P&T Committee Meeting Minutes
Commercial/Exchange/CHIP
October 2023 e-Vote

DRUG REVIEWS

ELREXFIO (elranatamab-bcmm)

Review: Elrexfio is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager, for adults with relapsed or refractory multiple myeloma (R/R MM) who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. Elrexfio binds BCMA on plasma cells, plasmablasts, and multiple myeloma cells and CD3 on T-cells leading to cytolysis of the BCMA-expressing cells. Elrexfio-activated T-cells caused proinflammatory cytokine release and resulted in multiple myeloma cell lysis.

Elrexfio is administered by subcutaneous injection by a qualified healthcare professional. Elrexfio is administered according to a step-up dosing schedule to reduce the incidence and severity of cytokine release syndrome (CRS). Patients should be hospitalized for 48 hours after administration of the first step-up dose and 24 hours after the second step-up dose.

Pretreatment should be administered prior to step-up dose 1, step-up dose 2, and the first treatment dose to reduce the risk of CRS. Elrexfio is supplied as 76 mg/1.9 mL (40 mg/mL) and 44 mg/1.1 mL (40 mg/mL) vials containing a ready-to-use solution.

The efficacy of Elrexfio was evaluated in MagnetisMM-3, a study in patients with relapsed or refractory multiple myeloma in an open-label, single arm study who were refractory to at least one proteasome inhibitor (PI), one immunomodulatory agent (IMiD) and one anti-CD38 monoclonal antibody. The trial included 123 patients naïve to prior BCMA-directed therapy (pivotal Cohort A) and 64 patients with prior BCMA-directed antibody drug conjugate (ADC) or chimeric antigen receptor (CAR) T-cell therapy (supportive Cohort B). Patients had measurable disease, ECOG scores of at least 2, and adequate baseline bone marrow and hepatic function. Eligible patients received the recommended subcutaneous dosage of Elrexfio.

The 123 patients in Cohort A received a median of 5 prior lines of therapy. The efficacy population was comprised of ninety-seven patients who were not exposed to prior BCMA-directed therapy and received at least four prior lines of therapy. Efficacy was based on response rate and duration of response assessed by BICR based on IMWG criteria.

Sixty-three of 64 patients enrolled in Cohort B received at least four prior lines of therapy (median:8, range 4-19). Seventy-three percent received prior BCMA-directed ADC and 32% received prior CAR-T cell therapy. Confirmed objective response rate was 33.3%. After median follow-up of 10.2 months among responders, median DOR was not reached and DOR rate at 9 months was 84.3%.

Elrexfio has a black box warning for Cytokine Release Syndrome and Neurologic Toxicity including Immune Effector Cell-Associated Neurotoxicity Syndrome and other warnings and precautions for risk of infections, neutropenia, hepatotoxicity, and embryo-fetal toxicity. During the MagnetisMM-3 trial, the most common adverse reactions were CRS, fatigue, injection site reaction, diarrhea, upper respiratory tract infection, musculoskeletal pain, pneumonia, decreased appetite, rash, cough, nausea, and pyrexia. Serious adverse reactions occurred in 68% of patients treated with Elrexfio, including pneumonia, sepsis, CRS, upper respiratory tract infection, acute kidney injury, urinary tract infection, COVID-19, encephalopathy, pyrexia, and febrile neutropenia. Fatal adverse reactions occurred in 10% of patients including pneumonia, sepsis, acute respiratory distress syndrome, cardio-respiratory arrest, cardiogenic shock, cardiopulmonary failure, COVID-19, failure to thrive, and pulmonary embolism. Permanent

discontinuation and dosage interruptions occurred in 17% and 73% of patients, respectively. The most common laboratory abnormalities were decreased lymphocytes, neutrophils, hemoglobin, white blood cells, and platelets. Due to the risk of CRS and neurologic toxicity including ICANS, a REM program is in place for Elrexfio treatment.

The safety and efficacy of Elrexfio in pediatric patients has not been established. Of the 183 patients with relapsed or refractory multiple myeloma treated with Elrexfio in MagnetisMM-3 at the recommended dosage, 62% were 65 years of age or older, and 19% were 75 years of age or older. No overall differences in safety and effectiveness were observed between patients 65-74 years compared to younger patients. Clinical studies did not include sufficient patients 75 years of age or older to determine whether they respond differently from younger patients.

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

Outcome: Elrexfio is a medical benefit drug and will be added to the medical benefit cost share list. When processed at a Specialty Pharmacy, Elrexfio will process on the Specialty tier or Brand NP tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Elrexfio is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of relapsed or refractory multiple myeloma **AND**
- Medical record documentation of treatment with at least four (4) prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody

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 the member experiences unacceptable 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.

SOGROYA (somapacitan-beco)

Review: Sogroya is a once-weekly human growth hormone analog indicated for the treatment of pediatric patients aged 2.5 years and older who have growth failure due to inadequate secretion of endogenous growth hormone (GH) and replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD). Sogroya binds the growth hormone receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamic effects. Some of these pharmacodynamic effects are primarily mediated by insulin-like growth factor 1 (IGF-1) produced in the liver, while others are primarily a consequence of the direct effects of somapacitan-beco.

Sogroya is administered by subcutaneous injection once weekly in the upper arms, thigh, abdomen, or buttocks with weekly rotation of injection site. The recommended dosage of Sogroya in pediatric patients is 0.16 mg/kg based on actual body weight once weekly for treatment -naïve patients and patients switching from daily growth hormone. The dosage should be individualized based on growth response. The recommended dosage of Sogroya in adult patients is an initial dosage of 1.5 mg once weekly for treatment naïve patients and patients switching from daily growth hormone. The dosage should be increased every 2 to 4 weeks by approximately 0.5 mg to 1.5 mg until the desired response is achieved. The maximum recommended dosage is 8 mg once weekly. For patients 65 years of age and older, the initial recommended dosage is 1 mg once weekly and smaller dosage increments are used to titrate to a maintenance dosage. Sogroya is supplied as a single-patient-use prefilled pen in three different doses: 5 mg/1.5 mL, 10 mg/1.5 mL, and 15 mg/1.5 mL.

The safety and efficacy of Sogroya in pediatric patients was evaluated in a randomized, open-label, active-controlled, parallel-group study in 200 treatment-naïve pediatric patients with growth hormone deficiency (GHD) comparing Sogroya (n=132) to somatropin (n=68). The primary efficacy endpoint was annualized height velocity at Week 52. Treatment with once weekly Sogroy for 52 weeks resulted in an annualized height velocity of 11.2 cm/year. Patients treated with daily somatropin achieved an annualized height velocity of 11.7 cm/year after 52 weeks of treatment.

The safety and efficacy of Sogroya in adult patients was evaluated in a 35 week, double-blind, placebo-controlled study in treatment naïve patients with GHD. Patients were randomized 2:1:2 to receive once weekly Sogroya (n=120) or placebo (n=60) or daily somatropin (n=119). Treated with Sogroya demonstrated superiority compared to placebo in reduction in truncal fat percentage as assessed by dual X-ray absorptiometry with a change of -1.06% for Sogroya compared to +0.47% for placebo (Table 4). Patients treated with daily somatropin achieved a change in truncal fat % of -2.23% after 34 weeks.

After 34 weeks, Sogroya normalized mean Insulin Growth Factor-1 (IGF-1) standard deviation score (SDS) level in treatment naïve patients with GHD with an IGF-1 SDS of -0.17 in Sogroya treated patients compared to -2.62 in placebo treated patients. The mean IGF-1 SDS levels in daily somatropin-treated patients was -2.53 at baseline and -0.23 at 34 weeks.

