P&T Committee Meeting Minutes
Commercial, Exchange, CHIP
July 14th, 2026

Present (via Teams):	**Absent:**
Bret Yarczower, MD, MBA – Chair	Alyssa Cilia, RPh
Amir Antonious, Pharm.D.	Kimberly Clark, Pharm.D.
Leslie Astleford, Pharm.D.	Bhargavi Degapudi, MD
Emily Bednarz, Pharm.D.	Michael Dubartell, MD
Kristen Bender, Pharm.D.	Michael Evans, RPh
Jeremy Bennett, MD	Tricia Heitzman, Pharm.D.
Angela Bolesta, Pharm.D.	Nichole Hossler, MD
Kim Castelnovo, RPh	Briana LeBeau, Pharm.D.
Keri Donaldson, MD, MSCE	Lisa Mazonkey, RPh
Kelly Faust, Pharm.D.	Tyreese McCrea, Pharm.D.
Jason Howay, Pharm.D.	Perry Meadows, MD
Keith Hunsicker, Pharm.D.	Jonas Pearson, RPh
Kelli Hunsicker, Pharm.D.	Luke Sullivan, DO
Emily Jacobson, Pharm.D.	Kevin Szczecina, RPh
Dennis Janosczyk, Pharm.D.	Amanda Taylor, MD
Alexandra Kempf-Malys, MSW, BSc	
Kerry Ann Kilkenny, MD	
Philip Krebs, R.EEG T	
Lauren Lesh, Pharm.D.	
Lisa Manoski, Pharm.D.	
Ted Marines, Pharm.D.	
Jamie Miller, RPh	
Mark Mowery, Pharm.D.	
Andrei Nemoianu, MD	
Kara Pabst, Pharm.D.	
Austin Paisley, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Sartori, Pharm.D.	
Angela Scarantino	
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.	
Ariana Wendoloski, Pharm.D.	
Brandon Whiteash, Pharm.D.	
Margaret Whiteash, Pharm.D.	
Sherry Beagle (non-voting participant)	
Molly Brautigam, Pharm.D. (non-voting participant)	
Rebecca Lucas, Pharm.D. (non-voting participant)	
Jordan Maroszek Pharm.D. (non-voting participant)	
Sydney Scott Pharm.D. (non-voting participant)	
Courtney Turowski, Pharm.D. (non-voting participant)	
Madelyn Zavada, Pharm.D. (non-voting participant)	

Call to Order:
Dr. Bret Yarczower called the meeting to order at 1:02 p.m., Tuesday, July 14, 2026.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the February 2026 e-vote and May 12, 2026 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

MYQORZO (aficamten)

Review: Myqorzo is a cardiac myosin inhibitor indicated for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM) to improve functional capacity and symptoms. Myqorzo reduces cardiac contractility and left ventricular outflow tract (LVOT) obstruction through myosin inhibition. Myqorzo will compete with Camzyos, another cardiac myosin inhibitor indicated for the treatment of adults with oHCM. Although Myqorzo and Camzyos appear to have similar efficacy and labeling, Myqorzo generally appears to have the better safety profile and REMS program. The most recent (2024) American Heart Association (AHA)/American College of Cardiology Foundation (ACC) guidelines recommend CMIs for patients with symptomatic oHCM who remain symptomatic despite having received first-line therapy with β-blockers or nondihydropyridine CCBs (e.g. verapamil, diltiazem).

Initiation or up-titration of MYQORZO in patients with LVEF < 55% is not recommended. Regular LVEF and Valsalva left ventricular outflow tract gradient (LVOT-G) assessment is needed for titration to achieve target LVOT-G while maintaining LVEF ≥ 50 % and avoiding heart failure symptoms. The recommended dosage of Myqorzo is 5 mg orally once daily. The dose is increased by 5 mg every 2 to 8 weeks until a maintenance dosage or the maximum dosage of 20 mg once daily is achieved. Maintenance dosage is individualized based on LVEF and LVOT-G (Table 5).

Table 5. Dosage adjustments for Myqorzo

LVEF	Valsalva LVOT-G	Dose Adjustment
≥55%	≥30 mmHg	Increase dose by 5 mg (up to the maximum dose of 20 mg once daily)
≥55%	<30 mmHg	Maintain Dose
<55% and ≥50%	Any	Maintain Dose
<50% and ≥40%	Any	Decrease dose by 5 mg[1] If already on 5 mg, interrupt treatment for at least 7 days
<40%	Any	Interrupt treatment for at least 7 days

1. Decrease dose as follows: 20 mg to 15 mg; 15 mg to 10 mg; 10 mg to 5 mg

Myqorzo is supplied as 5 mg, 10mg, 15 mg, and 20 mg tablets.

The efficacy of Myqorzo was evaluated in SEQOUIA-HCM, a randomized, double-blind, placebo-controlled study in 282 adults with symptomatic NYHA class II and III oHCM, LVEF ≥ 60%, and resting and post-Valsalva peak LVOT-G ≥ 30 and ≥ 50 mmHg at screening, respectively. Patients completing SEQUOIA -HCM were eligible to participate in an open-label, single-arm extension study, FOREST-HCM. Patients with a known infiltrative or storage disorder causing cardiac hypertrophy such as Noonan syndrome, Fabry disease or amyloidosis were excluded from the study.

Patients were randomized 1:1 to receive Myqorzo or placebo once daily for 24 weeks. Myqorzo was initiated at 5 mg once daily and then doses were individually titrated at week 2, 4, and 6 based on Valsalva LVOT-G and LVEF up to maximum dose of 20 mg.

At baseline, 76% of the randomized patients were NYHA class II and 24% were NYHA class III. The

median LVEF was 76%, the mean resting LVOT-G was 55 mmHg, the mean Valsalva LVOTG was 83 mmHg, and mean Kansas City Cardiomyopathy Questionnaire – Clinical Summary Score (KCCQ-CSS) was 74. Sixty-one percent of patients were on beta-blockers, 29% were on non-dihydropyridine calcium channel blockers, 13% were on disopyramide, and 15% were not taking any background medication for oHCM. Mean peak oxygen uptake (pVO2) by CPET at baseline was 18.5 mL/kg/min with 55% using treadmill and 45% using bicycle.

At week 24, in the Myqorzo group, 46% of patients were taking the 20 mg dose, 35% were on the 15 mg dose, 15% were on the 10 mg dose, and 4% were on the 5 mg dose.

The primary endpoint measuring change from baseline in pVO2 to week 24 was greater with Myqorzo than placebo (Table 6).

Table 6. Change from baseline in pVO2 by CPET at Week 24 in SEQUOIA-HCM

pVO_2	**MYQORZO (N = 142)**	**Placebo (N = 140)**
Baseline (mL/min/kg), mean (SD)	18.4 (4.4)	18.6 (4.5)
Change from baseline to Week 24		
LS mean (SE)[1]	1.7 (0.3)	0.0 (0.3)
LS mean difference vs. placebo (95% CI)[1]	1.7 (1.0, 2.4)	
p-value	<0.0001	

1. LS mean (SE), and LS mean difference (95% CI) were estimated from an ANCOVA model. A placebo-based multiple imputation approach was used to impute the missing data.

At Week 24, Myqorzo showed a greater improvement in secondary endpoints compared to placebo across all secondary points (Table 7).

Table 7. Results of Secondary Efficacy Endpoints in Sequoia-HCM

Endpoints	**MYQORZO N=142**	**Placebo N=140**	**LS Mean Difference (95% CI)**	**p-Value**
Mean Change from Baseline in KCCQ-CSS[1,3]				
Week 12	11.1 (0.9)	4.0 (0.9)	7.0 (4.6, 9.5)	<0.0001
Week 24	11.6 (1.0)	4.3 (1.0)	7.3 (4.6, 10.1)	<0.0001
Mean Change from Baseline in Valsalva LVOT-G (mmHg)[1]				
Week 12	-45.0 (2.4)	2.7 (2.4)	-47.7 (-54.5, -41.0)	<0.0001
Week 24	-46.7 (2.5)	2.2 (2.5)	-48.8 (-55.7, -42.0)	<0.0001
Mean Duration of SRT Eligibility[1]				
Days spent SRT-eligible during 24 Weeks of Treatment	35 (8)	113 (8)	−78 (−100, −56)	<0.0001
Mean Change from Baseline in Total Workload (Watts) during CPET[1]				
Week 24	13.1 (2.1)	0.9 (2.2)	12.2 (6.3, 18.1)	<0.0001
Endpoints	**MYQORZO N=142**	**Placebo N=140**	**Odds Ratio (95% CI)**	**p-Value**
Proportion of Patients with ≥1 NYHA Class Improvement[2]				
Week 12	69 (48.6)	25 (17.9)	OR: 4.6 (2.6, 8.4)	<0.0001
Week 24	83 (58.5)	34 (24.3)	OR: 4.4 (2.6, 7.6)	<0.0001
Proportion of Patients with Valsalva LVOT-G <30 (mmHg)[2]				
Week 12	73 (51.4)	8 (5.7)	OR: 16.9 (7.7, 37.2)	<0.0001
Week 24	70 (49.3)	5 (3.6)	OR: 22.9 (8.8, 59.6)	<0.0001

CPET: Cardiac Pulmonary Exercise Test; KCCQ CSS: Kansas City Cardiomyopathy Questionnaire – Clinical Summary Score; NYHA: New York Heart Association; LVOT-G: left ventricular outflow tract gradient; SRT: septal reduction therapy.

1. LS means (SE) and LS mean difference (95% CI) was estimated from an ANCOVA model (mixed model with repeated measures was used for longitudinal data) for continuous endpoints. Placebo-based multiple imputation approach was used to impute the missing data.
2. The number (percentage) of responders and common Odds Ratio (OR) obtained using Cochran-Mantel-Haenszel method (95% CI) are presented for binary endpoints.
3. The KCCQ-CSS score ranges from 0 to 100, with higher scores indicating better health status.

Myqorzo has a black box warning for risk of heart failure since Myqorzo reduces cardiac contractility, and in turn reduces LVEF and can cause heart failure due to systolic dysfunction. Myqorzo is only available through a REMS program due to this risk.

Myqorzo also carries warnings for Cytochrome P450 interactions that may lead to heart failure or loss of effectiveness. Myqorzo is metabolized primarily by CYP2C9, and to a lesser extent by CYP3A, CYP2D6, and CYP2C19 enzymes. Initiation of drugs that inhibit multiple p450 pathways of Myqorzo elimination or strong CYP2C9 inhibitors and discontinuation of moderate/strong CYP2A inducers may lead to increased concentrations of Myqorzo and increased risk of heart failure. Conversely, medications that induce P450 pathways may lead to decreased blood concentrations and potential loss of effectiveness.

During the SEQUOIA -HCM trial, hypertension was the only adverse reaction observed in > 5% of patients and occurred more commonly with Myqorzo compared to placebo.

The safety and efficacy of Myqorzo has not been established in pediatric patients. In SEQUOIA-HCM included 57 (40%) patients aged 65 and older of which 12 were 75 years and older. No overall differences in safety or efficacy have been established between older and younger patients.

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

Clinical Discussion: Bret asked if there was a time correlation between being on this medication and a reduction in EF/worsening of HF. Unsure, would need to look at studies more. No further comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (31 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: Myqorzo is a pharmacy benefit and will be added to the following tiers for Commercial, Marketplace, and GHP Kids formularies. The following prior authorization criteria will apply:

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2 – Brand	Tier 3 – Brand NP	Tier 4 – Specialty	Tier 6 - Specialty

- Medical record documentation that Myqorzo is prescribed by a cardiologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy **AND**
- Medical record documentation of left ventricular ejection fraction (LVEF) greater than or equal to 55% **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two of the following: beta-blockers, non-dihydropyridine calcium channel blockers, or disopyramide

MEDISPAN AUTHORIZATION LEVEL: GPI-12

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

AUTHORIZATION DURATION: Initial approval will be for 6 months. Subsequent approvals will be for an additional 12 months and will require medical record documentation of the following:

- Medical record documentation of left ventricular ejection fraction (LVEF) greater than or equal to 50% **AND**
- Medical record documentation of clinical improvement or maintenance of condition

RPH SIGNOFF REQUIRED: Yes. Rph Signoff will be required to ensure appropriate utilization.

Additional recommendations: Based on clinical findings showing comparable efficacy between Myqorzo and Camzyos, favorable safety efficacy of Myqorzo, and the opportunity for rebates with Myqorzo, it is recommended that Camzyos be removed from the Commercial, Marketplace, and GHP Kids formularies (34 approved, 0 rejected).

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

PIVYA (pivmecillinam)

Review: Pivya is penicillin antibiotic that is indicated for the treatment of female patients who are 18 years and older with uncomplicated urinary tract infections (uUTI's) caused by susceptible isolates of Escherichia coli (E.coli), Proteus mirabilis, and Staphylococcus saprophyticus. UTI's are the most common bacterial infections in women and the most common reason for outpatient visits in the United States. Approximately one-half of adult women will have a UTI in their lifetime. UTI's are classified as uncomplicated typically in patients who are healthy, non-pregnant adults (usually females) with normal urinary anatomy, who have no underlying conditions affecting the urinary tract, and the infection is limited to the lower urinary tract without signs or symptoms of upper tract, prostate, or systemic infection. Pivmecillinam is a prodrug containing the pivaloyloxymethylester of the amidinopenicillanic acid that is metabolized to the active form of the drug mecillinam. Mecillinam, a beta-lactam antibacterial, which interferes with the bacterial cell wall and has a mode of action different from other penicillin's by exerting high specificity against penicillin-binding protein 2 (PBP-2) in the gram-negative cell wall. Pivya is a tablet that has an FDA approved dose of 185mg three times daily for three to seven days. The guidelines and other countries who have been using this medication for over 40 years utilize the dosing of 400mg twice daily for three to seven days.

Guidelines from the Infectious Diseases Society of America (IDSA) and the European Society for Microbiology and Infectious Diseases (ESMID) in 2010 recommended several therapeutic options for empiric treatment of uUTIs, including nitrofurantoin and trimethoprim/sulfamethoxazole as appropriate first-line options. Fosfomycin and pivmecillinam are also suggested as potential first-line options. However, the guidelines note that they may have lower efficacy than nitrofurantoin and trimethoprim/sulfamethoxazole. Fluoroquinolones (ofloxacin, ciprofloxacin, and levofloxacin) and beta-lactams (amoxicillin-clavulanate, cefdinir, cefaclor, and cefpodoxime proxetil) are mentioned as alternative options when first-line agents cannot be used. The guidelines indicate that trimethoprim/sulfamethoxazole should not be used if local resistance rates are >20%. In the clinical ISDA guidelines, they do provide a comparative chart with the first line treatment regimens and expected early efficacy rates based upon each medications clinical trials. It is important to note, and the guidelines do state that these estimates cannot be accurately compared across agents due to different study designs, efficacy definitions, and therapy durations.

