P&T Committee Meeting Minutes
Commercial, Exchange, CHIP
August 2025 e-Vote

DRUG REVIEWS

AZMIRO (Testosterone cypionate)

Review:
Azmiro is the first and only FDA-approved prefilled testosterone cypionate injection indicated for testosterone replacement therapy in males for conditions associated with a deficiency or absence of endogenous testosterone.

Testosterone cypionate intramuscular injections are commonly used as a testosterone replacement therapy for patients with low testosterone by drawing up testosterone cypionate doses from a vial, then administering with a syringe.

Azmiro provides a prefilled option now available as a 200mg/ml single dose syringe. Dosing schedule depends on the patient's testosterone levels, but typical dosing is one injection every 7 days.

FDA approval of Azmiro was based primarily on a single, open-label, randomized, single dose, two-way crossover pharmacokinetic study of adult males with hypogonadism. In the clinical trial, 28 hypogonadal men (ages 18-65, BMI 18-35kg/m2) received a single intramuscular dose of Azmiro 200mg or a comparator testosterone cypionate product, then were assessed over 31 days. The primary purpose of the trial was to establish bioequivalence in pharmacokinetics between Azmiro and the established multidose formulation of testosterone cypionate. Secondarily, the trial aimed to assess safety and tolerability via adverse event monitoring with a focus on injection site reactions and general testosterone related events.

Azmiro demonstrated bioequivalence to the comparator product; pharmacokinetic profiles matched those of traditional testosterone cypionate injections.

The most common adverse events were mild injection site erythema (26%) and mild injection site reactions (4%). Safety in men with age-related hypogonadism and pediatric patients below 12 years old has not been established. The trial did not evaluate long-term cardiovascular outcomes.

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

Outcome: Azmiro is a pharmacy benefit and will not be added to the Commercial, Exchange, or GHP Kids formularies at this time. Recommend adding to Policy 726.0 Xyosted, with the following prior authorization criteria:

An exception for coverage of Xyosted and Azmiro may be made for members who meet the following criteria:

- Medical record documentation of one of the following:
    - Medical record documentation of use for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:
        - Primary hypogonadism (congenital or acquired) **OR**
        - Hypogonadotropic hypogonadism (congenital or acquired) **OR**
    - Medical record documentation of a diagnosis of gender dysphoria, as defined by the current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three formulary alternatives

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

FAST FACTS

AMVUTTRA (vutrisiran injection)

Clinical Summary: Amvuttra is a transthyretin-directed small interfering RNA previously indicated for the treatment of:

- Polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults

It is now also indicated for treatment of:

- Cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis in adults to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits

The efficacy of Amvuttra was evaluated in a multicenter, international, randomized, double-blind, placebo-controlled trial (HELIOS-B, NCT04153149) in 654 adult patients with wild-type or hereditary TTR-CM. Patients were randomized 1:1 and received either 25 mg of Amvuttra (n=326) subcutaneously once every 3 months or matching placebo (n=328). Treatment assignment was stratified by baseline tafamidis use (yes vs no), ATTR disease type (stATTR or hATTR amyloidosis), and by baseline New York Heart Association (NYHA) Class I or II and age <75 years vs all other. At baseline 40% of patients were on tafamidis. The mean age was 75 years old, 93% were male, 88% had wild type ATTR, 13% were NYHA Class I, 78% were Class II, and 9% Class III. No significant imbalance in baseline characteristics was observed between two treatment groups.

Participants were permitted to initiate open-label tafamidis during the study. A total of 85 participants initiated tafamidis: 44 (22%) in the Amvuttra arm and 41 (21%) in the placebo arm. The median time to initiation of tafamidis for these 85 participants was 18 months.

The primary efficacy endpoint was the composite outcome of all-cause mortality and recurrent CV events (CV hospitalizations and urgent heart failure [UHF] visits) during the double-blind treatment period up to 36 months, evaluated in the overall population and in the monotherapy population (defined as patients not receiving tafamidis at study baseline)

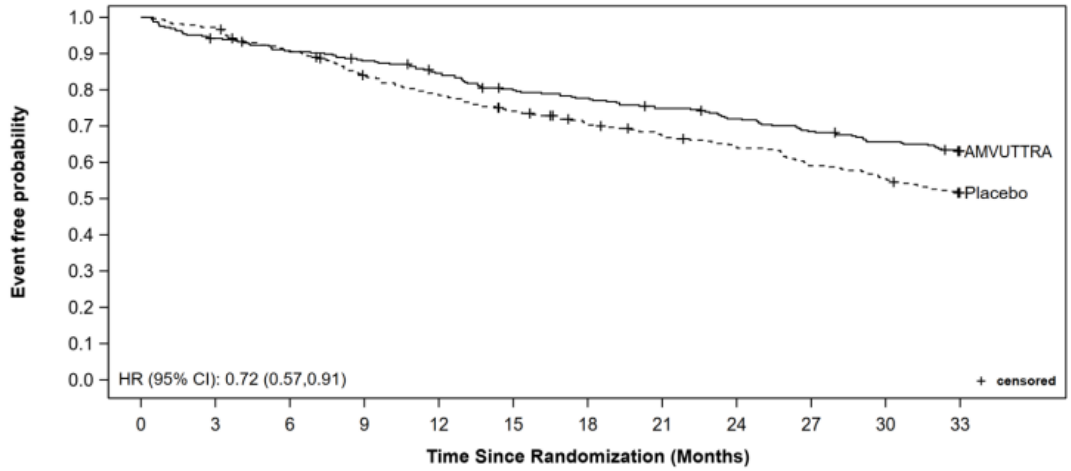
Amvuttra led to significant reduction in the risk of all-cause mortality and recurrent CV events compared to placebo in the overall and monotherapy population of 28% and 33% respectively shown in table 4. The majority of deaths (77%) were CV-related.

Table 4: Primary Composite Endpoint and its Individual Components in HELIOS-B

Endpoint		Overall population		Monotherapy population	
		AMVUTTRA (N=326)	Placebo (N=328)	AMVUTTRA (N=196)	Placebo (N=199)
Primary composite endpoint*	Hazard Ratio (95% CI)†	0.72 (0.55, 0.93)		0.67 (0.49, 0.93)	
	p-value†	0.01		0.02	
Components of the Primary Composite Endpoint					
All-cause mortality	Hazard Ratio (95% CI)‡	0.69 (0.49, 0.98)		0.71 (0.47, 1.06)	
CV hospitalizations and UHF visits	Hazard Ratio (95% CI)†	0.73 (0.55, 0.96)		0.67 (0.47, 0.96)	

Abbreviations: CI=confidence interval; CV=cardiovascular; UHF=urgent heart failure.
Heart transplantation and left ventricular assist device placement are treated as death. Deaths after study discontinuation are included in the all-cause mortality component analysis.
* Primary composite endpoint defined as: composite outcome of all-cause mortality and recurrent CV events. Primary analysis included at least 33 months (and up to 36 months) follow-up on all patients.
† Hazard Ratio (95% CI) and *p*-value are based on a modified Andersen-Gill model.
‡ Hazard Ratio (95% CI) is based on a Cox proportional hazard model.

Figure 5: Time to All-Cause Mortality or First CV Event (Overall population)



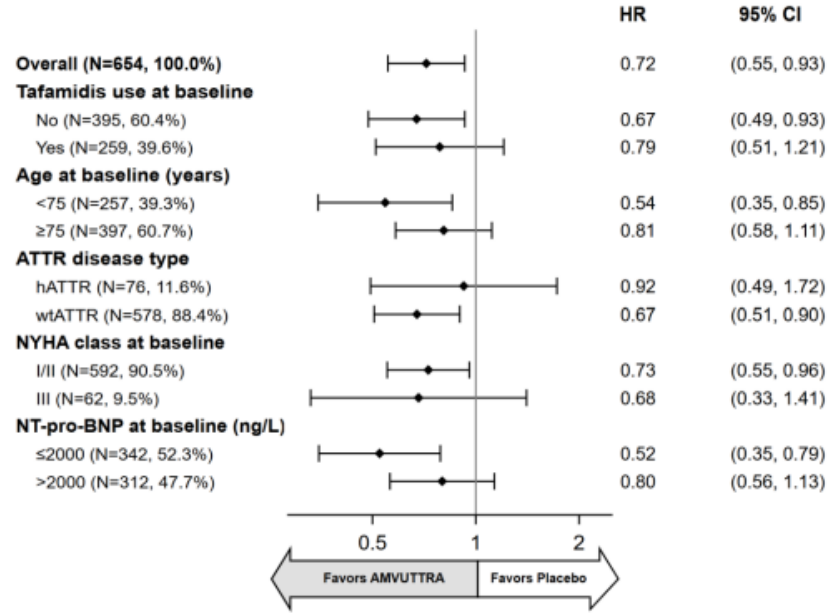
No. at Risk (Cumulative No. of Events)

AMVUTTRA	326(0)	306(19)	294(30)	284(39)	271(50)	254(65)	247(72)	237(81)	227(90)	216(101)	206(110)	185(118)
Placebo	328(0)	317(11)	295(31)	270(53)	253(70)	237(84)	221(96)	210(105)	199(115)	183(131)	172(142)	155(154)

Abbreviations: CI=confidence interval; CV=cardiovascular; HR = hazard ratio.

Heart transplantation and left ventricular assist device placement are treated as death. HR and 95% CI are based on a Cox proportional hazard model. First CV event = First CV hospitalization or urgent heart failure visit after randomization.

Figure 6: Subgroup Analyses of the Primary Composite Endpoint (Overall Population)



Abbreviations: ATTR = transthyretin amyloidosis; CI = confidence interval; hATTR = hereditary transthyretin amyloidosis; HR = hazard ratio; NT-pro-BNP = N-terminal prohormone of B-type natriuretic peptide; NYHA = New York Heart Association; wtATTR = wild-type transthyretin amyloidosis.

HR and 95% CI are based on modified Andersen-Gill model analyses.

The treatment effect of Amvuttra on functional capacity and health status were assessed by the change in baseline to month 30 in distance walked on a 6-minute Walk Test (6-MWT), and the Kansas City Cardiomyopathy Questionnaire-Overall summary (KCCQ-OS) score.

At month 30, the LS mean difference in change from baseline in distance walked on 6-MWT was 22 (95% CI: 8, 35; p=0.002) meters and 25 (95% CI: 7, 44; p=0.006) meters favoring AMVUTTRA over placebo in the overall population and monotherapy population, respectively

At Month 30, the LS mean difference in the change from baseline in KCCQ-OS was 6 (95% CI: 2, 9; p=0.001) and 8 (95% CI: 4, 13; p=0.0003) favoring AMVUTTRA over placebo in the overall population and monotherapy population respectively.

Current Formulary Status: Medical benefit requiring prior authorization.

Recommendation: There are no changes to the formulary status, authorization duration, or current quantity limits. It is recommended to add the following changes to the criteria for MBP 268.0:

- Prescription written by or in consultation with a neurologist, cardiologist board-certified medical geneticist, or specialist with experience in the treatment of hereditary transthyretin-mediated amyloidosis (hATTR) **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of one of the following
    - For hereditary transthyretin-mediated amyloidosis
        - Medical record documentation of diagnosis of hereditary transthyretin-mediated amyloidosis as confirmed by genetic testing to confirm a pathogenic mutation in TTR AND one of the following:
            - Biopsy of tissue/organ to confirm amyloid presence **OR**
            - A clinical manifestation typical of hATTR (Neuropathy and/or CHF) without a better alternative explanation **AND**
        - Medical record documentation of Amvuttra being used to treat polyneuropathy **AND**
        - Medical record documentation of familial amyloid polyneuropathy (FAP) stage 1-2 and/or polyneuropathy disability score (PND) indicating the patient is not wheelchair bound or bedridden **OR**
        - Medical record documentation Amvuttra is being used for cardiomyopathy to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits

      OR
    - For wild-type transthyretin-mediated amyloidosis
        - Medical record documentation of diagnosis of wild-type transthyretin-mediated amyloidosis as confirmed by genetic testing **AND**
        - Medical record documentation Amvuttra is being used for cardiomyopathy to reduce cardiovascular mortality, cardiovascular hospitalizations and urgent heart failure visits **AND**
- Medical record documentation of a dose and duration of therapy that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature **AND**
- Medical record documentation that Amvuttra will not be used in combination with other RNA interference treatment

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

BAQSIMI (glucagon)

Clinical Summary: In March 2025, the FDA expanded the approval of Baqsimi nasal powder to include treatment of severe hypoglycemia in patients aged 1 year and older with diabetes. Previously, Baqsimi was limited to use in patients 4 years of age and older.
The recommended dose of Baqsimi is 3mg (one actuation of single use device) into a single nostril. If there is no response, the dose may be repeated in 15 minutes using a new intranasal device. Baqsimi does not require inhalation during product actuation.

The expanded approval was based on data obtained from an open-label, single-arm, phase 1 study (A Study of Nasal Glucagon (LY900018) in Pediatric Participants With Type 1 Diabetes (RescuiNGkids)) that assessed both safety and tolerability of Baqsimi in patients aged 1 to less than years old with type 1 diabetes mellitus. The findings of this study achieved the primary efficacy endpoint that all study participants attained an increase in glucose of at least 20mg/dl from baseline within 30 minutes of Baqsimi administration.

The adverse reactions observed in this trial were comparable to those seen in trials involving older children and adults. The most common side effects reported with treatment include nausea, vomiting, headache, upper respiratory tract irritation, and nasal and ocular symptoms (e.g., watery eyes, redness of eyes, itchy nose, throat and eyes).

Current Formulary Status: Brand preferred on formulary with no prior authorization requirement

Recommendation: No recommended changes.

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

DEXTENZA (dexamethasone ophthalmic insert)

Clinical Summary: Dextenza is now indicated for the treatment of ocular inflammation and pain following ophthalmic surgery in pediatric patients and for the treatment of ocular itching associated with allergic conjunctivitis in pediatric patients aged 2 years and older. The use of Dextenza is not recommended for the treatment of ocular itching associated with allergic conjunctivitis in pediatric patients who require sedation for the insertion procedure. Previously, the same two indications were approved in the adult populations.

There were no changes to dosing as a result of the updated indication.

There were no new efficacy studies performed. Use of Dextenza for these indications is supported by evidence from well-controlled studies in adults with additional safety data from a single active-controlled study in pediatric patients aged birth to 5 years old.

There were no changes to the safety information for Dextenza – a similar safety profile was observed between pediatric and adult patients.

Current Formulary Status: Dextenza is a medical benefit requiring prior authorization

Recommendation: No changes recommended.

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

FUROSCIX (furosemide injection)

Clinical Summary: Furoscix is indicated for the treatment of edema in adult patients with chronic heart failure or chronic kidney disease (CKD), including the nephrotic syndrome.

The single-use, On-body Infusor with prefilled cartridge is pre-programmed to deliver 30 mg of furosemide over the first hour followed by 12.5 mg per hour for the subsequent 4 hours. Furoscix is not for chronic use and should be replaced with oral diuretics as soon as practical.

There were no new or updated clinical studies or safety considerations provided.

Current Formulary Status: Non-formulary

Recommendation: Recommend the following change to the Commercial/Exchange/CHIP policy 770.0 to reflect the additional indication for Furoscix. Formulary status, auth duration will remain the same.

- Medical record documentation that Furoscix is prescribed by or in consultation with a cardiologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of chronic heart failure **AND**
- Medical record documentation of congestion due to fluid overload **OR**
- Medical record documentation of chronic kidney disease (CKD), including the nephrotic syndrome **AND**
- Medical record documentation that member is stable on background loop diuretic therapy **AND**
- Medical record documentation of provider attestation that member will use Furoscix for short-term use only and will be transitioned to oral diuretics as soon as practical

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

IBRANCE (palbociclib)

Clinical Summary: Ibrance is now indicated in combination with inavolisib and fulvestrant for the treatment of adult patients with endocrine-resistant, PIK3CA-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy.