The safety profile of Sogroya is similar to that of other growth hormones and includes warnings and precautions for severe hypersensitivity, increased risk of neoplasm, glucose intolerance and diabetes mellitus, intracranial hypertension, fluid retention, hypoadrenalism, hypothyroidism, slipped capitol femoral epiphysis in pediatric patients, progression of preexisting scoliosis in pediatric patients, pancreatitis, and lipohypertrophy/lipoatrophy. The most common adverse reactions in pediatric patients were nasopharyngitis, headache, pyrexia, pain in extremities, and injection site reaction. The most common adverse reactions in adult patients were back pain, arthralgia, dyspepsia, sleep disorder, dizziness, tonsillitis, peripheral edema, vomiting, adrenal insufficiency, peripheral edema, vomiting, adrenal insufficiency, hypertensions, blood creatine phosphokinase increase, weight gain, and anemia.

The safety and efficacy of Sogroya have been established in patients 2.5 years of age and older based on evidence from the 52 week phase 3 trial in 200 treatment-naïve pediatric patients with GHD. The safety profile from the pediatric trial was similar to that reported in adults. In clinical trials, a total of 52 of the 333 Sogroya treated patients were 65 years of age and older and 3 patients were 75 years or older. Subjects older than 65 years appeared to have higher exposure than younger subjects at the same dose level. Elderly patients may be more sensitive to the action of somapacitan and therefore may be at increased risk for adverse reactions. A lower initial dose and smaller titration increments should be used when increasing the dose.

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

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

For Norditropin:

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

For all other Growth Hormone Agents:

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

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

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

GPI Level: GPI-12

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

TALVEY (talquetamab-tgvs)

Review: Talvey is a bispecific G protein-coupled receptor class C group 5 member D (GPRC5D)-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody. This was an accelerated approval based on response rate and durability of response. Talvey is the first bispecific antibody to target GPRC5D expressed on the surface of multiple myeloma cells and non-malignant plasma cells, as well as healthy tissues on the epithelial cells in keratinized tissues of the skin and tongue. It also binds the CD3 receptor expressed on the surface of T-cells. In vitro, Talvey activated T-cells caused the release of proinflammatory cytokines and resulted in the lysis of multiple myeloma cells. Talvey had anti-tumor activity in mouse models of multiple myeloma.

Talvey is administered as a subcutaneous injection and should be administered by a healthcare professional with appropriate medical support to manage severe reactions such as CRS and neurologic toxicity including ICANS. Due to the risk of CRS and neurologic toxicity, patients should be hospitalized for 48 hours after administration of all doses within the Talvey step-up dosing schedule. Premedication with a corticosteroid, antihistamine, and antipyretic should be administered 1-3 hours prior to each dose of Talvey in the step-up dosing schedule to reduce the risk of CRS. Dose Delays may be required to manage toxicities and may require the patient to repeat the step-up dosing, depending on the time from the last administered dose.

The efficacy of Talvey was evaluated in MonumenTAL-1, a single-arm, open-label study in patients with relapsed or refractory multiple myeloma. The study included patients who had previously received at least three prior systemic therapies, including a protease inhibitor, an immunomodulatory agents, and an anti-CD38 monoclonal antibody. The study exclude patients who experienced T-cell redirection therapy within 3 months, Grade-3 or higher CRS related to any T-cell redirection therapy, an autologous stem cell transplant within the past 12 weeks, an allogenic stem cell transplant within the past 6 months, ECOG performance score of 3 or higher, stroke or seizure withing the past 6 months, CNS involvement or clinical signs of meningeal involvement of multiple myeloma, plasma cell leukemia, and active or documented history of autoimmune disease.

Patients included in the trial received Talvey according to the recommended dosing schedule for weekly or biweekly dosing and patients were treated until disease progression or unacceptable toxicity. The efficacy population included 187 patients treated with Tavley who were not exposed to prior T-cell redirection therapy and who had received at least 4 prior lines of therapy. Ninety-four percent of patients were refractory to their last therapy and 74% were refractory to a proteasome inhibitor, immunomodulatory agent, and anti-CD38 antibody. Efficacy was based on overall response rate (ORR) and duration or response (DOR) as assessed by an Independent Review Committee using IMWG criteria.

The median duration of follow-up from the first response among responders receiving the 0.4 mg/kg weekly dosing and 0.8mg/kg biweekly dosing was 13.8 months and 5.9 months, respectively. Results for patients who received Talvey biweekly showed that an estimated 85% of responders maintained their response for at least 9 months.

Thirty-two patients were exposed to prior T-cell redirection therapy and had received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and anti-CD38 monoclonal antibody received the Talvey weekly dose. Patients received a median of 6 prior therapies, with 81% exposed to CAR-T cell therapy and 25% exposed to a bispecific antibody. Ninety-four percent of patients were exposed to prior T-cell redirection therapy directed at BCMA. The ORR per IRC assessment was 72%. With a median duration of follow up of 10.4 months, an estimated 59% of responders maintained a response lasting at least 9 months.

Talvey includes a black box warning for cytokine release syndrome (CRS) and neurologic toxicity, including Immune Effector Cell-associated neurotoxicity syndrome (ICANS) and additional warnings and precautions for oral toxicity and weight loss, risk of infections, cytopenias, skin toxicity, hepatotoxicity, and embryo-fetal toxicity. Serious adverse reactions occurred in 47% of patients who received Talvey and included CRS, bacterial infection, sepsis, pyrexia, ICANS, COVID-19, neutropenia, and upper respiratory tract infection. Fatal adverse reactions occurred in 3.2% of patients who received Talvey, including COVID-19, dyspnea, general physical health deterioration, bacterial infection, basilar artery occlusion, fungal infection, infection, and pulmonary embolism. Permanent discontinuation and dosage interruptions occurred in 9% and 56% of patients, respectively. The most common adverse reactions included pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight loss, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache. The most common Grade 3 or 4 lab abnormalities included decreased lymphocyte count, neutrophil count, white blood cells, and hemoglobin.

The safety and efficacy of Talvey have not been established in pediatric patients. Of 339 patients in clinical trials for RRMM, 178 (53%) patients were 65 years of age and older, while 57 (17%) were 75 years and older. No overall differences in safety or efficacy were observed in patients 65 to less than 74 years of age compared to younger patients. There was a higher rate of fatal adverse reactions in patients 75 years of age and older compared to younger patients. Clinical studies did not include sufficient numbers of patients 75 years of age and older to determine if they respond differently to younger patients.

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

Outcome: Talvey is a medical benefit drug and will be added to the medical benefit cost share list. When processed at a Specialty Pharmacy, Talvey will process on the Specialty tier or Brand NP tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Talvey is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of relapsed or refractory multiple myeloma **AND**
- Medical record documentation of treatment with at least four (4) prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody

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 the member experiences unacceptable 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.

FAST FACTS

AYVAKIT (avapritinib)

Clinical Summary: Ayvakit is now approved for the treatment of adult patients with indolent systemic mastocytosis (ISM). Ayvakit is not recommended for the treatment of patients with ISM with platelet counts of less than 50 X 109/L. The other indications for Ayvakit remain the same. These include the treatment of adults with unresectable or metastatic gastrointestinal stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including PDGFRA D842V mutations and the treatment of adult patients with advanced systemic mastocytosis (AdvSM). AdvSM includes patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with an associated hematological neoplasm (SMAHN), and mast cell leukemia (MCL), but Ayvakit is not recommended in patients with platelet counts less than 50 X 109/L.

The recommended dosage for Ayvakit for ISM is 25mg orally once daily. The dose should be reduced for those with severe hepatic impairment (Child-Pugh Class C).