Table 4. Treatment Regimens and Expected Early Efficacy Rates for Acute Uncomplicated Cystitis

	Mean percentage (range)			
Drug (dosage)	Estimated clinical efficacy[ab]	Estimated microbiological efficacy[b]	Common side effects	References
Nitrofurantoin monohydrate/ macrocrystals (100 mg twice daily for 5–7 days)	93 (84–95)	88 (86–92)	Nausea,headache	[36, 37, 39]
Trimethoprim-sulfamethoxazole (160/800 mg twice daily for 3 days)	93 (90–100)	94 (91–100)	Rash, urticaria,nausea, vomiting, hematologic	[36, 37]
Fosfomycin trometamol (3 g single-dose sachet)	91	80 (78–83)	Diarrhea, nausea,headache	[39, 40]
Pivmecillinam (400 mg twice daily for 3–7 days)	73 (55–82)	79 (74–84)	Nausea, vomiting, diarrhea	[29, 43]
Fluoroquinolones (dose varies by agent; 3–day regimen)[c]	90 (85–98)	91 (81–98)	Nausea/vomiting, diarrhea, headache, drowsiness, insomnia	[35, 43, 44, 46–52]
β-lactams (dose varies by agent; 3–5 day regimen)[d]	89 (79–98)	82 (74–98)	Diarrhea, nausea, vomiting, rash, urticaria	[38, 52, 54]

The safety and efficacy of Pivya was established based on four clinical trials. Trial 1 was a multicenter, randomized, double-blind study that was conducted in Sweden. It was designed to evaluate three different dosage regimens of Pivya compared to placebo. They included females who were 18 years of age or older with symptoms of uUTI's. The primary endpoint was the complete response rate, which was defined as the composite endpoint of clinical cure and microbiological response. The participants were randomized to receive one of the following: 185 mg TID for 7 days, 185 mg BID for 7 days, 370 mg BID for 3 days or placebo. Pivya demonstrated efficacy for the composite response of clinical cure and microbiological response at day 8-10. A complete response was achieved in 85/137 (62%) patients in the Pivya groups compared to 14/134 (10%) in the placebo group. Trial 2 was a multicenter, randomized, double-blind study in the United States that compared Pivya to cephalexin in females who were 18 years or older with a diagnosis of uUTI. It utilized the same primary end point as Trial 1 did. The interventions in this trial were Pivya 185 mg TID for 3 days or cephalexin 250mg QID for 7 days. The results showed a complete response rate achieved in 91/127 (72%) of patients in the Pivya group and 100/132 (76%) in the cephalexin group. Trial 3 did look at efficacy and was a safety only trial. Trial 4 was a multicenter, randomized, double-blind, noninferiority study in Denmark, Norway, and Sweden that compared Pivya to ibuprofen in females aged 18–60 years old with clinical symptoms of uUTI. The primary endpoint was the complete response rate at day 14. The participants were randomized to receive Pivya 185mg TID for 3 days or ibuprofen 600mg TID for 3 days. The results showed that Pivya demonstrated efficacy at day 14 in 69/105 patients (66%) achieving a complete response compared to 26/199 (22%) in the Ibuprofen group.

Trial 1, 2 and 3 were utilized to evaluate the safety of the medication. In Trial 1, the most common adverse reactions observed in ≥2% of the patients receiving Pivya included nausea (4.3%) and diarrhea (2.1%). In Trial 2 and Trial 3, the most common adverse reaction occurring in ≥1% of patients receiving Pivya was nausea with an incidence of 1.4% in Trial 2 and 3.6% in Trial 3. No serious adverse events were reported in any of the trials. Trial 4 did not evaluate safety of the medication. One contraindication to Pivya include hypersensitivity to pivmecillinam, other beta-lactam antibacterials (such as: penicillin's, cephalosporins, or carbapenems), or any component of the formulation. Additionally, Pivya is contraindicated in patients with a primary or secondary carnitine deficiency resulting from inherited disorders of mitochondrial fatty acid oxidation and carnitine metabolism, and other inborn errors of metabolism. This is due to potential carnitine depletion when using the medication long term but was not associated with short term use of the medication. Lastly, it is contraindicated in patients with porphyria, as it can lead to acute attacks.

There are no dose adjustments recommended in kidney or liver impairment. The active metabolite of Pivya does cross the placenta leading to low concentrations being detected in the fetus and amniotic fluid. As a class, penicillin antibiotics are widely used in pregnant patients. Based on available data, penicillin antibiotics are generally considered compatible for use during pregnancy, but maternal use of the medication may cause a false-positive test for isovaleric acidemia during newborn screening if administered shortly before delivery. Maternal adverse events may be increased with pivmecillinam compared to other antibiotics used for UTIs during pregnancy. Data is insuffient on the use to quantify the active metabolite in breast milk and recommended if used to monitor infants for GI disturbances such as diarrhea or thrush. Per the FDA labeling use is only recommended in adults aged 18 years or older. There is some limited data in children and adolescents. There are no additional considerations for use in the geriatric population.

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

Clinical Discussion: Bret asked to confirm the response rate in the clinical study of 66%. They looked at it as a composite endpoint, so the clinical and the microbiological together. No further comments or questions. 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 (33 approved, 0 rejected).

Outcome: Pivya is a pharmacy benefit which will not be added to the Commercial, Marketplace, or CHIP formularies. Exception requests will be reviewed with the following criteria:

- Medical record documentation of use for treatment of uncomplicated urinary tract infection in a female patient **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that the infection is caused by one of the following susceptible organisms: Escherichia coli (E. coli), Proteus mirabilis or Staphylococcus saprophyticus **AND**
- Medical record documentation of therapeutic failure on, intolerance to, contraindication to, or bacterial resistance to 2 formulary alternatives

GPI LEVEL: GPI-12

AUTHORIZATION DURATION: 7 days (per label)

QUANTITY LIMIT: 3 tablets per day

FORMULARY ALTERNATIVES: nitrofurantoin, sulfamethoxazole-trimethoprim, fosfomycin

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.

YUVIWEL (navepegritide)

Review: Yuviwel is a C-type natriuretic peptide (CNP) analog indicated to increase linear growth in pediatric patients 2 years of age and older with achondroplasia with open epiphyses. This was an accelerated approval based on an improvement in annualized growth velocity. The only other treatment approved for ACH is Voxzogo which is another CNP analog. Voxzogo is administered daily while Yuviwel is administered once weekly.

The recommended dosage is a once weekly subcutaneous administration based on patients body weight (Table 5).

Table 5. Recommended Yuviwel weekly dosage and Injection volume

Patient Body weight	Weekly Dose	Injection Volume	Vial Strength for Reconstitution*
8 to 9.9 kg	0.88 mg	0.4 mL	1.3 mg
10 to 13.4 kg	1.2 mg	0.55 mL	
13.5 to 17.5 kg	1.6 mg	0.35 mL	2.8 mg
17.6 to 23 kg	2.1 mg	0.45 mL	
23.1 to 30.5 kg	2.8 mg	0.6 mL	
30.6 to 41.2 kg	3.6 mg	0.65 mL	5.5 mg
41.3 to 55.9 kg	5 mg	0.9 mL	
56 to 73.5 kg	6.6 mg	1.2 mL (use 2 Kits) Administer 0.6 mL from each Kit	
73.6 to 90 kg	8.8 mg	1.6 mL (use 2 Kits) Administer 0.8 mL from each Kit	

*The concentration of navepegritide is 2.2 mg/mL in a reconstituted 1.3 mg vial; 4.6 mg/mL in a reconstituted 2.8 mg vial; and 5.5 mg/mL in a reconstituted 5.5 mg vial.

If switching from the once daily CNP analog, Yuviwel should be started the day after the last daily dose of CNP therapy. Patient growth should be monitored and the dosage should be adjusted accordingly. Yuviwel should be discontinued upon confirmation of no further growth potential, indicated by closure of the epiphyses. Yuviwel is supplied as single dose vials containing 1.3 mg, 2.8 mg, and 5.5 mg of Yuviwel for injection.

The efficacy of Yuviwel was established in Trial 1, a randomized, double-blind, placebo-controlled 52 week study, followed by a single arm, 52-week open-label extension period. Trial 1 enrolled 84 treatment naïve pediatric patients with genetically confirmed achondroplasia. Fifty-seven patients received Yuviwel while 27 patients received placebo.

The primary efficacy endpoint was annualized growth velocity (AGV) at Week 52. Height Z-scores calculated using reference data from untreated children with achondroplasia (achondroplasia-specific height Z-score) and using reference data from the general population (CDC-based height Z-score) were also evaluated.

Treatment with Yuviwel resulted in least-squares mean treatment difference in AVG of 1.5 cm/year and a least-squares mean increase from baseline in achondroplasia-specific height Z-score of 0.3 (Table 6).

Table 6: Growth Parameters in Pediatric Patients with Achondroplasia Treated with Yuviwel and Placebo at Week 52 in Trial 1

	NAVEPEGRITIDE (N = 57)	**Placebo (N = 27)**	**Treatment Difference [95% CI][a]**	**p-value**
Annualized growth velocity (cm/year)	5.9	4.4	1.5 [1.0, 1.9]	< 0.0001
Change from baseline				
Achondroplasia-specific height Z-score[b]	0.3	0.0	0.3 [0.2, 0.4]	< 0.0001
CDC height Z-score[c]	0.1	-0.2	0.3 [0.1, 0.5]	NA[d]

Note: Data presented are least-square (LS) means unless otherwise noted. Abbreviations: AGV, annualized growth velocity; CI, confidence interval; NA, not applicable. aTreatment differences between YUVIWEL and placebo were estimated from an analysis of covariance (ANCOVA) model that included treatment, strata (defined by sex and age), baseline age, and baseline achondroplasia-specific height Z-score as covariates. bCalculated using the reference data from untreated patients with achondroplasia (CLARITY Natural History Study). cCalculated using the Centers for Disease Control and Prevention (CDC) reference data from the general population. dThe endpoint was analyzed outside of the pre-specified multiple testing strategy.

In patients < 5 years of age, the least squares mean treatment difference for AGV at Week 52 was 1.0 cm/year. In patients ≥ 5 years of age, the least squares mean treatment difference was 1.8 cm/year.

In the OLE, AGV was maintained among those who had received 2 years of treatment with Yuviwel 0.1 mg/kg once weekly.

Warnings and precautions include risk of low blood pressure based on adverse reactions reported with once daily CNP analogs. In clinical trials, the most common reported adverse reactions were vomiting, injection-site reaction, pain in extremity, and nausea. Injection-site reactions could include swelling, erythema, bruising, pruritus, discoloration, hemorrhage, pain, vesicles, and edema.

The safety and effectiveness of Yuviwel to increase linear growth have been established in pediatric patients aged 2 years and older with achondroplasia with open epiphyses. Safety and efficacy has not

been established in pediatric patients less than 2 years of age.

Safety and effectiveness has not been evaluated in the geriatric population as it is only indicated in pediatric patients with open epiphyses.

Yuviwel is not recommended for patients with moderate or severe renal impairment. No dosage adjustment is needed for patients with mild 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 (31 approved, 0 rejected).

Financial Discussion: Bret asked why we wouldn't prefer Voxogo or require trial/failure of such. Kim will look into this further and will add to criteria if appropriate. No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (32 approved, 0 rejected).

Outcome: Yuviwel 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 a diagnosis of achondroplasia with genetic testing confirming a mutation of FGFR3 **AND**
- Medical record documentation that Yuviwel is prescribed by a pediatric endocrinologist **AND**
- Medical record documentation that member is greater than 2 years of age to less than 18 years of age **AND**
- Medical record documentation of evidence that member has open epiphyses **AND**
- Medical record documentation that member has not received (within the past 18 months) or plans to receive limb-lengthening surgery **AND**
- Medical record documentation that Yuviwel will not be used in combination with human growth hormone products **AND**
- Medical record documentation of glomerular filtration rate (GFR) greater than 60 ml/min/1.73m^2 **AND**
- Medical record documentation of member's current weight **AND**
- Medical record documentation that prescribed dose is appropriate for member's current weight **AND**
- Medical record documentation of baseline annualized growth velocity (AGV), calculated based on standing height measured over the course of 6 months prior to request **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to Voxzogo

AUTHORIZATION DURATION: Each treatment period will be defined as six (6) months. Re-review with occur every six (6) months. Yuviwel will no longer be covered if medical record documentation does not show:

- Medical record documentation of positive response to Yuviwel, as evidenced by improvement in annualized growth velocity (AGV) from baseline **AND**
- Medical record documentation of evidence that member continues to have open epiphyses **AND**
- Medical record documentation that member has not received (within the past 18 months) or plans to receive limb-lengthening surgery **AND**
- Medical record documentation that Yuviwel will not be used in combination with human growth hormone products **AND**
- Medical record documentation of glomerular filtration rate (GFR) greater than 60 ml/min/1.73m^2 **AND**
- Medical record documentation of member's current weight **AND**
- Medical record documentation that prescribed dose is appropriate for member's current weight

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT:

- 1.3 mg and 2.8 mg single-dose vials: 4 vials (4 kits) per 28 days, 28 day supply per fill
- 5.5 mg single-dose vial: 8 vials (8 kits) per 28 days, 28 day supply per fill

RPH SIGNOFF REQUIRED: Yes. Rph Signoff will be required to ensure appropriate utilization.

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

REZENOPY (naloxone nasal spray)

Review: Rezenopy is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression in adult and pediatric patients. Rezenopy is intended for immediate administration as emergency therapy in settings where opioids may be present and is not a substitute for emergency care.

Rezenopy is a 10mg/0.11mL nasal spray for intranasal use only and contains a single dose of naloxone. It is administered into one nostril, and nostrils should be alternated with each dose. If the desired response is not obtained after 2 to 3 minutes, an additional dose of Rezenopy may be administered. If there is still no response and additional doses are available, additional doses may be administered every 2 to 3 minutes, alternating nostrils, and using a new Rezenopy nasal spray until emergency medical assistance arrives. If the patient responds to Rezenopy and relapses back into respiratory depression before emergency medical assistance arrives, an additional dose should be administered along with continued surveillance of the patient.

No clinical studies were conducted for the approval of Rezenopy. Approval was based on a pharmacokinetic study in 30 healthy adults which compared a single dose of 10mg Rezenopy intranasally, 0.4mg naloxone intramuscularly, and 2mg naloxone intravenously. The study showed that Rezenopy had a significantly higher maximum concentration (Cmax) and area under the curve (AUC) compared to a single intramuscular injection of 0.4 mg naloxone shown in Table 1 and Figure 1. Since the plasma concentration threshold was met, clinical efficacy to reverse opioid effects was established.