There is no change to the recommended dosage for the new indication. The recommended dose of Ibrance is a 125 mg capsule taken orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a complete cycle of 28 days. When Ibrance is given in combination with inavolisib and fulvestrant therapy, patients should also be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to current clinical practice standards.

Support for the new indication comes from the INAVO120 trial, a randomized, double-blind, placebo-controlled trial evaluating the efficacy of inavolisib in combination with Ibrance and fulvestrant in adult patients with endocrine resistant PIK3CA-mutated, HR-positive, HER2-negative (defined as IHC 0 or 1+, or IHC 2+/ISH-), locally advanced or metastatic breast cancer whose disease progressed during or within 12 months of completing adjuvant endocrine therapy and who have not received prior systemic therapy for locally advanced or metastatic disease. Primary endocrine resistance was defined as relapse while on the first 2 years of adjuvant endocrine therapy (ET) and secondary endocrine resistance was defined as relapse while on adjuvant ET after at least 2 years or relapse within 12 months of completing adjuvant ET

Patients received either inavolisib 9 mg (n=161) or placebo (n=164) orally once daily, in combination with Ibrance 125 mg orally once daily for 21 consecutive days followed by 7 days off treatment to comprise a cycle of 28 days, and fulvestrant 500 mg administered intramuscularly on Cycle 1, Days 1 and 15, and then on Day 1 of every 28-day cycle. Patients received treatment until disease progression or unacceptable toxicity. In addition, all pre/perimenopausal women and men received an LHRH agonist throughout therapy.
Tamoxifen (57%) and aromatase inhibitors (50%) were the most commonly used adjuvant endocrine therapies. Eighty-three percent of patients had received prior chemotherapy (in the neo/adjuvant setting) and 1.2% of patients had been treated with a CDK4/6 inhibitor.

The major efficacy outcome measure was investigator-assessed progression free survival per RECIST v1.1. Additional efficacy outcome measures included overall survival and investigator-assessed complete response rate and duration of response. Results are shown in Table 1.

Table 1. Efficacy results in Patients with Locally Advanced or Metastatic Breast Cancer in INAVO120

Efficacy Endpoint	**IBRANCE plus Inavolisib and Fulvestrant N=161**	**IBRANCE plus Placebo and Fulvestrant N=164**
Progression-Free Survival [a,b]		
Patients with event (%)	82 (51)	113 (69)
Median, months (95% CI)	15.0 (11.3, 20.5)	7.3 (5.6, 9.3)
Hazard ratio (95% CI)	0.43 (0.32, 0.59)	
p-value	<0.0001	
Objective Response Rate [a,b,c]		
Patients with CR or PR (%)	94 (58)	41 (25)
95% CI	(50, 66)	(19, 32)
Duration of Response [b]		
Median DOR, months (95% CI)	18.4 (10.4, 22.2)	9.6 (7.4, 16.6)

CI=confidence interval; CR=complete response; DOR=duration of response; N=number of patients; PR=partial response.
[a] Per RECIST version 1.1.
[b] Based on investigator assessment.
[c] Based on confirmed ORR.

Serious adverse reactions occurred in 24% of patients who received Ibrance plus inavolisib and fulvestrant and included anemia (1.9%), diarrhea (1.2%), and urinary tract infection (1.2%). Fatal adverse reactions occurred in 3.7% of patients and included (0.6% each) acute coronary syndrome, cerebral hemorrhage, cerebrovascular accident, COVID-19 infection, and gastrointestinal hemorrhage. Permanent discontinuation of Ibrance associated with an adverse reaction occurred in 8 of 162 (4.9%) who received inavolisib and 0 of 162 patients who received placebo. Dose reduction and dose interruption occurred in 38% and 71% of patients respectively who received Ibrance + inavolisib + fulvestrant. Dose reduction and interruption occurred in 30% and 61% of patients, respectively who received Ibrance + placebo + fulvestrant. The most common (≥20%) adverse reactions, including laboratory abnormalities, were decreased neutrophils, decreased hemoglobin, increased fasting glucose, decreased platelets, decreased lymphocytes, stomatitis, diarrhea, decreased calcium, fatigue, decreased potassium, increased creatinine, increased alanine aminotransferase (ALT), nausea, decreased sodium, decreased magnesium, rash, decreased appetite, COVID-19 infection, and headache.

Current Formulary Status: Pharmacy Benefit, Oral Oncology Brand NP tier ($0 Copay), PA required for NSO

Recommendation: There are no changes recommended for the current formulary placement and quantity limits. The following updates are recommended to Commercial Policy 367.0 to incorporate the new indication:

Ibrance as Initial Endocrine Therapy
- Medical record documentation that Ibrance is prescribed by an oncologist **AND**
- Medical record documentation of a diagnosis of hormone receptor positive (HR-positive), HER2 negative advanced or metastatic breast cancer **AND**

- Ibrance is bring prescribed as initial endocrine based therapy in postmenopausal women **OR** men receiving testicular steroidogenesis suppression treated with a luteinizing hormone-releasing hormone (LHRH) agonist (i.e., goserelin, etc.) **AND**
- Medical record documentation that Ibrance will be prescribed in combination with an aromatase inhibitor (i.e., letrozole, etc.)

Ibrance Following Disease Progression on Endocrine Therapy
- Medical record documentation that Ibrance is prescribed by an oncologist **AND**
- Medical record documentation of a diagnosis of hormone receptor positive (HR-positive), HER2 negative advanced or metastatic breast cancer **AND**
- Ibrance is being prescribed after disease progression following endocrine therapy **AND**
- Medical record documentation that Ibrance is being used in combination with fulvestrant **AND**
- **If the request is for a pre/peri-menopausal woman:** Medical record documentation that the member is receiving ovarian suppression with a luteinizing hormone-releasing hormone (LHRH) agonist (i.e., goserelin, etc.)

Ibrance with PIK3CA mutation
- Medical record documentation that Ibrance is prescribed by an oncologist **AND**
- Medical record documentation of a diagnosis of hormone receptor positive (HR-positive), HER2 negative advanced or metastatic breast cancer **AND**
- Medical record documentation of a PIK3CA-mutation AND
- Medical record documentation of endocrine resistance* following recurrence on or after completing adjuvant endocrine therapy **AND**
- Medical record documentation that Ibrance is being used in combination inavolisib and fulvestrant t **AND**
- **If the request is for a pre/peri-menopausal woman:** Medical record documentation that the member is receiving ovarian suppression with a luteinizing hormone-releasing hormone (LHRH) agonist (i.e., goserelin, etc.)

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*
- QL FOR LETTER ONLY: 21 capsules per 28 days, 28 day supply per fill

RE-AUTHORIZATION CRITERIA: Ibrance is configured as a prior authorization for new starts only. Ibrance 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

*NOTE: In clinical trials, primary endocrine resistance was defined as relapse while on the first 2 years of adjuvant endocrine therapy (ET) and secondary endocrine resistance was defined as relapse while on adjuvant ET after at least 2 years or relapse within 12 months of completing adjuvant ET.

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

INZIRQO (hydrochlorothiazide oral suspension)

Clinical Summary: Inzirqo oral suspension [10 mg/ml] is a thiazide diuretic indicated for the following:
- The treatment of hypertension in adult and pediatric patients alone or in combination with other antihypertensive agents.
- The treatment of edema associated with congestive heart failure, hepatic cirrhosis and renal disease including the nephrotic syndrome in adult and pediatric patients.

Updated dosing:
- hypertension in adults: 25 mg once daily to 50 mg given once or twice daily
- edema in adults: 25 mg to 100 mg daily as a single or divided dose
- hypertension or edema in children: 1mg/kg to 2 mg/kg per day in singe or divided doses.
    - Max dose of 37.5 mg per day: less than 2 years of age.
    - Max dose of 100 mg per day: children 2 to less than 13 years of age.
    - Patients less than 6 months of age may require doses up to 3 mg/kg per day in two divided doses.

No updated clinical studies provided for review.

Summary of Safety Considerations:

- noted adverse reactions: impaired renal function, electrolyte abnormalities, metabolic disturbances, systemic lupus erythematosus, acute angle-closure glaucoma, acute myopia
- non melanoma skin cancer noted in post marketing experience: increased risk (1 additional case per 6,700 patients per year) of squamous cell carcinoma (SCC) in white patients taking large cumulative doses noted as greater than or equal to 50,000 mg

Current Formulary Status: Non-Formulary

Recommendation: No changes to formulary placement.

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

KEYTRUDA (pembrolizumab)

Clinical Summary:
Keytruda is now indicated for the treatment of adult patients with resectable locally advanced HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test, as a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without cisplatin and then as a single agent. There was also an update to the population for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma used combination with fluoropyrimidine- and platinum-containing chemotherapy. This is now restricted to patients whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test to reflect the population with a favorable risk-benefit assessment.

The recommended dosage of Keytruda for treated neo/adjuvant HNSCC is 200 mg every three weeks or 400 mg every 6 weeks. As neoadjuvant treatment, Keytruda is administered for 6 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity. For adjuvant treatment, Keytruda is administered in combination with radiotherapy with or without cisplatin, then continued as a single agent. Keytruda is continued until disease recurrence, unacceptable toxicity, or up to one year.

The efficacy and safety of Keytruda in the treatment of neoadjuvant and adjuvant treatment of locally advanced HNSCC for tumors expressing PD-L1 was evaluated in KEYNOTE-689, a randomized, open-label, active-controlled trial in 714 adults with resectable locally advanced (Stage III-IVA) HNSCC. Patients were randomized to receive:

- neoadjuvant Keytruda 200 mg for 2 cycles prior to surgical resection. Within 6 weeks following surgery, 3 cycles of adjuvant Keytruda 200 mg every 3 weeks in combination with radiotherapy (RT) with or without 3 cycles of cisplatin 100 mg/m2 every 3 weeks. This was followed by Keytruda 200 mg every 3 weeks for up to 12 cycles.
- no neoadjuvant treatment prior to surgery. Within 6 weeks following surgery, adjuvant RT with or without 3 cycles of concurrent cisplatin 100 mg/m2 every 3 weeks.

On both treatment arms, patients received cisplatin with adjuvant RT if high-risk pathological features (i.e., positive margins < 1 mm or extranodal extension) were present at surgery.

Treatment with KEYTRUDA continued until disease progression by RECIST v1.1 per BICR during the neoadjuvant phase that precluded surgery, local or metastatic recurrence during the adjuvant phase, completion of treatment, or unacceptable toxicity.

The major efficacy outcome measure was event-free survival (EFS) by BICR defined as the time from randomization to the first occurrence of any of the following events: progression of disease that precludes definitive surgery, local or distant disease progression or recurrence, or death due to any cause. Additional efficacy outcome measures were major pathological response (mPR) as assessed by BIPR, and overall survival (OS).

Seventy-six percent of patients in the Keytruda arm and 78% of patients in the SOC arm started the radiation phase of treatment. In the Keytruda arm, 35% of patients received Keytruda and cisplatin with concurrent RT, 57% of patients received Keytruda alone with concurrent RT, 3% of patients received cisplatin alone with concurrent RT, 5% of patients received RT alone and one patient (0.4%) received Keytruda alone without concurrent RT. On the SoC arm, 52% of patients received cisplatin with concurrent RT while 48% patients received RT alone. The trial demonstrated a statistically significant improvement in EFS for patients randomized to the Keytruda arm compared to those randomized to standard of care at the first interim analysis. Efficacy results are shown in Table 1.

Table 1. Efficacy Results for Perioperative KEYTRUDA with adjuvant RT with or without cisplatin in Patients with HNSCC CPS ≥1 inKEYNOTE-6891

Endpoint	KEYTRUDA 200 mg every 3 weeks with RT with or without cisplatin n=347	RT with or without cisplatin n=335
EFS		
Number of events, n (%)	128 (37%)	156 (47%)
Median in months* (95% CI)	59.7 (37.9, NR)	29.6 (19.5, 41.9)
Hazard ratio† (95% CI)	0.70 (0.55, 0.89)	
p-Value‡,	0.00140	

* From product-limit (Kaplan-Meier) method for censored data.
† Based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by primary tumor site and tumor stage.
‡ One-sided p-value based on log-rank test stratified by primary tumor site and tumor stage. Compared to a one-sided p-value boundary of 0.0124
NR = not reached

Changes to the first line treatment of gastric or GEJ adenocarcinoma used combination with fluoropyrimidine- and platinum-containing chemotherapy are based on additional overall survival data analysis of KEYNOTE-859. An exploratory analysis of overall survival (OS) in the PD-L1 CPS >1 (78% of patients in KEYNOTE-859) population showed a HR of 0.92 (95% CI 0.73, 1.17) indicating that the improvement in the ITT population was primarily attributed to the results observed in the subgroup of patients with PD-L1 CPS ≥1.

Current Formulary Status: Medical benefit requiring prior authorization.

Recommendation: No changes are needed for the formulary placement of Keytruda. The following changes are recommended for the authorization duration and prior authorization criteria in Medical Benefit Policy 119.0 to incorporate the new indication for HNSCC and changed indication for gastric cancer. Additionally, one change is recommended for first line treatment of squamous NSCLC, since this indication is not limited to those without EGFR or ALK mutations.

1. **Melanoma**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation of one of the following:

   <u>Unresectable or metastatic melanoma:</u>
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - A diagnosis of unresectable or metastatic melanoma **AND**
   - Keytruda is not being used in combination with any other agents for the treatment of unresectable or metastatic melanoma.

OR

<u>Adjuvant treatment of completely resected melanoma</u>
- Medical record documentation that patient is ≥ 12 years of age **AND**
- A diagnosis of Stage IIB, IIC, or III melanoma, which has been completely resected **AND**
- Keytruda is being used in the adjuvant setting (following complete resection) **AND**
- Keytruda is being used as a single agent.

2. **Neoadjuvant or Adjuvant Treatment of Non-Small Cell Lung Cancer (NSCLC)**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of one of the following:
   - Medical record documentation of Stage IB (T2a ≥ 4 cm), II, or IIIa non-small cell lung cancer (NSCLC) **AND**
   - Keytruda is being used in the adjuvant setting following resection and platinum-based chemotherapy **AND**
   - Keytruda is being used as a single agent

OR

- Medical record documentation of resectable (Tumors ≥ 4 cm or Node Positive) non-small cell lung cancer (NSCLC) **AND**
- Keytruda is being used in the neoadjuvant setting in combination with platinum containing chemotherapy then continued as a single agent in the adjuvant setting following resection

3. **Metastatic Non-Small Cell Lung Cancer (NSCLC)**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of a diagnosis of metastatic NSCLC meeting one of the following situations:
     - Medical record documentation of stage III NSCLC, metastatic NSCLC, OR that the member is not a candidate for surgical resection or definitive chemoradiation **AND**
     - Medical record documentation that Keytruda is being used as first-line treatment **AND**
     - Medical record documentation that Keytruda is being given as monotherapy **AND**
     - Medical record documentation that tumors express PD-L1 (TPS) ≥1% as determined by an FDA-approved test AND
     - Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

OR

     - Medical record documentation that Keytruda is being given as monotherapy **AND**
     - Medical record documentation that tumors express PD-L1 (TPS) ≥1% as determined by an FDA-approved test **AND**
     - Medical record documentation of disease progression on or after platinum-containing chemotherapy **AND**
     - For patients with EGFR or ALK genomic tumor aberrations: medical record documentation of disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.

