51, Vyondys 53, Viltepso, Amondys 45, and Elevidys.

The recommended dosage of Duvyzat is based on body weight and administered orally twice daily with food. In the case of adverse reactions, dosage reductions are recommended based on patient weight. Duvyzat is supplied as a peach flavored suspension containing 8.86 mg/mL givinostat.

The efficacy of Duvyzat for the treatment of Duchenne muscular dystrophy (DMD) was evaluated in EPIDYS, a randomized, double-blind, placebo-controlled 18-month study. A total of 179 patients were randomized 2:1 to receive either Duvyzat (n=118; dosed according to weigh-based dosing regimen) or placebo (n=61) in addition to standard of care (SOC) corticosteroids. The study include male patients 6 years of age and older with a confirmed diagnosis of DMD who were ambulatory and on a stable dose of corticosteroids.

The primary endpoint was change from baseline to Month 18 in 4-stair climb (4SC; measure of muscle function that tests time to climb 4 stairs) time for Duvyzat compared to placebo. A secondary endpoint was change from baseline to Month 18 in physical function as assessed by North Star Ambulatory Assessment (NSAA).

Patients treated with Duvyzat showed statistically significant less decline in the 4-stair climb compared to placebo. The Duvyzat treated group also experienced less worsening in NSAA scores, which was numerically significant but not statistically significant.

There are no black box warnings for Duvyzat. Warnings for Duvyzat are hematological changes, including dose-related thrombocytopenia and other myelosuppression; elevations in triglycerides, gastrointestinal disturbances, and prolongation of the QTc interval. During clinical trials, the most common adverse reactions (≥ 10% of Duvyzat treated patients) were diarrhea, abdominal pain, thrombocytopenia, nausea/vomiting, hypertriglyceridemia, and pyrexia.

Duvyzat is also being evaluated in the Ulysses trial which is evaluating the efficacy of Duvyzat in non-ambulatory males aged 9 to <18 years with DMD on a stable dose of corticosteroids.

The safety and efficacy of Duvyzat in children aged 6 years and older have been established. Safety and efficacy in pediatric patients below the age of 6 years have not been established. DMD is largely a disease of children and young adults, therefore, there is no experience with Duvyzat in geriatric DMD patients.

No study was conducted to evaluate pharmacokinetics of Duvyzat in subjects with hepatic impairment and no dosage adjustment recommendations can be made for patients with hepatic impairment. Duvyzat is mainly eliminated through hepatic metabolism and hepatic impairment is expected to increase the exposure of Duvyzat.

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 (30 approved, 0 rejected).

Financial Discussion: Dr. Bret Yarczower asked why we would only require failure on one of the formulary alternatives instead of both. Kimberly Reichard, Pharm.D., and Keith Hunsicker, Pharm.D., stated that the traditional "contraindication/intolerance" language was removed due to the need to be established on corticosteroid therapy to qualify for the drug. "OR" language to require failure of only one of the corticosteroids was utilized because while deflazacort has safety/tolerability advantages over prednisone, it wouldn't be expected that either of them have major efficacy differences. Dr. Yarczower asked if we can run the alternatives past a specialist provider to understand if “OR” vs “AND” language is more appropriate. The committee unanimously voted to accept the recommendations as presented. None were opposed (31 approved, 0 rejected).

Outcome: Duvyzat is a pharmacy benefit and will not be added to the Commercial, Marketplace, and GHP Kids. The following prior authorization criteria will apply:

- Medical record documentation that Duvyzat is prescribed by a neurologist or pediatric neurologist **AND**
- Medical record documentation of interdisciplinary team involvement including, but not limited to, neurology, pulmonology, and cardiology **AND**
- Medical record documentation of a diagnosis of Duchenne muscular dystrophy (DMD), confirmed by genetic testing **AND**
- Medical record documentation of provider attestation that the member is ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent) **AND**
- Medical record documentation that the member has not received any previous gene therapy for Duchenne muscular dystrophy **AND**
- Medical record documentation of age greater than or equal to 6 years **AND**
- Medical record documentation that member has been established on stable corticosteroid treatment for at least 6 months **AND**
- Medical record documentation of a therapeutic failure on prednisone or deflazacort

QUANTITY LIMIT: 420 mL per 30 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.

LAZCLUZE (lazertinib)

Review: Lazcluze is a kinase inhibitor indicated in combination with Rybrevant for the first time treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon21 L858R substitution mutations, as detected by an FDA-approved test.

The recommended dosage of Lazcluze is 240 mg by mouth once daily with or without food, given in combination with Rybrevant. Treatment is continued until disease progression or unacceptable toxicity. Administer Lazcluze at any time prior to Rybrevant when given on the same day.