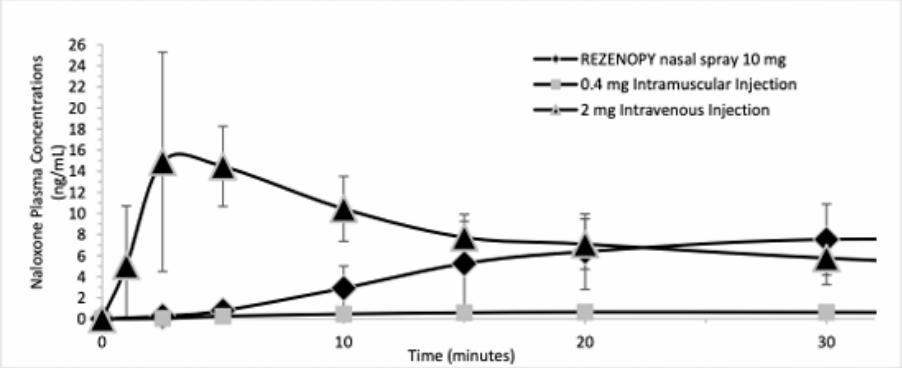
Table 1 Mean Pharmacokinetic Parameters (CV%) for REZENOPY nasal spray, Intramuscular and Intravenous Injections of Naloxone HCl to Healthy Subjects

Parameter	REZENOPY nasal spray 10 mg (n=29)	Naloxone HCl 0.4 mg Intramuscular Injection (n=30)	Naloxone HCl 2 mg Intravenous Injection (n=23)
t_{max} (h)†	0.75 (0.25, 1.03)	0.50 (0.17, 2.00)	0.08 (0.02, 0.18)
C_{max} (ng/mL)	9.11 (35.45)	0.74 (36.63)	18.41 (46.08)
AUCt (h·ng/mL)	19.19 (24.81)	1.92 (19.75)	12.18 (24.30)
$AUC_{0-\infty}$ (h·ng/mL)	19.52 (24.78)	1.98 (19.18)	12.25 (24.22)
$t_{½}$ (h)	1.33 (16.09)	1.22 (18.48)	1.18 (11.59)
Dose normalized absolute BA vs. IV††	0.34 (30.53)	0.84 (29.06)	-

† t_{max} reported as median (minimum, maximum)

†† N=22 and N=23, respectively for REZENOPY nasal spray 10 mg and Naloxone HCl 0.4 mg Intramuscular Injection for Dose normalized absolute BA vs. IV

Figure 1 Mean ± SD Plasma Concentration of Naloxone 0-30 minutes Following Intranasal, Intramuscular and Intravenous Administration.



No comparison studies have been conducted to show superiority compared to lower doses and no pediatric studies were conducted for Rezenopy. Use of Rezenopy in pediatric patients is supported by adult bioequivalence studies and evidence from the safe and effective use of other naloxone products.

Warnings and precautions are similar to other naloxone products which includes risk of recurrent respiratory and/or CNS depression, risk of limited efficacy with partial agonists or mixed agonist/antagonists such as buprenorphine and pentazocine, and precipitation of severe opioid withdrawal. Adverse reactions for Rezenopy are consistent with other naloxone products and additional adverse reactions specifically reported in the Rezenopy clinical study were upper abdominal pain, nasopharyngitis, and dysgeusia.

Currently, there are several FDA-approved naloxone products available in different strengths and formulations. All products act rapidly to reverse an opioid overdose, with no known difference in effectiveness between intranasal and intramuscular administration in community settings. Higher doses of naloxone are associated with an increased likelihood of withdrawal symptoms. Rezenopy was approved on pharmacokinetic data, and the manufacturer did not provide clinical evidence demonstrating improved efficacy for higher dose naloxone for reversing high-potency opioid overdose. Guidance from the Substance Abuse and Mental Health Services Administration (SAMHSA) indicates that administering higher doses or multiple doses of naloxone may not always be necessary, even when responding to a fentanyl overdose, and does not necessarily accelerate reversal or improve outcomes. According to the FDA's Benefit-Risk Assessment, approximately 92.9% of opioid overdose events are managed with one to two doses of naloxone, with only a small proportion receiving doses of 8 mg or more.

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 (33 approved, 0 rejected).

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

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

YARTEMLEA (narsoplimb-wuug)

Review: Yartemlea is indicated for the treatment of adult and pediatric patients 2 years of age and older with hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA). Yartemlea inhibits mannan-binding lectin-associated serine protease-2 and lectin-dependent activation of complement component 3 (C3) and C4, preventing lectin pathway-mediated cellular injury. Yartemlea does not affect the classical or alternative pathways of complement. Yartemlea is the first FDA approved treatment for TA-TMA.

Thrombotic microangiopathy (TMA) is widespread microvascular thrombosis that results in syndromes characterized by microangiopathic hemolytic anemia, thrombocytopenia, and organ injury, most commonly affecting the kidney and brain. TMA can be classified as primary which occurs in the absence of an underlying condition (i.e. thrombotic thrombocytopenic purpura [TTP] and hemolytic uremic syndrome [HUS]), or secondary which develops following a precipitating factor such as malignancy, autoimmune disease, or HSCT. Clinical presentation varies from patient to patient and can range from mild and self-limited to severe and rapidly progressing. Severe TMA resulting from a HSCT (TA-TMA) can lead to end-organ dysfunction, multiple organ dysfunction syndrome (MODS) and even death. TA-TMA can affect both adults and pediatric patients and can occur following both allogeneic and autologous HSCT (significantly higher following allo-HSCT).

Yartemlea is administered as an intravenous infusion based on patients' weight. For adults and pediatric patients 2 years and older weighing greater than or equal to 50 kg the recommended dosage is 370 mg once weekly. The dosage can be increased to twice weekly if there is inadequate improvement in TA-TMA signs and symptoms. For patients weighing less than 50 kg, the recommended dosage is 4 mg/kg once weekly (increased to twice weekly if needed). Yartemlea is supplied as single-dose vials containing 370 mg/2 mL.

The efficacy of Yartemlea was assessed in a single-arm, open-label in 28 adult patients with TA-TMA following HSCT and 19 adults and pediatric patients with TA-TMA enrolled in an expanded access program.

The TA-TMA Study patients had a confirmed diagnosis of TA-TMA per the diagnostic criteria as follows: platelet count < 150,000/μL, evidence of microangiopathic hemolysis (presence of schistocytes, serum LDH greater than the upper limit of normal [ULN] and/or haptoglobin less than the lower limit of normal [LLN]), and renal dysfunction. Patients in the EAP were similarly thrombocytopenic with evidence of microangiopathic hemolytic anemia. The primary efficacy endpoint was based on TMA response defined as both two laboratory TMA markers (LDH and platelet counts) and either improvement in organ function or independence from transfusions.

TA-TMA response was achieved in 17/28 (60.7%) patients in the TA-TMA study and 13/19 (68.4%) patients in the EAP (Table 3).

Table 3. Efficacy Results for TA-TMA Study and Expanded Access Program

	TA-TMA Study	Expanded Access Program (N = 19)	
	Adult (N = 28)	Pediatric (n = 6)	Adult (n = 13)
TMA response 95% CI [a]	17/28 (61%) (40.6, 78.5)	4/6 (67%) (22.3, 95.7)	9/13 (69%) (38.6, 90.9)
Improvement in TMA markers Platelet count LDH	17/28 (61%) 14/23 (61%)[b] 21/28 (75%)	4/6 (67%) 4/6 (67%) 5/6 (83%)	9/13 (69%) 9/13 (69%) 11/13 (85%)
Improvement in organ function	20/27 (74%)[b]	5/6 (83%)	11/13 (85%)
Freedom from red blood cell or platelet transfusion[c]	12/25 (48%)[b]	3/5 (60%)[b]	9/13 (69%)

[a]Confidence intervals were calculated using the exact (Clopper–Pearson) method.
[b]These component findings are based on the number of patients with evaluable data.
[c]Defined as no transfusions for at least the last 4 weeks from the last transfusion; only evaluated in patients who had received transfusions within 2 weeks prior to or on the first Yartemlea dose

In the TA-TMA Study and EAP study, 100-day survival from time of TMA diagnosis was 73.4% and 73.7%, respectively.

Warnings and precautions include the risk of serious and life-threatening infections, including sepsis, viral infections, pneumonia, bacteremia, fungal infection, gastroenteritis, respiratory tract infection, and urosepsis. In clinical trials, serious adverse reactions were reported in 61% of patients treated with Yartemlea, including acute kidney injury, confusional state, acute respiratory failure, neutropenic sepsis, septic shock, pulmonary edema, and vomiting. Fatal adverse reactions occurred in 7% of patients, including neutropenic sepsis and septic shock. Dose interruptions due to adverse reactions were reported in 7% of patients. The most common adverse reactions were viral infections, sepsis, hemorrhage, diarrhea, vomiting, nausea, neutropenia, pyrexia, fatigue, and hypokalemia.

The safety and efficacy of Yartemlea for the treatment of TA-TMA have been established in pediatric patients 2 years and older, supported by evidence from studies in adults and in 6 pediatric patients and additional safety data in 83 pediatric patients 2 years and older. Safety and efficacy have not been established in pediatric patients under 2 years of age. In the clinical trial and EAP for TA-TMA, 21 (8.4%) patients were 65 years of age and older while 1 (0.4%) were at least 75 years of age. Clinical studies did not include sufficient numbers of subjects 65 years of age or older to determine if they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between elderly 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: Bret asked if we should have a criteria point with this medication not being used with another complement inhibitor. Kim will research and/or ask specialists for input and will consider adding. No further 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 (28 approved, 0 rejected).

Outcome: Yartemlea is a medical benefit for Commercial, Marketplace, and GHP Kids. It will be added to the medical benefit cost share list. When processing at a Specialty pharmacy, Yartemlea will process on the following tiers:

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2 – Brand	Tier 3 – Brand NP	Tier 4 – Specialty	Tier 6 - Specialty

- Medical record documentation of age greater than or equal to 2 years of age **AND**
- Medical record documentation that Yartemlea is prescribed by a hematologist, oncologist, or a transplant specialist **AND**
- Medical record documentation of previous hematopoietic stem cell transplant (HSCT) **AND**
- Medical record documentation of a diagnosis of thrombotic microangiopathy (TMA) confirmed by the following:
    - Platelet count less than or equal to 150,000 / µL **AND**
    - Evidence of microangiopathic hemolysis, including but not limited to presence of schistocytes, serum lactate dehydrogenase (LDH) greater than the upper limit of normal (ULN) or haptoglobin less than the lower limit of normal (LLN) **AND**
    - Evidence of renal dysfunction **AND**
- If the initial request is for 370 mg twice weekly: Medical record documentation of inadequate response to signs and symptoms of hematopoietic stem cell transplant (HSCT)-associated thrombotic microangiopathy (TA-TMA) to 370 mg once weekly dosing

GPI LEVEL: GPI-12

QUANTITY LIMIT: 8 milliliters per 28 days, 28 day supply per fill

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

- Medical record documentation of a positive response to Yartemlea with improvement in the signs and symptoms of hematopoietic stem cell transplant (HSCT)-associated thrombotic microangiopathy (TA-TMA), including but not limited to improvement in platelet count, reduction of serum lactate dehydrogenase (LDH), increase of haptoglobin, improvement or stabilization of organ function, or reduction or elimination of red blood cell or platelet transfusion requirements **OR**
- Medical record documentation of inadequate response to signs and symptoms of hematopoietic stem cell transplant (HSCT)-associated thrombotic microangiopathy (TA-TMA) AND member requires an escalation in dosing frequency to a maximum of 370 mg administered twice weekly

RPH SIGNOFF REQUIRED: Yes. Rph Signoff will be required to ensure appropriate utilization.

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

ZYCUBO (copper histidinate)

Review: Zycubo is a copper replacement product indicated for the treatment of Menkes disease in pediatric patients. Zycubo is not indicated for the treatment of Occipital Horn Syndrome. Zycubo is the first treatment FDA-approved for Menkes disease.

Menkes disease is an X-linked recessive disorder caused by pathogenic variants in the copper transport ATPase encoded by ATP7A. Patients with Menkes disease have impaired absorption of copper from their diet, impaired transport of copper across the blood-brain barrier, and dysregulation of many copper-

dependent enzymes. Zycubo is a bioavailable copper replacement therapy that is administered as a subcutaneous injection to bypass the impaired gastrointestinal absorption observed in patients with Menkes disease.

The recommended dosage of Zycubo in pediatric patients less than 1 year of age is 1.45 mg administered subcutaneously twice daily (8-12 hours between injections). The recommended dose for pediatric patients 1 year of age to less than 17 years of age is 1.45 mg administered subcutaneously once daily.

Zycubo is manufactured as 2.9 mg of copper histidinate (equivalent to 0.5 mg elemental copper) as a blue lyophilized powder or cake in a single-dose vial for reconstitution.
The primary efficacy analysis compared the overall survival in patients in the Zycubo-ET and EC-ET cohorts. Patients in the Zycubo-ET cohort had a significant improvement in overall survival compared to patients in the EC-ET cohort, with a 78% reduction in the risk of death. In the Zycubo-ET cohort, 48% of patients survived > 6 years, including 23% of patients who survived > 12 years. In the EC-ET cohort, no patients survived > 6 years. The primary efficacy results are summarized in Table 2.

Table 2: Overall Survival in Zycubo Early Treatment and External Control Early Treatment Cohorts with Menkes Disease

	ZYCUBO-Early Treatment (n=31)	**External Control-Early Treatment (n=17)**
Number (%) of Patients Alive	16 (52%)	2 (12%)
Median survival time (months) (95% CI)	177.1 (33, NE)	17.6 (11.5, 28.6)
Hazard Ratio (95% CI)	0.22 (0.10, 0.49)	

CI=Confidence Interval; NE=Not estimable
Note: If death dates were unknown, patients were censored at the last known date alive.

The secondary efficacy analysis compared the overall survival in patients in the Zycubo-LT cohort with patients in the EC-LY cohort. Patients in the Zycubo-LT cohort had a significant improvement in overall survival compared to patients in the EC-LT cohort, with a 73% reduction in the risk of death. In the Zycubo-LT cohort, 31.4% of patients survived > 6 years, including 1 patient who survived > 12 years. In the EC-LT cohort, no patients survived > 6 years.

The most common adverse reactions (incidence ≥ 7%) were pneumonia, viral infection, respiratory failure, seizure, bacterial infection, hemorrhage, hypotension, vomiting, tachycardia, pyrexia, volume depletion, fracture, dyspnea, transaminases elevation, diarrhea, fungal infection, anemia, and local administration reaction

Menkes disease is a disease of pediatric patients so clinical trials did not include patients 65 years of age and older

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (28 approved, 0 rejected).

Financial Discussion: Bret asked if we have any members with Menkes disease and if we've had any utilization of Zycubo to date. Mark confirm that we have two members who have received Zycubo in the GHP Family line of business. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (29 approved, 0 rejected).