OR

     - Medical record documentation of metastatic nonsquamous NSCLC **AND**
     - Medical record documentation that Keytruda will be given in combination with pemetrexed AND either carboplatin or cisplatin **AND**
     - Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

OR

     - Medical record documentation of metastatic squamous NSCLC **AND**
     - Medical record documentation that Keytruda will be given in combination with carboplatin AND either paclitaxel or nab-paclitaxel AND
     - Medical record documentation that Keytruda, carboplatin, and paclitaxel (or nab-paclitaxel) are being used as first-line treatment **AND**
     - ~~Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations~~

4. **Head and Neck Squamous Cell Carcinoma**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of one of the following:
     - A diagnosis of Head and Neck Squamous Cell Carcinoma that is recurrent or metastatic **AND**
     - Disease progression on or after platinum-containing chemotherapy **AND**
     - Keytruda is being used as a single agent.

OR

     - A diagnosis of metastatic or unresectable, recurrent Head and Neck Squamous Cell Carcinoma **AND**
     - Keytruda is being used as a first-line treatment **AND**
     - Keytruda is being used as a single agent **AND**
     - Tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test

OR

     - A diagnosis of metastatic or unresectable, recurrent Head and Neck Squamous Cell Carcinoma **AND**
     - Keytruda is being used as a first-line treatment **AND**
     - Keytruda is being administered in combination with platinum chemotherapy and fluorouracil (FU)

OR

     - A diagnosis of resectable locally advanced Head and Neck Squamous Cell Carcinoma **AND**
     - Tumors express PD-L1 [Combined Positive Score (CPS) ≥ 1] as determined by an FDA-approved test
     - Keytruda is being used as a single agent for neoadjuvant treatment, followed by adjuvant treatment in combination with radiotherapy (RT) with or without cisplatin and then as a single agent

5. **Classical Hodgkin Lymphoma**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation of Classical Hodgkin Lymphoma **AND**
   - One of the following:
     a. Medical record documentation of a diagnosis of refractory Classical Hodgkin Lymphoma **OR**
     b. Medical record documentation of age greater than or equal to 18 years AND relapse following one (1) or more prior lines of therapy **OR**

c. Medical record documentation of age less than 18 years AND relapse following two (2) or more prior lines of therapy

6. Microsatellite Instability-High Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors OR colorectal cancer

AND

- For solid tumors:
  - Medical record documentation of progression following prior treatment(s) **AND**
  - Medical record documentation of no satisfactory alternative treatment options

7. Urothelial Carcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of locally advanced or metastatic urothelial carcinoma **AND**
- Medical record documentation of one of the following:
  - Disease progression during or following platinum-containing chemotherapy

OR

  - Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

OR

  - Patient is not eligible for any platinum-containing chemotherapy

OR

  - Patient has high-risk, non-muscle invasive bladder cancer (NMIBC)** **AND**
  - Patient's disease is unresponsive to an adequate trial of Bacillus Calmette-Guerin (BCG) therapy** **AND**
  - Patient is ineligible for or has elected not to undergo cystectomy

OR

  - Keytruda is being used in combination with Padcev

**Note:

- BCG-unresponsive high-risk NMIBC is defined as persistent disease despite adequate BCG therapy, disease recurrence after an initial tumor-free state following adequate BCG therapy, or T1 disease following a single induction course of BCG.
- Adequate BCG therapy was defined as administration of at least five of six doses of an initial induction course plus either of: at least two of three doses of maintenance therapy or at least two of six doses of a second induction course.

8. Gastric Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that Keytruda will be used as first-line treatment **AND**
- Medical record documentation of one of the following:
  - Medical record documentation of a diagnosis of locally advanced unresectable or metastatic HER-2 positive gastric or gastroesophageal junction adenocarcinoma **AND**
  - Medical record documentation that tumors express PD-L1 (CPS≥1) as approved by an FDA approved test **AND**
  - Medical record documentation that Keytruda will be used in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy

OR

  - Medical record documentation of locally advanced unresectable or metastatic HER-2 negative gastric or gastroesophageal junction (GEJ) adenocarcinoma **AND**
  - Medical record documentation that tumors express PD-L1 (CPS≥1) as approved by an FDA approved test **AND**
  - Medical record documentation that Keytruda will be used in combination with fluoropyrimidine- and platinum-containing chemotherapy

9. **Cervical Cancer**

- Prescription written by a hematologist/oncologist **AND**
- One of the following:
    - Medical record documentation of recurrent or metastatic cervical cancer **AND**
    - Medical record documentation that tumors express PD-L1 (CPS≥1) **AND**
    - Medical record documentation of disease progression after receiving at least one prior line of therapy

OR

    - Medical record documentation of persistent, recurrent or metastatic cervical cancer **AND**
    - Medical record documentation that tumors express PD-L1 (CPS≥1) **AND**
    - Medical record documentation that Keytruda will be used in combination with chemotherapy (paclitaxel, cisplatin or carboplatin), with or without bevacizumab

OR

    - Medical record documentation of FIGO 2014 Stage III-IVA cervical cancer **AND**
    - Medical record documentation that Keytruda will be used in combination with chemoradiotherapy (cisplatin and external beam radiation therapy [EBRT] followed by brachytherapy [BT])

*Note: FIGO 2014 Stage III-IVA includes patients with tumor involvement of the lower vagina with or without extension onto pelvic sidewall or hydronephrosis/non-functioning kidney or has spread to adjacent pelvic organs.

10. **Primary Mediastinal Large B-cell Lymphoma (PMBCL)**

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of refractory primary mediastinal large B-cell lymphoma (PMBCL) **OR**
- Medical record documentation of relapse following two (2) prior lines of therapy

11. **Hepatocellular Carcinoma (HCC)**

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of a diagnosis of hepatocellular carcinoma secondary to Hepatitis B **AND**
- Medical record documentation of at least one (1) prior systemic therapy other than a PD-1 and PD-L1 containing regimen

12. **Merkel Cell Carcinoma (MCC)**

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of a diagnosis of Merkel Cell Carcinoma **AND**
- Medical record documentation of metastatic and/or recurrent disease

13. **Renal Cell Carcinoma (RCC)**

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of one of the following:

Advanced Renal Cell Carcinoma

    - Medical record documentation of a diagnosis of advanced renal cell carcinoma **AND**
    - Medical record documentation that Keytruda is being used in combination with axitinib (Inlyta) OR lenvatinib (Lenvima) **AND**
    - Medical record documentation that Keytruda in combination with axitinib (Inlyta) OR lenvatinib (Lenvima) is being used as first-line treatment for advanced disease

Note: In clinical trials, advanced disease included newly diagnosed or recurrent Stage IV renal cell carcinoma.

OR

Adjuvant treatment of Renal Cell Carcinoma

    - A diagnosis of renal cell carcinoma **AND**
    - Documentation of intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions **AND**
    - Keytruda is being used in the adjuvant setting **AND**
    - Keytruda is being used as a single agent

Note: In clinical trials, intermediate-high risk category included: pT2 with Grade 4 or sarcomatoid features; pT3, any Grade without nodal involvement (N0) or distant metastases (M0); and high risk included: pT4, any Grade N0 and M0; any pT, any Grade with nodal involvement and M0. The M1 no evidence of disease (NED) category includes patients with metastatic disease who had undergone complete resection of primary and metastatic lesions.

14. Esophageal Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- One of the following:
    - Medical record documentation of a diagnosis of locally advanced or metastatic squamous cell carcinoma of the esophagus or gastroesophageal junction (GEJ) **AND**
    - Medical record documentation that tumors express PD-L1 (CPS ≥10) as determined by an FDA-approved test **AND**
    - Medical record documentation of disease progression after one or more prior lines of systemic therapy for advanced disease.
- **OR**
    - Medical record documentation of a diagnosis of locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) carcinoma not amenable to surgical resection or definitive chemoradiation **AND**
    - Medical record documentation of use in combination with platinum (oxaliplatin or cisplatin) and fluoropyrimidine-based (fluorouracil or capecitabine) chemotherapy

15. Endometrial Carcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of a diagnosis of primary advanced or recurrent endometrial carcinoma **AND**
    - Medical record documentation that Keytruda will be used in combination with carboplatin and paclitaxel followed by Keytruda as a single agent

OR

    - Medical record documentation of a diagnosis of advanced endometrial carcinoma **AND**
    - Medical record documentation of disease progression following at least one prior systemic therapy **AND**
    - Medical record documentation that patient is not a candidate for curative surgery or radiation **AND**
    - Medical record documentation of one of the following:
        - Medical record documentation that tumors are **not** microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) **AND**
        - Medical record documentation that Keytruda will be given in combination with lenvatinib (Lenvima)

OR

        - Medical record documentation that Keytruda will be used as a single agent for treatment of tumors that are microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)

16. Tumor Mutational Burden – High (TMB-H) Solid Tumors

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of unresectable or metastatic solid tumors **AND**
- Medical record documentation that tumors are tumor mutational burden-high (TMB-H), defined as greater than or equal to 10 mutations per megabase (≥10 mut/Mb), determined by an FDA-approved test **AND**
- Medical record documentation of progression following prior treatment(s) **AND**
- Medical record documentation of no satisfactory alternative treatment options

17. Cutaneous Squamous Cell Carcinoma (cSCC)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of locally advanced, recurrent, OR metastatic cutaneous squamous cell carcinoma **AND**
- Medical record documentation that the patient's disease is not curable by surgery **AND**
- Medical record documentation that the patient's disease is not curable by radiation.

18. Triple Negative Breast Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) **AND** both of the following:

- Medical record documentation that tumors express PD-L1 [Combined Positive Score (CPS) greater than or equal to 10] as determined by an FDA approved test **AND**
- Medical record documentation that Keytruda will be given in combination with chemotherapy (paclitaxel, paclitaxel protein-bound, or gemcitabine and carboplatin).

OR

- Medical record documentation of high-risk, early-stage triple-negative breast cancer (TNBC) **AND**
- Medical record documentation that Keytruda will be given in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery

LIMITATIONS: The treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.

18. **Biliary Tract Cancer**

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of locally advanced unresectable or metastatic biliary tract cancer **AND**
- Medical record documentation that Keytruda will be used in combination with gemcitabine and cisplatin

19. **Malignant Pleural Mesothelioma (MPM)**

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is ≥ 18 years of age **AND**
- Medical record documentation of unresectable advanced or metastatic malignant pleural mesothelioma (MPM) **AND**
- Medical record documentation that Keytruda is being used as first-line treatment in combination with pemetrexed and platinum chemotherapy.

AUTHORIZATION DURATION:

For adjuvant treatment of metastatic melanoma (completely resected melanoma), neoadjuvant/adjuvant treatment of early-stage triple negative breast cancer, neoadjuvant/adjuvant treatment of non-small cell lung cancer, and adjuvant treatment of renal cell carcinoma:

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

- Authorization of Keytruda for the adjuvant treatment of metastatic melanoma, of non-small cell lung cancer, and of renal cell carcinoma should not exceed the FDA-approved treatment duration of 1 year (12 months).
- Authorization of Keytruda for the treatment of early-stage triple negative breast cancer should not exceed the approved treatment duration of 24 weeks for neoadjuvant therapy and 27 weeks for adjuvant therapy.
- Authorization for the treatment of neoadjuvant/adjuvant treatment of non-small cell lung cancer should not exceed the approved treatment duration of 12 weeks of neoadjuvant treatment and 39 weeks of adjuvant therapy.

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

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

For neoadjuvant/adjuvant treatment of head and neck squamous cell carcinoma:

Initial approval will be for 6 months. Additional approval will be for up to an additional 12 months or less if determined medically appropriate by the reviewing provider and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

- Authorization for the treatment of neoadjuvant/adjuvant treatment of head and neck squamous cell carcinoma should not exceed the approved treatment duration of 6 weeks of neoadjuvant treatment and 12 months of adjuvant treatment.

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

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

For all other indications:

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

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

MONJUVI (tafasitamab-cxix)

Clinical Summary: Monjuvi is a CD19-directed cytolytic antibody previously indicated in combination with lenalidomide for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise

for autologous stem cell transplant in combination with lenalidomide iphoma (FL). A limitation of use treatment of patients with relapsed

proved indication of relapsed or dy weight, to be given mide is to be given on days 1-21 juvi are summarized in Table 1.

Outcome per Investigator	MONJUVI in Combination with Lenalidomide and Rituximab (N = 273)	Placebo in Combination with Lenalidomide and Rituximab (N = 275)
Overall response rate[c], n (%) (95% CI)	228 (84) (79, 88)	199 (72) (67, 78)

CI = confidence interval; NE = not evaluable
[a] Kaplan-Meier estimate.
[b] Hazard ratio based on a stratified Cox proportional hazard model.
[c] Complete response plus partial response

Cycle[a]	Dosing Schedule
Cycles 1 to 3	Days 1, 8, 15, and 22
Cycles 4 to 12	Days 1 and 15

[a] Each treatment cycle is 28-days.

The efficacy of Monjuvi in relapsed or refractory follicular lymphoma (FL) was evaluated in inMIND (NCT04680052) a randomized, double-blind, placebo controlled trial in 548 patients with relapsed or refractory FL. Patients had Grade 1, 2, or 3a disease and has at least one systemic therapy previously, which had to include one anti-CD20 antibody (given for at least 4 doses). The median age was 64 years (range 31-88 years), median number of prior lines of systemic therapy was 1 (range 1-10) with 55% receiving 1 prior line, 25% receiving 2 prior lines, and 20% receiving 3 or more prior lines. 32% of patients had progression of disease (POD) within 24 months of initial diagnosis, and 43% had refractory disease prior to CD-20 directed therapy. Exclusion criteria was significant for patients in partial remission after their last line of therapy, history of transformed lymphoma, congestive heart failure, HCV/HBV infection, known CNS involvement, life expectancy <6 months, and prior use of lenalidomide in combination with rituximab.

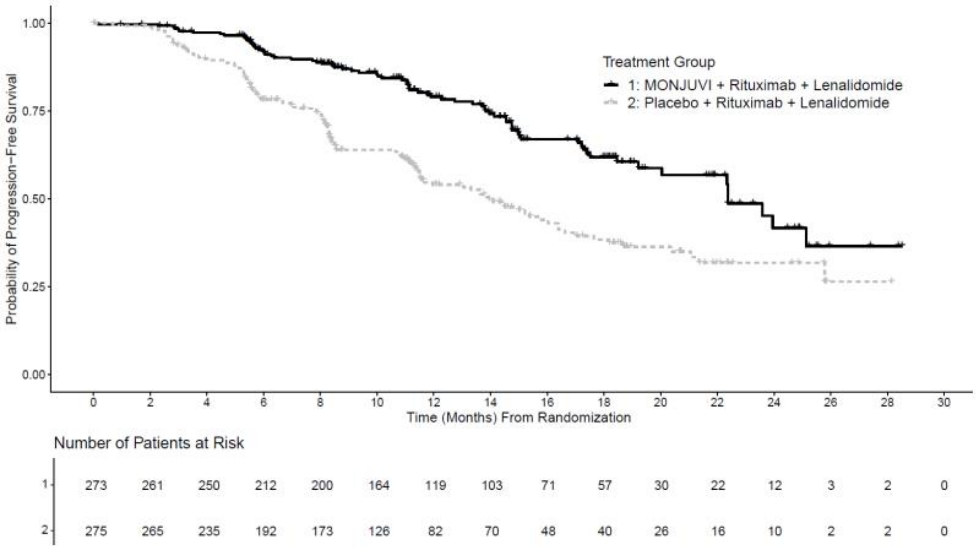
Patients were randomized 1:1 to receive Monjuvi or placebo in combination with lenalidomide and rituximab, with randomization being stratified by POD within 24 months, refractoriness to CD-20 antibody therapy, and the number of prior lines of therapy (less than 2 versus greater than or equal to 2). Treatment was administered in 28 day cycles according to the dosing recommendations provided in the prescribing information.