When initiating treatment with Lazcluze and Rybrevant, patients should receive anticoagulant prophylaxis to prevent venous thromboembolic events (VTE) for the first four months of treatment. If there are no signs and symptoms of VTE during the first four months of treatment, anticoagulation prophylaxis discontinuation can be considered. Patients should also be treated with alcohol-free emollient cream, limit sun exposure, wear protective clothing, and use broad spectrum UVA/UVB sunscreen during and for two months after treatment to reduce the risk of dermatologic adverse reactions.

In the case of adverse reactions, Lazcluze recommended dosage can be reduced to 160 mg once daily for the first dose reduction, then 80 mg once daily for the second dose reduction. Patients requiring a third dosage reduction should discontinue treatment. Lazcluze is supplied as 80 mg tablets and 240 mg tablets.

The efficacy of Lazcluze and Rybrevant was evaluated in MARIPOSA, a randomized, active-controlled. Eligible patients were required to have untreated locally advanced or metastatic NSCLC with either exon 19 deletions or exon 21 L858R substitution EGFR mutations, not amenable to curative therapy. Patients with asymptomatic or previously treated and stable intracranial metastases were eligible to enroll. Patients were randomized (2:2:1) to receive Lazcluze and Rybrevant (n=429), Tagrisso (osimertinib) (n=429), or Lazcluze monotherapy (unapproved regimen for NSCLC) until disease progression or unacceptable toxicity.

The major efficacy endpoint measure was progression-free survival (PFS) as assessed by blinded independent central review (BICR). Additional efficacy outcome measures included overall survival (OS), overall response rate (ORR) and duration of response (DOR). Among 858 patients with EGFR exon 19 deletion or L858R substitution mutations that were randomized between the Lazcluze + Rybrevant and Tagrisso arm, 544 had evaluable results, 527 were positive for EGFR exon 19 deletion or L858R substitution mutations, while 17 were negative.

Results from MARIPOSA demonstrated a statistically significant improvement in PFS by BICR assessment for Lazcluze + Rybrevant compared to Tagrisso.

Although OS results were immature at the current analysis, 55% of pre-specified deaths for the final analysis were reported and no trend towards detriment was observed. Of all randomized patients, 367 patients had baseline intracranial lesions assessed by BICR using modified RECIST.

There are no black box warnings for Lazcluze. The warnings and precautions for Lazcluze include increased risk of venous thromboembolic events (VTE), new or worsening interstitial lung disease (ILD)/ pneumonitis, severe dermatologic adverse reactions (including severe rash and acneiform dermatitis), new or worsening ocular adverse reactions (including keratitis), and embryo-fetal toxicity. During clinical trials, the most common adverse reactions were rash, nail toxicity, infusion-related reaction (Rybrevant), musculoskeletal pain, edema, stomatitis, VTE, paresthesia, fatigue, diarrhea, constipation, COVID-19, hemorrhage, dry skin, decreased appetite, pruritus, nausea, and ocular toxicity. The most common Grade 3 or 4 laboratory abnormalities were decreased albumin, sodium, potassium, hemoglobin, and increased ALT, AST, GGT, and magnesium.

The safety and efficacy of Lazcluze in pediatric patients has not been established. Of the 421 patients with locally advanced or metastatic NSCLC treated with Lazcluze in combination with Rybrevant in MARIPOSA, 45% were 65 years and older and 12% were 75 years and older. No overall differences in safety or effectiveness were observed between patients aged 65 years and older and younger patients.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (30 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (32 approved, 0 rejected).

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

- Medical record documentation that Lazcluze is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years of age **AND**

- Medical record documentation of locally advanced or metastatic non-small cell lung cancer (NSCLC) **AND**
- Medical record documentation of epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858Rsubstitution mutations, as detected by an FDA-approved test **AND**
- Medical record documentation that Lazcluze will be used in combination with amivantamab (Rybrevant) for first-line treatment

AUTHORIZATION DURATION: Lazcluze is configured as a prior authorization for new starts only. Lazcluze 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:

- **80 mg Tablets:** 2 tablets per day, 30 day supply per fill
- **240 mg Tablets:** 1 tablet per day, 30 day supply per fill

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.

FAST FACTS

RYBREVANT (amivantamab-vmjw)

Clinical Summary: Rybrevant is now indicated in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor. Rybrevant is also indicated in combination with lazertinib for the first line-treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, as determined by and FDA-approved test. Previous indications include Rybrevant in combination with carboplatin + pemetrexed for first-line treatment of NSCLC with EGFR exons 20 insertion mutations, and as a single agent for previously treated NSCLC with EGFR exon 20 insertion mutations.