The efficacy of Ayvakit was demonstrated in PIONEER (NCT03731260), a randomized, double-blind, placebo-controlled trial conducted in adult patients with Indolent Systemic Mastocytosis (ISM) based on World Health Organization (WHO) classification. Enrolled patients had moderate to severe symptoms despite receiving at least 2 symptom directed therapies. Patients were randomized to receive 25 mg Ayvakit orally once daily with best supportive care versus placebo with best supportive care. The majority of patients who received Ayvakit (99.3%) or placebo (100%) received concomitant best supportive care at baseline (median of 3 therapies in the Ayvakit group and 4 in the placebo group). The most common therapies in the Ayvakit group were H1 antihistamines (97%), H2 antihistamines (66%), leukotriene inhibitors (35%) and cromolyn sodium (30%). The treatment duration was over a 24-week period, during the randomized portion of the study. Efficacy was based on the absolute mean change from baseline to Week 24 in the Indolent Systemic Mastocytosis-Symptom Assessment Form (ISM-SAF) total symptom score (TSS). The ISM-SAF is a patient-reported outcome measure assessing ISM signs and symptoms: abdominal pain, nausea, diarrhea, spots, itching, flushing, bone pain, fatigue, dizziness, headache, brain fog. Scores ranged from 0 (“none”) to 10 (“worst imaginable”). The item scores were summed to calculate a daily ISM-SAF TSS (range 0110), with higher scores indicating greater symptom severity. A biweekly average ISM-SAF TSS was used to evaluate efficacy endpoints. Additional supportive results included the proportion of Ayvakit-treated patients achieving greater than or equal to 50% reduction from baseline through Week 24 in TSS compared to placebo. Objective measures of mast cell burden were assessed including the proportion of Ayvakit-treated patients with a greater than or equal to 50% reduction from baseline through Week 24 in serum tryptase, peripheral blood KIT D816V allele fraction and bone marrow mast cells.

The warnings and precautions have been updated to include a broad spectrum of cognitive adverse reactions can also occur in patients receiving Ayvakit for ISM. Depending on the severity, continue Ayvakit at same dose, withhold and then resume at same or reduced dose upon improvement, or permanently discontinue.

Current Formulary Status: Ayvakit is a pharmacy benefit requiring a prior authorization with a quantity limit. It is on the oral oncology brand non-preferred tier ($0 copay).

Recommendation: No changes recommended to the formulary placement of Ayvakit at this time. However, it is recommended to update policy 611.0 to include the following changes. The Medispan authorization level change will only apply to the ISM criteria as the only dosing recommended for this indication is 25mg orally once daily.

Indolent Systemic Mastocytosis (ISM)

- Medical record documentation that Ayvakit 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 platelet count greater than or equal to 50 x 10^9/L **AND**
- Medical record documentation of indolent systemic Mastocytosis (ISM) **AND**
- Medical record documentation of a dose consistent with FDA approved labeling

MEDISPAN AUTHORIZATION LEVEL: GPI-14, number of claims authorized = 1, enter for the remainder of the calendar year

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

- QL FOR LETTER ONLY: 1 tablet per day, 30 day supply per fill
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RE-AUTHORIZATION CRITERIA: Ayvakit is configured as a prior authorization for new starts only. Ayvakit 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

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

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

BREO ELLIPTA (fluticasone-vilanterol)

Clinical Summary: Breo Ellipta is a combination corticosteroid/ long-acting beta2 adrenergic agonist (LABA) inhaler indicated for the maintenance treatment of asthma in patients 5 years of age and older. It was previously indicated for the maintenance treatment of asthma and chronic obstructive pulmonary disease (COPD) in patients 18 years of age and older.

The efficacy of Breo Ellipta for the maintenance treatment of asthma in pediatric patients aged 5 to 17 years of age was based on Trial 14 (NCT03248128), a 24-week, randomized, double-blind, stratified, parallel-group clinical trial. This trial evaluated the efficacy of Breo Ellipta compared with fluticasone furoate in 902 pediatric patients with asthma aged 5 to 17 years who were uncontrolled on their current inhaled corticosteroid (ICS) treatment. All inhalations were administered once daily in the morning. At trial entry patients had at least a 6-month history of asthma and had been receiving stable asthma therapy for at least 4 weeks prior to screening. Patients had to have a pre-bronchodilator FEV1 >50% to ≤100% of predicted normal and demonstrate a ≥12% reversibility of FEV1 within 15 to 40 minutes following 2 to 4 inhalations of albuterol inhalation aerosol (or 1 nebulized treatment with albuterol solution). Patients entered a 4-week open-label run-in period during which all patients received fluticasone propionate 100 mcg twice daily. Patients reporting symptoms and/or rescue beta2-agonist medication use during the last week of the run-in period were continued in the trial and were stratified by age. Pediatric patients aged 12 to 17 years (n = 229) were randomized 1:1 to Breo Ellipta 100/25 mcg once daily (n = 117) or fluticasone furoate 100 mcg once daily (n = 112). Pediatric patients aged 5 to 11 years (n = 673) were randomized 1:1 to Breo Ellipta 50/25 mcg once daily (n = 337) or fluticasone furoate 50 mcg once daily (n = 336).

The primary endpoint was weighted mean FEV1 (0 to 4 hours) at Week 12. Lung function improvements based on the primary endpoint of weighted mean FEV1 (0 to 4 hours) are presented in Table 1. Difference in least squares (LS) mean change from baseline at Week 12 for Breo Ellipta 100/25 mcg compared with fluticasone furoate 100 mcg was 106 mL (95% CI: -8, 220) in pediatric patients 12 to 17 years of age, and difference in LS mean change from baseline at Week 12 for Breo Ellipta 50/25 mcg compared with fluticasone furoate 50 mcg was 73 mL (95% CI: 28, 118) in pediatric patients 5 to 11 years of age.

Orally inhaled corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. The safety and effectiveness of Breo Ellipta have not been established in pediatric patients less than 5 years of age. Monitor the growth of pediatric patients receiving Breo Ellipta routinely (e.g., via stadiometry). To minimize the systemic effects of orally inhaled corticosteroids, titrate each patient's dose to the lowest dosage that effectively controls his/her symptoms.

Current Formulary Status: Pharmacy Benefit; preferred, no QL, no Prior Authorization required

Recommendation: Recommend adding Breo Ellipta 50mcg/25mcg to same tier as 100mcg/25mcg and 200mcg/25mcg strengths. Recommend adding a QL of 2 per day to all strengths (50mcg/25mcg, 100mcg/25mcg, 200mcg/25mcg)* No other recommended changes.

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

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

BYLVAY (odevixibat)

Clinical Summary: Bylvay (odevixibat) is now indicated in the treatment of cholestatic pruritus in patients 12 months of age and older with Alagille syndrome. Previously, Bylvay was approved for the treatment of the treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis (PFIC).

The recommended dosage of Bylvay for Alagille Syndrome is 120 mcg/kg taken orally once daily. This is an increase from the recommended dosage for PFIC, which is 40 mcg/kg taken once a day.

Bylvay comes in two formulations: oral pellets and capsules. Both formulations share the same indications but differ in strengths. Bylvay oral pellets are intended for use by patients weighing less than 19.5 kilograms while the capsules are intended for use by patients weighing 19.5 kilograms or above.

Current Formulary Status: Bylvay is a pharmacy benefit on specialty tier or brand non-preferred tier for members with a three- tier benefit, requiring prior authorization with a quantity limit.