The major efficacy outcome was investigator-assessed progression-free survival (PFS) using the Lugano criteria. The median duration of progression free survival follow-up was 14.1 months. Efficacy results are summarized in Table 2 and Figure 1. To note: At the time of PFS analysis the median overall survival had not been reached in either arm

Table 2. Efficacy Results in Patients with Relapsed or Refractory FL in inMIND

Outcome per Investigator	MONJUVI in Combination with Lenalidomide and Rituximab (N = 273)	Placebo in Combination with Lenalidomide and Rituximab (N = 275)
Progression-free survival		
Patients with event, n (%)	75 (27.5)	131 (47.6)
Disease progression	67 (24.5)	124 (45.1)
Death	8 (2.9)	7 (2.5)
Median PFS (95% CI), months[a]	22.4 (19.2, NE)	13.9 (11.5, 16.4)
Hazard ratio[b] (95% CI)	0.43 (0.32, 0.58)	
p-value	< 0.0001	

Figure 1. Kaplan-Meier Curve for PFS by Investigator Assessment in inMIND



No new contraindications or warnings and precautions were added as a result of the newly approved indication. Serious adverse reactions occurred in 33% of patients in the Monjuvi arm of inMIND and included serious infections (24%), renal insufficiency (3.3%), second primary malignancies (2.9%), and febrile neutropenia (2.6%). Adverse reactions leading to permanent discontinuation occurred in 11% of patients and dose interruptions in 74% of patients. The most common adverse reactions were respiratory tract infections, diarrhea, rash, fatigue, constipation, musculoskeletal pain, and cough.

Current Formulary Status: Medical benefit requiring prior authorization.

Recommendation: There are no changes recommended to the formulary placement or authorization duration of Monjuvi. It is recommended to change the prior authorization criteria for MBP 221.0 as a result of the updated indication.

1. **Relapsed or Refractory Diffuse Large B-Cell Lymphoma (DLBCL)**
   - Medical record documentation of age greater than or equal to 18 years **AND**
   - Medical record documentation that Monjuvi is prescribed by a hematologist or oncologist **AND**
   - Medical record documentation of relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low grade lymphoma **AND**
   - Medical record documentation that the member is not eligible for autologous stem cell transplant (ASCT) **AND**
   - Medical record documentation that Monjuvi will be used in combination with Revlimid (lenalidomide)

2. **Relapsed or Refractory Follicular Lymphoma (FL)**
   - Medical record documentation of age greater than or equal to 18 years **AND**
   - Medical record documentation that Monjuvi is prescribed by a hematologist or oncologist **AND**
   - Medical record documentation of relapsed or refractory follicular lymphoma (FL) **AND**
   - Medical record documentation that Monjuvi will be used in combination with lenalidomide (Revlimid) and rituximab

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

Limitation of use: Monjuvi is not indicated and is not recommended for the treatment of patients with relapsed or refractory marginal zone lymphoma outside of controlled clinical trials

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

NEFFY (epinephrine nasal spray)

Clinical Summary: Neffy is now approved for children who are aged 4 years and older and weigh 15 to 30 kilograms (33 to < 66 lb). It is indicated in this population of children and adults for the treatment of Type 1 allergic reactions, including anaphylaxis. With this approval came the development of a lower 1mg dose of Neffy to allow for administration of the lower recommended dose. Dosing recommendations are as follows:

Patients Weight	Dosage
30 kg or Greater	One spray of neffy 2 mg
15 kg to less than 30 kg	One spray of neffy 1 mg

The approval of Neffy 1 mg is based on data from extensive clinical trials, including pharmacokinetic (PK) and pharmacodynamic (PD) responses in pediatric and adult subjects that were consistent with those of epinephrine injection products. Adverse events in pediatric trials were generally mild and transient consisting of nasal discomfort, nasal congestion, paresthesia, rhinorrhea, sneezing, upper respiratory tract congestion, epistaxis, rhinalgia, nasal dryness, dry throat, fatigue, and feeling jittery.

Current Formulary Status: Non-formulary requiring formulary exception review.

Recommendation: Non-formulary requiring formulary exception review; Neffy 1 mg will be non-formulary to match the placement of the Neffy 2 mg dosage. The following changes are recommended to commercial policy 840.0

- Medical record documentation of member weight greater than or equal to 15 kilograms **AND**
- Medical record documentation of member age of 4 years or older **AND**
- Medical record documentation of use for the treatment of type I allergic reactions, including anaphylaxis **AND**
- Medical record documentation that member does not have nasal polyps, or a history of nasal surgery, fracture, or injury **AND**
- Medical record documentation that the patient and their caregiver has shown the inability to properly use the injectable generic epinephrine (EpiPen) device

Approve by GPI-14:
Neffy 1mg - 38900040002040
Neffy 2mg – 38900040002080

Quantity limit: QL FOR LETTER ONLY: 2 devices per fill

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

PLUVICTO (lutetium Lu 177 vipivotide tetraxetan)

Clinical Summary: On March 28, 2025, The FDA expanded the indication for Pluvicto to include the treatment of adult patients with prostate-specific membrane antigen-positive (PSMA+) metastatic castrate-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor (ARPI) therapy and are considered appropriate to delay taxane-based chemotherapy. Pluvicto was previously approved for adult patients with PSMA+ mCRPC who were previously treated with an ARPI and taxane-based chemotherapy. The recent label expansion broadens the eligible patient population by allowing the use of Pluvicto on taxane-naïve patients.

Novartis, OncoHealth, and the Geisinger Hematology/Oncology department were all consulted regarding when it is appropriate to defer taxane-based chemotherapy. Novartis' response was that eligibility in the clinical trial was not determined by any protocol-specified criteria but was instead based on the clinical judgement of the treating physician. OncoHealth was also consulted and responded with the same information as Novartis. Geisinger Hematology/Oncology was able to provide some information. The following are considerations to allow taxane-based chemotherapy to be delayed:

- Asymptomatic/minimally symptomatic patients: if the patient has slow progression on imaging or PSA and do not have significant symptoms, chemotherapy could be deferred in favor of Pluvicto (or other androgen receptor pathway inhibitors. They are often better tolerated and can help maintain quality of life.
- Poor performance status: if a patient is considered frail or has significant comorbidities, they may not tolerate taxane chemotherapy well. A delay could be considered while optimizing other medical management or reviewing palliative care decisions.
- Low disease burden: taxane chemotherapy can be delayed in low-volume metastatic hormone sensitive prostate cancer, especially if the patient prefers oral chemotherapy or has concerns for chemotherapy toxicity.

- Recent surgeries or infection: Chemotherapy can be deferred until the patient recovers
- Patient preference: patients may prefer oral chemotherapy or concerns for adverse effects of chemotherapy

There is no updated dosing for the new indication. The dosing continues to be 7.4 GBq (200 mCi) every 6 weeks for 6 doses.

The efficacy of Pluvicto for taxane-naïve patients was evaluated in PSMAfore (NCT04689828), a randomized (1:1), multicenter, open-label trial that evaluated Pluvicto (N=234) versus a change in ARPI (N=234) in patients with progressive, PSMA-positive mCRPC. Randomization was stratified by setting of prior ARPI use (CRPC vs. hormone-sensitive prostate cancer (HSPC) and by symptomatology (asymptomatic or mildly symptomatic vs. symptomatic). Patients were required to have a castrate level of serum/plasma testosterone by either medical castration or prior orchiectomy at study entry. Patients were required to have progressed only once on an ARPI (abiraterone, enzalatumide, darolutamide, or apalutamide). Prior taxane-based chemotherapy was only allowed in the adjuvant or neoadjuvant setting greater than 12 months before enrollment. Patients were considered appropriate for delay of taxane-based chemotherapy by the investigator. Patients were required to have PSMA-positive mCRPC defined as having at least one tumor lesion (soft tissue or bone) with gallium Ga 68 gozetotide uptake greater than in normal liver. Patients were considered ineligible if any intraprostatic lesion or any one lesion larger than size criteria (organs ≥ 1 cm in longest diameter, lymph nodes ≥ 2.5 cm in short axis, bones ≥ 1 cm in longest diameter) has gallium Ga 68 gozetotide uptake less than or equal to uptake in normal liver.

Patients used Pluvicto 7.4 GBq (200 mCi) every 6 weeks for 6 doses or a change in ARPI. Supportive care administered at the investigator's discretion included bone-targeted agents, androgen deprivation therapy (ADT), or palliative radiotherapy.

The major efficacy outcome was radiographic progression-free survival (rPFS) as determined by blinded independent central review (BICR) per Prostate Cancer Working Group 3 (PCWG3)-modified Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria. Additional efficacy outcome measures were Overall Survival (OS) and Overall Response Rate (ORR). PSMAfore demonstrated a statistically significant improvement in rPFS for Pluvicto compared to a change in ARPI. Of patients that were randomized to receive a change in ARPI, 141 patients (60%) crossed over to receive Pluvicto after confirmation of radiographic disease progression by BICR. Efficacy results are presented in Table 1.

Table 1: Efficacy Results in PSMAfore

	PLUVICTO	ARPI
Radiographic progression-free survival (rPFS)[a]	N = 233[b]	N = 234
Events (progression or death), n (%)	60 (26)	106 (45)
Median, months (95% CI)[c]	9.3 (7, NE)	5.6 (4, 6)
Hazard ratio (95% CI)[d]	0.41 (0.29, 0.56)	
P-value[e]	< 0.0001	
Overall survival (OS)	N = 234	N = 234
Deaths, n (%)	142 (61)	157 (67)
Median, months (95% CI)[c]	24.5 (19.5, 28.9)	23.1 (19.6, 25.5)
Hazard ratio (95% CI)[d]	0.91 (0.72, 1.14)	
P-value[e]	NS	
Overall response rate (ORR)[a,f]		
Patients with measurable disease at baseline	N = 72	N = 72
ORR (CR + PR), n (%) (95% CI)	35 (49) (37, 61)	10 (14) (7, 24)
Complete response (CR), n (%)	15 (21)	2 (2.8)
Partial response (PR), n (%)	20 (28)	8 (11)

ARPI = androgen receptor pathway inhibitor; NE = Not estimable; NS = Not statistically significant
[a]By BICR per PCWG3-modified RECIST v1.1 criteria.
[b]Excludes one patient in the PLUVICTO arm who was randomized after the data cut-off for the rPFS primary analysis.
[c]Based on Kaplan-Meier estimate.
[d]Hazard ratio based on the stratified Cox PH model.
[e]Stratified log-rank test one-sided p-value.
[f]Responses are based on soft tissue and bone lesion assessment.

Current Formulary Status: Pluvicto is a medical benefit requiring prior authorization.

Recommendation: Pluvicto is a medical benefit and will require a prior authorization. The following updated prior authorization criteria will apply:

Prior Authorization Criteria Medicare [Medical])

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

- Medical record documentation of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) **AND**
- Medical record documentation that a gonadotropic-releasing hormone (GnRH) analog will be used concurrently OR member has had bilateral orchiectomy **AND**
- Medical record documentation of prior treatment with an androgen-receptor pathway inhibitor **AND**
- One of the following:
    - Medical record documentation of prior treatment with taxane-based chemotherapy **OR**
    - Medical record documentation that the patient is considered appropriate to delay taxane-based chemotherapy

AUTHORIZATION DURATION: Approval will be for a one-time authorization of 6 visits (15 months) of therapy. 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 labeling.

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

POSFREA (palonosetron)

Clinical Summary: Posfrea is now FDA approved for pediatric patients 1 month to less than 17 years of age for prevention of acute nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including highly emetogenic cancer chemotherapy (HEC).

The recommended dosage for Posfrea in new the patient population, pediatric patients 1 month to less than 17 years of age, is 20 micrograms per kilogram (max 1.5 mg) as a single dose to be infused over 15 minutes beginning approximately 30 minutes before the start of chemotherapy. The recommended weight based dosing in pediatric patients is a different unit that the recommended weight based dosing for adults – micrograms (mcg) for pediatric patients and milligrams (mg) for adult patients. Posfrea (brand and generic) is supplied as IV single dose vials.

The efficacy of Posfrea for the prevention of nausea and vomiting associated with emetogenic chemotherapy, Including HEC in pediatric patients was evaluated in a one double-blind, active-controlled clinical trial was conducted in pediatric cancer patients. The total population (N = 327) had a mean age of 8.3 years (range two months to 16.9 years) and were 53% male; and 96% white. Patients were randomized and received a 20 mcg/kg (maximum 1.5 mg) intravenous infusion of palonosetron 30 minutes prior to the start of emetogenic chemotherapy (followed by placebo infusions four and eight hours after the dose of palonosetron) or 0.15 mg/kg of intravenous ondansetron 30 minutes prior to the start of emetogenic chemotherapy (followed by ondansetron 0.15 mg/kg infusions four and eight hours after the first dose of ondansetron, with a maximum total dose of 32 mg). Emetogenic chemotherapies administered included doxorubicin, cyclophosphamide (<1500 mg/m2), ifosfamide, cisplatin, dactinomycin, carboplatin, and daunorubicin. Adjuvant corticosteroids, including dexamethasone, were administered with chemotherapy in 55% of patients.

Complete Response in the acute phase of the first cycle of chemotherapy was defined as no vomiting, no retching, and no rescue medication in the first 24 hours after starting chemotherapy. Efficacy was based on demonstrating non-inferiority of intravenous palonosetron compared to intravenous ondansetron. Non-inferiority criteria were met if the lower bound of the 97.5% confidence interval for the difference in Complete Response rates of intravenous palonosetron minus intravenous ondansetron was larger than -15%. The non-inferiority margin was 15%. Intravenous palonosetron 20 mcg/kg (maximum 1.5 mg) demonstrated non-inferiority to the active comparator during the 0 to 24-hour time interval.

Prevention of Acute Nausea and Vomiting (0 to 24 Hours) Associated with Emetogenic Chemotherapy in Pediatric Patients: Complete Response Rates

Palonosetron 20 mcg/kg intravenously (N=165)	Ondansetron 0.15 mg/kg for three intravenous doses (N=162)	Difference [97.5% Confidence Interval][a]: Palonosetron minus intravenous Ondansetron Comparator
59.4%	58.6%	0.36% [-11.7%, 12.4%]

[a] To adjust for multiplicity of treatment groups, a lower-bound of a 97.5% confidence interval was used to compare to -15%, the negative value of the non-inferiority margin.

There are no new warnings and precautions for Posfrea.

Current Formulary

Status: Medical benefit requiring prior authorization.

Recommendation: It is recommended that Posfrea require a prior authorization and a medical benefit policy is created.

For Moderately or Highly Emetogenic Chemotherapy:

- Medical record documentation that Posfrea is being used for prevention of acute or delayed nausea and vomiting associated with initial and repeat courses of moderately or highly emetogenic cancer chemotherapy **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to palonosetron (generic Aloxi)

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 that member continues to receive a moderately to highly emetogenic cancer chemotherapy regimen AND has been benefiting from Posfrea.

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

RIVFLOZA (nedosiran)

Clinical Summary: Rivfloza (nedosiran) is now approved to lower urinary oxalate levels in children 2 years of age and older and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function, e.g., eGFR ≥ 30 mL/min/1.73 m^2.

Rivfloza was previously approved for this indication in children 9 years of age and older and adults.

Updated dosing for New Indication: The recommended once monthly subcutaneous dose of Rivfloza for the expanded age group (children 2 to 9 years of age) is dependent on body weight:

- Less than 39 kg: 3.3 mg/kg once monthly (max dose: 128 mg/dose per prescribing information)
- 39 kg to less than 50 kg: 128 mg once monthly
- 50 kg and above: 160 mg once monthly

	Body weight		
	Less than 39 kg	**39 kg to less than 50 kg**	**50 kg and above**
Age 2 to less than 12 years	3.3 mg/kg	128 mg	160 mg
Age 12 years and older	128 mg		160 mg

The approval of Rivfloza for the expanded indication was based on a single-arm study in 15 patients that were 2 years to less than 12 years of age with PH1 and eGFR ≥ 30 mL/min/1.73 m2. Patients received Rivfloza once monthly for 6 months. Efficacy was based on the percent change from baseline at month 6 in spot urinary oxalate to creatinine ratio. Treatment with Rivfloza reduced the spot urinary oxalate to creatinine ratio by 64% (95% CI: 44, 84) from baseline, with an absolute risk reduction of 0.25 mmol/mmol (95% CI: 0.21, 0.29). The adverse event profile in this study did not reveal any new safety concerns for Rivfloza and was in line with previous clinical studies in Rivfloza.

