P&T Committee Meeting Minutes
Commercial/Exchange/CHIP
February 2024 e-Vote

DRUG REVIEWS

AIRSUPRA (albuterol and budesonide oral inhalation)

Review: Airsupra is a combination of albuterol, a beta-2-adrenergic agonist and budesonide, a corticosteroid, indicated for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma 18 years of age and older.

It is supplied as an inhalation aerosol: pressurized metered dose inhaler that delivers a combination of albuterol 90mcg and budesonide 80mcg per actuation. Each aerosol can contains 120 doses. It is recommended to use in addition to maintenance therapy, if prescribed. Recommended dosage: 2 actuations of albuterol/budesonide (90mcg/80mcg) by oral inhalation as needed for asthma symptoms. Do not take more than 6 doses (12 inhalations) in a 24-hour period.

MANDALA – a multinational, Phase 3, double-blind, randomized, parallel-group, event-driven trial. N=3132 underwent randomization, and 3123 were assessed for efficacy end points. Adults and adolescents (age greater than 12 years and up) were assigned 1:1:1 randomly to 3 trial groups: a fixed-dose 180 µg of albuterol and 160 µg of budesonide [higher-dose combination group], a fixed-dose 180 µg of albuterol and 80 µg of budesonide [lower-dose combination group], or 180 µg of albuterol [albuterol-alone group]. Children aged 4 through 11 were only assigned to the fixed-dose 180 µg of albuterol and 80 µg of budesonide [lower-dose combination group], or 180 µg of albuterol [albuterol-alone group]. The primary efficacy end point was the first event of severe asthma exacerbation in a time-to-event-analysis, in the intent to treat population. This was defined as a requirement of systemic corticosteroids for at least 3 days or an emergency room visit that led to the use of systemic corticosteroids for at least 3 days or a hospitalization due to asthma for at least 24 hours. The study had a variable length with at least a 24-week duration.

Patients were included in the trial if they had moderate to severe symptomatic asthma, history of at least 1 severe asthma exacerbation in the year prior to screening, pre-bronchodilator FEV1 40 to < 90% of predicted normal (for patients aged 12 to < 18 years old, ≥ 60%), and a confirmed reversibility to albuterol. They were required to be on maintenance asthma treatment (medium to high dose ICS or low to high dose ICS/long-acting beta2-adrenergic agonists (LABA), with or without another controller medicine as maintenance therapy). All patients continued on their maintenance treatment during the trial. Secondary endpoints were the mean annualized total systemic corticosteroid exposure, severe exacerbation rate (annualized), asthma control and health-related quality of life.

The results (for adult only) included-- a severe asthma exacerbation was reduced by 28% in the higher-dose combination of albuterol-budesonide than with as-needed use with albuterol-alone (hazard ratio, 0.72; 95% confidence interval [CI], 0.60 to 0.86; P=0.001). The secondary end point of mean annualized total systemic corticosteroid exposure, higher-dose combination of albuterol and budesonide (Airsupra) demonstrated a statistically significant reduction in systemic corticosteroid exposure. The treatment group also demonstrated a statistically significant reduction in the annualized severe exacerbation rate. Adverse events were similar across the treatment groups and were consistent with the known safety profiles of the individualized components. The most common adverse events were nasopharyngitis and headache.

DENALI – a double blind, Phase 3, active-comparator and placebo-controlled lung function study that was conducted over 12 weeks. N=1001 (964 adults, aged 18 and over), evaluated the efficacy of albuterol-budesonide (Airsupra) on lung function in patients aged 12 and over. These patients had mild to moderate asthma and were previously treated with an as-needed, short-acting beta2 agonist (SABA) alone or with a low-dose ICS maintenance inhaler plus an as needed SABA. This study was designed to address the efficacy of each component in a combination product.

Patients were randomly assigned to one of the following five treatment groups in a 1:1:1:1:1 ratio: Airsupra 180/160mcg four times daily (excluding children aged 4–11 years), albuterol/budesonide 180/80mcg four times daily, albuterol 180mcg four times daily, budesonide 160mcg four times daily (excluding children aged 4–11 years) and placebo four times daily. There were two primary efficacy endpoints: the change from baseline in FEV1 area under the curve 0-6 hours over 12 weeks of Airsupra compared to budesonide to assess the effect of albuterol and change from baseline in trough FEV1 at Week 12 of Airsupra compared to albuterol to assess the effect of budesonide. Secondary endpoints included the time to onset and duration of response on day one, number of patients who achieved a clinically meaningful improvement in asthma control from baseline at Week 12 and trough FEV1 at Week 1. 989 patients were evaluated for efficacy (aged ≥ 12 years old). The change of baseline in FEV1 AUC 0-6 hours was greater with albuterol-budesonide 180/160 mcg versus budesonide 160 mcg. The change in trough FEV1 at week 12 was greater with albuterol-budesonide 180/160 and 180/80 mcg versus albuterol 180mcg. The day 1 time to onset and the duration of bronchodilation with albuterol-budesonide were similar to those with albuterol alone. The safety and adverse events profile was similar in all groups.