Recommendation: There are no changes recommended to formulary placement of Bylvay at this time. However, it is recommended to update the prior authorization criteria in the current policy to include the following:

Progressive Familial Intrahepatic Cholestasis (PFIC)

- Medical record documentation that Bylvay is prescribed by or consultation with a hepatologist or gastroenterologist **AND**
- Medical record documentation of a diagnosis of progressive familial intrahepatic cholestasis (PFIC) confirmed by genetic testing **AND**
- Medical record documentation of the presence of moderate to severe pruritus **AND**
- Medical record documentation of age greater than or equal to 3 months **AND**
- Medical record documentation that the member is receiving an appropriate dose* based on the member's weight **AND**
- Medical record documentation of concurrent use or therapeutic failure on, intolerance to, or contraindication to ursodiol

***NOTE:** The recommended dosage of Bylvay for PFIC is 40 mcg/kg once daily. If there is no improvement in pruritus after 3 months, the dosage may be increased in 40 mcg/kg increments up to 120 mcg/kg once daily not to exceed a total daily dose of 6 mg (6000 mcg). See https://bylvay.com/pdf/021066_Bylvay_Dosing_Guide.pdf

OR

Alagille Syndrome

- Medical record documentation of a diagnosis of Alagille Syndrome (ALGS) **AND**
- Medical record documentation of the presence of moderate to severe pruritis **AND**
- Medical record documentation that member is 12 months of age or older **AND**
- Medical record documentation that Bylvay is prescribed by or in consultation with a hepatologist or gastroenterologist **AND**
- Medical record documentation that member is receiving an appropriate dose* based on the member's weight **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ursodiol and one of the following: cholestyramine, rifampin, or naltrexone.

***NOTE:** The recommended dosage of Bylvay for Alagille Syndrome is shown in the table below:

Table 2. Recommended Dosage for ALGS in Patients aged 12 months and older (120 mcg/kg/day)

Body Weight (kg)	Once Daily Dosage (mcg)
7.4 and below	600
7.5 to 12.4	1,200
12.5 to 17.4	1,800
17.5 to 25.4	2,400
25.5 to 35.4	3,600
35.5 to 45.4	4,800
45.5 to 55.4	6,000
55.5 and above	7,200

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 the following:

- Medical record documentation of improvement in pruritus and/or reduction in serum bile acid **AND**
- Medical record documentation that the member is receiving an appropriate dose* based on the member's weight

QUANTITY LIMIT:

- **QL FOR LETTER ONLY:**
  - 200 mcg pellets: ~~30 capsules per day~~, up to a 34 day supply per fill
    - → 36 capsules per day, up to a 34 day supply per fill
  - 600 mcg pellets: ~~10 capsules per day~~, up to a 34 day supply per fill
    - → 12 capsules per day, up to a 34 day supply per fill
  - 400 mcg capsules: ~~15 capsules per day~~, up to a 34 day supply per fill
    - → 18 capsules per day, up to a 34 day supply per fill
  - 1200 mcg capsules: ~~5 capsules per day,~~ up to a 34 day supply per fill
    - → 6 capsules per day, up to a 34 day supply per fill

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

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

FARXIGA (dapagliflozin)

Clinical Summary: Farxiga is now indicated to reduce the risk of cardiovascular death~~, and~~ hospitalization for heart failure, and urgent heart failure visit in adults with heart failure ~~with reduced ejection fraction (NYHA class II-IV).~~

An update was also made to the limitations of use for Farxiga. Previously the package insert stated that Farxiga was not recommended for patients with type 1 diabetes mellitus as it may increase risk of diabetic ketoacidosis in these patients. Now it states that Farxiga is not recommended for use to improve glycemic control in patients with type 1 diabetes mellitus.

No updated dosing for the heart failure indication however, recommendations have been made for use prior to major surgery. It is now recommended to withhold Farxiga for at least 3 days, if possible, prior to major surgery or procedures associated with prolonged fasting. Resume Farxiga when the patient is clinically stable and has resumed oral intake.

The efficacy and safety of Farxiga 10mg for use in heart failure was assessed in two phase 3 studies, Dapagliflozin And Prevention of Adverse outcomes in Heart Failure (DAPA-HF, NCT03036124) and Dapagliflozin Evaluation to Improve the LIVEs of Patients with PReserved Ejection Fraction Heart Failure (DELIVER, NCT03619213). The DAPA-HF study was an international, multicenter, randomized, double blind, placebo-controlled study in patients with heart failure with reduced ejection fraction. Of 4744 patients, 2373 were randomized to Farxiga and 2371 to placebo and were followed for a medium of 18 months. The DELIVER study was an international, multicenter, randomized, double-blind, placebo-controlled study in patients with heart failure with LVEF >40% and evidence of structural heart disease. Of 6263 patients, 3131 were randomized to Farxiga 10mg and 3132 to placebo and were followed for a median of 28 months. This study also included 654 heart failure patients who were randomized during hospitalization for heart failure or within 30 days of discharge. In both studies, Farxiga reduced the incidence of the primary composite endpoint of CV death, hospitalization for heart failure or urgent heart failure visits.

In both studies, all three components of the primary composite endpoint individually contributed to the treatment effect. In both studies, the Farxiga and placebo event curves separated early and continued to diverge over the study period. In DAPA-HF, Farxiga reduced the total number of hospitalizations for heart failure events and CV death, with 567 and 742 total events in the Farxiga treated vs placebo group (Rate Ratio 0.75 [95% CI 0.65, 0.88]; p=0.0002). In DELIVER, Farxiga reduced the total number of heart failure events and CV death, with 815 and 1057 total events in the Farxiga treated vs placebo group (Rate Ratio 0.77 [95% CI 0.67, 0.89]; p=0.0003). The treatment effect of Farxiga on the composite endpoint of cardiovascular death, hospitalization for heart failure or urgent heart failure was consistent across the LVEF range as evaluated in the DAPA-HF and Deliver studies.

In patients with type 1 diabetes mellitus, Farxiga significantly increases the risk of diabetic ketoacidosis beyond the background rate. In placebo-controlled trials of patients with type 1 diabetes, the risk of ketoacidosis was markedly increased in patients who received SGLT2 inhibitors compared to patients who received placebo. Farxiga is not indicated for glycemic controlled in patients with type 1 diabetes mellitus. Urinary glucose excretion persists for 3 days after discontinuing Farxiga; however there have been post marketing reports of ketoacidosis and/or glucosuria lasting greater than 6 days and some up to 2 weeks after discontinuation of SGLT2. Withhold Farxiga, if possible, in temporary clinical situations that could predispose patients to ketoacidosis. Resume Farxiga when the patient is clinically stable and has resumed oral intake.

Current Formulary Status: Pharmacy benefit on the brand preferred tier with a quantity limit of 1 tablet per day. No prior authorization is required.

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

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

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

JEMPERLI (dostarlimab-gxly)

Clinical Summary: Jemperli is now indicated, in combination with carboplatin and paclitaxel, followed by Jemperli as a single agent for the treatment of adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR), as determined by an FDA approved test, or microsatellite instability-high (MSI-H). This indication is approved under accelerated approval, based on tumor response rate and durability of response. Previously, Jemperli was approved as a single agent for adult patients with dMMR recurrent or advanced endometrial cancer following progression on a platinum-containing regimen and as a single agent for the treatment of adult patients with dMMR recurrent or advanced solid tumors.

The recommended dosage for the new indication is a 30 minute intravenous administration of Jemperli 500 mg every 3 weeks for 6 doses followed by 1000 mg monotherapy every 6 weeks. For the first six doses, Jemperli is administered prior to carboplatin and paclitaxel. Monotherapy treatment will continue until disease progression, unacceptable toxicity, or up to 3 years.