Rybrevant is administered intravenously based on body weight at baseline. For week 1, the dosage should be split and given on Day 1 and Day 2. For week 2 and beyond, Rybrevant can be administered as a single dose. For patients weighing less than 80 kg, the recommended dose is 1450 weekly from weeks 1 to 4, no dose on weeks 5-6, then 1750 mg every 3 weeks from Week 7 onward. For patients weighing greater than or equal to 80 kg, the recommended dose is 1750 mg weekly for weeks 1 to 4, no dose on weeks 5-6, then 2100 mg every 3 weeks starting from Week 7 onward. Table 1 shows the order of administration and regimen for Rybrevant when administered with carboplatin and pemetrexed.

Premedication with glucocorticoids is required for Week 1, Day 1 and 2 only and upon re-initiation after prolonged dose interruptions, then as necessary for subsequent infusions. Antihistamines and antipyretics should be administered prior to all infusions.

The recommended dosage of Rybrevant in combination with lazertinib is based on baseline body weight. For patients weighing less than 80 kg, the recommended dose is 1050 mg weekly from Weeks 1 to 5, no dose on Week 6, then every 2 weeks from Week 7 onwards. For patients weighing greater than or equal to 80 kg, the recommended dose is 1400 mg weekly from Weeks 1 to 5, no dose on Week 6, then every 2 weeks from Week 7 onwards. When given on the same day, Rybrevant is administered at any time after lazertinib.

The efficacy of Rybrevant in combination with carboplatin and pemetrexed was evaluated in MARIPOSA-2, a randomized, open-label trial in patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations and progressive disease on or after receiving osimertinib. Patients with asymptomatic or previously treated and stable intracranial metastases were eligible to enroll. Patients were randomized (1:2:2) to receive Rybrevant in combination with carboplatin and pemetrexed (Rybrevant-CP, N=131), carboplatin and pemetrexed (CP, N-263), or Rybrevant as part of another combination regimen. The evaluation of efficacy for metastatic NSCLC was based on comparing Rybrevant-CP to the CP group.

The patients included in the trial had a baseline ECOG performance status of 0 (40%) or 1 (60%); 65% never smoked, 45% had a history of brain metastases, and 99.7% had Stage IV cancer at study enrollment.

The major efficacy outcome was progression-free survival (PFS) as assessed by blinded independent central review (BICR). Overall survival (OS) and overall response rate (ORR) as assessed by BICR were also assessed. Results demonstrated a statistically significant improvement in PFS by BICR for Rybrevant in combination with carboplatin and pemetrexed compared to carboplatin and pemetrexed.

At the prespecified second interim analysis of OS with 85% of deaths needed for final analysis, there was no statistically significant difference in OS. The median OS was 17.7 months. Pre-specified secondary analyses of intracranial ORR by BICR in the subset of 91 (23%) patients with baseline intracranial disease were performed. Data were only available for intracranial complete responses and not available

for intracranial partial responses. Intracranial ORR was 20% (95% CI: 8, 39) in the 30 patients with baseline intracranial disease in the ACP arm and 7% (95% CI: 1.8, 16) in the 61 patients with baseline intracranial disease in the CP arm.

The safety of Rybrevant in combination with carboplatin and pemetrexed was consistent with the known safety profiles of the agents and previous trials of Rybrevant + carboplatin + pemetrexed for first line treatment of locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations.

The efficacy of Lazcluze and Rybrevant was evaluated in MARIPOSA, a randomized, active-controlled. Eligible patients were required to have untreated locally advanced or metastatic NSCLC with either exon 19 deletions or exon 21 L858R substitution EGFR mutations, not amenable to curative therapy. Patients with asymptomatic or previously treated and stable intracranial metastases were eligible to enroll. Patients were randomized (2:2:1) to receive Lazcluze and Rybrevant (n=429), Tagrisso (osimertinib) (n=429), or Lazcluze monotherapy (unapproved regimen for NSCLC) until disease progression or unacceptable toxicity.

The major efficacy endpoint measure was progression-free survival (PFS) as assessed by blinded independent central review (BICR). Additional efficacy outcome measures included overall survival (OS), overall response rate (ORR) and duration of response (DOR). Among 858 patients with EGFR exon 19 deletion or L858R substitution mutations that were randomized between the Lazcluze + Rybrevant and Tagrisso arm, 544 had evaluable results, 527 were positive for EGFR exon 19 deletion or L858R substitution mutations, while 17 were negative.
Results from MARIPOSA demonstrated a statistically significant improvement in PFS by BICR assessment for Lazcluze + Rybrevant compared to Tagrisso.

Although OS results were immature at the current analysis, 55% of pre-specified deaths for the final analysis were reported and no trend towards detriment was observed. Of all randomized patients, 367 patients had baseline intracranial lesions assessed by BICR using modified RECIST.