Outcome: Zycubo will be a pharmacy benefit and will be added to the Commercial/Exchange/CHIP

formularies at the Specialty tier or the Brand Non-Preferred tier for those with a three-tier benefit. The following prior authorization criteria will apply:

- Medical record documentation that the member is less than 17 years of age **AND**
- Medical record documentation that Zycubo is prescribed by or in consultation with a geneticist, neonatologist, neurologist, or a provider who specializes in the diagnosis and treatment of Menkes disease **AND**
- Medical record documentation of a confirmed diagnosis of Menkes disease demonstrated by ALL of the following:
    - One of the following:
        - Molecular genetic testing confirming ATP7A gene mutation **OR**
        - Plasma catecholamine analysis findings that are consistent with a diagnosis of Menkes disease (DOPAC:DHPG ratio greater than 5 or DA:NE ratio greater than 0.2) **AND**
    - Documentation of clinical signs and symptoms consistent with a diagnosis of Menkes disease (e.g., characteristic hair abnormalities [sparse, hypopigmented, brittle, and crinkly hair], osteoporosis, seizures, hypotonia, unstable body temperature, failure to thrive, developmental delay or regression) **AND**
- Medical record documentation of baseline serum copper and ceruloplasmin levels to be used to evaluate efficacy upon renewal **AND**
- Medical record documentation of a prescribed dose and administration that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

NOTE TO REVIEWER: Zycubo is not indicated for the treatment of Occipital Horn Syndrome, a milder type of Menkes disease.

AUTHORIZATION DURATION: Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of continued disease improvement or lack of disease progression as evidenced by:

- Improvement in serum copper and ceruloplasmin levels compared to baseline AND
- Improvement in signs and symptoms of Menkes disease

The medication will no longer be covered if patient experiences toxicity or worsening of disease.

QUANTITY LIMIT:

- Less than 1 year of age: 1.45 mg twice daily (2 vials per day)
- 1 year to < 17 years of age: 1.45 mg daily (1 vial per day)

RPH SIGNOFF REQUIRED: Yes

MEDISPAN AUTHORIZATION LEVEL: GPI-12

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

AVOPEF (etoposide)

Review: Avopef is a new formulation of etoposide supplied in multi-dose vials containing ready to use solution (no reconstitution needed). It is supplied as 100 mg/5mL solution for injection. At this time, Avopef is approved for the treatment of refractory testicular cancer and small cell lung cancer.

Avopef solution is diluted to 0.2 to 0.4 mg/mL which is then administered over 30 to 60 minutes by intravenous infusion. The recommended dosage for refractory testicular cancer is 50 mg/m^2 to 100 mg/m^2 daily on Days 1 to 5 or 100 mg/m^2 intravenously daily on Days 1, 3, and 5. The cycle is repeated every 3 to 4 weeks. The recommended dosage for Small Cell Lung Cancer is 35 mg/m^2 intravenously daily on Days 1 to 4 or 50 mg/m^2 intravenously daily on Days 1 to 5. The cycle is repeated every 3 to 4 weeks.

No new clinical trials were conducted to evaluate Avopef and safety and efficacy is based on clinical findings of etoposide.

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 (26 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (27 approved, 0 rejected).

Outcome: Avopef is a medical benefit and will require a prior authorization. It will be added to the medical benefit cost share list. When processed at a Specialty Pharmacy, Avopef will process on the following tiers:

2 Tier/CHIP	**3 Tier**	**4 Tier**	**ACA**
Tier 2 – Brand	Tier 3 – Brand NP	Tier 4 – Specialty	Tier 6 - Specialty

The following prior authorization criteria will apply:

- Medical record documentation that Avopef 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 refractory testicular cancer **OR** Medical record documentation of small cell lung cancer **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to generic etoposide products

GPI LEVEL: GPI-12

AUTHORIZATION DURATION: 6 months

RPH SIGNOFF REQUIRED: Yes. Rph signoff will be required to ensure appropriate utilization.

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

FAVLYXA (fluorouracil)

Review: Favlyxa is a new formulation of fluorouracil supplied in multi-dose vials containing ready to use solution (no reconstitution needed). It is supplied as 250 mg/10mL single-dose vial solution for injection. Favlyxa is approved for the treatment adenocarcinoma of the colon and rectum, adenocarcinoma of the breast, gastric adenocarcinoma, and pancreatic adenocarcinoma.

Favlyxa is recommended for administration as an intravenous bolus or an intravenous infusion at the following doses:

Adenocarcinoma of the Colon and Rectum

- In combination with leucovorin or as a component of a multidrug chemotherapy regimen that includes leucovorin (infusional regimen): 400 mg/m^2 for one dose, followed by 2,400 mg/m^2 to 3,000 mg/m^2 over 46 hours on day 1 of each 2-week cycle or

- In combination with leucovorin (bolus regimen): 500 mg/m^2 on days 1, 8, 15, 22, 29 and 36 of each 8-week cycle.

Adenocarcinoma of the Breast

- in combination with a cyclophosphamide based multidrug regimen: 500 mg/m^2 or 600 mg/m^2 on days 1 and 8 of each 28-day cycle (bolus regimen).

Gastric Adenocarcinoma

- in combination with a platinum-containing multidrug regimen: 200 mg/m^2 to 1,000 mg/m^2 over 24 hours (infusional regimen).

Pancreatic Adenocarcinoma

- in combination with leucovorin or as a component of a multidrug chemotherapy regimen that includes leucovorin: 400 mg/m^2 on day 1, followed by 2,400 mg/m^2 over 46 hours every 2 weeks (infusional regimen).

No new clinical trials were conducted to evaluate Favlyxa and safety and efficacy is based on clinical findings of fluorouracil. The safety and efficacy has not been established in pediatric 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 (27 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (29 approved, 0 rejected).

Outcome: Favlyxa is a medical benefit and will require a prior authorization. It will be added to the medical benefit cost share list. It will be excluded from Specialty pharmacy. The following prior authorization criteria will apply:

- Medical record documentation that Avopef 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 one of the following:
    - Adenocarcinoma of the Colon and Rectum **OR**
    - Adenocarcinoma of the Breast **OR**
    - Gastric Adenocarcinoma **OR**
    - Pancreatic Adenocarcinoma **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to generic fluorouracil products

GPI LEVEL: GPI-12

AUTHORIZATION DURATION: 6 months

Require RPH Sign off: Yes. Rph signoff will be required to ensure appropriate utilization.

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

BYSANTI (milsaperidone)

Review: Bysanti is an oral atypical antipsychotic indicated for the treatment of schizophrenia in adults AND for the acute treatment of manic or mixed episodes associated with bipolar I disorder (BD-I) in adults. Milsaperidone is a new chemical entity; however, it rapidly interconverts in vivo with iloperidone which is approved as Fanapt (iloperidone) by the same manufacturer, Vanda Pharmaceuticals, for the same indications as Bysanti. The mechanism of action of Bysanti is unknown, but it is thought that the

efficacy of milsaperidone could be mediated through a combination of dopamine type 2 (D2) and serotonin type 2 (5-HT2) antagonism and it has an in vitro receptor binding profile similar to iloperidone.

Schizophrenia is a complex mental health condition that significantly impacts patients and their families, characterized by hallucinations, delusions, disordered thinking, and cognitive impairment. Schizophrenia is typically diagnosed in patient's late teens to early 30s, generally affects males and females equally (possible earlier onset in males), and is estimated that the U.S. prevalence is between 0.25% and 1.62%. Patients with schizophrenia may have difficulty maintaining employment, living independently, and managing relationships. Bipolar disorder (BD) is also a complex mental health condition. BD can be chronic or episodic, usually involving extreme ranges of mood changes from manic/excessively elevated moods to depressive phases, with the duration and severity varying between individuals. BD has subtypes that include BD-I and bipolar II disorder (BD-II). BD-I is characterized by manic episodes lasting at least 7 days or during which the severity of the manic symptoms requires hospital care; depressive episodes in patients with BD-I typically last at least 2 weeks. BD-II is characterized by at least one episode of hypomania, one episode of major depression, and no history of mania. It is estimated that the U.S. prevalence of BD is 2.8%.

There is no cure for schizophrenia; the treatment approach includes both pharmacologic agents and psychological interventions for first-episodes of psychosis, acute exacerbations, and preventing relapse. First-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs) are effective for acute and maintenance phases of schizophrenia, with both having established efficacy in the positive symptoms (i.e. hallucinations, delusions) but limited efficacy in cognitive or negative symptoms. FGAs and SGAs have high rates of sides effects, including extrapyramidal side effects (EPSs), weight gain, QTc prolongation, and increased risk for diabetes. It is estimated that 30% of patients have treatment-resistant schizophrenia (defined as persistence of positive symptoms despite 2 or more trials of antipsychotic medication). Clozapine is the only pharmacotherapy indicated for treatment-resistant schizophrenia but is associated with severe adverse events. The APA Practice Guideline for the Treatment of Patients with Schizophrenia (APA 2020) highlights the challenge in developing a treatment algorithm for FGAs and SGAs due to limited data and trial designs; therefore, there is no definitive evidence to support one antipsychotic as consistently superior, with the potential exception of clozapine. This makes treatment selection for schizophrenia complex and patient specific. The treatment of BD involves medications, psychotherapy, or a combination of treatments. Mood stabilizers and SGAs are the most common medications used in treatment of BD. Antidepressants are not used alone for treatment of BD because they can trigger a manic episode and may cause rapid cycling, but they may be added on in patients with BD experiencing a depressive episode.

Bysanti is an oral atypical antipsychotic available as 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, and 12 mg tablets. Bysanti should be titrated to reduce the risk of orthostatic hypotension and can be administered with or without food. It is administered orally twice daily at a maintenance dose of 6-12 mg for schizophrenia or 12 mg for BD-I, following a titration period. It is recommended to consider CYP2D6 genetic testing to determine the patient's metabolizer status prior to Bysanti initiation. The following tables summarize the titration schedules in adult patients and in patients who are CYP2D6 poor metabolizers.

Table 1. Bysanti Recommended Dosage in Adults with Schizophrenia or Manic or Mixed Episodes Associated with Bipolar I Disorder

Population	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Recommended Maintenance Dosage
Schizophrenia	1 mg twice daily	2 mg twice daily	4 mg twice daily	6 mg twice daily	8 mg twice daily*	10 mg twice daily*	12 mg twice daily*	6 mg to 12 mg twice daily

Manic or Mixed Episodes Associated with Bipolar I Disorder	1 mg twice daily	3 mg twice daily	6 mg twice daily	9 mg twice daily	12 mg twice daily	Titration complete	12 mg twice daily

* Patients with schizophrenia may either (1) follow the recommended titration schedule, OR (2) starting on Day 5, continue 6 mg twice daily BYSTANTI dosing. As needed, titrate subsequent doses based on tolerability and response within the recommended maintenance dosing range of 6 mg to 12 mg twice daily.

Table 2. Bysanti Recommended Dosage in Adults, with Schizophrenia or Manic or Mixed Episodes Associated with Bipolar I Disorder, Who are CYP2D6 Poor Metabolizers.

Population	Day 1	Day 2	Day 3	Day 4	Recommended Maintenance Dosage
Schizophrenia	1 mg twice daily	2 mg twice daily	4 mg twice daily*	6 mg twice daily*	3 mg to 6 mg twice daily
Manic or Mixed Episodes Associated with Bipolar I Disorder	1 mg twice daily	3 mg twice daily	6 mg twice daily	Titration complete	6 mg twice daily

* Patients with schizophrenia may either (1) follow the recommended titration schedule, OR (2) starting on Day 3, initiate and continue 3 mg twice daily BYSANTI dosing. As needed, titrate subsequent doses based on tolerability and response within the recommended maintenance dosing range of 3 mg to 6 mg twice daily.

Bysanti efficacy and safety for schizophrenia and BD-I manic and mixed episodes are supported by the clinical studies described in the Fanapt package insert. Vanda Pharmaceuticals focused on demonstrating bioequivalence to Fanapt, allowing Bysanti to be characterized as a New Chemical Entity (NCE) while using the safety and efficacy data of Fanapt.

Bysanti has a black box warning for increased mortality in elderly patients with dementia-related psychosis. There is no available data for use during pregnancy; the available data from iloperidone use during pregnancy is not sufficient to determine a drug-associated risk for major birth defects and miscarriage. Neonates exposed to Bysanti during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. There are risks to pregnant mothers associated with untreated schizophrenia or BD-I. It is advised to not breastfeed during Bysanti treatment and for 6 days after the last dose in CYP2D6 normal metabolizers (8 days after last dose in CYP2D6 poor metabolizers) due to potential for severe adverse reactions in the breastfed infant. Safety and effectiveness of Bysanti in pediatric patients have not been established. Clinical studies of iloperidone in the treatment of schizophrenia did not include enough patients aged 65 and over to determine difference in response in geriatric patients. There is a black box warning for increased risk of death compared to placebo in elderly patients with dementia-related psychosis treated with Bysanti; Bysanti is not approved for treatment of patients with dementia-related psychosis. Antipsychotic drugs increase risk of tardive dyskinesia, with this risk appearing to be the highest among elderly patients (particularly elderly women). Bysanti is not recommended for patients with severe hepatic impairment (Child-Pugh class C); a lower dose should be considered in patients with moderate hepatic impairment (Child-Pugh class B) and no dose adjustment is recommended in patients with mild hepatic impairment (Child-Pugh class A).

Contraindications	Known hypersensitivity to milsaperidone or the inactive ingredients of Bysanti
Black Box Warning	Increased risk of mortality in elderly patients with dementia-related psychosis

Warnings and Precautions	Cerebrovascular adverse reactions in elderly patients with dementia-related psychosis QTc interval prolongation Neuroleptic malignant syndrome (NMS) Tardive dyskinesia Metabolic changes Orthostatic hypotension and syncope Seizures Leukopenia, neutropenia, and agranulocytosis Priapism Potential for cognitive and motor impairment Intraoperative floppy iris syndrome (IFIS)
Adverse Reactions (incidence ≥ 5% and 2-fold greater than placebo)	Schizophrenia: dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypotension, somnolence, tachycardia, and weight increased Bipolar mania: tachycardia, dizziness, dry mouth, hepatic enzymes increased, nasal congestion, weight increased, hypotension, and somnolence
Drug Interactions	Strong CYP2D6 Inhibitors: Reduce the dosage of Bysanti when administered with a strong CYP2D6 inhibitor Strong CYP3A4 Inhibitors: Reduce the dosage of Bysanti when administered with a strong CYP3A4 inhibitor Strong CYP2D6 and Strong CYP3A4 Inhibitors: Reduce the dosage of Bysanti if administered concomitantly with both a CYP2D6 and a CYP3A4 inhibitor Drugs that lower blood pressure: Avoid concomitant administration of Bysanti with alpha-adrenergic blocking agents and consider lowering the dosage of other drugs that lower blood pressure

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 (approved 27, rejected 0).