The new indication is supported by results from the RUBY trial, a randomized, double-blind, placebo controlled trial in 122 patients with dMMR/MSI-H primary advanced or recurrent endometrial cancer. Treatment with Jemperli continued until disease progression, unacceptable toxicity, or a maximum of 3 years. Administration of J Jemperli was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator. The major efficacy outcome in the dMMR/MSI-H subgroup was investigator-assessed progression-free survival (PFS) using RECIST v1.1. Additional efficacy outcome measures included overall survival (OS), Objective Response Rate (ORR), and Duration of Response (DOR). Overall survival data in this subpopulation was immature with 27% deaths.

The safety of Jemperli in combination with carboplatin and paclitaxel was evaluated in RUBY in 52 patients who received Jemperli. Serious adverse reactions occurred in 13% of patients receiving Jemperli + carboplatin + paclitaxel, most commonly sepsis. Fatal adverse reactions occurred in 6% of patients received Jemperli, including septic shock, and myelosuppression. Jemperli was permanently discontinued due to adverse reactions in 8 patients, including 1 case of each: maculo-papular rash, fatigue, generally physical health deterioration, acute kidney injury, infusion-related reaction, keratitis, muscular weakness, and myelosuppression. The most common adverse reactions included rash, diarrhea, hypothyroidism, and hypertension. The most common Grade 3 or 4 laboratory abnormalities were decreased neutrophils, hemoglobin, white blood cell count, lymphocytes, and platelets, and increased glucose.

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

Recommendation: No changes are recommended to the formulary placement or authorization duration of Jemperli. The following prior authorization criteria and changes will be added to MBP 236.0:

Endometrial Cancer

- Medical record documentation that Jemperli 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 one of the following:
    - Medical record documentation of a diagnosis of recurrent or advanced endometrial cancer **AND**

- Medical record documentation of mismatch repair deficient (dMMR) as determined by an FDA approved test **AND**
- Medical record documentation of disease progression on or following prior treatment with a platinum-containing regimen **AND**
- Medical record documentation that member is not a candidate for curative surgery or radiation

OR

- Medical record documentation of primary advanced or recurrent endometrial cancer **AND**
  - Medical record documentation that Jemperli will be used in combination with carboplatin and paclitaxel for 6 doses, followed by Jemperli as a single agent **AND**
  - Medical record documentation of mismatch repair deficient (dMMR) as determined by an FDA approved test **OR** microsatellite instability-high (MSI-H)

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

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

LINZESS (linaclotide)

Clinical Summary: Linzess is now approved for functional constipation in pediatric patients aged 6 to 17 years of age. Previously, it was approved for irritable bowel syndrome with constipation and chronic idiopathic constipation in adults. The dosing is 72mcg once daily for FC for pediatric patients.

Efficacy for the new indication was established in a 12-week double-blind, placebo-controlled, randomized, multicenter trial where a total of 328 patients aged 6-17 years of age received Linzess 72mcg once daily or placebo once daily. Patients were required to have < 3 spontaneous bowel movements (SBM) per week and 1 or more of the following at least once per week for the 2 months before the screening visit: history of stool withholding or excessive voluntary stool retention, history of painful or hard bowel movements, history of large diameter stools that may obstruct the toilet, presence of a large fecal mass in the rectum, at least 1 episode of fecal incontinence per week. Patients were also required to have an average of < 3 SBM per week during the 2-week baseline period. The primary endpoint was the 12-week change from baseline in SBM frequency rate. Patients who received Linzess had statistically significant improvements compared to placebo.

Current Formulary Status: Linzess is on the brand preferred tier without a prior authorization but with an age restriction of a minimum of 18 years of age.

Recommendation: Recommend removing the age restriction.

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

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

LONSURF (trifluridine and tipiracil)

Clinical Summary: Lonsurf is now indicated for the treatment of adult patients with metastatic colorectal cancer as a single agent or in combination with bevacizumab who have been previously treated with

fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy. Previously, this was only indicated as a single agent in this patient population.

The dosage for the treatment metastatic colorectal cancer in combination with bevacizumab is the same as it was as a single agent, 35 mg/m2/dose twice daily on days 1 to 5 and days 8 to 12 of a 28-day cycle, until disease progression, or unacceptable toxicity.

The safety and efficacy of Lonsurf in combination with bevacizumab were assessed in SUNLIGHT (NCT 04737187), an international, randomized (1:1), open label study of patients previously treated for metastatic colorectal cancer. Patients could not have received more than two prior treatments for advanced disease including a fluoropyrimidine, irinotecan, oxaliplatin, an anti-VEGF monoclonal antibody (optional) and an anti-EGFR monoclonal antibody for patients with RAS wild-type. Patients were randomized 1:1 to receive Lonsurf 35 mg/m2 twice daily on Days 1 to 5 and 8 to 12 of each 28-day cycle with or without bevacizumab 5 mg/kg administered intravenously every 2 weeks (on Day 1 and Day 15) of each 4-week cycle until disease progression or unacceptable toxicity. There were a total of 492 patients that were randomized to receive Lonsurf in combination with bevacizumab (246 patients) or Lonsurf as a single agent (246 patients). The primary efficacy outcome was overall survival (OS) and an additional efficacy outcome measure was progression-free survival (PFS).

The most common adverse reactions occurring in ≥20% of patients for this patient population included neutropenia, anemia, thrombocytopenia, fatigue, nausea, increased AST, increased ALT, increased alkaline phosphatase, decreased sodium, diarrhea, abdominal pain, and decreased appetite. No new warnings, contraindications, or black box warnings were identified.

Current Formulary Status: Pharmacy Benefit on the Oral Oncology Brand NP tier, requires a prior authorization.

Recommendation: No changes are recommended to the formulary placement of Lonsurf. The following criteria will be added to Commercial Policy 396.0 for Lonsurf to incorporate the new indication.

Metastatic Colorectal Cancer

- Medical record documentation that Lonsurf 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 metastatic colorectal cancer **AND**
- Medical record documentation of previous treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF (vascular endothelial growth factor) biological therapy, and is RAS wild-type, an anti-EGFR (epidermal growth factor receptor) therapy **AND**
- Medical record documentation that Lonsurf will be prescribed as a single agent or in combination with bevacizumab

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

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

PREVYMIS (letermovir)

Clinical Summary: Prevymis is now indicated for prophylaxis of CMV disease in adult kidney transplant recipients at high risk (Donor CMV seropositive/Recipient CMV seronegative [D+/R-]).

The recommended dosage of Prevymis is 480 mg administered orally or intravenously once daily. Dosage of Prevymis should be adjusted when co-administered with cyclosporine. For kidney transplant,

initiate Prevymis between Day 0 and Day 7 post-transplant and continue through Day 200 post-transplant. If oral or intravenous Prevymis is co-administered with cyclosporine, the dosage of Prevymis should be decreased to 240 mg once daily.

To evaluate Prevymis prophylaxis as a preventive strategy for CMV disease in kidney transplant recipients, the efficacy of Prevymis was assessed in a multicenter, double-blind, active comparator controlled non-inferiority Phase 3 trial (P002, NCT03443869) in adult kidney transplant recipients at high risk [D+/R-]. Subjects were randomized (1:1) to receive either Prevymis or valganciclovir. Prevymis was administered at a dose of 480 mg once daily (adjusted to 240 mg when co-administered with cyclosporine). Prevymis was given concomitantly with acyclovir. Valganciclovir was given concomitantly with a placebo to acyclovir. Randomization was stratified by the use or nonuse of highly cytolytic, antilymphocyte immunotherapy during induction. Study drug was initiated between Day 0 and Day 7 post-kidney transplant and continued through Week 28 (~200 days) post-transplant. Study drug was administered either orally or IV; the dose of Prevymis was the same regardless of the route of administration. Three subjects received IV Prevymis for a mean duration of 1.7 days. Subjects were monitored through Week 52 post-transplant.