Airsupra is contraindicated in patients with a hypersensitivity to albuterol, budesonide, or any component of the formulation. Warnings and precautions include adrenal suppression, bronchospasm, hypersensitivity reactions, immunosuppression, and oral candidiasis. Disease-related concerns include: bone mineral density, cardiovascular disease, diabetes, glaucoma, hepatic impairment, hyperthyroidism, hypokalemia, renal impairment, and seizure disorders. Drug Interactions: caution for use in combination with strong CYP3A4 inhibitors, as this may cause a systemic corticosteroid effect. Use cautiously with other short-acting beta agonists. If taking a beta-blocker, Airsupra's effectiveness may be decreased, and severe bronchospasm may occur. Consider alternatives to beta-blockers or if a beta-blocker is required, use a cardio selective one. Caution for use with diuretics, as this could potentiate hypokalemia or EKG changes. Airsupra can decrease digoxin levels. Use Airsupra with extreme caution if using concomitantly with MAOs or TCAs. Adverse effects: the most common adverse effects include: headache, oral candidiasis, cough, and dysphonia.

Dr. Paul Simonelli, Pulmonologist from GMC. He believes Airsupra will not be used as stand-alone therapy. He made an important point to compare the costs of an ICS inhaler and albuterol versus Airsupra in two inhalers. He states S(MART) therapy hasn't been adapted really in the US and worries about plan restrictions and limitations. We have our quantity limits updated to allow for SMART therapy using budesonide-formoterol. He thinks we have to keep in mind to allow use of an ICS for PRN use for exacerbations as in Track 2 of the GINA Guidelines. Under cost considerations, I listed a chart to compare costs of controller medications along with reliever medications.

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

Outcome: Airsupra is a pharmacy benefit and will not be added to the Commercial/Exchange/CHIP formularies. The following prior authorization criteria will apply:

- Medical record documentation of age ≥ 18 years old **AND**
- Medical record documentation for as needed use to treat or prevent asthma attacks **AND**
- Medical record documentation of therapeutic failure, intolerance to, or contraindication to one beta-2 agonist (albuterol or levalbuterol) AND budesonide-formoterol (Symbicort)

NOTE: Airsupra is not FDA approved as maintenance therapy.

QUANTITY LIMIT: 32.1 gm per 30 days

FORMULARY ALTERNATIVES: albuterol HFA, levalbuterol HFA, budesonide-formoterol* (*quantity limits apply)

RPH SIGNOFF REQUIRED: no

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

AUGTYRO (repotrectinib)

Review: Augtyro is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic ROS-1 positive non-small cell lung cancer (NSCLC). Augtyro inhibits the proto-oncogene tyrosine-protein kinase ROS1 and the tropomyosin receptor tyrosine kinases (TRKs) TRKA1, TRKB1, and TRKC.

The recommended dosage of Augtyro is 160 mg orally once daily with or without food for 14 days, then increased to 160 mg twice daily and continued until disease progression or unacceptable toxicity. In the event of adverse reactions, the dosage can be reduced to 120 mg for the first reduction and to 80 mg for the second reduction. Augtyro is supplied as 40 mg capsules.

The efficacy of Augtyro was evaluated in TRIDENT-1, a single-arm, open-label, clinical trial in patients with ROS1-positive locally advanced or metastatic NSCLC. Patients were treated with Augtyro 160 mg orally once daily for 14 days, then increased to 160 mg twice daily until disease progression or unacceptable toxicity.

The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR) according to RECIST v1.1 assessed by blinded independent central review (BICR). Intracranial response according to modified RECIST v1.1 was assessed by BICR. The efficacy population included 71 ROS-1 TKI-naïve patients who received up to 1 prior line of platinum-based chemotherapy and/or immunotherapy and 56 patients who received 1 prior ROS1 TKI with no prior platinum-based chemotherapy or immunotherapy. Among ROS-1 TKI-naïve patients, 94.4% of patients had metastatic disease and 25.4% had CNS metastases by BICR at baseline. Among the patients who received 1 prior ROS1 TKI with no prior platinum-based chemotherapy or immunotherapy, 98.2% of patients had metastatic disease and 42.9% had CNS metastases by BICR.