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

Outcome: Bysanti is a pharmacy benefit and will be added to the following tiers of the Commercial, Marketplace, and GHP Kids formularies. The following prior authorization criteria will apply:

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2 – Brand	Tier 3 – Brand NP	Tier 4 – Specialty	Tier 6 – Specialty

- Medical record documentation of age 18 years or older **AND**
- Medical record documentation of diagnosis of schizophrenia **OR** manic or mixed episodes associated with bipolar I disorder (BD-I) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three formulary atypical antipsychotics

FORMULARY ALTERNATIVES: aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone, clozapine

GPI LEVEL: GPI-10

QUANTITY LIMIT:

- Tablets (1 mg, 2mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg): 2 tablets per day
- Titration Packs: 1 pack per 180 days

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.

IDVYNSO (doravirine/islatravir)

Review: Idvynso is indicated as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen with no history of virologic treatment failure and no known substitutions associated with resistance to doravirine. Idvynso is a two drug combination of doravirine and islatravir, an HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI) and a nucleoside analog reverse transcriptase inhibitor (NRTI).

The recommended dosage is one tablet once daily with or without food in adults. If Idvynso is administered with rifabutin, Idvynso is administered once daily as recommended followed by one tablet of doravirine 100 mg 12 hours after a dose of Idvynso for the duration of rifabutin co-administration. Each Idvynso tablet contains 100 mg doravirine and 0.25 mg of islatravir in bottles of 30 tablets.

The efficacy of Idvynso was evaluated in Trial 051 and Trial 052, two randomized, active-controlled, non-inferiority trials in virologically-suppressed participants living with HIV. Included patients were stably suppressed on baseline regimen for at least 3 months prior to trial entry and had no history of treatment failure. Participants with active HBV infection were excluded from the trials.

Trial 051 was open-label and randomized 551 patients 2:1 to either switch from an oral ART regimen to Idvynso or remain on their baseline ART. At enrollment, 64% of the participants were receiving InSTI-based regimens, 5% PI-based regimens (including combinations with InSTI), and 30% other regimens.

Trial 052 was double-blind and randomized 513 patients 2:1 to switch from bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) to Idvynso or remain in BIC/FTC/TAF.

The primary endpoint of Trial 051 and Trial 052 was the proportion of participants with HIV-1 RNA ≥50 copies/mL at Week 48.

Table 7: Virologic Outcomes in Trial 051 and Trial 052 at Week 48 in Virologically-Suppressed Adults Who Switched to Idvynso

Outcomes	Trial 051		Trial 052	
	IDVYNSO N=366	Baseline ART N=185	IDVYNSO N=342	BIC/FTC/TAF N=171
HIV-1 RNA ≥50 copies/mL	1%	5%	1%	1%
Treatment Difference (95% CI)*	-3.6% (-7.8%, -0.8%)		0.9% (-1.9%, 2.9%)	
HIV-1 RNA <50 copies/mL	96%	92%	92%	94%
No Virologic Data at Week 48 Window	3%	3%	7%	5%
Discontinued study due to AE or Death†	1%	1%	2%	2%
Discontinued study for Other Reasons‡	2%	2%	5%	4%
On study drug but missing data in window	1%	1%	-	-

* CIs were calculated based on the stratified Miettinen and Nurminen method with Cochran-Mantel-Haenszel weights for Trial 051 (with baseline ART as stratification factors), and unstratified Miettinen and Nurminen method for Trial 052; non-inferiority (NI) was assessed using a NI margin of 4% † Includes participants who discontinued because of AE or death if this resulted in no virologic data on treatment during the Week 48 window ‡ Other reasons include: lost to follow-up, physician decision, and withdrawal by participant

In Trial 051, the mean increase from baseline at Week 48 in CD4+ T-cell counts in the Idvynso and baseline ART groups were 5 and 18 cells/mm3, respectively. In Trial 052, the mean increase from baseline at Week 48 in CD4+ T-cell counts in the Idvynso and BIC/FTC/TAF groups was 30 and 28 cells/mm3, respectively.

Warnings and precautions include severe skin reactions, including Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) which have been reported in doravirine-containing regimens. During clinical trials, the most common adverse reaction reported were diarrhea, dizziness, fatigue, abdominal distension, headache, and weight gain.

The safety and efficacy of Idvynso have not been established in pediatric patients less than 18 years of age. Clinical trials of Idvynso included 81 patients aged 65 years and older, 10 of whom were aged 75 years and older. No overall differences in safety or effectiveness were observed between older and younger patients.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (28 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (29 approved, 0 rejected).

Outcome: Idvynso is a pharmacy benefit and will be added to the following tiers of the Commercial, Marketplace, and GHP Kids. It will not require a prior authorization. The following quantity limits will apply:

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2: Brand	Tier 2: Brand P	Tier 2: Brand P	Tier 4: Brand P

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

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

YEZTUGO (lenacapavir)

Review: Yeztugo is formulation of lenacapivir indicated for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults and adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition. Lenacapivir was previously approved under the brand name Sunlenca for use in heavily treatment-experienced adults with multidrug-resistant HIV-1, in combination with other antiretrovirals. Lenacapivir is a selective HIV-1 capsid inhibitor which interferes with multiple steps of the viral life-cyle to inhibit HIV-1 replication.

Yeztugo is the fourth medication approved for PrEP and the second long acting formulation. Other approved products include Apretude (long acting injectable), Truvada, and Descovy.

Prior to the initiation of Yeztugo and each subsequent injection, patients should test negative for HIV-1. The recommended dosage of Yeztugo in adults and adolescents weighing at least 35 kg consists of initiation dosing using both subcutaneous injections and oral tablets followed by continuation dosing once every 6 months using subcutaneous injections (Table 1).

Table 1. Dosing Schedule for YEZTUGO Initiation and Continuation in Adults and Adolescents Weighing at Least 35 kg[1]

Time	
	Dosage of YEZTUGO: Initiation[a]
Day 1	927 mg by subcutaneous injection (2 x 1.5 mL injections) and 600 mg orally (2 x 300 mg tablets)
Day 2	600 mg orally (2 x 300 mg tablets)
	Dosage of YEZTUGO: Continuation
Every 6-months (26 weeks)[b] +/-2 weeks	927 mg by subcutaneous injection (2 x 1.5 mL injections)

a. The complete initiation dosing schedule, consisting of subcutaneous injections and oral tablets, is required; the efficacy of YEZTUGO has only been established with this dosing schedule.
b. From the date of the last injection.

If the Day 2 oral initiation dose is missed, it should be taken as soon as possible. The Day 1 and Day 2 oral initiation doses should not be taken on the same day. During the continuation dosing, if the scheduled injection is delayed by more than 2 weeks (26-28 weeks since last injection), Yeztugo tablets can be taken on an interim basis at 300 mg once every 7 days for up to 6 months if needed. The continuation injection should be resumed within 7 days after the last oral dose. If it has been over 28 weeks since the last injection of Yeztugo and the tablets were not taken, patients should reinitiate with the initiation dosing schedule from Day 1. Patients treated with strong or moderate CYP3A inducers will require supplemental doses of Yeztugo on the day of induction and every 6 months for the duration of CYP3A inducer treatment. Yeztugo as tablets containing 300 mg of lenacapavir and single-dose vials containing 463.5/1.5 mL of lenacapavir.

The safety and efficacy of Yeztugo was evaluated in PURPOSE 1 and PURPOSE 2, two randomized, double-blind, active-controlled trials evaluating the risk reduction of HIV-1 acquisition.

PURPOSE 1
PURPOSE 1 included 5,338 cisgender adolescent girls and young women aged 16 to 25 who tested HIV-1 negative at screening and who were at risk of acquiring HIV-1 based on sexual activity with male partners. Patients were randomized 2:2:1 to receive Yeztugo, once daily Descovy, or once daily Truvada.

In PURPOSE 1, 99% of injections were administered into the abdomen and each dose was administered in 2 locations. A total of 32 pregnant participants received Yeztugo injections in the thigh and each dose was administered bilaterally (one in the right/one in the left).

The efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to Yeztugo compared to Truvada. Yeztugo demonstrated superiority with 100% reduction in the risk of incident HIV-1 infection over Truvada (Table 2).

Table 2. Overall HIV-1 Infection Outcomes in PURPOSE 1[a,1]

	YEZTUGO N=2134	TRUVADA N=1068	Rate Ratio (95% CI)
Person-years	1939	949	-
HIV-1 infections (incidence rate per 100 person-years)	0 (0.00)	16 (1.69)	YEZTUGO / TRUVADA: 0.000 (0.000, 0.101) p <0.0001

CI = confidence interval

a. The determination of efficacy was based on planned interim analyses (which became the final analyses) following sequential testing of HIV-1 incidence for YEZTUGO compared to background followed by YEZTUGO compared to TRUVADA, all at alpha level of 0.0026 when 50% of randomized participants completed at least 52 weeks of follow-up or prematurely discontinued from the study. YEZTUGO also demonstrated superiority in the risk of incident HIV-1 infection over background HIV-1 incidence.

PURPOSE 2

PURPOSE 2 included 3,265 cisgender men, transgender women, transgender men, and gender non-binary individuals 16 years of age and older who tested negative for HIV-1 at baseline and who were at risk of acquiring HIV-1 based on sexual activity with male partners. Patients were randomized 2:1 to receive Yeztugo or once daily Truvada.

In PURPOSE 2, injections were administered into the abdomen and each dose was administered in 2 locations.

The efficacy endpoint was the rate of incident HIV-1 infections per 100 person-years in participants randomized to Yeztugo compared to Truvada. Yeztugo demonstrated superiority with an 89% reduction in the risk of incident HIV-1 infection over Truvada.

Table 3. Overall HIV-1 Infection Outcomes in PURPOSE 2[a,1]

	YEZTUGO N=2179	TRUVADA N=1086	Rate Ratio (95% CI)
Person-years	1938	967	-
HIV-1 infections (incidence rate per 100 person-years)	2 (0.1)	9 (0.93)	YEZTUGO / TRUVADA: 0.111 (0.024, 0.513) p = 0.00245

CI = confidence interval

a. The determination of efficacy was based on planned interim analyses (which became the final analyses) following sequential testing of HIV-1 incidence for YEZTUGO compared to background followed by YEZTUGO compared to TRUVADA, all at alpha level of 0.0026 when 50% of randomized participants completed at least 52 weeks of follow-up or prematurely discontinued from the study. YEZTUGO also demonstrated superiority in the risk of incident HIV-1 infection over background HIV-1 incidence.

Yeztugo carries a black box warning for potential drug resistance to develop when used in patients with undiagnosed HIV-1 infection. It is contraindicated in patients with unknown or positive HIV-1 status. Other warnings include potential risk associated with residual concentrations of lenacapavir due to long-acting properties which increase the exposure and risk of adverse reactions and serious injection site reactions, including necrosis and ulcer, when administered improperly (intradermal).
The most common adverse reactions were injection site reactions, headache, and nausea.

The safety and efficacy of Yeztugo for HIV-1 PrEP in adolescents weighing at least 35 kg who are at risk for HIV-1 acquisition is supported by PURPOSE 1 and PURPOSE 2 in a total of 129 patients, 59 of whom received Yeztugo. Safety data reported was consistent with those reported in adults. Adolescents may benefit from additional counseling and appointment reminders to support adherence to the dosing and testing schedule. Safety, efficacy, and pharmacokinetics of Yeztugo have not been established in pediatric populations weighing less than 35 kg.

Clinical studies did not include sufficient numbers of participants aged 65 years and over to determine if they respond differently from younger patients. In general, caution should be used when administered in elderly individuals, reflecting greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

Yeztugo has not been studied in individuals with ESRD (CrCl < 15 mL/min) but no dosage adjustment is recommended in patients with mild, moderate, or severe renal impairment. Yeztugo has not been studied in patients with severe hepatic impairment (Child-Pugh Class C) but no dosage adjustment is recommended in patients with mild or moderate hepatic impairment.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (29 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: Yeztugo is a pharmacy benefit and will be added to the Commercial, Marketplace, and GHP Kids formulary. No prior authorization will be required. It will have a $0 copay when used for PrEP. The following quantity limit will apply:

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2 – Brand	Tier 2 – Brand P	Tier 2 – Brand P	Tier 1 - $0 Copay Tier

QUANTITY LIMIT:

- Tablets: 4 tablets per 28 days, 28 day supply per fill
- Single Dose Vials: 3 milliliters per 6 months, 6 months per fill

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

LOARGYS (pegzilarginase-nbln)

Review: Loargys is an arginine-specific enzyme indicated for the treatment of hyperargininemia in adult and pediatric patients 2 years of age and older with arginase 1 deficiency (ARG1-D), in conjunction with dietary protein restriction. This indication is approved under accelerated approval based on reduction of plasma arginine. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

ARG1-D, also known as hyperargininemia, is one of the eight urea cycle disorders (UCD) subtypes. The urea cycle is responsible for the clearance of nitrogen waste that results from protein turnover and nitrogen metabolism. Urea cycle disorders are inherited deficiencies in the enzymes or transporters involved in the urea cycle pathway, when these enzymes are deficient, toxic ammonia compounds cannot be cleared from the body. ARG1-D is an ultra-rare and autosomal recessive inherited metabolic disorder characterized by the complete or partial absence of ARG1 enzyme in the liver and red blood cells. In the absence of ARG1, an overaccumulation of plasma arginine and its toxic metabolites occurs, resulting in hyperargininemia. Patients with ARG1-D are often diagnosed in late infancy or childhood and if left untreated, symptoms may include seizures, spasticity, short stature, loss of ambulation, developmental delay, and severe intellectual disability.

ARG1-D is diagnosed through a combination of plasma arginine levels and confirmatory molecular genetic testing identifying biallelic pathogenic variants in the ARG1 gene or absent red blood cell arginase enzyme activity (<1% of normal).

Treatment options is based on reducing ammonia and arginine concentrations in blood plasma and preventing excess ammonia formation and reducing nitrogen intake (dietary protein restriction). Reduction of plasma ammonia concentration is accomplished through dialysis when severe symptoms are present or with IV fluids and/or pharmacologic therapy. Pharmacologic therapy consists of a combination of sodium phenylacetate and sodium benzoate, co-formulated in an IV formulation (Ammonul), and oral formulations of phenylbutyrate (Buphenyl, Ravicti, Phenburane, Olpruva). All agents are nitrogen scavengers that conjugate with glutamine, forming phenylacetylglutamine which gets excreted by the kidneys and provides an alternate route of nitrogen excretion. All are approved for use as adjunctive therapies (i.e. dietary protein restriction and/or amino acid supplementation) in patients with urea cycle disorders, none are specifically approved for the treatment of ARG1-D. Patients with ARG1-D are expected to require lifelong arginine depletion therapy and Loargys is the first and only option.

Loargys provides an exogenous source of the deficient ARG1 activity in patients with ARG1-D and reduces plasma arginine by converting it to urea and ornithine. It is the first disease modifying therapy for the treatment of ARG1-D.