Among the 589 treated subjects, 292 subjects received Prevymis and 297 received valganciclovir. The median age was 51 years (range: 18 to 82 years); 72% were male; 84% were White; 9% were Black; 3% were multiple; 2% were Asian; 1% Alaskan native or American Indian; 17% were Hispanic or Latino; and 60% received a kidney from a deceased donor. The most common primary reasons for transplant were congenital cystic kidney disease (17%), hypertension (16%), and diabetes/diabetic nephropathy (14%).

CMV Disease The primary efficacy endpoint of Trial P002 was the incidence of CMV disease (CMV end-organ disease or CMV syndrome, confirmed by an independent adjudication committee) through Week 52 post-transplant. The Observed Failure (OF) approach was used, where subjects who discontinued prematurely from the study for any reason or were missing data at the timepoint were not counted as failures. The number of subjects who discontinued from the study before Week 52 was 32 (11%) in the Prevymis arm and 28 (9%) in the valganciclovir arm. The number of subjects with a missing outcome in the Week 52 visit window was 24 (8%) in the Prevymis arm and 25 (8%) in the valganciclovir arm. Efficacy was comparable across all subgroups, including the use/nonuse of highly cytolytic, anti-lymphocyte immunotherapy during induction.

In an exploratory analysis of the incidence of CMV disease through Week 28 post-transplant, the difference (Prevymis – Valganciclovir) was -1.7% with 95% CI of (-3.4, 0.1). No subjects in the Prevymis group experienced CMV disease through Week 28 post-transplant (end of treatment period) compared with 5 subjects in the valganciclovir group.

Adult Kidney Transplant Recipients [D+/R-] The safety of Prevymis was evaluated in a Phase 3 randomized, double-blind, active comparator controlled trial (P002) in which 589 subjects were treated with Prevymis (N=292) or valganciclovir (N=297) through Week 28 post-transplant. Adverse events were those reported while subjects were on study medication or within two weeks of study medication completion/discontinuation. In these subjects, diarrhea was reported in at least 10% of subjects in the Prevymis group and at a frequency greater than valganciclovir (Prevymis, 32%; valganciclovir, 29%). Study drug was discontinued due to an adverse event in 4% of Prevymis subjects and 14% of valganciclovir subjects. The most frequently reported adverse events that led to study drug discontinuation were neutropenia (Prevymis, 1%; valganciclovir, 2%) and leukopenia (Prevymis, 1%; valganciclovir, 5%).

Current Formulary Status: Prevymis is a formulary medication covered under commercial policy 505.0

Recommendation: The following changes are recommended to commercial policy 505.0 to reflect the new indication for Prevymis:

- Medical record documentation that member is a recipient of an allogeneic hematopoietic stem cell transplant **OR** is a recipient of an adult kidney transplant **AND**

Discussion: No comments or questions.

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

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

REXULTI (brexpiprazole)

Clinical Summary: The new indication for Rexulti is for the treatment of agitation associated with dementia due to Alzheimer's disease. [It is not indicated as an as needed treatment for this condition]. Previous indications include use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder in adults and treatment of schizophrenia in adults and pediatric patients ages 13 years and older.

The recommended dosing for the treatment of agitation associated with dementia due to Alzheimer's disease is 0.5 mg taken once daily on days 1 to 7, increase to 1 mg on days 8 to 14 and on day 15, increase dose to 2 mg once daily. The recommended target dose is 2 mg once daily. The dosage can be increased to the maximum recommended daily dosage of 3 mg once daily after at least 14 days of therapy, based on clinical response and tolerability. The recommended maximum daily dosage in severe hepatic impairment or renal impairment is 2 mg once daily for this indication**.**

The safety and efficacy of Rexulti in the treatment of agitation associated with dementia due to Alzheimer's disease was demonstrated in two 12-week, randomized, double-blind, placebo-controlled, fixed-dose studies in 503 patients, ages 51 to 90, with a probable diagnosis of agitation associated with dementia due to Alzheimer's Disease.

Study 6 included 433 patients, mean age of 74 years old, range of 51 to 90 years old; 45% male; 96%, 3% and 1% were White, Black or African American, and Asian, respectively; 16 % and 83% were Latino/Hispanic and not Latino/Hispanic respectively. Study 7 included 345 patients, mean age of 74, range of 56 to 90 years old; 44% male; 95%, 4% and 1% were White, Black or African American, and Asian, respectively; 31% and 69% were Latino/Hispanic and not Latino/Hispanic, respectively.

The primary efficacy endpoint in these two studies was the change from baseline in the Cohen-Mansfield Agitation Inventory total (CMAI) score at week 12. This is a clinician rated questionnaire consisting of 29 items which assess the frequency of manifestations of agitated behaviors in elderly patients based on caregiver input. Three specific factors can be derived from the CMAI scale: (1) Aggressive Behavior such as screaming, throwing things, cursing, verbal aggression, kicking, pushing, scratching, hurting self or others; (2) Physically Non-Aggressive Behavior (e.g., repetitive mannerisms, general restlessness, pacing); (3) Verbally Agitated Behavior (e.g., complaining, repetitive questions, constant requests for attention). Each CMAI behavior was rated on a scale of 1 (never) to 7 (very frequent agitated behaviors). The total CMAI scores range from 29 (best) to 203 (worst) with a negative change indicating improvement.

In Study 6, patients in the Rexulti 2 mg group showed improved total CMAI scores compared to patients in the placebo group at Week 12 and in Study 7, patients in the Rexulti 2 mg and 3 mg group showed improved CMAI scores compared to patients in the placebo group at Week 12. The table below shows the mean change from baseline in the total CMAI score after 12 weeks in the 2 mg or 3 mg Rexulti group was statistically significantly superior to the placebo group. The 1 mg Rexulti group did not demonstrate significantly greater mean changes from baseline for the total CMAI score as compared to placebo therefore this dose is not approved and /or recommended for the treatment of agitation associated with dementia due to Alzheimer's Disease.

Current Formulary Status: Rexulti is currently non-formulary requiring prior authorization and a quantity limit.

Recommendation: Recommend adding the following highlighted indication and bullets to Policy 388.0:

Agitation Associated with Dementia due to Alzheimer's Disease:

- Medical record documentation of a diagnosis of agitation associated with dementia due to Alzheimer's Disease **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three generic, formulary antipsychotics used for the treatment of agitation associated with dementia (such as but not limited to quetiapine, risperidone, olanzapine, etc.) **AND**
- Medical record documentation that Rexulti will not be used "as needed" for this indication

Discussion: No comments or questions.

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

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

REBLOZYL (luspatercept-aamt)

Clinical Summary: Reblozyl is now indicated for anemia failing an erythropoiesis stimulating agent (ESA) and requiring 2 or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).

The dosing for Reblozyl for anemia remains the same as previous at 1 mg/kg once every 3 weeks by subcutaneous injection. The dose is to be adjusted per Table 1 below, with the recommendations remaining unchanged after the new indication was added. The patient's hemoglobin and transfusion record should be reviewed prior to each dose, and Reblozyl should be discontinued if no decrease in transfusion burden (including no increase from baseline hemoglobin) after 9 weeks of treatment at the maximum dose (1.75 mg/kg) is observed.