Current Formulary Status: Non-formulary

Recommendation: It is recommended to update the policy for Rivfloza to:

- Medical record documentation of primary hyperoxaluria type 1 (PH1) as confirmed by one of the following:
  - Molecular genetic testing that confirms a mutation of alanin:glyoxylate aminotransferase (AGXT) gene* **OR**
  - A liver biopsy to confirm absent or significantly reduced alanin:glyoxylate aminotransferase (AGT) **AND**
- Medical record documentation that Rivfloza is prescribed by or in consultation with an appropriate specialist with experience managing hyperoxaluria (i.e., a nephrologist, urologist, geneticist, or hepatologist) **AND**
- Medical record documentation of age greater than or equal to ~~9 years~~ 2 years **AND**

- Medical record documentation of increased urinary oxalate excretion (i.e., generally greater than 0.7 mmol/1.73 m^2 per day or greater than the upper limit of normal) **AND**
- Medical record documentation of relatively preserved kidney function as defined by one of the following:
    - Medical record documentation patient has an estimated glomerular filtration rate (eGFR) greater than or equal to 30 mL/min/1.73m^2 **OR**
    - If estimated glomerular filtration rate (eGFR) is not calculated due to age limitations, a serum creatine within the normal age-specific reference range **AND**
- Medical record documentation that the member does not have a history of a liver transplant **AND**
- Medical record documentation that the member will not be receiving Rivfloza in combination with Oxlumo **AND**
- Medical record documentation of a prescribed dose and administration that is consistent with Food and Drug Administration (FDA)-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature **AND**
- Medical record documentation of failure, contraindication, or intolerance to Oxlumo

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

SIVEXTRO (tedizolid phosphate)

Clinical Summary: Sivextro is an oxazolidinone antibacterial now indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following gram-positive microorganisms: Staphylococcus aureus (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus Group (including Streptococcus anginosus, Streptococcus intermedius, and Streptococcus constellatus), and Enterococcus faecalis, in adult and pediatric patients (at least 26 weeks gestational age and weighing at least 1 kg).

Previously, Sivextro was indicated in adult and pediatric patients 12 years of age and older for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of the following Gram-positive microorganisms: Staphylococcus aureus (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus Group (including Streptococcus anginosus, Streptococcus intermedius, and Streptococcus constellatus), and Enterococcus faecalis.

The dosing for Sivextro has been updated to include a recommendation to not administer medication if patients weigh less than 35kg. The intravenous dosing in pediatric patients has changed from 200mg once daily to the recommendations summarized in Table 1 below. The intravenous dosing in adult patients has remained the same at 200mg intravenously once daily, given over 1 hour, for a total duration of 6 days. The oral dosing in pediatric and adult patients has remained the same at 200mg given once daily for 6 days.

Table 1. Recommended Intravenous Dosage of Sivextro for Injection for Pediatric Patients

Weight Band (kg)	Dose	Frequency	Infusion Time	Duration of Treatment
Pediatric Patients Weighing Less than 2 kg				
1 to less than 2*	3 mg/kg	Twice daily	1 hour	6 days
Pediatric Patients Weighing at Least 2 kg				
2 to less than 3	6 mg	Twice daily	1 hour	6 days
3 to less than 6	12 mg			
6 to less than 10	20 mg			
10 to less than 14	30 mg			
14 to less than 20	40 mg			
20 to less than 35	60 mg			
Pediatric Patients Weighing at Least 35 kg				
Greater than or equal to 35	200 mg	Once daily	1 hour	6 days

*Recommended Dosage for 1 kg to less than 2 kg is based on actual body weight.

The efficacy of Sivextro in pediatric patients aged 4 months to less than 12 years was evaluated in Pediatric Trial 2 (NCT03176134), a randomized, single blind, active-controlled trial of 100 patients with clinically documented ABSSSI. Patients had to have at least one suspected or documented gram-positive pathogen and symptoms had to have started within 14 days of study's day 1. Patients were excluded if they had significant or life-threatening disease or organ system condition, suspected or documented gram-negative pathogens with cellulitis/erysipelas or major cutaneous disease, however mixed infections were allowed provided they could receive treatment with aztreonam and/or metronidazole for gram-negative or anaerobic coinfections.

Patients were randomized 3:1 to receive Sivextro (IV or oral) for 6-10 days or comparator for 10-14 days. Dosing of Sivextro was weight based and as follows: ≥50kg once-daily 200 mg dose, ≥30kg to <50kg 2 mg/kg once every 12 hours, and 3.2kg to <30kg 2.5 mg/kg every 12 hours. Oral Sivextro was given to patients in a not-currently-approved oral suspension formulation, and the decision for oral or IV was at the discretion of the investigator, however 50% or more of the patients had to receive IV for at least 24 hours. The comparator was chosen by the investigator from a pre-specified list per local standard of care and included vancomycin, linezolid, clindamycin, flucloxacillin, and cefazolin.

Clinical response at the test of cure visit was assessed in the ITT population (all randomized patients) between day 18 and 25. Patients needed to have resolution or near-resolution of all related signs and symptoms such that no further antibacterial therapy was needed in order to be considered a clinical success. Early clinical response was also assessed in the ITT population and was defined as at least a 20% reduction in lesion size at 48-72 hours after the start of treatment. To note, this trial was not powered for comparative inferential efficacy analysis. At the test of cure visit, the clinical success rate was 93.3% (70/75) in the Sivextro group and 92.0% (23/25) in the comparator group (difference: 1.3%, 95% CI: -10.7, 13.4). Early clinical response was not adequately assessed in Pediatric Trial 2 because an in-person outpatient visit at this timepoint was not required during the COVID-19 pandemic.

No new contraindications or warnings and precautions were added as a result of the newly patient population. The most common adverse reactions occurring in the clinical trial were infusion or injection-related adverse reactions. One patient treated with Sivextro developed thrombocytopenia with a platelet count less than 100 x 10^3/mm^3.

Current Formulary Status:

- IV: Medical benefit requiring prior authorization
- Oral: Pharmacy benefit requiring prior authorization, Tier 3 for Triple Choice

Recommendation: There are no changes recommended to the formulary placement or authorization duration of Sivextro. It is recommended to change the prior authorization criteria for MBP 122.0 and Pharmacy Commercial Policy 348.0 as a result of the updated indication.

MBP 122.0 Sivextro (tedizolid phosphate) IV

Sivextro (tedizolid phosphate) IV will be considered medically necessary for the commercial, exchange, CHIP, and Medicaid lines of business when all of the following criteria are met:

- ~~Medical record documentation that patient is ≥ 12 years of age **AND**~~
- Medical record documentation of a diagnosis of an acute bacterial skin and skin structure infection (including cellulitis/erysipelas, wound infection, and major cutaneous abscess) caused by: Staphylococcus aureus, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus, Streptococcus intermedius, Streptococcus constellatus, or Enterococcus faecalis which has been diagnosed and documented with Infectious Disease consultation **AND**
- Medical record documentation of a prescribed dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature **AND**
- Medical record documentation of a culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity **OR**
- If Sivextro was initiated during an inpatient stay, medical record documentation of a culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity

AUTHORIZATION LIMIT: If approved, Sivextro IV will be authorized for a maximum of 6 daily doses.
(Facets RX Count: 200 (J3090 units) per dose)

Pharmacy Commercial Policy 348.0 Sivextro Tablets

- ~~Medical record documentation that patient is greater than or equal to 12 years of age **AND**~~
- Medical record documentation of a diagnosis of a grade 2 or greater acute bacterial skin and skin structure infection (including cellulitis/erysipelas, wound infection, and major cutaneous abscess) caused by: *Staphylococcus aureus, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus anginosus, Streptococcus intermedius, Streptococcus constellatus,* or *Enterococcus faecalis* which have been diagnosed and documented with Infectious Disease consultation **AND**
- Medical record documentation of a prescribed dose that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature **AND**
- Medical record documentation of culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity **OR**
- Medical record documentation that Sivextro therapy was started during an inpatient setting

MEDISPAN AUTHORIZATION LEVEL: GPI-12

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

- QL FOR LETTER ONLY: 6 tablets

AUTHORIZATION DURATION: one-time, 6 day approval, RX count 1

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

SOLIRIS (eculizumab)

Clinical Summary: Soliris (eculizumab) is a monoclonal antibody that works by binding to the complement protein C5, thereby inhibiting its cleavage to C5a and C5b and preventing the generation of the terminal complement complex C5b-9, a part of the immune system that can contribute to inflammation and cell destruction. Soliris is indicated in the treatment of paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), generalized myasthenia gravis (gMG), and nueromyletitis optica spectrum disorder (NMOSD). Soliris is administered via IV infusion and is available only through a REMS (Risk Evaluation and Mitigation Strategy) program due to the risk of meningococcal infections.

Soliris was granted FDA approval for treatment of pediatric patients aged six (6) years and older with generalized myasthenia gravis (gMG) who are anti-acetylcholine receptor positive on March 10, 2025. Soliris became the first and only FDA approved therapy for pediatrics with gMG. Soliris is indicated for use as chronic immunosuppressive therapy in refractory anti-acetylcholine receptor antibody positive (AChR+) myasthenia gravis in select patients (eg, dependence on maintenance IVIG or plasma exchange or lack of response to at least one other immunosuppressant).

Updated Dosing for generalized myasthenia gravis via IV infusion (6 years - < 18 years) :

Weight Range	Induction Phase Dosing	Maintenance Phase Dosing
5 kg - < 10 kg	300 mg single dose at week 1	300 mg at week 2; then 300 mg 3 weeks
10 kg - < 20 kg	600 mg single dose at week 1	300 mg at week 2; then 300 mg every 2 weeks
20 kg - < 30 kg	600 mg for the first 2 weeks	600 mg at week 3; then 600 mg every 2 weeks
30 kg - < 40 kg	600 mg for the first 2 weeks	900 mg at week 3; then 900 mg every 2 weeks
>40 kg	900 mg weekly for the first 4 weeks	1200 mg at week 5; then 1200 mg every 2 weeks

**In the setting of concomitant plasmapheresis or plasma exchange, or fresh frozen plasma infusion (PE/PI) or with concomitant IVIG treatment; supplemental dosing is required, see package insert.

In a 26-week, multicenter, open-label, single-arm, phase 3 trial study evaluating the safety and efficacy of Soliris in 11 pediatric patients with gMG 12 to 17 years of age (NCT03759366/Study ECU-MG-303), adverse reactions were consistent with those 16 observed in adult patients with gMG. The study's main goal was to assess changes in the Quantitative Myasthenia Gravis (QMG) scores from the study's start to week 26. Changes in MG-ADL scores also were evaluated as a key secondary goal. Results showed QMG scores dropped by a mean of 5.8 points and MG-ADL scores decreased by a mean of 2.3 points over six months, suggesting less severe disease. Improvements in these and other

clinical outcomes became apparent as early as one week after treatment initiation and were sustained through week 26. The safety profile in children was consistent with its profile in adult patients. The most common side effects observed in the study were headache and cold-like symptoms. Inclusion criteria included the presence of refractory gMG, defined as participants with gMG who have 1 or more of the following:
(a) failed treatment ≥1 year with at least 1 immunosuppressive therapies (IST), defined as follows:
(1) persistent weakness with impairment of activities of daily living;
(2) myasthenia gravis (MG) exacerbation and/or crisis while on treatment; or
(3) intolerance to ISTs due to side effect or comorbid condition(s).
(b) Require maintenance plasma exchange (PE) or intravenous immunoglobulin (IVIg) to control symptoms; and/or
(c) in the opinion of the Investigator, MG poses a significant functional burden despite current MG treatment.

Current Formulary Status: Medical Benefit requiring prior authorization.

Recommendation: It is recommended to update Medical Benefit Policy 51.0 Soliris (eculizumab) to include the updated indication:

Soliris (eculizumab) will be considered medically necessary for the commercial, exchange, CHIP, and Medicaid lines of business when all of the following criteria are met per indication:

Generalized Myasthenia Gravis (gMA)

- Medical record documentation supporting a confirmed diagnosis of Generalized Myasthenia Gravis **AND**
- Medical record documentation that member is anti-acetylcholine receptor (AchR) antibody positive **AND**
- Prescribed by or in consultation with a neuromuscular specialist **AND**
- Medical record documentation of age ≥ 6 years **AND**
- Medical record documentation of a prescribed dose and administration that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature **AND**
- Medical record documentation of Myasthenia Gravis Foundation of America Clinical Classification (MGFA) Class II to IV **AND***
- For members 18 years of age or older: Medical record documentation Myasthenia Gravis-Activities of Daily Living (MG-ADL) score of 6 or more at baseline **AND**
- For members under the age of 18 years: Medical record documentation of baseline Myasthenia Gravis-Activities of Daily Living (MG-ADL), Quantitative Myasthenia Gravis (QMG) or Myasthenia Gravis Composite (MGC) score **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids **AND**
- Medical record documentation of therapeutic failure on intolerance to, or contraindication to at least two (2) non-steroidal immunosuppressive therapies **OR** has failed at least one (1) immunosuppressive therapy and required chronic plasmapheresis or plasma exchange (PE) **AND**
- Medical record documentation of failure on intolerance to, or contraindication to intravenous immunoglobulin (IVIG)

AUTHORIZATION DURATION: Initial approval will be given for **6 months**.
Subsequent approvals will be for an additional **6 months** and will require:

- Medical record documentation of continued disease improvement or lack of disease progression **AND**
- For members 18 years of age or older: Medical record documentation that the member is responding positively to therapy as evidenced by a 3-point reduction in MG-ADL total score**;
  The medication will no longer be covered if patient experiences toxicity or worsening of disease.

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

TREMFYA (guselkumab)

Clinical Summary: Tremfya is now indicated for the treatment of adult patients with moderately to severely active Crohn's disease. It was previously indicated in moderately to severely active ulcerative colitis, moderate to severe plaque psoriasis, and active psoriatic arthritis

Updated Dosing:

- *Induction:* 200 mg administered by intravenous (IV) infusion over at least one hour at Week 0, Week 4, and Week 8 or 400 mg administered by subcutaneous (SubQ) injection at Week 0, Week 4, and Week 8.
- *Maintenance:* 100 mg administered by SubQ injection at Week 16, and every 8 weeks thereafter, or 200 mg administered by SubQ injection at Week 12, and every 4 weeks thereafter. Use the lowest effective recommended dosage to maintain therapeutic response.

The efficacy and safety of Tremfya were assessed in three randomized, double-blind, placebo-controlled trials that enrolled adult subjects with moderately to severely active Crohn's disease who had a history of inadequate response, loss of response, or intolerance to oral corticosteroids, immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), and/or biologic therapy (TNF blockers or vedolizumab). Moderately to severely active Crohn's disease was defined as a Crohn's Disease Activity Index (CDAI) score of ≥220 and a Simple Endoscopic Score for Crohn's Disease (SES-CD) of ≥6 (or ≥4 for subjects with isolated ileal disease). Subjects were permitted to use stable doses of oral corticosteroids (prednisone ≤40 mg/day or equivalent), immunomodulators (azathioprine, 6-mercaptopurine, methotrexate), and/or aminosalicylates.