Loargys is available in 2 mg/0.4mL or 5 mg/mL single-dose vials. Loargys should be administered under the supervision of a healthcare provider with knowledge in the management of hypersensitivity reactions including anaphylaxis also it should be administered in a healthcare setting with appropriate medical monitoring and support measures. A baseline plasma arginine concentration should be obtained. Patients could be pre-medicated with antihistamines. The recommended starting dose of Loargys is 0.1 mg/kg administered as an intravenous infusion once weekly. Actual body weight should be used for the calculation. Dose adjustments should be aimed at achieving a pre-dose level of plasma arginine near the upper limit of normal. After 4 weeks of administration, measure pre-dose plasma arginine (168 hours after prior dose) to determine the need for a dose adjustment. If two consecutive weekly pre-dose plasma arginine measurements are not in the desired therapeutic range, the dose should be adjusted as follows: below 50 micromolar, reduce the weekly Loargys dosage by 0.05 mg/kg; above 150 micromolar, increase the weekly Loargys dosage by 0.05 mg/kg. The maximum recommended dose is 0.2 mg/kg once weekly. Plasma arginine levels should be monitored weekly for 2 weeks after any Loargys dosage adjustment and as clinically indicated. After 8 weeks of once weekly intravenous Loargys, patients may be switched from intravenous administration to subcutaneous administration at the same dosage of intravenous therapy. If a dose is missed, Loargys must be administered as soon as possible. Do not administer two Loargys doses on the same day or within 4 days of each other to make up for a missed dose. Ensure there is a minimum of four days between doses. Samples must be collected into Immedica Pharma's Nor-NOHA Blood Collection Tues, which contain Nω-hydroxy-nor-Arginine (nor-NOHA), an enzyme inhibitor used to inhibit post-sampling degradation of arginine by Loargys. Arginine concentration must be measured using Immedica Pharma's Loargys Arginine Assay. Loargys is only available to a patient if the patient is enrolled in Study IMM-PEG-005 to obtain Immedica Pharma's Nor-NOHA Blood Collection Tubes and Loargys Arginine Assay. For intravenous administration, Loargys should be diluted with 0.9% sodium chloride and administered over at least 30 minutes. For subcutaneous administration, administer the undiluted solution subcutaneously into abdomen, lateral part of thigh, or the side or back of the upper arms. If a patient tolerates maintenance subcutaneous administration, they may receive administration at home under the supervision of a healthcare provider. In the case of missed or delayed injections, contact a healthcare provider as subsequent injections may need to occur in a supervised clinical setting.

The effectiveness of Loargys for the treatment of hyperargininemia in adult and pediatric patients with ARG1-D was evaluated in the Pegzilarginase Effect on Arginase 1 Deficiency Clinical Endpoints (PEACE) study. The study consisted of a screening period; a 24-week randomized double blind treatment period; an open-label long-term extension period of up to 150 weeks; and a follow-up visit for final safety assessments. There were 32 patients enrolled in the trial aged 2 to 29 years old. Majority (90%) of patients were between 2 and 17 years of age at enrollment. Patient enrolled in the trial needed to be 2 years of age or older, documented diagnosis of ARG1-D, pArg ≥250 µmol/L (mean of all screening values), impairment on any secondary functional mobility assessment. Patients were excluded in they had symptomatic hyperammonemia (ammonia ≥ 100 µM requiring acute care or hospitalization) within 6 weeks before first Loargys dose, extreme mobility impairment (i.e. unable to complete assessments), prior liver or hematopoietic transplant. Patients were randomized 2:1 to receive one of the following, IV

once weekly, for 24 weeks: Loargys (n-21) titrated to a dosing range of 0.05-0.2 mg/kg as clinically indicated to achieve target pArg level or placebo (n=11). Patients who previously had an ARG1-D-related dietary regimen or ammonia scavengers continued to receive these treatments throughout the initial trial period. The percentage of patients who remained on background therapy was not reported. The primary endpoint was change from baseline in pArg at Week 24. The key secondary endpoint was functional mobility per mean change from baseline in GMFM-E, Gross Motor Function Measure Part E (evaluates walking and running; score 0–72, with lower scores indicating greater impairment) or 2-minute walk test at Week 24. Other secondary endpoints include change from baseline in GMFM-D, Gross Motor Function Measure Part D (evaluates sitting and standing; score 0–39, with lower scores indicating greater impairment), percentage of patients with pArg <200 µmol/L (guideline level) and percentage of patients with normal pArg (40–115 µmol/L); change from baseline in guanidino compounds (ARGA, GAA, GVA, and NAArg); and change from baseline in ornithine, all after 24 weeks. A total of 31 patients completed the double blind period, one patient discontinued for personal reasons. Loargys significantly reduced mean pArg levels by approximately 77% compared to placebo at Week 24. Placebo patients had no meaningful reduction in pArg. Additionally, 90% of Loargys-treated patients achieved normalized pArg levels (40 µmol/L–115 µmol/L) by Week 24. All 31 patients who completed the double blind period, entered the long term extension period and received open-labeled treatment of Loargys. After 8 weeks in the long term extension period, patients could switch to subcutaneous (SC) injections at the same dose as the IV. All patients switched from IV to SC. During the long term extension period, patients who switched from placebo to Loargys achieved similar reductions in mean pArg levels as those who received Loargys from the start of the study. For patients who received Loargys the entire study, mean improvements in all 3 clinical outcomes (2-meter walk test and Gross Motor Function Measure Parts D&E) exceeded thresholds for clinically important response. Clinically important difference was not achieved in patients who received placebo/Loargys.

The most common adverse reactions are vomiting, pyrexia, infusion associated reactions, and constipation. There are no contraindications to use. The warnings and precautions include hypersensitivity reactions, if a severe one occurs, Loargys should be discontinued and appropriate medical treatment should be initiated including epinephrine. The safety and effectiveness of Loargys have not been established for the treatment of hyperargininemia in pediatric patients less than 2 years of age with ARG1-D. Clinical studies of Loargys did not include patients 65 years of age and older.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (26 approved, 0 rejected).

Financial Discussion: Bret requested that we evaluate our eligible population for this therapy. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (30 approved, 0 rejected).

Outcome: Loargys is a medical benefit for Commercial, Marketplace, and GHP Kids. It will be added to the medical benefit cost share list. When processed at a specialty pharmacy, Loargys will process on the following tiers. Loargys will require a prior authorization with the following criteria:

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2 – Brand	Tier 3– Brand NP	Tier 4-Specialty	Tier 6-Specialty

- Prescription written by a metabolic disease specialist b
- Medical record documentation of age ≥ 2 years **AND**
- Medical record documentation of a diagnosis of Arginase 1 Deficiency as evidenced by one of the following:
    - Pathogenic variants in ARG1 on molecular genetic testing; **OR**
    - Diminished erythrocyte arginase enzyme activity (i.e., <1% of normal in red blood cell extracts) **AND**
- Medical record documentation that the member is enrolled in Study IMM-PEG-005 to obtain

Immedica Pharma's Nor-NOHA Blood Collection Tubes and Loargys Arginine Assay **AND**
- Medical record documentation of baseline plasma arginine levels ≥250 µmol/L **AND**
- Medical record documentation that Loargys will be used in conjunction with a protein-restricted diet **AND**
- Medical record documentation of member's weight **AND**
- Medical record documentation that the dose does not exceed 0.2 mg/kg once weekly

AUTHORIZATION DURATION: 6 months initial and 12 month subsequent

REAUTHORIZATION CRITERIA:
- Medical record documentation of one of the following:
  - Plasma arginine levels between 50 µmol/L–150 µmol/L **OR**
  - Plasma arginine levels are outside normal range and medical record documentation that the dose will be adjusted per labeling* **AND**
- Medical record documentation of member's weight **AND**
- Medical record documentation that the dose does not exceed 0.2 mg/kg once weekly

**If two consecutive weekly pre-dose (168 hours after prior dose) plasma arginine measurements are not in the desired therapeutic range, increase or decrease the weekly Loargys dosage as follows:*
- *Below 50 micromolar, reduce the weekly Loargys dosage by 0.05mg/kg*
- *Above 150 micromolar, increase the weekly Loargys dosage by 0.05 mg/kg*

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.

LIFYORLI (relacorilant)

Review: Lifyorli is a glucocorticoid receptor antagonist indicated in combination with nab-paclitaxel for the treatment of adults with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens, at least one of which included bevacizumab. Lifyorli enhanced apoptosis and antitumor activity when administered with paclitaxel.

The recommended dosage of Lifyorli is 150 mg orally once on the day before, the day of, and the day after each nab-paclitaxel infusion until disease progression or unacceptable toxicity. The recommended dosage for nab-paclitaxel is 80 mg/m^2 administered as an intravenous infusion on Days 1, 8, and 15 of each 28 day cycle until disease progression or unacceptable toxicity. In the event of adverse events, Lifyorli can be reduced to 125 mg once the day before, the day of, and the day after nab-paclitaxel infusion. Patients unable to tolerate Lifyorli after the dose reduction should permanently discontinue treatment. Lifyorli is supplied as 25 mg and 100 mg capsules.

The efficacy of Lifyorli was evaluated in ROSELLA, an open-label, active-controlled, randomized, two-arm trial in patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer. Patients were permitted to receive up to three lines of systemic therapy and prior bevacizumab was required. The trial excluded patients who required chronic or frequent use of glucocorticoids. Patients were randomized 1:1 to receive:
- LIFYORLI 150 mg orally the day before, the day of, and the day after administration of nab paclitaxel 80 mg/m2 intravenous infusion on Days 1, 8 and 15 of each 28-day cycle (188) or
- nab-paclitaxel 100 mg/m2 intravenous infusion on Days 1, 8 and 15 of each 28-day cycle (193)

Treatment was administered until disease progression or unacceptable toxicity. Tumor response assessments occurred every 8 weeks for the first 40 weeks and every 12 weeks thereafter.

The major efficacy outcome measures were progression-free survival (PFS) assessed by blinded independent central review (BICR) and overall survival (OS). PFS was evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST v1.1).

Nine percent of patients had received 1 prior line of systemic therapy, 48% of patients had received 2 prior lines of systemic therapy, and 44% of patients had received 3 prior lines of systemic therapy. Thirty-nine percent of patients received prior systemic therapy for platinum-resistant disease. All patients received prior bevacizumab, 99.5% had received a prior taxane (19% in the last line of therapy and 4% in the platinum-resistant setting) and 61% had received a prior PARP inhibitor.
Lifyorli demonstrated a statistically significant improvement in PFS and OS for patients randomized to Lifyorli in combination with nab-paclitaxel compared to nab-paclitaxel monotherapy (Table 5).

Table 5. Efficacy Results in ROSELLA

	LIFYORLI and Nab-Paclitaxel N=188	**Nab-Paclitaxel N=193**
Progression-free Survival (PFS) by BICR [a]		
Number (%) of patients with events	113 (60)	121 (63)
Median, months (95% CI)	6.5 (5.6, 7.4)	5.5 (3.9, 5.9)
Hazard ratio (95% CI)[b]	0.70 (0.54, 0.91)	
p-value[c]	0.0076	
Overall Survival (OS)[d]		
Number (%) of patients with events	129 (69)	159 (82)
Median, months (95% CI)	16.0 (13.0, 18.3)	11.9 (10.0, 13.8)
Hazard ratio (95% CI)[b]	0.65 (0.51, 0.83)	
p-value[e]	0.0004	

BICR = Blinded Independent Central Review; CI = Confidence Interval a Results at the pre-specified final PFS analysis. b Based on the stratified Cox proportional hazard model. c Two-sided p-value based on stratified log-rank test (compared to a significance level of 0.04). d Results at the pre-specified final OS analysis. e Two-sided p-value based on stratified log-rank test (compared to a significance level of 0.0499).

Warnings and precautions include risk neutropenia and severe infections, adrenal insufficiency, exacerbation of conditions treated with glucocorticoids, and embryo-fetal toxicity. In clinical trials, serious adverse reactions occurred in 35% of patients who received Lifyorli + nab-paclitaxel, including neutropenia, pneumonia, pleural effusion, febrile neutropenia, and fatigue. Fatal adverse reactions occurred in 2.1% of patients, including septic shock, cardiac arrest, ischemic stroke, and intestinal perforation. Permanent discontinuation occurred in 9% of patients. Dose interruptions occurred in 72% of patients and dose reductions occurred in 7.4% of patients. The most common adverse reactions were decreased hemoglobin, decreased neutrophils, fatigue, nausea, diarrhea, decreased platelets, rash, and decreased appetite.

The safety and efficacy of Lifyorli has not been established in pediatric patients. Of the 188 patients with platinum-resistant epithelial ovarian cancer who received Lifyorli, 38% were 65 years or older and 9.6% were 75 years or older. A higher incidence of Grade 3-4 adverse events and dosage modification occurred in patients 65 years or older when compared to younger patients. No difference in efficacy was observed between older and younger patients.

Lifyorli should be avoided in patients with moderate of severe hepatic impairment due to potential for increased relacorilant and paclitaxel exposures.

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 (26 approved, 0 rejected).

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed (29 approved, 0 rejected).

Outcome: Lifyorli is a pharmacy benefit and should be added to the Commercial, Marketplace, and GHP Kids formularies to the following tiers.

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2 – Brand (Oral Oncology $0 Copay)	Tier 3 – Brand NP (Oral Oncology $0 Copay)	Tier 3 – Brand NP (Oral Oncology $0 Copay)	Tier 1 – Brand NP (Oral Oncology $0 Copay)

It will require a prior authorization for new starts only and should be added to Commercial Policy 896.0 with the following quantity limits.

Commercial Policy 896.0 Oral Oncology Agents

- Medical record documentation that the oral oncology agent is prescribed by or in consultation with a hematologist, oncologist, or other appropriate specialist **AND**
- Medical record documentation of a diagnosis that is supported by one of the following:
    - U.S. Food and Drug Administration (FDA)- approved package labeling **OR**
    - The National Comprehensive Cancer Network (NCCN) guidelines **OR**
    - American Society of Clinical Oncology (ASCO) **AND**
- Medical record documentation of an age consistent with Food and Drug Administration (FDA) approval or medically accepted indication **AND**
- Medical record documentation that the medication is being prescribed at a dose and duration that is consistent with Food and Drug Administration (FDA)-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature **AND**
- For a non-preferred product with a therapeutically equivalent generic or biosimilar, medical record documentation of a history of therapeutic failure of or a contraindication or an intolerance to the preferred therapeutically equivalent generic or biosimilar

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT: Lifyorli 125 mg Dose Pack: 18 capsules per 28 days, 28 day supply per fill
Lifyorli 150 mg Dose Pack: 27 capsules per 28 days, 28 day supply per fill

RE-AUTHORIZATION CRITERIA FOR NEW START ONLY: All products (unless listed below) are configured as a prior authorization for new starts only. The requested medication 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

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

FAST FACTS

JAKAFI/ JAKAFI XR (ruxolitinib (extended release))

Clinical Summary: Jakafi and Jakafi XR are indicated for the treatment of:

- intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis in adults.
- polycythemia vera in adults who have had an inadequate response to or are intolerant of hydroxyurea.
- steroid-refractory acute graft-versus-host disease in adult and pediatric patients 12 years and older.
- chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older.