During clinical trials, the most common adverse reactions were rash, nail toxicity, infusion-related reaction (Rybrevant), musculoskeletal pain, edema, stomatitis, VTE, paresthesia, fatigue, diarrhea, constipation, COVID-19, hemorrhage, dry skin, decreased appetite, pruritus, nausea, and ocular toxicity. The most common Grade 3 or 4 laboratory abnormalities were decreased albumin, sodium, potassium, hemoglobin, and increased ALT, AST, GGT, and magnesium.

Current Formulary Status: Medical Benefit, PA required, MBP 239.0 , When processed at Specialty Pharmacy, processes at Specialty tier or Brand NP tier for members with a three-tier benefit.

Recommendation: No changes are recommended to the formulary placement and authorization duration of Rybrevant.

Medical Benefit Policy 239.0

- Medical record documentation that Rybrevant is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation of a diagnosis of with locally advanced or metastatic non-small cell lung cancer (NSCLC) **AND**
- **One of the following:**
    - Medical record documentation of epidermal growth factor receptor (EGFR) exon 20 insertion mutations as determined by an FDA approved test* **AND** one of the following:
        - Medical record documentation of disease progression on or following prior treatment with a platinum-based chemotherapy AND that Rybrevant will be used as a single agent **OR**
        - Medical record documentation that Rybrevant is being used as first line treatment AND that Rybrevant will be used in combination with carboplatin and pemetrexed

OR

- Medical record documentation of epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations as determined by an FDA-approved test **AND** one of the following:
    - Medical record documentation that Rybrevant is being used as first-line treatment AND Rybrevant will be used in combination with Lazcluze (Lazertinib)

    OR
    - Medical record documentation of disease progression on or following treatment with an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor AND Rybrevant will be used in combination with carboplatin and pemetrexed

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

***NOTE:** The FDA approved test for Rybrevant to detect the presences of EGFR exon 20 insertion mutations is the Guardant360® CDx

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (31 approved, 0 rejected).

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

ELEVIDYS (delandistrogene moxeparvovec)

Clinical Summary: Elevidys is an adeno-associated virus vector-based gene therapy that was previously indicated in patients at least 4 years of age but no older than 5 years of age, in patients who are ambulatory and have a confirmed mutation in the Duchenne muscular dystrophy (DMD) gene. Elevidys is now indicated for all individuals at least 4 years of age with a mutation in the DMD gene, for both ambulatory and non-ambulatory patients. The indication for non-ambulatory patients was approved under accelerated approval based on expression of Elevidys micro-dystrophin in skeletal muscle and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. Per IPD Analytics, the label expansion goes beyond the patient population for which data from randomized control trials is available. In a press release the FDA stated the expanded approval is based on the "totality of the evidence, including the potential risks associated with the product, the life-threatening and debilitating nature of the disease, and the urgent unmet medical need."

The dosing appears to have remained the same at 1.33 × 1014 vector genomes per kilogram (vg/kg) of body weight (or 10 mL/kg body weight) for patients weighing less than 70 kg. Or 9.31 × 1015 vg total fixed dose for patients weighing 70 kg or greater. The maximum dose of Elevidys is 9.31 x 10 1015 vg. The prescribing information goes on to state that there is limited safety data available for patients who weighed 70kg or more and received the maximum dose. Prior to infusion, the following should be done: assess liver function, obtain platelet count and troponin-I levels, and measure baseline anti-adeno-associated virus serotype rh74 (anti-AAVrh74) antibody titers. Patients should be selected for treatment if their anti-AAVrh74 total binding antibody titers are <1:400. Pre- and post-Elevidys corticosteroids are recommended. Elevidys comes in a customized kit to meet the dosing requirements of each patient, with the dosing requirements laid out in a table, which is filtered by patient's weight, then dictates how many vials will come in the kit that is needed, with a maximum of 10 vials for patients weighing 69.5 kg and above.

It appears as though one study was added to the prescribing information titled Study 3 (NCT 05096221). Study 3 is a multi-center, randomized, double-blind, placebo-controlled, confirmatory study that evaluated 125 ambulatory male patients aged 4-7 years. Patients were included if they had a confirmed frameshift, splice site, premature stop codon, or other disease-causing mutation in the DMD gene starting at or after exon 18. Patients were excluded if they had exon 45 (inclusive), or in-frame deletions, in-frame duplications, and variants of uncertain significance ("VUS").

All patients received a dose of 1.33 x 1014 vg/kg of Elevidys as a single intravenous infusion and corticosteroids for DMD according to the dosing tables in the prescribing information. All patients also had anti-AAVrh74 antibody titers <1:400.

The efficacy outcome was physical function as assessed by the North Star Ambulatory Assessment (NSAA) total score at week 52 after infusion of Elevidys or placebo. Other outcome measures were expression of microdystrophin in skeletal muscle, time to rise from floor, time of 10-meter walk/run, time of 100-meter walk/run, and time to ascend 4 steps. The difference between Elevidys and placebo for the primary outcome was not statistically significant (p=0.24). The least squares mean change was 2.57 points for Elevidys (95%CI: 1.80, 3.34) and 1.92 points for placebo (95%CI: -0.45, 1.74). Relevant changes were noted in secondary endpoints including time to rise from the floor, 10-meter walk/run and time to ascend 4 steps.