The efficacy of Reblozyl in patients who were ESA-naïve with anemia in Revised International Prognostic Scoring System (IPSS-R) very low, low, or intermediate-risk MDS or myelodysplastic/ myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN RS-T) was evaluated in a multi-center, open-label, randomized active-controlled trial called COMMANDS (NCT03682536). Patients had endogenous serum EPO (sEPO) levels of <500 U/L, had 2 to 6 RBC units for 8 weeks immediately preceding randomization, and were ESA naïve. 356 patients were randomized 1:1 to Reblozyl or epoetin alfa. Reblozyl was started at 1 mg/kg every 3 weeks, and two dose increases were allowed up to 1.33 mg/kg and 1.75 mg/kg, with doses reduced if hemoglobin increased by ≥2 g/dL from the prior cycle. Doses were held if pre-dose hemoglobin was ≥12 g/dL. Doses were also held and subsequently reduced for adverse reactions. Epoetin alfa was given once weekly. All patients also received RBC transfusions as needed. Patients were treated and evaluated for efficacy at 24 weeks, with option to continue therapy based upon response to treatment and absence of disease progression.

The primary endpoint was achievement of RBC transfusion independence (RBC-TI), defined as the absence of any RBC transfusion, and an associated concurrent mean improvement in hemoglobin by at least 1.5 g/dL for any consecutive 12 week period. Secondary endpoints were achievement of hematologic improvement-erythroid (HI-E) response for ≥ 8 weeks per IWG 2006 criteria, RBC-TI for at least 24 weeks and for at least 12 weeks, and safety. The interim efficacy analysis, done after 301 patients (about 85%) completed 24 weeks of therapy, established the efficacy of Reblozyl in the treatment

of anemia in ESA-naïve patients with MDS. Efficacy was established based on the proportion of patients who reached the primary efficacy endpoint. Results are summarized in Table 3. The trial concluded that Reblozyl improved the rate at which RBC-TI and hemoglobin increase was achieved, compared to epoetin alfa. The data showed superiority of Reblozyl over ESA in ESA-naïve patients and could represent a new standard of care for patients with transfusion dependent, lower-risk MDS, per the American Society of Clinical Oncology (ASCO). Reblozyl led to clinically meaningful and statistically significant improvements in red blood cell transfusion independence and its durability, erythroid response, and reduction of transfusion burden.

There are no changes to the contraindications or warnings and precautions with the updated indication. There are no contraindications listed. Warnings and precautions are still significant for thrombosis/thromboembolism, hypertension, extramedullary hematopoietic masses, and embryo fetal toxicity. In the COMMANDS trial, of the patients treated with Reblozyl, 9.6% (17/178) discontinued dosing due to adverse events, 27% (48/178) interrupted dosing due to adverse events, and 2.8% (5/178) reduced dosing due to adverse events. The most common adverse events (>10%) were diarrhea, fatigue, hypertension, peripheral edema, nausea, and dyspnea.

Current Formulary Status: Reblozyl is a medical benefit requiring prior authorization. If processed at a specialty pharmacy, Reblozyl will process at the Specialty tier or Brand non-preferred tier for members with a three tier benefit.

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

1. Anemia due to Beta thalassemia

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of beta thalassemia **AND**
- Medical record documentation that patient requires regular* red blood cell (RBC) transfusions **AND**
- Medical record documentation of baseline number of transfusions and red blood cell (RBC) units required for the previous six (6) months **AND**
- Medical record recommendation that Reblozyl is being dosed consistent with FDA-approved labeling**.

2. Anemia due to myelodysplastic syndromes or myelodysplastic/myeloproliferative neoplasm
For ESA-refractory disease:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T) with one of the following:
    - Documentation of greater than or equal to 15% ring sideroblasts **OR**
    - Documentation of greater than or equal to 5% ring sideroblasts AND an SF3B1 mutation **AND**
- Medical record documentation of very low to intermediate risk disease per the Revised International Prognostic Scoring System (IPSS-R) **AND**
- Medical record documentation that patient requires 2 or more red blood cell units over 8 weeks **AND**
- Medical record documentation of baseline number of transfusions and red blood cell (RBC) units required for the previous six (6) months **AND**
- Medical record documentation of therapeutic failure, intolerance to, or contraindication to an erythropoiesis stimulating agent **AND**
- Medical record recommendation that Reblozyl is being dosed consistent with FDA-approved labeling**.

For ESA-naïve disease:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of myelodysplastic syndromes with or without ring sideroblasts **AND**
- Medical record documentation of very low to intermediate risk disease per the Revised International Prognostic Scoring System (IPSS-R) **AND**
- Medical record documentation that patient requires an average of at least 2 red blood cell units per 8 weeks **AND**
- Medical record documentation of baseline number of transfusions and red blood cell (RBC) units required for the previous six (6) months **AND**
- Medical record recommendation that Reblozyl is being dosed consistent with FDA-approved labeling**.

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

- a decrease in red blood cell (RBC) transfusion burden from baseline **AND**
- Reblozyl being dosed consistent with the FDA-approved labeling**

Ongoing subsequent approvals will be for a **duration of six (6) months** or less if the reviewing provider feels it is medically appropriate, requiring medical record documentation of:

- a sustained reduction of red blood cell (RBC) transfusion burden from baseline **AND**
- Reblozyl being dosed consistent with the FDA-approved labeling**

LIMITATIONS: Reblozyl will no longer be covered if the patient does not experience a decrease in transfusion burden after nine (9) weeks of treatment (administration of three (3) doses) at the maximum dose level or if unacceptable toxicity occurs at any time.

NOTES:
*In clinical trials For Beta Thalassemia, “regular red blood cell transfusions” was considered to be 6 to 20 red blood cell units per 24 weeks with no transfusion-free period greater than 35 days.

**Per current labeling: For Beta Thalassemia: 1mg/kg every 3 weeks increasing to a maximum of 1.25mg/kg every 3 weeks after two doses if a reduction in transfusion burden is not seen. Dose should not exceed 1.25mg/kg every 3 weeks

For MDS associated anemia ~~-RS and MDS/MPN-RS-T~~: 1mg/kg every 3 weeks increasing to a dose of 1.33 mg/kg every 3 weeks after two doses if a reduction in transfusion burden is not seen , then increasing up to a maximum of 1.75mg/kg every 3 weeks after two doses if a reduction in transfusion burden is not seen. Dose should not exceed 1.75mg/kg every 3 weeks

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

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

RINVOQ (upadacitinib)

Clinical Summary: Rinvoq is the first oral medication approved by the FDA to treat moderate to severely active Crohn’s disease. Patients should start with 45 mg of Rinvoq once daily for 12 weeks. Following the

12-week period, the recommended maintenance dosage is 15 mg once a day. A maintenance dosage of 30 mg once daily can be considered for patients with refractory, severe, or extensive Crohn's disease. Patients with severe renal impairment (eGFR 15 to < 30 mL/min/1.73m2) do require a dosage adjustment. Similarly, patients with mild to moderate hepatic impairment (Child-Pugh A or B) also require a dose adjustment.

The efficacy and safety of Rinvoq were evaluated in two randomized induction trials of 857 patients with moderately to severely active Crohn's disease, CD-1 (NCT03345836) and CD-2 (NCT03345849). Patients were randomized 2:1 to receive 45 mg of Rinvoq or placebo once a day for 12 weeks. Enrolled patients in both studies were permitted to use stable doses of CD-related antibiotics, aminosalicylates, or methotrexate. Concomitant corticosteroids (up to 30 mg/day prednisone or equivalent) were permitted at enrollment; tapering was initiated at Week 4. The co-primary endpoints were the proportion of patients achieving clinical remission (by the Crohn's Disease Activity Index (CDAI) at Week 12, and the proportion of patients achieving endoscopic response (by Simple Endoscopic Score for Crohn's Disease (SES-CD) at Week 12. At week 12, a greater proportion of patients treated with 45 mg of Rinvoq, as compared to placebo, achieved clinical remission based on the CDAI. Similarly, a greater proportion of patients treated with 45 mg of Rinvoq demonstrated improvement in intestinal inflammation as assessed by SES-CD.