Among TKI-naïve patients, 8 had measurable CNS metastases at baseline as assessed by BICR. Response in intracranial lesions were observed in 7 of 8 patients. Among TKI pretreated patients with no prior platinum-based chemotherapy, 12 had measurable CNS metastases at baseline. Responses in intracranial lesions were observed in 5 of 12 patients.

Among the 56 ROS-1 treated patients, 8 had resistance mutations following TKI therapy. Responses were observed in 6 of these 8 patients.

Warnings and precautions for Augtyro include central nervous system adverse reactions, interstitial lung disease/pneumonitis, hepatotoxicity, myalgia with creatine phosphokinase elevation, hyperuricemia, skeletal fractures, and embryo fetal toxicity.

Among 351 patients treated with Augtyro, a broad spectrum of central nervous system adverse reactions occurred in 75% of patients, including dizziness, ataxia, and cognitive disorders. Grade 3 or 4 CNS adverse reactions occurred in 4% of patients. The incidence of CNS adverse reactions observed were similar in patients with or without CNS metastases.

Serious adverse reactions in TRIDENT-1 occurred in 33% of patients treated with Augtyro, including pneumonia, dyspnea, pleural effusion, and hypoxia. Fatal adverse reactions occurred in 4.2% of patients who received Augtyro, including death, pneumonia, pneumonia aspiration, cardiac arrest, sudden cardiac death, cardiac failure, sudden death, hypoxia, dyspnea, respiratory failure, tremor, and disseminated intravascular coagulation. Permanent discontinuation of Augtyro occurred in 8% of patients due to adverse reactions, including dyspnea, pneumonitis, and muscular weakness. Dose interruptions and dose reductions occurred in 48% and 35% of patients. The most common adverse reactions included dizziness, dysgeusia, peripheral neuropathy, constipation, dyspnea, ataxia, fatigue, cognitive disorders,

and muscular weakness. The most common Grade 3 and 4 laboratory abnormalities included decreased hemoglobin, lymphocytes, leukocytes, neutrophils, and phosphate and increased alanine aminotransferase, gamma glutamyl transferase, alkaline phosphatase, urate, and magnesium.

The safety and efficacy of Augtyro has not been established in pediatric patients with ROS1-positive NSCLC. Daily oral administration of repotrectinib to juvenile rats for 8 weeks starting on postnatal day 12 resulted in toxicities similar to adult rats, though juvenile animals showed decreased body weight gain and decreased femur lengths which persisted following 4 weeks of recovery.

Of the 351 patients who received Augtyro, 21% were 65 to 75 years of age and 7% were 75 years of age or older. There were no clinically meaningful differences in safety and efficacy between patients younger than 65 years of age and patients 65 years of age and older.

The recommended dosage of Augtyro has not been established in patients with severe renal impairment or kidney failure and patients on dialysis. No dosage modification is recommended for patients with mild or moderate renal impairment. The recommended dosage of Augtyro has not been established in patients with moderate or severe hepatic impairment. No dosage modification is recommended for patients with mild hepatic impairment.

NCCN recommends Augtyro as a preferred first line agent in patients with recurrent, advanced, or metastatic ROS1 rearrangement positive tumors with NSCLC (Category 2B for locoregional recurrence or symptomatic local disease with no evidence of disseminated disease and Category 2A for all others). Other preferred first line agents for patients with ROS-1 positive NSCLC include Xalkori and Rozlytrek.

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

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

- Medical record documentation that Augtyro is prescribed by an oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive

QUANTITY LIMIT: QL for letter: 8 capsules per day, 30 day supply per fill

GPI-LEVEL: GPI-12

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

RPH SIGNOFF REQUIRED: yes

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

BALFAXAR (prothrombin complex concentrate, human-lans)

Review: Balfaxar is a blood coagulation factor replacement product indicated for the urgent reversal of acquired coagulation factor deficiency induced by Vitamin K antagonist (VKA, e.g., warfarin) therapy in adult patients with need for an urgent surgery/invasive procedure. VKA therapy is used to prevent blood clots in a variety of circumstances, including to prevent deep vein thrombosis (DVT) and pulmonary embolism (PE), to lower the risk of stroke in atrial fibrillation (AF), and after a heart attack or valve surgery. Due to its anti-clotting properties, warfarin increases the risk of bleeding, which could be a serious complication during surgery. The incidence of warfarin-associated hemorrhage is unclear, but some reports indicate that the annual rate of fatal hemorrhage may be approximately 1% (24,000 patients) per year.