Per IPD Analytics, to fulfill the post-marketing requirements for the accelerated approval in non-ambulatory patients specifically, Sarepta will submit results from the Phase 3 trial, ENVISION (NCT05881408) to confirm benefit in this population. The estimated primary completion date of ENVISION is January 1, 2026.

Elevidys is contraindicated in patients with any deletion in exon 8 or exon 9 in the DMD gene. Warnings and precautions include infusion-related reactions, acute serious liver injury, immune-mediated myositis, myocarditis, and pre-existing immunity against AAVrh74.

Current Formulary Status: Elevidys is a medical benefit requiring prior authorization. Elevidys is on the medical benefit cost share list. Elevidys is not eligible to be processed at a specialty pharmacy.

Recommendation: There are no changes recommended to the formulary placement of Elevidys. It is recommended to update the following criteria as a result of the new indication.

MBP 307.0 Elevidys (delandistrogene moxeparvovec-rokl)

Elevidys (delandistrogene moxeparvovec-rokl) will be considered medically necessary for the commercial, exchange, CHIP, and Medicare lines of business when ALL of the following criteria are met:

- Medical record documentation of a diagnosis of Duchenne Muscular Dystrophy confirmed by a genetic mutation in the Duchenne Muscular Dystrophy gene **AND**
- One of the following:
    - Medical record documentation that the member is a male based on assigned sex at birth

    OR

    - Medical record documentation that the member is a female based on assigned sex at birth AND
    - Medical record documentation that the member has a confirmed X-inactivation of the unmutated X-chromosome OR confirmed biallelic variants in the *DMD* gene (cytogenetic or molecular) alteration involving the Xp21 locus

    AND
- Medical record documentation of patient age of at least 4 ~~but no older than 5,~~ years of age **AND**
- Medical record documentation that the patient does NOT have a deletion in exon 8 and/or exon 9 in the Duchenne Muscular Dystrophy gene **AND**

- Medical record documentation that the patient has anti-adeno-associated virus serotype rh74 (anti-AAVrh74) antibody titers <1:400 **AND**
- Medical record documentation of provider attestation that the member is ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent) **AND**
- Medical record documentation that Elevidys is prescribed by a neurologist or pediatric neurologist **AND**
- Medical record documentation that patient has been initiated on corticosteroids for Duchenne muscular dystrophy one day prior to Elevidys infusion and medical documentation that patient will continue the regimen after for 60 days* **AND**
- Medical record documentation that the patient is on the appropriate weight-based dose **AND**
- Medical record documentation that the patient has never received Elevidys treatment in their lifetime **AND**
- Medical record documentation that the member has not received any previous gene therapy for Duchenne muscular dystrophy **AND**
- Medical record documentation that the patient will not receive exon-skipping therapies for Duchenne Muscular Dystrophy [e.g., Amondys (casimersen), Exondys 51 (eteplirsen), Viltepso (viltolarsen), Vyondys 53 (golodirsen)] concomitantly with Elevidys treatment. (Note: Any current authorizations for exon-skipping therapy will be terminated upon Elevidys approval.)

* Deflazacort is not recommended for use as a peri-Elevidys infusion corticosteroid

AUTHORIZATION DURATION: One (1) time approval (auth duration: 2 months) per lifetime. Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

Elevidys (delandistrogene moxeparvovec-rokl) is considered unproven for:
- Use in non-ambulatory patients

Note to Reviewer: Based on the Elevidys prescribing information, patients with deletions in the DMD gene in exons 1 to 17 and /or exons 59 to 71 may be at risk for severe immune-mediated myositis reaction.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (33 approved, 0 rejected).

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

UPDATES

VOWSTSTRENSIQ (asfotase alfa)

Background: The following updates were proposed based on the Antimicrobial Subcommittee recommendations to recognize Vowst as first-line in this clinical space. These changes will affect Policy 775.0 Vowst.

Vowst (fecal microbiota spores, live-brpk) is now the recommended/preferred therapy for recurrent *Cdiff* prevention over Rebyota (fecal microbiota, live-jslm) due to positive clinical outcomes as well as storage/administration advantages. Rebyota requires enema administration via gravity flow until entire dose is delivered and requires storage in an ultracold freezer (-60ºC to -90ºC) OR in refrigerator for up to 5 days. Vowst is an oral medication that does not require a clinic appointment to administer nor ultracold freezer storage. Currently there are no head-to-head trial comparisons favoring Rebyota over Vowst.