To assess Rinvoq as a maintenance treatment, CD-3 (NCT03345823) evaluated 343 patients who responded to 12 weeks of 45 mg of Rinvoq once daily. Patients were re-randomized to receive a maintenance regimen of 15 or 30 mg of Rinvoq once daily or placebo for 52 weeks, representing a total of at least 64 weeks of therapy. The co-primary endpoints were again clinical remission (by CDAI) and endoscopic response (by SESCD) and were assessed at Week 52. At week 52, a greater proportion of patients treated with 15 mg or 30 mg of Rinvoq, as compared to placebo, achieved clinical remission based on the CDAI and demonstrated improvement in intestinal inflammation as assessed by colonoscopy.

The safety profile observed in patients with Crohn's disease treated with Rinvoq was consistent with the known safety profile for Rinvoq in other indications. The most common side effects consisted of respiratory tract infections, anemia, fever, acne, herpes zoster, and headache. Rinvoq is not recommended for use in combination with other Janus kinase (JAK) inhibitors, biological therapies for Crohn's disease, or with strong immunosuppressants such as azathioprine and cyclosporine. Additionally, serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis have occurred with JAK inhibitors such as Rinvoq.

Current Formulary Status: Pharmacy benefit requiring prior authorization; specialty tier or brand non preferred for members with a 3 tier benefit.

Recommendation: Addition to policy 605.0 Rinvoq.

<u>Crohn's Disease</u>

- Medical record documentation that Rinvoq is prescribed by a gastroenterologist **AND**
- Medical record documentation of age greater than of equal to 18 years **AND**
- Medical record documentation of moderately to severely active Crohn's disease **AND**
- Medical record documentation that the medication is not being used in combination with a TNF blocker, other JAK inhibitor, biological therapy for Crohn's disease, or with potent immunosuppressants such as azathioprine and cyclosporine **AND**
- Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of Humira

Reauthorization Criteria: Rinvoq is configured as a prior authorization for new starts only. Rinvoq 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

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT: 45 mg once daily for 12 weeks
In PA Hub: Add PA, OQL, number of claims authorized 1, max quantity dispensed 84 with a duration of 12 weeks

- **QL FOR LETTER:** Loading dose: 84 tablets per 180 days; Maintenance dose: 1 tablet per day, 30 day supply per fill

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

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

UPDATES

MEDICAL BENEFIT POLICY UPDATES

Background: During the process of annual review, it was determined Enbrel would be another acceptable preferred agent to include in the alternative list for the indication of Rheumatoid Arthritis for the Commercial, Exchange, CHIP, and Medicaid lines of business, given its formulary placement.

Recommendation: The following changes have been recommended to be made with annual review.
MBP 48.0 Rituxan (rituximab), Truxima (rituximab-abbs), Ruxience (rituximab-pvvr), and Riabni (rituximab-arrx)

Rituxan (rituximab), Truxima (rituximab-abbs), Ruxience (rituximab-pvvr), and Riabni (rituximab-arrx) will be considered medically necessary for commercial, exchange, CHIP and Medicaid lines of business when all of the following criteria are met:

1. **For Rheumatoid Arthritis:**
   All of the following criteria must be met:
   - Physician documentation of a diagnosis of moderate to severe rheumatoid arthritis in accordance with the American College of Rheumatology Criteria for the Classification and Diagnosis of Rheumatoid Arthritis; **AND**
   - At least 18 years of age or older; **AND**
   - Prescription written by a rheumatologist; **AND**
   - Medical record documentation that an effective dose of methotrexate will be continued during rituximab therapy; **AND**
   - Medical record documentation that Rituxan is not being used concurrently with a TNF blocker **AND**
   - Physician documentation of an inadequate response to 12 weeks of therapy with Humira*, Enbrel*, Rinvoq*, OR Xeljanz*

   AND
   - For rituximab reference product requests (i.e. Rituxan), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to rituximab-pvvr (Ruxience) AND rituximab-arrx (Riabni) AND rituximab-abbs (Truxima).

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

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

QULIPTA (atogepant)

Background: We were asked to look into Qulipta and the possibility of adding it to a preferred tier at parity with Aimovig, Emgality, and Nurtec ODT. From a rebate perspective, we would not lose any of our current rebates and we would gain a rebate on Qulipta. Clinically, there is promising NNT data based on a post hoc analysis of the ADVANCE trial from Abbvie that has not been published yet. Also, Abigail Chua MD, Geisinger neurology, fully supports adding Qulipta to the preferred tier, to match the other formulary CGRP receptor antagonists. She said she would use it more if she could bypass Nurtec ODT as a preventive. She said patients do well on Qulipta and prefer the daily option (easier to remember to take) rather than every other day dosing of Nurtec ODT.

Recommendation: It is recommended to add Qulipta to the Brand Preferred tier. There will be no changes to quantity limits, authorization duration, or reauthorization criteria. However, it is recommended to update the policy to the following:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**

- Medical record documentation that Qulipta will not be used concomitantly with another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the preventive treatment of migraine **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least two (2) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/sodium valproate
    - Amitriptyline
    - Venlafaxine **AND**
- Medical record documentation that Qulipta will not be used in combination with botulinum toxin for the preventive treatment **OR**
    - Medical record documentation of therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Additional Recommendations: Ajovy and Vyepti
There are no changes recommended to formulary status, authorization duration, or quantity limits. However, it is recommended to update the current criteria to include Qulipta as a formulary alternative.

Ajovy

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least two (2) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/sodium valproate
    - Amitriptyline
    - Venlafaxine **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) of the following: Aimovig, Emgality, Nurtec ODT, and Qulipta **AND**
- Medical record documentation that Ajovy will not be used concomitantly with another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the preventive treatment of migraine **AND**
- Medical record documentation that Ajovy will not be used in combination with botulinum toxin **OR**
- If the request is for use in combination with Botox, all of the following must be met:
    - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox
- **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Vyepti

- Medical record documentation of the patient age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura **AND**
- Medical record documentation of the number of baseline migraine or headache days per month **AND**
- Medical record documentation of the patient experiencing 4 or more migraines per month **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two of the following: Aimovig, Emgality, Nurtec ODT, and Qulipta **AND**
- If the request is for Vyepti 300 mg every 3 months, medical record documentation of therapeutic failure on Vyepti 100 mg every 3 months **AND**
- If the request is for use in combination with Botox, all of the following must be met:

    - Medical record documentation of therapeutic failure on a minimum 3 month trial of at least one calcitonin gene-related peptide (CGRP) receptor antagonist without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of calcitonin gene-related peptide (CGRP) receptor antagonist **AND**
- Medical record documentation that Vyepti will not be used concomitantly with another calcitonin gene-related peptide (CGRP) receptor antagonist indicated for the preventive treatment of migraine (e.g. Aimovig, Ajovy, Emgality, Nurtec ODT, Qulipta)

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

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

ZOLADEX (goserelin) UPDATE

Background: Zoladex for the Commercial, Exchange and CHIP lines of business is currently a medical benefit that is covered without the need for prior authorization. It was discovered that Zoladex is not on the Commercial, Exchange, and CHIP pharmacy formularies.

Recommendation: It is recommended to add Zoladex (goserelin) to the Commercial, Exchange, and CHIP pharmacy formularies. Zoladex should process at the Specialty tier or the Brand Non-preferred tier for members with a three tier benefit. It is recommended that still no prior authorization be required for coverage of Zoladex. The following quantity limit should apply:

Zoladex 3.6mg subcutaneous implant: Quantity Limit: 28 days supply per fill
Zoladex 10.8mg subcutaneous implant: Quantity Limit: 84 days supply per fill

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

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

Voting responses were received from 28 of 49 members. The vote was unanimously approved.

The next bi-monthly scheduled meeting will be held on November 21st, 2023 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.