Balfaxar dosing should be individualized based on the patient's baseline International Normalized Ratio (INR) value and body weight. Vitamin K should be administered concurrently to patients receiving Balfaxar to maintain factor levels once the effects of Balfaxar have diminished. Repeat dosing is not recommended due to unknown safety and effectiveness. Balfaxar should be administered at a rate of 0.12 ml/kg/min (~3 units/kg/min) up to a maximum rate of 8.4 ml/min (~210 units/min).

The 2022 American College of Chest Physicians (ACCP) Guidelines for Perioperative Management of Antithrombotic Therapy outline balancing risk of thrombosis and bleeding for individual patients to direct therapy. The current therapies used for urgent warfarin reversal include fresh frozen plasma (FFP), vitamin K, and Kcentra. Balfaxar and Kcentra are both four-factor prothrombin complex concentrate (4F-PCC) therapies that avoid fluid overloading and correct coagulation quicker than alternative options.

Balfaxar was compared head-to-head with Kcentra in a phase 3, randomized, double-blind, multicenter study comparing the efficacy and safety in reversal of VKA-induced anticoagulation in adult patients needing urgent surgery. The study included 208 patients randomized to a single dose of Balfaxar (n=105) or Kcentra (n=103). The doses were based on body weight and baseline INR (25, 35, 50 IU/kg per 2-<4, 4-6, >6, respectively). The single IV dose was given at a rate of 0.12 mL/kg/min (~3 IU/kg/min), up to a maximum rate of 8.4 mL/min (~210 IU/min). The primary efficacy endpoint was hemostatic efficacy rating at the end of the surgery, assessed using the Independent Endpoint Adjudication Board (IEAB). The interim analysis showed statistically significant efficacy results, with 94.6% of the Balfaxar group and 93.5% of the Kcentra group achieving effective homeostasis, meeting the primary objective. Balfaxar was determined to be non-inferior to Kcentra based on the non-inferiority analysis of the 1.1% difference (98% CI; $p<0.001$). At the final analysis at the study conclusion, 94.3% of the Balfaxar group and 94.2% of the Kcentra group achieved effective homeostasis, with a 0.1% difference (95% CI).

There is no data on use of Balfaxar in pregnancy or breastfeeding. Balfaxar safety and efficacy has not been evaluated in pediatric patients. Of the patients in the clinical trial, 59% were 65 years or older and 20% were 75 years or older; there is no evidence suggesting Balfaxar safety or effectiveness is different in the geriatric population.

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

OTHER RECOMMENDATIONS: Kcentra will be removed from Commercial/Exchange/CHIP formularies.

Outcome: Balfaxar is a medical benefit and will be added to the medical benefit cost share list, not requiring prior authorization.

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

LOQTORZI (toripalimab-tpzi)

Review: Loqtorzi is a programmed death receptor-1 (PD-1) blocking antibody indicated in combination with cisplatin and gemcitabine, for first-line treatment of adults with metastatic or with recurrent locally advanced nasopharyngeal carcinoma (NPC) and as a single agent for the treatment of adults with recurrent unresectable or metastatic NPC with disease progression on or after a platinum-containing chemotherapy. Loqtorzi is a humanized IgG4 monoclonal antibody that binds the PD-1 receptor, blocking its interaction with PD-L1 and PD-L2, leading to PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. Loqtorzi is the first and only FDA approved treatment for nasopharyngeal carcinoma. NCCN recommends Loqtorzi as a preferred treatment regimen with cisplatin/gemcitabine for patients with recurrent, unresectable, oligometastatic, or metastatic disease (with no surgery or RT options) (Category 1) or for subsequent-line regimen if disease progression on or after a platinum-containing chemotherapy (Category 2A).

The recommended dosage of Loqtorzi is 240 mg every three weeks by intravenous infusions for first-line treatment of NPC (in combinations with cisplatin and gemcitabine) until disease progression, unacceptable toxicity, or up to 24 months. The recommended dosage of Loqtorzi for the treatment of recurrent NPC is 3 mg/kg every two weeks by intravenous infusion until disease progression or unacceptable toxicity. There are no dosage adjustments recommended for Loqtorzi. In general, Loqtorzi should be withheld for severe immune mediated adverse reactions. Loqtorzi should be permanently discontinued for patients with life-threatening immune-mediated adverse reactions, recurrent severe immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce prednisone to 10 mg per day or less withing 12 weeks of initiating steroids. Loqtorzi is supplied as 240 mg/6 mL (40 mg/mL) solution in a single-dose vial.