Recommendation: Due to administration and storage advantages, it is recommended that the following criterion be removed from Commercial Policy 775.0 Vowst:*

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

Discussion: The committee questioned the cost implications of this change. Vowst is around $22k, Rebyota is around $11k. Because of the cost difference we didn't want to require failure of Vowst ahead of Rebyota or Zinplava. The storage requirements and the favorable administration method prompted the Antimicrobial Subcommittee to prefer this product over Rebyota. Additionally the ACG guidelines recommend Vowst as a preferred option. Additional questions remain including what are the cost implications of administering Rebyota and is there additional savings by eliminating the need for the gravity flow enema administration?

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (30 approved, 0 rejected).

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

STRENSIQ (asfotase alfa)

Background: Due to the complexity of the disease being treated by Strensiq, and the financial considerations of Strensiq, a re-review of policy criteria was completed. Areas of opportunity to clearly define diagnosis and dose were identified.

Recommendation: It is recommended to update the prior authorization and reauthorization criteria for Strensiq to more closely resemble medically accepted uses of the medication.

- Medical record documentation that Strensiq is prescribed by an endocrinologist or metabolic specialist **AND**
- Medical record documentation of a diagnosis of perinatal/infantile- or juvenile-onset hypophosphatasia (HPP) **AND**
- Medical record documentation of disease onset prior to the age of 18 years (note: If member is 18 years or older at the time of request, documentation must be provided that member began experiencing symptoms prior to 18 years old) **AND**
- ~~Medical record documentation of low total serum alkaline phosphatase activity (see chart below for typical lowest normal reference values)~~ ~~**AND**~~

- Medical record documentation that member will receive a weight and diagnosis appropriate dosing regimen **AND**
- Medical record documentation that the member will receive the appropriate vials, as stated in the prescribing information, for the dose that is being prescribed **AND**
- Medical record documentation of the following:
    - A pathological mutation in the alkaline phosphatase (ALPL) gene as determined by molecular genetic testing

    OR
    - Low total serum alkaline phosphatase activity (see chart below for typical lowest normal reference values) **AND**
    - One of the following:
        - Radiographic evidence* supporting the diagnosis of hypophosphatasia **OR**
        - An elevated substrate of tissue non-specific alkaline phosphatase (TNSALP), including but not limited to pyridoxal-5´-phosphate (PLP), inorganic pyrophosphate (PPi), or phosphoethanolamine (PEA) in serum, tissues, or urine

Table 2. Typical Lowest Normal Reference Values for Serum Alkaline Phosphatase Activity in North America

Age	Lowest Normal Total Serum or Plasma Alkaline Phosphatase Activity (U/L)	
	Male	Female
0-30 days	60	60
1-11 months	70	70
1-3 years	125	125
4-11 years	150	150
12-13 years	160	110
14-15 years	130	55
16-19 years	60	40
>20 years	40	40

MEDISPAN AUTHORIZATION LEVEL: GPI-12

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

- QL FOR LETTER ONLY: 30 day supply per fill

AUTHORIZATION DURATION: Initial approval will be for a period of 3 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require:

- Medical record documentation that Strensiq is prescribed by an endocrinologist or metabolic specialist **AND**
- Medical record documentation of continued disease improvement or lack of disease progression **AND**
- Medical record documentation that member will receive a weight and diagnosis appropriate dosing regimen **AND**
- Medical record documentation that the member will receive the appropriate vials, as stated in the prescribing information, for the dose that is being prescribed

NOTE:

- *Radiographic evidence
    - In clinical trials this included but was not limited to osteopenia, rachitic chest/deformed ribs, metaphyseal fraying/flaring/tongues, physeal widening, long bone bowing, thin gracile bones, sclerosis, bony spurs, fracture (non-union), or absence of some/all bones

- Perinatal/Infantile-Onset HPP
  - Recommended dosage regimen is 2 mg/kg administered subcutaneously three times per week, or 1 mg/kg administered six times per week. Injection site reactions may limit the tolerability of the six times per week regimen.
  - The dose may be increased to 3 mg/kg three times per week for insufficient efficacy.
- Juvenile-Onset HPP
  - Recommended dosage regimen is 2 mg/kg administered subcutaneously three times per week, or 1 mg/kg administered six times per week. Injection site reactions may limit the tolerability of the six times per week regimen.
- Preparation and Weight-Based Dosing Tables
  - Patient weights should be rounded to the nearest kilogram when determining dose. Use the following tables based on the frequency per week and the indication.