The recommended starting dose of Jakafi and Jakafi XR for myelofibrosis is based on the platelet count (Table 1). Doses may be titrated based on safety and efficacy.

Table 1. Jakafi/Jakafi XR Starting Doses for Myelofibrosis[1]

Platelet Count	JAKAFI Starting Dose	JAKAFI XR Starting Dose
Greater than 200×10^9/L	20 mg orally twice daily	44 mg orally once daily
100×10^9/L to 200×10^9/L	15 mg orally twice daily	33 mg orally once daily
50×10^9/L to less than 100×10^9/L	5 mg orally twice daily	11 mg orally once daily

The recommended starting dose of Jakafi XR for Polycythemia Vera is 22 mg orally once daily.

The recommended dose of Jakafi XR for acute GVHD is 11 mg given orally once daily. Consider increasing the dose to 22 mg once daily after at least 3 days of treatment if the ANC and platelet counts are not decreased by 50% or more relative to the first day of dosing with Jakafi XR.

The recommended dosage of Jakafi XR for chronic GVHD is 22 mg once daily. Patients should consider tapering Jakafi XR after 6 months of treatment in patients with response who have discontinued therapeutic doses of corticosteroids. It should be tapered by one dose level approximately every 8 weeks to Jakafi XR 11mg and then discontinued.

Jakafi XR is supplied as 11 mg, 22 mg, 33 mg, 44 gm, and 55 mg tablets.

No new clinical trials were conducted to evaluate the safety and efficacy of Jakafi XR. Approval was based on previous findings for Jakafi and pharmacokinetic data. No new safety signals were identified with the new formulation.

Current Formulary Status: Jakafi; Pharmacy Benefit, PA

Recommendation: Jakafi XR is a pharmacy benefit and will be added to the following tiers for Commercial, Marketplace, and GHP Kids formulary. An exception for coverage of Jakafi/Jakafi XR may be made for members who meet the following criteria:

2 Tier/CHIP	3 Tier	4 Tier	ACA
Tier 2 – Brand (Oral Oncology $0 Copay)	Tier 3 – Brand NP (Oral Oncology $0 Copay)	Tier 3 – Brand NP (Oral Oncology $0 Copay)	Tier 1 – Brand NP (Oral Oncology $0 Copay)

Commercial Policy 250.0
An exception for coverage of Jakafi/Jakafi XR may be made for members who meet the following criteria:

For Myelofibrosis

- Medical record documentation that Jakafi/Jakafi XR is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis **AND**
- Medical record documentation of platelet count greater than or equal to 50 x 10^9/L **AND**
- Medical record documentation of splenomegaly as measured by computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound **AND**
- Medical record documentation of a baseline Total Symptom Score as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF) **AND**
- Medical record documentation that Jakafi/Jakafi XR will not be used concurrently with Inrebic

NOTE: Intermediate or High-Risk Myelofibrosis is defined by having at least 2 of the following factors:

- ✓ Age > 65 years
- ✓ WBC > 25 x 10^9/L
- ✓ Hemoglobin < 10 g/dL
- ✓ Blood Blasts ≥ 1%
- ✓ Presence of Constitutional Symptoms (weight loss, fever, excessive sweats, etc.)
- ✓ Transfusion dependency
- ✓ Platelets less than 100 X 10^9/L
- ✓ Unfavorable karyotype

AUTHORIZATION DURATION: Each treatment period will be defined as six (6) months. Re-review with occur every six (6) months. Jakafi/Jakafi XR will no longer be covered if medical record documentation does not show:

- Medical record documentation of platelet count greater than or equal to 50 x 10^9/L **AND**
- The member has achieved a reduction from pretreatment baseline of at least 35% in spleen volume as measured by computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound **OR**
- The member has achieved a 50% or greater reduction in the Total Symptom Score from baseline as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF)

For Polycythemia Vera

- Medical record documentation of a diagnosis of polycythemia vera **AND**
- Medical record documentation that member requires phlebotomy **AND**
- Medical record documentation of splenomegaly **AND**
- Medical record documentation of an inadequate response or intolerance to hydroxyurea **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to interferon therapy **OR** medical record documentation of post –polycythemia vera myelofibrosis with hydroxyurea-refractory symptomatic splenomegaly **OR** severe constitutional symptoms

AUTHORIZATION DURATION: Initial approval will be given for 6 months or less is 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 the member experiences unacceptable toxicity or worsening of disease.

For Graft versus Host Disease

- Medical record documentation that Jakafi/Jakafi XR is prescribed by a hematologist/oncologist or transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**

- Medical record documentation of a diagnosis of steroid refractory graft-versus-host disease (GVHD) **OR**
- Medical record documentation of both of the following:
  - Documentation of a diagnosis of chronic graft-versus-host disease (cGVHD) **AND**
  - Documentation of therapeutic failure of one or two prior lines of systemic therapy

AUTHORIZATION DURATION: Initial approval will be given for 6 months or less is 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 the member experiences unacceptable toxicity or worsening of disease.

Note for GVHD: Tapering of Jakafi/Jakafi XR may be considered after 6 months of treatment in patients with response who have discontinued therapeutic doses of corticosteroids. Taper will take at least 4 months. If signs/symptoms recur during or after the taper, Jakafi can be restarted.

MEDISPAN AUTHORIZATION LEVEL: GPI-12

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

- **JAKAFI:** QL FOR LETTER ONLY: 2 tablets per day, 30 day supply per fill
- **JAKAFI XR:** QL FOR LETTER ONLY: 1 tablet per day, 30 day supply per fill

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.

OMISIRGE (omidubicel-onlv)

Clinical Summary: Omisirge is a nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood now indicated for the treatment of adults and pediatric patients 6 years and older with severe aplastic anemia (SAA) following reduced intensity conditioning. Previously, Omisirge was indicated for, and is still also indicated for, adults and pediatric patients 12 years and older with hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative conditioning to reduce the time to neutrophil recovery and the incidence of infections.

The dosing of Omisirge remained unchanged for the new indication of SAA and is a one-time infusion, administered by a center with expertise in hematopoietic stem cell transplants, delivered in two separate bags consisting of:

- a Cultured Fraction (CF): a minimum of 8.0×10^8 total viable cells of which a minimum of 8.7% is CD34+ cells and a minimum of 9.2×10^7 CD34+ cells, and
- a Non-cultured Fraction (NF): a minimum of 4.0×10^8 total viable cells with a minimum of 2.4×10^7 CD3+ cells

Infusion of the NF bag should be completed within one hour of infusion of the CF bag. For SAA, it is recommended to administer a reduced intensity conditioning regimen according to institutional guidelines. Premedication for SAA specifically includes oral or IV prednisone/methylprednisolone for patients receiving anti-thymocyte globulin (ATG). Also, for pediatric patients with SAA, premedication with diphenhydramine and acetaminophen are recommended based on institutional guidelines. Omisirge is supplied in two shipping containers: 1) a liquid nitrogen dry vapor shipper containing the CF and NF and

2) a refrigerated shipping container containing two infusion solutions for dilution of the CF and NF. Omisirge is shipped to the transplant center for a specific patient.

The efficacy of Omisirge in patients with SAA was evaluated in an open-label, single center study (Study 17- H-0091, NCT 03173937). Patients had intolerance or failure to immunosuppressive therapy and availability of at least one ≥ 4/8 HLA-matched (HLA-A, B, C and DR loci) cord blood unit. Patients were included if they had bone marrow cellularity <30% (excluding lymphocytes) associated with either RBC transfusion dependence or platelet transfusion dependence and/or neutropenia. Patients could also be included if they had a history of SAA transformed to MDS and the following: International Prognostic Scoring System (IPSS) risk category of INT-1 or greater, and b) < 5% myeloblasts and < 30% of cellularity in the bone marrow on screening morphologic analysis. Patients were excluded if there was an identical (12/12) HLA-matched donor, related or unrelated. Median age was 17 years (range 6-45 years), median absolute neutrophil count at baseline was 0.3×10^9 /L (range, 0.0 – 1.0 /L), and median platelet count at baseline was 35×10^9 /L (range, 10-89 /L). Hematopoietic stem cell transplantation (HSCT) specific comorbidity index was ≥ 3 in 76% and 0-2 in 24% of patients.

A total of 17 patients were treated with Omisirge, with 3 patients receiving combination therapy with haploidentical CD34+ cells. Only the 14 patients treated with Omisirge alone were included in the efficacy evaluation. The median CD34+ cell dose of Omisirge was 9.5×10^6 cells/kg (range, 2.3 - 21.4 cells/kg) and all patients received reduced intensity conditioning with cyclophosphamide, fludarabine, Total Body Irradiation (TBI), and horse-ATG. Lastly, GvHD prophylaxis was administered according to institutional guidelines.

The primary efficacy outcome was the incidence of early and sustained neutrophil recovery, defined as ANC ≥500 cells/µl for 3 consecutive measurements on different days, including: by Day 26, maintained at both Day 42, and Day 100 post-transplant. Secondary efficacy outcomes were: neutrophil recovery (days to first of three consecutive ANC≥500 cells/µL), red blood cell transfusion independence (days to 30-day transfusion independence), platelet recovery (days to first of 3 consecutive platelet count of 20,000/µL with no preceding transfusion in 7 days), and platelet transfusion independence (days to 30-day platelet transfusion independence). Efficacy results are summarized in Table 1.

Table 1. Efficacy Results from Study 17-H-0091

Efficacy Outcome	**N=14**
Patients with early and sustained neutrophil recovery at 100 days n (%) (95% CI)[1]	 12 (86%) (57%, 98%)
Time to neutrophil recovery[2] Median days (min - max)[3]	 11 (7 – 20)
Time to RBC transfusion independence No. patients who achieved (%) Median days (min - max) [3]	 12 (86%) 58.5 (42 – 446)
Time to platelet 20,000/µl recovery No. patients who achieved within a year (%) Median days (min – max) [3]	 12 (86%) 31.5 (20 – 197)
Time to platelet transfusion independence No. patients who achieved (%) Median days (min - max) [3]	 11 (79%) 53.0 (43 – 93)

[1] 95% CI was calculated by the Clopper-Pearson method.
[2] Time to neutrophil recovery was defined as ANC ≥500 cells/µl for 3 consecutive measurements on different days.
[3] Based on patients who achieved the events.
Abbreviation: CI: Confidence interval; min: Minimum; max: Maximum; N: number.

Omisirge has black box warnings that include: GvHD, infusion reactions, autoimmune cytopenias, graft failure, and engraftment syndrome. Contraindications include patients with known hypersensitivity to dimethyl sulfoxide (DMSO), Dextran 40, gentamicin, human serum albumin, or bovine products. Warnings and precautions are significant for graft-versus-host disease, hypersensitivity/infusion related reactions, autoimmune cytopenias, graft failure, malignancies of donor origin, engraftment syndrome, transmission of serious infections, and transmission of rare genetic diseases.

Serious adverse reactions in Study 17-H-0091 included: infections (n=15), diarrhea (3), nausea/vomiting (n=4), pyrexia (n=2), hypoxia (n=2), thrombotic microangiopathy (note: n=1 for the remaining adverse reactions), cardiac arrest, pericarditis, colitis, febrile neutropenia, cholecystitis, portal vein thrombosis, graft-versus-host disease, weight decreased, dehydration, Guillain-Barre Syndrome, uterine hemorrhage, pleural effusion, pulmonary hemorrhage, and respiratory failure. One patient had a fatal adverse reaction, caused by disseminated adenovirus infection. The most common Grade 3-5 adverse reactions were: febrile neutropenia (41%), bacterial infections (41%), hyperglycemia (41%), Epstein-Barr virus infection (29%), immune thrombocytopenia (24%) and pneumonia (24%). Safety and efficacy have been established in pediatric patients with SAA who are 6 years of age and older, with 7 pediatric patients included in Study 17-H-0091. It is unclear if patients 65 years and older respond differently from younger patients since clinical studies did not include these patients.

Current Formulary Status: Medical benefit requiring prior authorization.

Recommendation: It is recommended not to update the formulary placement or authorization duration of Omisirge. It is recommended to update the prior authorization criteria of MBP 292.0 Omisirge (omidubicel-onlv).

MBP 292.0 Omisirge (omidubicel-onlv)

- Medical record documentation that Omisirge is prescribed by a hematologist and/or oncologist **AND**
- Medical record documentation of age greater than or equal to 12 years of age **AND**
- Medical record documentation of a diagnosis of a hematological malignancy planned for umbilical cord blood transplantation following myeloablative conditioning **AND**
- Medical record documentation that a matched related donor (MRD), matched unrelated donor (MUD), mismatched unrelated donor (MMUD), or haploidentical donor is not readily available **AND**
- Medical record documentation that patient has not had a prior allogeneic hematopoietic stem cell transplantation (HSCT)

OR

- Medical record documentation that Omisirge is prescribed by a hematologist and/or oncologist **AND**
- Medical record documentation of age greater than or equal to 6 years of age **AND**
- Medical record documentation of a confirmed diagnosis of aplastic anemia (AA) **AND**
- Medical record documentation of severe disease, as defined by two (2) of the following:
    - Absolute neutrophil count (ANC) less than 500/microL (or $0.5x10^9$/L)
    - Platelet count less than 20,000/microL (or $20x10^9$/L)
    - Reticulocyte count less than 60,000/microL (or $60x10^9$/L)

  AND
- Medical record documentation that reduced intensity conditioning will be administered prior to infusion with Omisirge **AND**
- Medical record documentation that an identically matched (12/12) donor (related or unrelated) is not readily available **AND**
- Medical record documentation that patient has not had a prior allogeneic hematopoietic stem cell transplantation (HSCT)

AUTHORIZATION DURATION: One time authorization for one administration of Omisirge

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.

UPDATES

XPOVIO (selinexor)

Background: The following indication was withdrawn for Xpovio:

for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from follicular lymphoma, after at least 2 lines of systemic therapy

This was previously approved through the accelerated approval. The Phase 3 confirmatory trial was not completed and Karyopharm Therapeutics requested to voluntarily withdraw the indication.

Recommendation: No changes recommended to the formulary placement of Xpovia. It is recommended that the policy updated from the Commercial Admin Policy to the Oral Oncology Policy 896.0 with the following quantity Limits:

- QL FOR LETTER ONLY:

40 mg once weekly	10 mg tablets	16 tablets per 28 days
40 mg once weekly	40 mg tablets	4 tablets per 28 days
40 mg twice weekly	40 mg tablets	8 tablets per 28 days
60 mg once weekly	60 mg tablets	4 tablets per 28 days
60 mg twice weekly	20 mg tablets	24 tablets per 28 days
80 mg once weekly	40 mg tablets	8 tablets per 28 days
80 mg twice weekly	20 mg tablets	32 tablets per 28 day
100 mg once weekly	50 mg tablets	8 tablets per 28 days

Discussion: No comments or questions.