Trials CD1 and CD2:

- In CD1 (NCT03466411), 361 subjects were randomized to receive IV Tremfya 200 mg at Weeks 0, 4, and 8 (N = 285) or placebo (N = 76). The median baseline CDAI score was 285 (range: 220 - 442), and the median baseline SES-CD score was 11 (range: 4 - 39). Of the randomized subjects, 52% of subjects had previously failed (inadequate response, loss of response, or intolerance) treatment with at least one biologic therapy, 43% were biologic-naïve, and 6% had previously received but had not failed a biologic. At baseline, 37% of subjects were receiving oral corticosteroids and 30% of subjects were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate).
- In CD2 (NCT03466411), 360 subjects were randomized to receive IV Tremfya 200 mg at Weeks 0, 4, and 8 (N = 288) or placebo (N = 72). The median baseline CDAI score was 286 (range: 220 - 442) and the median baseline SES-CD score was 11 (range: 4 - 42). Of the randomized subjects, 52% of subjects had previously failed (inadequate response, loss of response, or intolerance) treatment with at least one biologic therapy, 41% were biologic-naïve, and 7% had previously received but had not failed a biologic. At baseline, 36% of the subjects were receiving oral corticosteroids and 31% of the subjects were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate). The results of efficacy endpoints at Week 12 for CD1 and CD2 are shown in Table 11.

Table 11: Proportion of Subjects with Crohn's Disease Meeting Efficacy Endpoints at Week 12 in CD1 and CD2

	CD1			CD2		
Endpoint	**Placebo**	**TREMFYA 200 mg Intravenous Infusion[a]**	**Treatment Difference vs Placebo (95% CI)[b]**	**Placebo**	**TREMFYA 200 mg Intravenous Infusion[a]**	**Treatment Difference vs Placebo (95% CI)[b]**
Clinical remission[c] at Week 12						
Total population	N=76 20%	N=285 47%	27% (17%, 38%)[d]	N=72 15%	N=288 47%	31% (21%, 41%)[d]
Prior biologic failure[e]	N=39 21%	N=147 44%		N=39 15%	N=148 47%	
Without prior biologic failure[f]	N=37 19%	N=138 49%		N=33 15%	N=140 48%	
Endoscopic response[g] at Week 12						
Total population	N=76 9%	N=285 36%	27% (19%, 35%)[d]	N=72 13%	N=288 34%	21% (11%, 30%)[d]
Prior biologic failure[e]	N=39 3%	N=147 26%		N=39 8%	N=148 28%	
Without prior biologic failure[f]	N=37 16%	N=138 47%		N=33 18%	N=140 40%	
Clinical remission[c] at Week 12 and endoscopic response[g] at Week 12						
Total population	N=76 3%	N=285 20%	17% (11%, 23%)[d]	N=72 3%	N=288 21%	18% (12%, 24%)[d]
Prior biologic failure[e]	N=39 3%	N=147 14%		N=39 3%	N=148 19%	
Without prior biologic failure[f]	N=37 3%	N=138 26%		N=33 3%	N=140 24%	

[a] TREMFYA 200 mg as an intravenous infusion at Weeks 0, 4, and 8.
[b] The adjusted treatment difference and the confidence intervals (CIs) were based on the common risk difference test using Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification variables used were baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), BIO-Failure status (Yes or No), and baseline corticosteroid use (Yes or No).
[c] Clinical remission is defined as CDAI score <150.
[d] p <0.001
[e] Includes inadequate response, loss of response, or intolerance to biologic therapy (TNF blockers, vedolizumab) for Crohn's disease.
[f] Includes subjects that were biologic naïve and subjects with prior biologic exposure who did not meet criteria for failure. In CD1, 3 subjects in the placebo group and 18 subjects in the intravenous TREMFYA 200 mg group were previously exposed to but did not fail a biologic therapy. In CD2, 6 subjects in the placebo group and 19 subjects in the intravenous TREMFYA 200 mg group were previously exposed to but did not fail a biologic therapy.
[g] Endoscopic response is defined as >50% improvement from baseline in SES-CD score.

Greater reductions in stool frequency and abdominal pain were observed as early as Week 4 in subjects treated with intravenous Tremfya compared to placebo.

- **Trial CD3:**
- In CD3, 340 subjects were randomized in a 1:1:1 ratio to receive SubQ Tremfya 400 mg at Weeks 0, 4, and 8 followed by subcutaneous Tremfya 100 mg every 8 weeks (with the first dose given at Week 16); SubQ Tremfya 400 mg at Weeks 0, 4, and 8 followed by SubQ Tremfya 200 mg every 4 weeks (with the first dose given at Week 12); or placebo. The median baseline CDAI score was 291 (range: 220 - 447), and the median baseline SES-CD score was 10 (range: 4 - 40). Of the randomized subjects, 46% of subjects had previously failed (inadequate response, loss of response, or intolerance) treatment with at least one biologic therapy, 47% were biologic naïve, and 7% had previously received but had not failed a biologic. At baseline, 30% of the subjects were receiving oral corticosteroids and 29% of the subjects were receiving immunomodulators (azathioprine, 6-mercaptopurine, methotrexate).
- In CD3, the coprimary endpoints were clinical remission at Week 12 and endoscopic response at Week 12 compared to placebo. Additional efficacy endpoints included clinical response at Week 12, clinical remission at Week 24, clinical remission at Week 48, and endoscopic response at Week 48. The results of analyses of multiplicity-controlled efficacy endpoints in CD3 are shown in Table 12.

Table 12: Proportion of Subjects with Crohn's Disease Meeting Efficacy Endpoints in CD3

Endpoint	Placebo	TREMFYA 400 mg Subcutaneous Injection at Weeks 0, 4, and 8[a]	Treatment Difference vs Placebo (95% CI)[b]
Week 12			
Clinical Remission[c]			
Total population	N=115 22%	N=225 56%	34% (24%, 44%)[d]
Prior biologic failure[e]	N=53 17%	N=104 60%	
Without prior biologic failure[f]	N=62 26%	N=121 52%	
Endoscopic Response[g]			
Total population	N=115 15%	N=225 34%	19% (10%, 28%)[d]
Prior biologic failure[e]	N=53 11%	N=104 27%	
Without prior biologic failure[f]	N=62 18%	N=121 40%	
Clinical Response[h]			
Total population	N=115 33%	N=225 72%	39% (29%, 50%)[d]
Prior biologic failure[e]	N=53 28%	N=104 76%	
Without prior biologic failure[f]	N=62 37%	N=121 69%	

Table 12: Proportion of Subjects with Crohn's Disease Meeting Efficacy Endpoints in CD3 (continued)

Endpoint	Placebo	TREMFYA 400 mg Subcutaneous Injection at Weeks 0, 4, and 8[a]		Treatment Difference vs Placebo (95% CI)[b]	
Weeks 24 and 48					
Endpoint	**Placebo**	**TREMFYA 100 mg Subcutaneous Injection every 8 weeks starting at Week 16**	**TREMFYA 200 mg Subcutaneous Injection every 4 weeks starting at Week 12**	**Treatment difference vs Placebo (95% CI)[b]**	
				TREMFYA 100 mg	**TREMFYA 200 mg**
Clinical Remission[c] at Week 24					
Total population	N=115 21%	N=114 61%	N=111 58%	39% (28%, 51%)[d]	37% (25%, 48%)[d]
Prior biologic failure[e]	N=53 19%	N=54 63%	N=50 52%		
Without prior biologic failure[f]	N=62 23%	N=60 58%	N=61 62%		
Clinical Remission[c] at Week 48					
Total population	N=115 17%	N=114 59%	N=111 65%	41% (30%, 52%)[d]	47% (36%, 58%)[d]
Prior biologic failure[e]	N=53 9%	N=54 56%	N=50 60%		
Without prior biologic failure[f]	N=62 24%	N=60 62%	N=61 69%		
Endoscopic Response[g] at Week 48					
Total population	N=115 5%	N=114 39%	N=111 48%	34% (24%, 44%)[d]	42% (32%, 53%)[d]
Prior biologic failure[e]	N=53 0%	N=54 33%	N=50 52%		
Without prior biologic failure[f]	N=62 10%	N=60 45%	N=61 44%		

[a] At baseline, subjects were randomized 1:1: 1 to receive subcutaneous TREMFYA 400 mg at Weeks 0, 4, and 8 followed by subcutaneous TREMFYA 100 mg every 8 weeks; subcutaneous TREMFYA 400 mg at Weeks 0, 4, and 8 followed by subcutaneous TREMFYA 200 mg every 4 weeks; or placebo. Because dosing is identical through Week 12, subjects in both TREMFYA groups are combined for the analysis of the Week 12 endpoints.

[b] The adjusted treatment difference and the CIs were based on the common risk difference test using Mantel-Haenszel stratum weights and the Sato variance estimator. The stratification variables used were baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), BIO-Failure status (Yes or No). CI = confidence interval

[c] Clinical remission is defined as CDAI score <150.

[d] p <0.001

[e] Includes inadequate response, loss of response, or intolerance to biologic therapy (TNF blockers, vedolizumab) for Crohn's disease.

[f] Includes subjects that were biologic naïve and subjects with prior biologic exposure who did not meet criteria for failure. Of these, 8 subjects in the placebo group and 17 subjects in the subcutaneous TREMFYA 400 mg group, were previously exposed to but did not fail a biologic therapy.

[g] Endoscopic response is defined as >50% improvement from baseline in SES-CD score.

[h] Clinical response is defined as ≥100-point decrease from baseline in CDAI total score.

[i] Includes subjects that were biologic naïve and subjects with prior biologic exposure who did not meet criteria for failure. Of these, 8 subjects in the placebo group, 7 subjects in the subcutaneous TREMFYA 100 mg group, and 10 subjects in the subcutaneous TREMFYA 200 mg group were previously exposed to but did not fail a biologic therapy.

Greater reductions in stool frequency and abdominal pain were observed as early as Week 4 in subjects treated with Tremfya 400 mg SubQ compared to placebo.

- **Endoscopic Remission at Week 48**: Endoscopic remission was defined as an SES-CD score ≤4 and at least a 2-point reduction from baseline and no subscore greater than 1 in any individual component. In CD3, a greater proportion of subjects treated with either Tremfya regimen (i.e., SubQ TREMFYA 400 mg at Weeks 0, 4, and 8 followed by SubQ Tremfya 100 mg at Week 16 and every 8 weeks thereafter or SubQ Tremfya 400 mg at Weeks 0, 4, and 8 followed by SubQ Tremfya 200 mg at Week 12 and every 4 weeks thereafter) achieved endoscopic remission, compared to placebo-treated subjects (31% and 40%, respectively, vs. 6%).

- **Summary of Updated Safety Considerations**: none

Current Formulary Status: Pharmacy Benefit, Specialty tier or Brand NP tier for members with a three tier benefit, PA for NSO, QL

Recommendation: Recommend the following updates to policy 484.0 and Medical Benefit Policy (MBP) 330.0. Recommend adding Tremfya Crohn's Induction 200 MG/2ML SOLN A-INJ to formulary, PA required; QL as noted below.

Commercial Policy 484.0 Tremfya

Crohn's Disease

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Tremfya is prescribed by a gastroenterologist **AND**
- Medical record documentation of a diagnosis of moderately to severely active Crohn's disease **AND**
- Medical record documentation that Tremfya is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- Medical record documentation of one of the following:
  - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids and immunomodulators (e.g. azathioprine and 6 mercaptopurine) **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy **OR**
  - Medical record documentation of moderate/high risk patient as defined by age at initial diagnosis less than 30 years, extensive anatomic involvement, perianal and/or severe rectal disease, deep ulcers, prior surgical resection, and structuring and/ or penetrating behavior

MEDISPAN AUTHORIZATION LEVEL: GPI-14

QUANTITY LIMIT: *Quantity limit must be entered in authorization.*

IV for Induction/ SubQ for Maintenance:

- Prefilled 100 mg/mL Syringe or Autoinjector, Tremfya 200 mg IV at Weeks 0, 4, and 8, then Tremfya 100 mg at Week 16, then every 8 weeks thereafter
  1. In PA Hub: Add Treat As "Include" Process Modifier, max number of claims authorized 1, max quantity dispensed 1, with a duration of four months.
     - QL FOR LETTER: 1 mL per 56 days
- Prefilled 200 mg/2 mL Syringe or Autoinjector, Tremfya 200 mg IV at Weeks 0, 4, and 8, then Tremfya 200 mg at Week 12, then every 4 weeks thereafter
  1. In PA Hub: Add Treat As "Include" Process Modifier, max number of claims authorized 1, max quantity dispensed 2, with a duration of four months.
     - QL FOR LETTER: 2 mL per 28 days
- ***Note to reviewer:*** **If IV doses will be purchased through pharmacy benefit, must enter a one-time override for IV.**

Renewal (SubQ for Maintenance ONLY):

- Tremfya 100 mg every 8 weeks
  1. In PA Hub: Add Treat As "Include" Process Modifier, max number of claims authorized 1, max quantity dispensed 1, with a duration of one month.
     - QL FOR LETTER: 1 mL per 56 days
- Tremfya 200 mg every 4 weeks
  1. In PA Hub: Add Treat As "Include" Process Modifier, max number of claims authorized 1, max quantity dispensed 2, with a duration of one month.
     - QL FOR LETTER: 2 mL per 28 days

SubQ for Induction AND Maintenance:

- Prefilled 100 mg/mL Syringe or Autoinjector for Maintenance, Tremfya 400mg SubQ (as 2 consecutive 200mg injections) at Weeks 0, 4, and 8, then Tremfya 100 mg at Week 16, then every 8 weeks thereafter
  1. In PA Hub: Add Treat As "Include" Process Modifier, max number of claims authorized 3, max quantity dispensed 4, with a duration of three months.
     - QL FOR LETTER: Loading dose: 1 mL per 28 days (max 3 fills); Maintenance Dose: 1 mL per 56 days

- Prefilled 200 mg/2 mL Syringe or Autoinjector for Maintenance, Tremfya 400mg SubQ (as 2 consecutive 200 mg injections) at Weeks 0, 4, and 8, then Tremfya 200 mg at Week 12, then every 4 weeks thereafter
    1. In PA Hub: Add Treat As "Include" Process Modifier, max number of claims authorized 3, max quantity dispensed 4, with a duration of three months.
    - QL FOR LETTER: Loading dose: 4 mL per 28 days (max 3 fills); Maintenance dose: 4 mL per 28 days

RE-AUTHORIZATION CRITERIA: Tremfya is configured as a prior authorization for new starts only. Tremfya 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

Medical Benefit Policy 330.0 Tremfya

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

Crohn's Disease

- Medical record documentation that Tremfya is prescribed by a gastroenterologist **AND**
- Member must be at least 18 years of age **AND**
- Medical record documentation of moderately to severely active Crohn's disease **AND**
- Medical record documentation that Tremfya is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- Medical record documentation of Tremfya 200 mg /20 mL vials for IV infusion are being prescribed for induction therapy at weeks 0, 4, and 8 **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids **AND** immunomodulators (e.g. azathioprine and 6-mercaptopurine) **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy **OR**
    - Medical record documentation of moderate/high risk patient as defined by age at initial diagnosis less than 30 years, extensive anatomic involvement, perianal and/or severe rectal disease, deep ulcers, prior surgical resection, and structuring and/or penetrating behavior

Ulcerative Colitis

- Medical record documentation that Tremfya is prescribed by a gastroenterologist **AND**
- Medical record documentation of a diagnosis of moderately to severely active ulcerative colitis **AND**
- Medical record documentation that Tremfya is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to one conventional systemic therapy* (e.g. corticosteroids, immunomodulators such as azathioprine, 6 mercaptopurine, cyclosporine, tacrolimus) **OR** medical record documentation of a therapeutic failure on or intolerance to one prior biologic therapy other than the requested agent **AND**
- Medical record documentation of Tremfya 200 mg /20 mL vials for IV infusion are being prescribed for induction therapy at weeks 0, 4, and 8.

*Note: A trial of a mesalamine product does not count as a systemic therapy for ulcerative colitis.