Table 1: Weight-Based Dosing for Administration of 2 mg/kg Three Times per Week

Body Weight (kg)*	Dose to Inject	Volume to Inject	Vial Configuration
3	6 mg	0.15 mL	18 mg/0.45 mL
4	8 mg	0.2 mL	18 mg/0.45 mL
5	10 mg	0.25 mL	18 mg/0.45 mL
6	12 mg	0.3 mL	18 mg/0.45 mL
7	14 mg	0.35 mL	18 mg/0.45 mL
8	16 mg	0.4 mL	18 mg/0.45 mL
9	18 mg	0.45 mL	18 mg/0.45 mL
10	20 mg	0.5 mL	28 mg/0.7 mL
15	30 mg	0.75 mL	40 mg/1 mL
20	40 mg	1 mL	40 mg/1 mL
25	50 mg	1.25 mL	Two 28 mg/0.7 mL vials
30	60 mg	1.5 mL	Two 40 mg/1 mL vials
35	70 mg	1.75 mL	Two 40 mg/1 mL vials
40	80 mg	0.8 mL	80 mg/0.8 mL
50	100 mg	1 mL	Two 80 mg/0.8 mL vials
60	120 mg	1.2 mL**	Two 80 mg/0.8 mL vials
70	140 mg	1.4 mL**	Two 80 mg/0.8 mL vials
80	160 mg	1.6 mL**	Two 80 mg/0.8 mL vials

* Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg *[see Clinical Pharmacology (12.3)]*.

** When preparing a volume for injection greater than 1 mL, split the volume equally between two syringes, and administer two injections. When administering the two injections, use two separate injection sites.

Table 2: Weight-Based Dosing for Administration of 1 mg/kg Six Times per Week

Body Weight (kg)*	Dose to Inject	Volume to Inject	Vial Configuration
3	3 mg	0.08 mL	18 mg/0.45 mL
4	4 mg	0.1 mL	18 mg/0.45 mL
5	5 mg	0.13 mL	18 mg/0.45 mL
6	6 mg	0.15 mL	18 mg/0.45 mL
7	7 mg	0.18 mL	18 mg/0.45 mL
8	8 mg	0.2 mL	18 mg/0.45 mL
9	9 mg	0.23 mL	18 mg/0.45 mL
10	10 mg	0.25 mL	18 mg/0.45 mL
15	15 mg	0.38 mL	18 mg/0.45 mL
20	20 mg	0.5 mL	28 mg/0.7 mL
25	25 mg	0.63 mL	28 mg/0.7 mL
30	30 mg	0.75 mL	40 mg/1 mL
35	35 mg	0.88 mL	40 mg/1 mL
40	40 mg	1 mL	40 mg/1 mL
50	50 mg	0.5 mL	80 mg/0.8 mL
60	60 mg	0.6 mL	80 mg/0.8 mL
70	70 mg	0.7 mL	80 mg/0.8 mL
80	80 mg	0.8 mL	80 mg/0.8 mL
90	90 mg	0.9 mL	Two 80 mg/0.8 mL vials
100	100 mg	1 mL	Two 80 mg/0.8 mL vials

* Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg *[see Clinical Pharmacology (12.3)]*.

Table 3: Weight-Based Dosing for Administration of 3 mg/kg Three Times per Week – Only for Perinatal/Infantile-Onset HPP*

Body Weight (kg)**	Dose to Inject	Volume to Inject	Vial Configuration
3	9 mg	0.23 mL	18 mg/0.45 mL
4	12 mg	0.3 mL	18 mg/0.45 mL
5	15 mg	0.38 mL	18 mg/0.45 mL
6	18 mg	0.45 mL	18 mg/0.45 mL
7	21 mg	0.53 mL	28 mg/0.7 mL
8	24 mg	0.6 mL	28 mg/0.7 mL
9	27 mg	0.68 mL	28 mg/0.7 mL
10	30 mg	0.75 mL	40 mg/1 mL
15	45 mg	1.13 mL***	Two 28 mg/0.7 mL vials
20	60 mg	1.5 mL***	Two 40 mg/1 mL vials
25	75 mg	1.88 mL***	Two 40 mg/1 mL vials

* A regimen of 3 mg/kg three times per week is recommended only for patients with perinatal/infantile-onset HPP *[see Dosage and Administration (2.2)]*

** Do not use the 80 mg/0.8 mL vial of STRENSIQ in pediatric patients weighing less than 40 kg *[see Clinical Pharmacology (12.3)]*.

*** When preparing a volume for injection greater than 1 mL, split the volume equally between two syringes, and administer two injections. When administering the two injections, use two separate injection sites.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (31 approved, 0 rejected).

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

MEDICAL BENEFIT POLICY UPDATES

Pombiliti Update

Recommendations: It is recommended that the same criteria that was approved for the commercial, exchange, CHIP and Medicaid lines of business also apply to the Medicare line of business for the medical benefit.