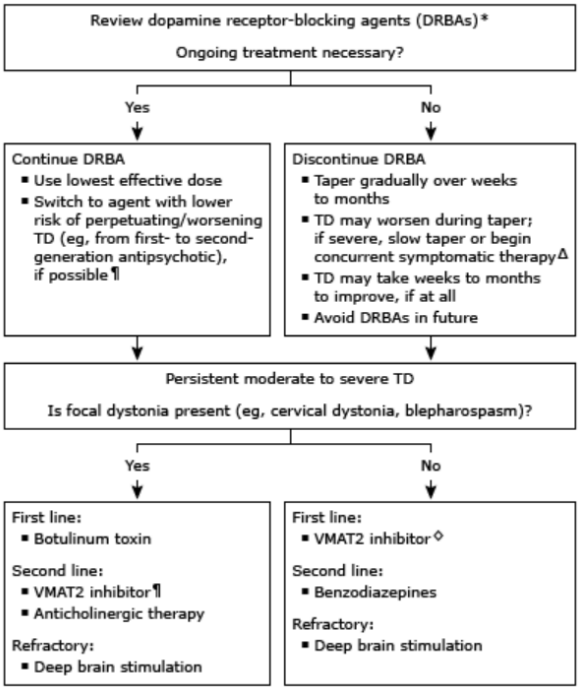
Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (32 approved, 0 rejected).

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

VMAT INHIBITOR UPDATES

Background: Since the introduction of VMAT2 inhibitors, Ingrezza and Austedo/Austedo XR, treatment guidelines have been updated to recommend VMAT2 inhibitors as first line treatment in patients without focal dystonia and second line treatment following botox for patients with focal dystonia. The current recommended treatment algorithm is shown in Table 1.

Table 1. Tardive Dyskinesia Treatment Aglorithm[1]



VMAT2: vesicular monoamine transporter type 2

* The most common causes of TD are first-generation antipsychotics, second-generation antipsychotics, metoclopramide, and prochlorperazine.
¶ Among second-generation antipsychotics, clozapine and quetiapine have the lowest risk of perpetuating/worsening TD.
Δ Symptomatic therapies include VMAT2 inhibitors, benzodiazepines, botulinum toxin (for focal dystonia), and anticholinergic therapy (for focal dystonia).
◊ VMAT2 inhibitors for TD include valbenazine, deutetrabenazine, and tetrabenazine. The three drugs have not been compared directly, and regional availability and cost may vary. Valbenazine and deutetrabenazine are generally preferred over tetrabenazine based primarily on longer half-life and convenience

Although amantadine has shown some efficacy for adjunctive treatment of tardive dyskinesia in patients who require antipsychotics, evidence is limited in support of routine use of amantadine in TD and is not currently recommended in clinical guidelines.

Recommendation: It is recommended that the Commercial policies for Ingrezza and Austedo/Austedo XR be updated to remove failure of amantadine from the TD prior authorization criteria as follows:

Ingrezza Policy 465.0
Tardive Dyskinesia

- Medical record documentation of age greater than or equal to 18 years **AND**
  - Medical record documentation that Ingrezza is prescribed by, or in consultation with, a psychiatrist or neurologist **AND**
  - Medical record documentation of a diagnosis of tardive dyskinesia (TD) as evidenced by one of the following:
    - Moderate to severe abnormal body movement (AIMS score 3 or 4) in greater than or equal to 1 body area **OR**
    - Mild abnormal body movements (AIMS score 1 or 2) in greater than or equal to 2 body areas **AND**
  - Medical record documentation that the member was assessed for and determined to have no other causes of involuntary movements **AND**
  - Medical record documentation of the member's baseline AIMS score prior to initiating therapy **AND**

- If member's symptoms are related to use of a first-generation antipsychotic, medical record documentation that a switch to a second-generation antipsychotic has been attempted and did not resolve tardive dyskinesia symptoms **OR** provider rationale as to why a switch to a second-generation antipsychotic would not be appropriate for the member **AND**
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to amantadine~~

Austedo/Austedo XR Policy 465.0
Tardive Dyskinesia

- Medical record documentation of age greater than or equal to 18 years **AND**
  - Medical record documentation that Austedo is prescribed by, or in consultation with, a psychiatrist or neurologist **AND**
  - Medical record documentation of a diagnosis of tardive dyskinesia (TD) as evidenced by one of the following:
    - Moderate to severe abnormal body movement (AIMS score 3 or 4) in greater than or equal to 1 body area **OR**
    - Mild abnormal body movements (AIMS score 1 or 2) in greater than or equal to 2 body areas **AND**
  - Medical record documentation that the member was assessed for and determined to have no other causes of involuntary movements **AND**
  - Medical record documentation of the member's baseline AIMS score prior to initiating therapy **AND**
  - One of the following:
    - If patient has a history of prior suicide attempt, bipolar disorder, or major depressive disorder: Medical record documentation that patient was evaluated and treated by a psychiatrist **OR**
    - For all others: Medical record documentation of a mental health evaluation performed by the prescriber **AND**
  - If member's symptoms are related to use of a first-generation antipsychotic, medical record documentation that a switch to a second-generation antipsychotic has been attempted and did not resolve tardive dyskinesia symptoms **OR** provider rationale as to why a switch to a second-generation antipsychotic would not be appropriate for the member **AND**
  - ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to amantadine~~

Discussion: Dr. Shepherd commented that the Behavioral Health Medical Directors are in agreement with this update. No additional comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (29 approved, 0 rejected).

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

XPOVIO (selinexor)

Background: We were presented with a rebate opportunity if we were to remove any "documentation" notation in the policies and replace it with "attestation" from our preferred CGRP antagonist policies. This update needs to also apply to Ubrelvy.

Recommendation: It is recommended to update the Ubrelvy policy as follows:

Ubrelvy (Policy 626.0)

- ~~Medical record documentation~~ Patient of age greater than or equal to 18 years **AND**
- ~~Medical record documentation~~ Physician attestation that Ubrelvy will be used for the acute treatment of migraine with or without aura **AND**
- ~~Medical record documentation~~ Physician attestation of therapeutic failure on, intolerance to, or contraindication to one (1) formulary triptan **AND**
- ~~Medical record documentation~~ Physician attestation that Ubrelvy will not be used concomitantly with another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the acute treatment of migraine (e.g., Nurtec ODT)

Discussion: Bret asked us to confirm that someone is monitoring rebates to ensure we are obtaining the value as expected. Jamie and Aubrielle confirmed that we are. No additional comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented. None were opposed (29 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 GENERIC DRUG UPDATE

Background: All current medical benefit drug policies were reviewed and drugs that have a therapeutically equivalent generic available were identified. Currently, there is no language in the identified medical benefit drug policies requiring the use of a generic formulation first before the use of a brand formulation. Using a generic drug first may provide cost savings for Geisinger Health Plan especially if a medication is being fulfilled by a specialty pharmacy. It is recommended to require a generic first before the use of a brand, when the generic formulation is available.

Recommendation: It is recommended that the following wording be added to applicable medical benefit policies for drugs that have a therapeutically equivalent generic available. The medical benefit list of drugs will continue to be reviewed annually to identify drugs with newly released generic formulations. Policies identified containing drugs with therapeutically equivalent generics will be updated with the below language.

AND (if a brand drug is being requested when a therapeutically equivalent generic drug exists):

- Medical record documentation of a therapeutic failure on, or intolerance to the generic formulary agent(s) **OR**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to the inactive ingredients of the generic formulary agent(s)

Newly Identified Drugs with Available Therapeutically Equivalent Generic Formulations

- Halaven (eribulin mesylate) MBP 88.0
- Sandostatin LAR (octreotide acetate) MBP 99.0
- Dalvance (dalbavancin) MBP 121.0
- Radicava IV (edaravone) MBP 154.0

Discussion: Bret asked if we are in sync with the clinical enterprise for when they will need to order generics vs. a brand. We confirmed they are. No additional 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 UPDATES (YERVOY, IDOSE TR, DARZALEX FASPRO, PORTRAZZA)

Background: Yervoy Update

Discussion: Previously, the Yervoy policy criteria for unresectable/metastatic melanoma aligned with NCCN recommendations. After reviewing further, it appears some NCCN recommendations for unresectable/metastatic melanoma and Yervoy are not accounted for in the policy. Additionally, other indications for Yervoy, along with other oncology medication policies, align closely with the FDA approved indication.

Recommendations: It is recommended to update the prior authorization criteria for Yervoy and the indication of unresectable/metastatic melanoma to align with the FDA approved indication, consistent with both other indications within the policy and other oncology policies at Geisinger Health Plan.

MBP 91.0 Yervoy (Ipilimumab)

1. Melanoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 12 years of age or older **AND**
- Medical record documentation that Yervoy will be used as a single agent or in combination with nivolumab (Opdivo) **AND**
- Medical record documentation of unresectable or metastatic melanoma ~~**AND**~~
- ~~One of the following:~~
    - ~~Medical record documentation of use in combination with nivolumab for first line therapy **OR**~~
    - ~~Medical record documentation of use as a single agent or in combination with nivolumab as second-line or subsequent therapy for disease progression if not previously used **OR**~~
    - ~~Medical record documentation of use as a single-agent reinduction therapy in select patients who experienced no significant systemic toxicity during prior ipilimumab therapy and who relapse after initial clinical response or progress after stable disease >3 months~~

OR

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or older **AND**
- Medical record documentation of use as a single agent for adjuvant therapy:
    - For Stage IIIA with metastases > 1 mm, or Stage IIIB or Stage IIIC cutaneous melanoma with nodal metastases following a complete lymph node dissection or resection **OR**
    - Following complete lymph node dissection and/or complete resection of nodal recurrence

iDose TR Update

Recommendations: It is recommended to update the authorization duration and reauthorization criteria for iDose TR based on specialist feedback and internal discussion.

MBP 369.0 iDose TR (travoprost intracameral implant) – for Commercial/Exchange/CHIP/Medicare

Authorization Duration: Initial approval will be for a period of 6 months to allow for one-time administration. ~~12 months or less if the reviewing provider feels it is medically appropriate.~~ Subsequent approvals will be for a period of 6 months to allow for one-time administration. ~~an additional 12 months or less if the reviewing provider feels it is medically appropriate and~~ all subsequent requests will require:

- ~~Medical record documentation of continued or sustained improvement in the signs and symptoms of the treated indication while on therapy~~ Medical record documentation of improvement from baseline in the signs and symptoms of the treated indication sustained for a duration of 12 months or more **AND**
- Medical record documentation that symptoms have returned to such a degree that repeat implantation is required **AND**
- Medical record documentation that the patient has not received a previous administration of iDose TR to the requested eye within the past 12 months **AND**

- Medical record documentation a pre-implantation, central corneal endothelial cell density prior to the readministration of iDose TR

IVIG Update

Recommendations: It is recommended to update the prior authorization criteria for IVIG and the indication of dermatomyositis and polymyositis to also allow for rheumatologist prescribing.

MBP 4.0 Intravenous Immune Globulin (IVIG)

- **Dermatomyositis and Polymyositis**
  All of the following criteria must be met:
  1. Diagnosis of dermatomyositis or polymyositis confirmed by biopsy **AND**
  2. Documented evidence of active disease **AND**
  3. Must be prescribed by a neurologist or rheumatologist **AND**
  4. Documented evidence that the condition is refractory to both of the following therapies:
     - First line therapy: corticosteroids (at least 4 months of therapy)
     - Second line therapy: at least two immunosuppresants (e.g. cyclosporine, azathioprine, methotrexate, cyclophosphamide)

Darzalex Faspro Update

Recommendations: It is recommended to update the authorization duration for Darzalex Faspro per PARP recommendations.

MBP 230.0 Darzalex Faspro (daratumumab/hyaluronidase)

AUTHORIZATION DURATION
Multiple Myeloma
Initial approval will be for 3 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 the following:

- Continued disease improvement or lack of disease progression **AND**
- ~~An FDA approved dose and dosing interval~~ A dose and dosing interval that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

The medication will no longer be covered if patient experiences toxicity or worsening of disease ~~or a non-FDA approved dose or dosing interval.~~ or a dose or dosing interval that is not consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

For requests of a treatment duration exceeding United States Food and Drug Administration (FDA) labeling, National Comprehensive Cancer Network® (NCCN), or indication specific peer-reviewed literature, medical record documentation of the following is required:

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

High-Risk Smoldering Multiple Myeloma
Initial approval will be for 3 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 the following:

- Continued disease improvement or lack of disease progression **AND**
- ~~An FDA approved dose and dosing interval~~ A dose and dosing interval that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

The medication will no longer be covered if patient experiences toxicity or worsening of disease ~~or a non-FDA approved dose or dosing interval.~~ or a dose or dosing interval that is not consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

Authorization of Darzalex Faspro for ~~light chain (AL) amyloidosis~~ high-risk smoldering multiple myeloma should not exceed the FDA-approved treatment duration of 3 years (36 months). For requests exceeding the above limit, medical record documentation of the following is required:

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

Light Chain (AL) Amyloidosis

Initial approval will be for 3 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 the following:

- Continued disease improvement or lack of disease progression **AND**
- ~~An FDA approved dose and dosing interval.~~ A dose and dosing interval that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

The medication will no longer be covered if patient experiences toxicity, worsening of disease, ~~or a non-FDA approved dose or dosing interval.~~ or a dose or dosing interval that is not consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

Authorization of Darzalex Faspro for light-chain (AL) amyloidosis should not exceed the FDA-approved treatment duration of 2 years (24 months). For requests exceeding the above limit, medical record documentation of the following is required:

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

Portrazza Update

Recommendations: It is recommended to retire MBP 142.0 Portrazza. The manufacturer has let the NDC go inactive on 5/29/26 and the National Cancer Institute lists the NDC as status: no longer used and discontinued as of 5/27/26.

Discussion: Keith commented regarding the authorization duration of iDOSE TR. No additional comments or questions (30 approved, 0 rejected).

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

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

QUARTERLY CASE AUDIT

Background: Quarterly case audit for 1st quarter 2026 was held on June 11, 2026.

Recommendation: There were no formulary changes proposed at this meeting. We will continue to monitor requests for non formulary insulins for commercial and non formulary albuterol sulfate HFA requests at the next case audit meeting to help determine if a policy should be created. We will continue to look for additional opportunities to create more drug specific policies at future quarterly case audit meetings.

Discussion: No comments or questions.

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

Meeting adjourned at 3:33 pm.

The next bi-monthly scheduled meeting will be held on September 8th, 2026 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.