AUTHORIZATION DURATION: One-time 3-month authorization (maximum of 3 visits for loading dose administration)

Additional Recommendations: Recommend updating Medical Benefit Policy 267.0 Skyrizi to add conventional therapies to commercial, exchange, and CHIP lines of business align with Tremfya and Stelara policies.

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

Crohn's Disease

- Medical record documentation that Skyrizi is prescribed by a gastroenterologist **AND**
- Member must be at least 18 years of age **AND**
- Medical record documentation of moderately to severely active Crohn's disease **AND**
- Medical record documentation that Skyrizi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**

- Medical record documentation of Skyrizi 600 mg/ 10 mL vials for IV infusion is being prescribed for induction therapy at weeks 0, 4 and 8. **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids **AND** immunomodulators (e.g. azathioprine and 6-mercaptopurine) **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy **OR**
    - Medical record documentation of moderate/high risk patient as defined by age at initial diagnosis less than 30 years, extensive anatomic involvement, perianal and/or severe rectal disease, deep ulcers, prior surgical resection, and structuring and/or penetrating behavior

Ulcerative Colitis

- Medical record documentation that Skyrizi is prescribed by a gastroenterologist **AND**
- Medical record documentation of a diagnosis of moderately to severely active ulcerative colitis **AND**
- Medical record documentation that Skyrizi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to one conventional systemic therapy* (e.g. corticosteroids, immunomodulators such as azathioprine, 6 mercaptopurine, cyclosporine, tacrolimus) OR medical record documentation of a therapeutic failure on or intolerance to one prior biologic therapy other than the requested agent **AND**
- Medical record documentation of two Skyrizi 600 mg /10 mL vials for IV infusion are being prescribed for induction therapy at weeks 0, 4, and 8.

AUTHORIZATION DURATION: One-time 3-month authorization (maximum of 3 visits for loading dose administration)

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

VALTOCO (diazepam nasal spray)

Clinical Summary: Valtoco is a benzodiazepine that was indicated for the treatment of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern in patients with epilepsy 6 years of age and older. It is now indicated in patients 2 years of age and older.

The recommended dose of Valtoco nasal spray is 0.2mg/kg to 0.5mg/kg, depending on the patient's age and weight. The maximum dose is up to 2 doses for a single episode

Table 1: Recommended Dose Based on Age

Age (Years)	Recommended Dose
2 through 5	0.5 mg/kg
6 through 11	0.3 mg/kg
12 and older	0.2 mg/kg

Table 2: Recommended Dosage and Administration for Adults and Pediatric Patients 2 Years of Age and Older

Dose Based on Age and Weight				Administration	
2 to 5 Years of Age (0.5 mg/kg)	**6 to 11 Years of Age (0.3 mg/kg)**	**12 Years of Age and Older (0.2 mg/kg)**	**Dose (mg)**	**Number of Nasal Spray Devices**	**Number of Sprays**
Weight (kg)					
6 to 11	10 to 18	14 to 27	5	One 5 mg device	One spray in one nostril
12 to 22	19 to 37	28 to 50	10	One 10 mg device	One spray in one nostril
23 to 33	38 to 55	51 to 75	15	Two 7.5 mg devices	One spray in each nostril
	56 to 74	76 and up	20	Two 10 mg devices	One spray in each nostril

Second Dose (if needed): A second dose, when required, may be administered after at least 4 hours after the initial dose. If the second dose is to be administered, use a new blister pack of VALTOCO.

No additional studies were completed for the updated indication. Safety and effectiveness of valtoco have been established in pediatric patients 2 years to 16 years of age. Use of valtoco in this age group is supported by evidence from adequate and well-controlled studies of diazepam rectal gel in adult and pediatric patients, adult bioavailability studies comparing valtoco with diazepam rectal gel, patient pharmacokinetic data, and open-label safety studies of valtoco including patients 2 years to 16 years of age. Safety and effectiveness of valtoco in pediatric patients below the age of 2 years have not been established.

No updated safety considerations for the new indication.

Current Formulary Status: Brand preferred tier with age limit (6 to 999 years) and quantity limit of 10 per 30 days.

Recommendation: There are no changes to the formulary status or current quantity limits. Based on the updated indication, I recommend removing the age limit edit and retiring policy 617.0.

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

WELIREG (belzutifan)

Clinical Summary: Welireg is now indicated for the treatment of adult and pediatric patients 12 years and older with locally advanced, unresectable, or metastatic pheochromocytoma or paraganglioma (PPGL). It also has an update to the advanced renal cell carcinoma indication to clarify that the use of the drug product is intended for patients with advanced RCC with a clear cell component.

There is no change to the dosage of Welireg for adult patients for the new indication. For adult patients, the recommended dosage is 120 mg once daily with or without food. For pediatric patients 12 years and older, the recommended dosage is based on bodyweight: 120 mg orally once daily for patients weighing greater than or equal to 40 kg and 80 mg orally once daily for patients weighing less than 40 kg. Welireg is supplied as 40 mg tablets.

No new studies were done for the change to the advanced RCC indication. Changes were made to clarify the clear cell component in the RCC population, which was included in the original clinical trial, LITESPARK-005.

Support for the new indication comes from LITESPARK-015 trial, an open-label, clinical trial in 72 patients with measurable disease verified by BICR per RECIST v1.1, documented histopathological diagnosis of pheochromocytoma or paraganglioma (PPGL), locally advanced or metastatic disease that was not amenable to surgery or curative treatment, and adequately controlled blood pressure with no change in antihypertensive medications for patients with concomitant hypertension for at least 2 weeks prior to start of study treatment. Patients received Welireg 120 mg orally once daily until disease progression or unacceptable toxicity.

The median number of prior therapies was 1. A total of 50% of patients received prior chemotherapy, 44% received prior radiopharmaceuticals, and 25% received prior VEGF-TKIs.

The major efficacy outcome measures for the treatment of locally advanced PPGL was objective response rate (ORR) was measured by BICR using RECIST v1.1. Duration of response, time to response, and proportion of patients who had a reduction in at least one antihypertensive medication by at least 50% maintained for at least 6 months. The results are summarized in Table 1. Median TTR was 11.0 Months (range 1.7 to 24.8 months).

Table 1. Efficacy results for PPGL in LITESPARK-015

Efficacy Outcome Measure	WELIREG n=72
Confirmed Objective Response Rate *,†	
ORR, % (95% CI)	26% (17, 38)
Duration of Response*	
Median in months (95% CI)‡	20.4 (8.3, NR)
Range	5.6+, 29.6+
% with duration ≥ 12 months	53%
Reduction in at least one antihypertensive medication by at least 50% maintained for at least 6 months	
Number of patients	19
Proportion of patients (95% CI¶)§	32% (20, 45)

* Based on BICR.
† All responses were partial responses.
‡ Based on Kaplan-Meier estimates.
¶ Calculated using the Clopper-Pearson method.
§ Based on the number of patients who were on antihypertensive medications at baseline (N=60).
NR = not reached
+ = Denotes ongoing response.
Data cut-off: October 23, 2024

Adverse reactions were consistent with previous clinical trials of Welireg and no new safety signals were identified. Serious adverse reactions occurred in 36% of patients and included anemia and hypertension (4.2% each) and pyelonephritis, pneumonia, hypoxia, dyspnea and hemorrhage (2.8% each). Permanent discontinuation occurred in 2 patients, cause by increased alanine aminotransferase and paraparesis. Dose interruptions occurred in 40% of patients and dose reductions occurred in 14% of patients.

The safety and efficacy of Welireg in pediatric patients 12 years and older is supported by evidence from an adequate and well-controlled study of WELIREG in adults with additional pharmacokinetic data demonstrating that belzutifan exposure is predicted to be within range of that observed in adults, and that the course of locally advanced, unresectable, or metastatic pheochromocytoma or paraganglioma is sufficiently similar in adults and pediatric patients to allow extrapolation of data in adults to pediatric patients.

Current Formulary Status: Pharmacy Benefit, Oral Oncology Brand NP tier ($0 Copay), PA required for NSO

Recommendation: No changes are recommended to the formulary placement, authorization duration, or quantity limits for Welireg. The following prior authorization criteria changes to commercial policy 680.0 are recommended to update the RCC indication and add the new PPGL indication.

Advanced Renal Cell Carcinoma
- Medical record documentation of a diagnosis of advanced renal cell cancer with a clear cell component **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Welireg is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of therapeutic failure on, contraindication to, or intolerance to a PD-1 inhibitor or PD-L1 inhibitor (i.e., Bavencio, Keytruda, Opdivo) **AND**
- Medical record documentation of therapeutic failure on, contraindication to, or intolerance to a VEGF-TKI (i.e., Cabometyx, Fotivda, Inlyta, Lenvima, sorafenib, sunitinib, Votrient)

Von Hippel-Lindau (VHL) Disease
- Medical record documentation that Welireg is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**

- Medical record documentation of a diagnosis of von Hippel-Lindau (VHL) disease confirmed with a germline VHL alteration and at least one of the following:
    - associated renal cell carcinoma (RCC) **OR**
    - associated central nervous system (CNS) hemangioblastomas **OR**
    - associated pancreatic neuroendocrine tumors (pNET)

  AND
- Medical record documentation that patient does not require immediate surgery

Pheochromocytoma or Paraganglioma (PPGL)
- Medical record documentation that Welireg is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation of locally advanced, unresectable, or metastatic pheochromocytoma or paraganglioma (PPGL)

MEDISPAN APPROVAL LEVEL: GPI-12, number of claims authorized = 1, enter for 1 month duration

QUANTITY LIMIT: *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*
- QL FOR LETTER ONLY: 90 tablets per 30 days

RE-AUTHORIZATION CRITERIA: Welireg is configured as a prior authorization for new starts only. Welireg 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.

ZYNYZ (retifanlimab-dlwr)

Clinical Summary: On May 15, 2025, the FDA approved Zynyz in combination with carboplatin and paclitaxel for the first-line treatment of adults with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC). The FDA also approved Zynyz as monotherapy for adults with locally recurrent or metastatic SCAC whose disease has progressed on or who are intolerant to platinum-based chemotherapy. There is no biomarker requirement for use in either setting. Zynyz was initially approved for only metastatic or recurrent locally advanced Merkel cell carcinoma.

There is no updated dosing for the new indications. The dosing is 500 mg as an intravenous infusion every 4 weeks.

The efficacy of Zynyz in combination with carboplatin and paclitaxel was evaluated in study PODIUM-303/InterAACT 2 (NCT04472429), a randomized, multicenter, double-blind study in 308 patients with chemotherapy-naïve inoperable locally recurrent or metastatic SCAC. Patients who had not received prior systemic therapy other than a radiosensitizing agent or neoadjuvant or adjuvant therapy completed > 6 months prior to the study were eligible. The study did not enroll patients who received prior treatment with PD-(L)1-directed therapies. Patients were randomized to receive either Zynyz 500 mg IV every 4 weeks on day 1, carboplatin AUC 5 on day 1, and paclitaxel 80 mg/m^2 on days 1, 8, and 15 for 6 cycles followed by Zynyz 500 mg IV every 4 weeks, or placebo IV every 4 weeks on day 1, carboplatin AUC 5 on day 1, and paclitaxel 80 mg/m^2 on days 1, 8, and 15 for 6 cycles followed by placebo 500 mg IV for 4 weeks. Treatment with Zynyz continued until disease progression, unacceptable toxicity, death, or withdrawal of consent, for up to 12 months. The major efficacy outcomes were progression-free survival (PFS) and overall survival (OS). Additional efficacy outcome measures included objective response rate (ORR) and duration of response (DOR). There were 69 patients (45%) from the placebo arm who received Zynyz as a single agent after disease progression. The results are summarized in Table 1.

Table 1: Efficacy Results from study PODIUM-303/InterAACT 2 (NCT04472429)

Endpoint	ZYNYZ in Combination with Carboplatin and Paclitaxel (N = 154)	Placebo in Combination with Carboplatin and Paclitaxel (N = 154)
Progression-free survival		
Events, n (%)	92 (60)	110 (71)
Median (months) (95% CI)	9.3 (7.5, 11.3)	7.4 (7.1, 7.7)
Hazard ratio[a] (95% CI)	0.63 (0.47, 0.84)	
p-value[b]	0.0006	
Overall survival		
Deaths, n (%)	53 (34)	73 (47)
Median (months) (95% CI)	29.2 (24.2, NE)	23 (15.1, 27.9)
Hazard ratio[a] (95% CI)	0.70 (0.49, 1.01)	
Objective response rate		
Objective response rate (%) (95% CI)	56 (48, 64)	44 (36, 52)
Complete response, n (%)	34 (22)	21 (14)
Partial response, n (%)	52 (34)	47 (31)
Median duration of response, in months (95% CI)	14.0 (8.6, 22.2)	7.2 (5.6, 9.3)

CI = confidence interval; NE = not evaluable.
[a] Based on stratified Cox model.
[b] One-sided p-value based on stratified log-rank test.

Study PODIUM-202: As a Single Agent for the Treatment of Platinum-refractory or Intolerant Locally Recurrent or Metastatic Squamous Cell Carcinoma of the Anal Canal

The efficacy of Zynyz was evaluated in study PODIUM-202 (NCT03597295), an open-label, multicenter, single-arm study in 94 patients with locally recurrent or metastatic SCAC who progressed on or were intolerant of platinum-based chemotherapy. Patients received Zynyz IV every 4 weeks until disease progression, unacceptable toxicity, or up to 24 months. The major efficacy outcomes were ORR and DOR. The results are summarized in Table 2.

Table 2: Efficacy Results from Study PODIUM-202

Endpoint	ZYNYZ (N = 94)
Objective Response Rate (95% CI)	14% (8, 23)
Complete response, n (%)	1 (1.1)
Partial response, n (%)	12 (13)
Duration of Response	
Median, months	9.5 (4.4, NE)
Patients with DOR ≥ 6 months (95% CI)	65% (31, 85)
Patients with DOR ≥ 12 months (95% CI)	41% (11, 69)

CI = confidence interval; DOR = duration of response; NE = not evaluable.

Current Formulary Status: Zynyz is a medical benefit requiring prior authorization.

Recommendation: It is recommended to update the criteria in the medical benefit policy to include the new indication:

1. **Merkel Cell Carcinoma**

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

2. **Squamous Cell Carcinoma of the Anal Canal**

- Medical record documentation that Zynyz is written by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years of age **AND**
- Medical record documentation of a diagnosis of locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC) **AND**
- One of the following:
    - Medical record documentation of inoperable disease **AND**
    - Medical record documentation of use in the first-line setting **AND**
    - Medical record documentation of use in combination with carboplatin and paclitaxel

OR

- Medical record documentation that Zynyz will be used as a single agent **AND**
- Medical record documentation of disease progression on or intolerance to platinum-based chemotherapy

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

QUANTITY LIMIT: 20mL per 28 days

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

UPDATES

HB 1993 DAY SUPPLY UPDATES

Background: Due to HB 1993, several specialty medications were removed from the specialty drug list since they no longer met the specialty definition. Once the specialty edit was removed from these medications, they would no longer have the specialty day supply limitation (i.e. 34 day supply).

Recommendation: It is recommendation that day supply edits are added to the following medications to ensure the dispensing pharmacy submits an appropriate day supply.

Drug	Day Supply
Anagrelide	Max: 34 day supply
Droxidopa	Max: 34 day supply
Irinotecan	Min: 28 day supply Max: 42 day supply
Penicillamine	Max: 34 day supply
Penicillamine	Max: 34 day supply
Penicillamine	Max: 34 day supply
Palonosetron	Max: 34 day supply
Palonosetron	Max: 34 day supply
Paragard	Max: 3650 day supply
Paragard	Max: 3650 day supply
Miudella	Max: 1095 day supply
Xatmep	Max: 34 day supply

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

Medical Benefit Drug Prior Authorization List Update

Background: Recently, GHP engaged with outside consulting. During this process the GHP medical benefit prior authorization (PAL) list was compared to that of three competitors. Discrepancies between GHP's PAL and at least 2 other competitors' lists were flagged by the consultant for GHP review.