MBP 326.0 Pombiliti (cipaglucosidase alfa-atga)

Pombiliti (cipaglucosidase alfa-atga) will be considered medically necessary for all lines of business when all of the following criteria are met:

- Medical record documentation of a diagnosis of late-onset Pompe disease supported by:
    - Acid alpha-glucosidase (GAA) assay performed on dried blood spots, skin fibroblasts or muscle biopsy **AND**
    - Genetic testing showing a mutation in the GAA gene

AND

- Medical record documentation of a consultation with a metabolic specialist and/or biochemical geneticist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of baseline percent-predicted forced vital capacity (% FVC) and 6-minute walk test (6MWT) **AND**
- Medical record documentation of member weight ≥ 40 kg **AND**
- Medical record documentation that Opfolda and Pombiliti will be used in combination **AND**
- Medical record documentation that member is currently receiving enzyme replacement therapy (e.g. Lumizyme, Nexviazyme) and is not experiencing improvement **AND**
- Medical record documentation that Pombiliti and Opfolda will not be used concurrently with other enzyme replacement therapy (e.g. Lumizyme, Nexviazyme)

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

- Medical record documentation of improvement or stabilization in percent-predicted forced vital capacity (% FVC) and/or 6-minute walk test (6MWT) **AND**
- Medical record documentation of member weight ≥ 40 kg **AND**
- Medical record documentation that Opfolda and Pombiliti will be used in combination **AND**
- Medical record documentation that Pombiliti and Opfolda will not be used concurrently with other enzyme replacement therapy (e.g. Lumizyme, Nexviazyme)

Tecelra Update

Recommendations: It is recommended that the “and” be changed to an “or” in the HLA-A criteria point, per package labeling.

MBP 327.0 Tecelra (afamitresgene autoleucel)

- Medical record documentation that Tecelra is prescribed by a hematologist or oncologist **AND**

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of unresectable or metastatic synovial sarcoma **AND**
- Medical record documentation of at least one (1) prior chemotherapy treatment **AND**
- Medical record documentation that member is HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P, ~~and~~ or HLA-A*02:06P allele–positive* **AND**
- Medical record documentation that the member has not had a prior allogeneic hematopoietic stem cell transplant **AND**
- Medical record documentation of tumor expression of melanoma-associated antigen A4 (MAGE-A4)

*Tecelra is contraindicated for patients who are heterozygous or homozygous for HLA-A*02:05P based on an alloreactivity screen which indicated in vitro alloreactivity against HLA-A*02:05

Humira Update

Recommendations: It is recommended to update all policies that contain a criteria point pertaining to Humira to include Humira biosimilars as acceptable alternatives.

Unspecified MBP's
Change "Humira" to "a preferred adalimumab product"

SOC Updates

Recommendations: It is recommended that Sunlenca be removed from the site of care program, as no prior authorization is or should be required for this medication.

MBP 181.0 Site of Care Review Guidelines for Infusion Drugs and Specialty Medications
~~38. Lenacapavir (Sunlenca)~~

DHS Updates

Recommendations: It is recommended to make the following changes based on DHS feedback.

MBP 177.0 Prevymis IV (letermovir)
Kidney Transplant

- Medical record documentation that Prevymis is prescribed by or in consultation with a transplant or infectious disease specialist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that member is a recipient of a kidney transplant **AND**
- Medical record documentation that member is at high risk of CMV [defined as CMV seropositive donor and CMV seronegative recipient (D+/R-)] **AND**
- Medical record documentation that Prevymis is being used for cytomegalovirus (CMV) prophylaxis **AND**
- Medical record documentation that Prevymis is being initiated between Day 0 and Day 7 post-transplantation **AND**
- Medical record documentation that Prevymis is not being used in combination with pimozide, ergot alkaloids (ergotamine and dihydroergotamine), and/or pitavastatin and simvastatin (if co-administered with cyclosporine) **AND**
- Medical record documentation of intolerance to or contraindication to Prevymis tablets.

MBP 132.0 Avycaz (cetfazidime/avibactam)

- Prescribed by or in consultation with an infectious disease specialist **AND**
- Medical record documentation of one of the following:

- A diagnosis of complicated intra-abdominal infection caused by caused by the following susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Enterobacter cloacae, Klebsiella oxytoca, Citrobacter freundii* complex *and Pseudomonas aeruginosa* **OR**
- A diagnosis of complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Citrobacter freundii* complex, *Proteus mirabilis*, and *Pseudomonas aeruginosa* **OR**
- A diagnosis of Hospital-acquired Bacterial Pneumonia ~~and~~ or Ventilator-associated Bacterial Pneumonia (HABP/VABP) caused by the following susceptible microorganisms: *Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa and, Serratia marcescens*

AND

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

MBP 325.0 Adzynma (ADAMTS13, recombinant-krhn)

- If being used for prophylactic treatment: Medical record documentation that member is currently receiving prophylactic therapy OR medical record documentation of at least one thrombotic thrombocytopenia purpura (TTP) event

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (30 approved, 0 rejected).

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 January 21st, 2025 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.