Recommendation: Based on GHP's review and leadership direction, the following changes are recommended.

Drug	Policy	Current PA Status	Proposed PA Status	Other Actions Required
Xiaflex (Collagenase clostridium histolyticum)	MBP 80.0	PA=Yes	PA=No	Retire MBP 80.0, Remove Xiaflex from MBP 300.0
Zulresso (Brexanolone)	MBP 201.0	PA=Yes	PA=No	Retire MBP 201.0 (Note: this drug was removed from market)
Triptodur (triptorelin ER)	MBP 204.0	PA=Yes	PA=No	Retire MBP 204.0
Iluvien (fluocinolone acetonide)	MBP 129.0	PA=Yes	PA=No	Retire MBP 129.0
Clolar (clofarabine)	MBP 38.0	PA=Yes	PA=No	Retire MBP 38.0
Zaltrap (ziv-aflibercept)	MBP 101.0	PA=Yes	PA=No	Retire MBP 101.0
Somatuline Depot (lanreotide)	N/A	PA=No	PA=Yes	Create policy. See proposed criteria below.
Bendamustine (multiple generics and brands)	N/A	PA=No	PA=Yes (except generic Treanda)	Create policy. See proposed criteria below

Proposed criteria for lanreotide:
Acromegaly

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of acromegaly **AND**
- One of the following:
    - Medical record documentation that the patient has an insufficient response to surgery and/or radiotherapy **OR**
    - Medical record documentation that the patient is not a candidate for surgery and/or radiotherapy

Carcinoid Syndrome

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of histologically-confirmed neuroendocrine tumor **AND**
- Medical record documentation of carcinoid syndrome (flushing and/or diarrhea)

Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of well or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumor (GEP-NET) **AND**
- All of the following:
    - Medical record documentation that the tumor is unresectable **AND**
    - Medical record documentation that the tumor is non-functioning **AND**
    - Medical record documentation that the tumor is without hormone-related symptoms

AND

- Medical record documentation that the medication is being used to improve progression-free survival

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

Proposed criteria for bendamustine:
For all lines of business: Generic Treanda will not require prior authorization. Brand Treanda, Belrapzo (and its generics), Bendeka, and Vivimusta, will be considered medically necessary when ALL of the following criteria are met. Part B Step therapy will apply.

For a request for brand Treanda:

- 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)

For Belrapzo (or its generics) and Bendeka requests:

- Medical record documentation of a therapeutic failure of, intolerance to, or contraindication to generic Treanda

For Vivimusta requests (Commercial/Exchange/CHIP/Medicaid):

- Medical record documentation of a therapeutic failure of, intolerance to, or contraindication to generic Treanda **AND**
- Medical record documentation of a therapeutic failure of, intolerance to, or contraindication to both of the following: Belrapzo (or its generics)* AND Bendeka*

For Vivimusta requests (Medicare ONLY):

- Medical record documentation of a therapeutic failure of, intolerance to, or contraindication to generic Treanda **AND**
- Medical record documentation of a therapeutic failure of, intolerance to, or contraindication to one of the following: Belrapzo (or its generics)* OR Bendeka*

*prior authorization required (note: generic Treanda is preferred and does not require prior authorization)

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

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

Medical Benefit Policy Update – Aliqopa and Arzerra

Recommendations: It is recommended to retire the medical benefit policy for Aliqopa MBP 161.0 Aliqopa (copanlisib) & Arzerra MBP 73.0 Arzerra (ofatumumab). Aliqopa was withdrawn from the market March 2024 and Arzerra was moved to a patient access program via manufacturer only on August 2020.

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

Medical Benefit Policy Update – Drug Optimization Program Update

Recommendations: The following (highlighted) drug products are recommended to be added to the Medical Benefit Drug Optimization Program effective on 12/1/25. No other changes are recommended to the program at this time.

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

I. Policy:
Medical Benefit Drug Optimization Program

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

1. AbobotulinumtoxinA (Dysport)
2. Ado-Trastuzumab Emtansine (Kadcyla)
3. Amivantamab (Rybrevant)
4. Aripiprazole (Abilify Maintena, Abilify Asimtufii)
5. Aripiprazole lauroxil (Aristada Initio, Aristada)
6. Arsenic Trioxide (Trisenox)
7. Asparaginase (Erwinia [Recombinant]) (Rylaze)
8. Atezolizumab (Tecentriq)
9. Avelumab (Bavencio)
10. Belatacept (Nulojix)
11. Belinostat (Beleodaq)
12. Blinatumomab (Blincyto)
13. Brentuximab Vedotin (Adcetris)
14. Bortezomib
15. Cabazitaxel (Jevtana)
16. Carfilzomib (Kyprolis)
17. Cemiplimab (Libtayo)
18. Collagenase (Xiaflex)
19. Datopotamab Deruxtecan (Datroway)
20. Daunorubicin and Cytarabine (Liposomal) (Vyxeos)
21. Daratumumab (Darzalex)
22. Daratumumab and Hyaluronidase (Darzalex Faspro)
23. DaxibotulinumtoxinA (Daxxify)
24. Dostarlimab (Jemperli)
25. Durvalumab (Imfinzi)
26. Elotuzumab (Empliciti)
27. Elranatamab (Elrexfio)
28. Epcoritamab (Epkinly)
29. Eribulin (Halaven)
30. Enfortumab Vedotin (Padcev)
31. Fam-Trastuzumab Deruxtecan (Enhertu)
32. Fluphenazine deconate
33. Gemtuzumab Ozogamicin (Mylotarg)
34. Haloperidol deconate
35. IncobotulinumtoxinA (Xeomin)
36. Inotuzumab Ozogamicin (Besponsa)
37. Ipilimumab (Yervoy)
38. Irinotecan liposomal (Onivyde)
39. Isatuximab (Sarclisa)
40. Loncastuximab Tesirine (Zynlonta)
41. Lurbinectedin (Zepzelca)
42. Margetuximab (Margenza)

43. Mirvetuximab Soravtansine (Elahere)
44. Mogamulizumab (Poteligeo)
45. Mosunetuzumab (Lunsumio)
46. Naxitamab (Danyelza)
47. Necitumumab (Portrazza)
48. Nivolumab (Opdivo)
49. Nivolumab and hyaluronidase-nvhy (Opdivo Qvantig)
50. Obinutuzumab (Gazyva)
51. Octreotide (Sandostatin LAR)
52. Olanzapine (Zyprexa Relprevv)
53. OnabotulinumtoxinA (Botox)
54. Paliperidone (Invega Sustenna, Invega Hafyera, Invega Trinza)
55. Panitumumab (Vectibix)
56. Pegloticase (Krystexxa)
57. Pembrolizumab (Keytruda)
58. Polatuzumab Vedotin (Polivy)
59. Ramucirumab (Cyramza)
60. Relatlimab and nivolumab (Opdualag)
61. Retifanlimab (Zynyz)
62. RimabotulinumtoxinB (Myobloc)
63. Risperidone (Perseris, Risperdal Consta, Rykindo, Uzedy)
64. Rituximab (Rituxan)
65. Rituximab and Hyaluronidase (Rituxan Hycela)
66. Romidepsin (Istodax)
67. Romiplostim (Nplate)
68. Siltuximab (Sylvant)
69. Sipuleucel-T (Provenge)
70. Sutimlimab (Enjaymo)
71. Tafasitamab (Monjuvi)
72. Tagraxofusp (Elzonris)
73. Tarlatamab (Imdelltra)
74. Tebentafusp (Kimmtrak)
75. Temsirolimus (Torisel)
76. Telisotuzumab Vedotin (Emrelis)
77. Thiotepa (Tepadina)
78. Tislelizumab (Tevimbra)
79. Tisotumab Vedotin (Tivdak)
80. Toripalimab (Loqtorzi)
81. Trabectedin (Yondelis)
82. Trastuzumab (Herceptin)
83. Tremelimumab (Imjudo)
84. Zolbetuximab (Vyloy)

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

Site of Care Update

Discussion: Currently, the below medications (highlighted in green) are medical benefits that require prior authorization for the commercial line of business and are not on the Site of Care Program. After review of the respective FDA-approved labels, it has been determined that the below medications are acceptable candidates for the Site of Care program.

Recommendations: It is recommended the following changes (highlighted in green) be made to MBP 181.0 so that this policy may reflect the addition of the below medications to the Site of Care Program. The addition of tocilizumab biosimilars to the self-injected drug list is recommended. Also, the removal of ustekinumab from the SOC list is recommended given dosing and administration considerations.

MBP 181.0 Site of Care
I. Policy:
Site of Care Review Guidelines for Infusion Drugs and Specialty Medications

II. Purpose/Objective:

To provide a policy of coverage regarding the use of hospital-based outpatient facilities as a site of care for drugs that require administration via intravenous infusion or injection. This policy applies to these medications:

1. Abatacept (Orencia IV)
2. ADAMTS13 [Recombinant] (Adzynma)
3. Agalsidase Beta (Fabrazyme)
4. Alglucosidase Alfa (Lumizyme)
5. Alpha1-Proteinase Inhibitor [Human] products
6. Anifrolumab-fnia (Saphnelo)
7. Avalglucosidase alfa-ngpt (Nexviazyme)
8. Axatilimab (Niktimvo)
9. Belimumab (Benlysta IV)
10. Benralizumab (Fasenra)
11. Beremagene Geperpavec (Vyjuvek)
12. Burosumab (Crysvita)
13. C1 esterase Inhibitor [Human] (Cinryze)
14. Canakinumab (Ilaris)
15. Casimersen (Amondys 45)
16. Certolizumab (Cimzia)
17. Cipaglucosidase alfa (Pombiliti)
18. Crizanlizumab (Adakveo)
19. Crovalimab (PiaSky)
20. Denosumab & denosumab biosimilars ~~(Prolia, Xgeva)~~
21. Eculizumab & eculizumab biosimilars ~~(Soliris)~~
22. Edaravone (Radicava)
23. Elapegademase-lvlr (Revcovi)
24. Elosulfase alfa (Vimizim)
25. Emapalumab (Gamifant)
26. Eptinezumab (Vyepti)
27. Efgartigimod Alfa (Vyvgart & Vyvgart Hytrulo)
28. Eteplirsen (Exondys 51)
29. Evinacumab (Evkeeza)
30. Galsulfase (Naglazyme)
31. Givosiran (Givlaari)
32. Golodirsen (Vyondys 53)
33. Golimumab (Simponi Aria)
34. Idursulfase (Elaprase)
35. Immune Globulin (IVIG)
36. Imiglucerase (Cerezyme)
37. Inclisiran (Leqvio)
38. Inebilizumab (Uplizna)
39. Infliximab & infliximab biosimilar products
40. Laronidase (Aldurazyme)
41. Lumasiran (Oxlumo)
42. Mepolizumab (Nucala)
43. Natalizumab & natalizumab biosimilars ~~(Tysabri)~~
44. Ocrelizumab (Ocrevus & Ocrevus Zunovo)
45. Olipudase alfa-rpcp (Xenpozyme)
46. Omalizumab (Xolair)
47. Patisiran (Onpattro)
48. Pegunigalsidase Alfa (Elfabrio)
49. Pozelimab (Veopoz)
50. Ravulizumab (Ultomiris)
51. Reslizumab (Cinqair)
52. Romosozumab (Evenity)
53. Rozanolixizumab (Rystiggo)
54. Sebelipase alfa (Kanuma)
55. Secukinumab (Cosentyx IV)
56. Sutimlimab (Enjaymo)
57. Taliglucerase alfa (Elelyso)
58. Teprotumumab (Tepezza)
59. Testosterone udecanoate (Aveed)
60. Tezepelumab (Tezspire)
61. Tildrakizumab (Ilumya)
62. Tocilizumab IV & tocilizumab IV biosimilars ~~(Actemra IV)~~
63. Ublituximab-xiiy (Briumvi)
64. ~~Ustekinumab (Stelara)~~
65. Vedolizumab (Entyvio)
66. Velaglucerase alfa (Vpriv)
67. Velmanase alfa (Lamzede)
68. Vestronidase alfa-vjbk (Mepsevii)
69. Viltolarsen (Viltepso)
70. Vutrisiran (Amvuttra)

III. Responsibility:

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

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.
6. Site of Care – choice of physical location for administration of intravenous infusions or injections. Site of care locations include hospital inpatient, hospital based outpatient facilities, physician's office, ambulatory infusion centers, or home infusion services.
7. Alternative less intensive site of care facilities include non-hospital affiliated outpatient infusion centers such as ambulatory infusion centers or physician's offices and home infusion
8. Hospital based outpatient facilities include ER services, intravenous drug infusions or injections, observation services, outpatient surgery, lab tests, or x-rays, or any other hospital services where the patient is not admitted as an inpatient.

V. Additional Definitions

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

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

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

c. in accordance with current standards good medical treatment practiced by the general medical community;

d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and

e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

DESCRIPTION:

Specific intravenous and injectable drugs must meet applicable medical necessity criteria for coverage. If these criteria are met, this coverage policy will be used to determine the medical necessity of administration in the hospital based outpatient setting. If medical necessity criteria for administration in the hospital based outpatient setting are not met, an alternative less intensive site of care facility should be utilized.

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

Administration in the hospital-based outpatient setting will be considered medically necessary and LIMITED to a duration of 60 days (for Xolair (omalizumab), a duration of up to 90 days if the reviewing provider determines it is medically appropriate) when one of the following criteria are met:

- This is the initial medication infusion **OR**
- Member is reinitiating treatment after not receiving any treatments for at least 6 months.

AUTHORIZATION DURATION: Initial approval will be for a duration of 60 days (for Xolair, up to 90 days). Administration in the hospital-based outpatient setting for longer than the initially approved amount will be required to meet the authorization criteria in the section below.

Administration in the hospital-based outpatient setting will be considered medically necessary for a duration of greater than 60 days when one of the following criteria are met:

- The medication has a site of care restriction for administration per the FDA approved label **OR**
- Documented previous history of severe or potentially life-threatening adverse event during or following administration and the adverse event cannot be managed using pre-medication(s) or adjusting the rate of infusion **OR**
- All of the following:
    - All alternate non-hospital outpatient settings are not within a reasonable distance from the member's home (within 50 miles) **AND**
    - Home healthcare or infusion provider has determined that the patient, home caregiver, or home environment is not appropriate for home infusion or home infusion services are not available due to limited network access **AND**
    - For request of a provider administered drug, for which a self-administered formulation is available, including but not limited to abatacept, belimumab, benralizumab, certolizumab, golimumab, mepolizumab, omalizumab, secukinumab, tezepelumab, and tocilizumab & tocilizumab biosimilar products~~, and ustekinumab~~: medical record documentation of a therapeutic failure of or intolerance to a 3 month trial of the self-administered formulation of the respective product.

  OR

- For IVIG any of the above criteria **OR**
    - Change of immune globulin products (one infusion will be permitted in the hospital outpatient setting) **OR**
    - Laboratory confirmed immunoglobulin A (IgA) deficiency with anti-IgA antibodies

  OR
- For Xgeva (denosumab) or Xgeva biosimilars any of the above criteria **OR**
    - Patient is receiving Xgeva concomitantly with intravenous chemotherapy as part of the same encounter

  AUTHORIZATION DURATION: Initial approval will be for the same length of time as the authorization of the specific drug being administered. Subsequent approvals will be required if the specific drug requires subsequent authorizations.

NOTE: To prevent a delay in care and allow adequate transition time for members to an alternate infusion site, members already established on therapy who do not meet any of the above criteria will be given a 60-day transition auth to allow them to continue receiving therapy at their current hospital based outpatient facility while they transition to a different infusion site.

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

Voting responses were received from 32 of 49 members. The vote was unanimously approved.

The next bi-monthly scheduled meeting will be held on September 9th, 2025 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.