The efficacy in combination with cisplatin and gemcitabine was evaluated in JUPITER-02, a randomized, double-blind, placebo-controlled trial in 289 patients with metastatic and recurrent, locally advanced NPC who had not been previously treated with systemic chemotherapy for recurrent or metastatic disease. Patients with recurrent NPC after treatment with curative intent were required to have an interval of at least 6 months between the last dose of radiotherapy or chemotherapy and recurrence. Patients were randomized to receive one of the following:

- LOQTORZI 240 mg intravenously every 3 weeks in combination with cisplatin 80 mg/m2 on Day 1 every 3 weeks gemcitabine 1000 mg/m2 on Days 1 and 8 for up to 6 cycles, followed by LOQTORZI 240 mg once every 3 weeks, or
- Placebo intravenously every 3 weeks in combination with cisplatin 80 mg/m2 on Day 1 every 3 weeks and gemcitabine 1000 mg/m2 on Days 1 and 8 for up to 6 cycles, followed by placebo once every 3 weeks.

Treatment with Loqtorzi or placebo continued until disease progression per RECIST v1.1, unacceptable toxicity, or a maximum of 2 years. Administration of Loqtorzi was permitted beyond radiographic progression if the patient was deriving benefit as assessed by the investigator. The main efficacy outcome measure was Blinded Independent Review Committee (BIRC) – assessed progression-free survival (PFS) according to RECIST v1.1. Additional efficacy outcome measures include BIRC-assessed overall response rate (ORR) and overall survival (OS). The trial demonstrated statistically significant improvements in BIRC-assessed PFS, ORR, and OS for patients randomized to Loqtorzi in combination with cisplatin/gemcitabine compared to cisplatin and gemcitabine with placebo.

The efficacy of Loqtorzi in previously treated unresectable or metastatic NPC was evaluated in POLARIS-02, an open-label, multi-cohort trial in 172 patients who had received prior platinum-based chemotherapy for treatment of recurrent or metastatic NPC or had disease progression within 6 months of completion of platinum-based chemotherapy administered as neoadjuvant, adjuvant, or definitive chemoradiation treatment for locally advanced disease. The major efficacy outcome was confirmed ORR and duration of response (DOR) assessed by Blinded Independent Review Committee (BIRC) using RECIST v1.1.

Warnings and precautions include severe and fatal immune-mediated adverse reactions, infusion-related reactions, complications of allogeneic HSCT, and embryo-fetal toxicity. Immune-mediated reactions can

be severe or fatal, can occur in any organ system or tissue, and can affect more than one body system simultaneously. Immune-mediate reactions can include pneumonitis, colitis, hepatitis and hepatotoxicity, endocrinopathies, nephritis and renal dysfunction, and dermatologic reactions.

In JUPITER-02 in patients with recurrent locally advanced or metastatic nasopharyngeal carcinoma (NPC) that was not previously treated with systemic chemotherapy for recurrent or metastatic disease, serious adverse reactions occurred in 43% of patients, including thrombocytopenia, decreased neutrophil count, pneumonia, anemia, abnormal hepatic function, and rash. Three fatal adverse reactions (2.1%) occurred due to epistaxis, one due to intracranial hemorrhage associated with immune-related thrombocytopenia and coagulopathy, and one due to pneumonia. Permanent discontinuation and dose interruptions occurred in 12% and 50% of patients, respectively.

In POLARIS-02 in patients with previously treated, unresectable or metastatic nasopharyngeal carcinoma (NPC), serious adverse reactions occurred in 24% of patients, including pneumonia, abnormal hepatic function, and hyperbilirubinemia. Fatal adverse reactions occurred in 3.7% of patients, including death not otherwise specified, tumor hemorrhage, hepatic failure and thrombocytopenia, hyponatremia, and sudden death. Permanent discontinuation and dosage interruptions occurred in 9% and 23% of patients.

The most common adverse reactions were nausea, vomiting, decreased appetite, constipation, hypothyroidism, rash, pyrexia, diarrhea, peripheral neuropathy, cough, musculoskeletal pain, upper respiratory infection, insomnia, dizziness, and malaise. The most common Grade 3 and 4 laboratory abnormalities were decreased neutrophils, lymphocytes, hemoglobin, platelets, potassium, sodium, and calcium, and increased alanine aminotransferase, aspartate aminotransferase, and bilirubin, and increased or decreased magnesium.

The safety and efficacy of Loqtorzi has not been established in pediatric patients. Of the 146 patients with NPC who were treated with Loqtorzi in combination with cisplatin and gemcitabine, 7 patients were 65 years or older and now patients were 75 years or older. Clinical studies did not include a sufficient number of patients to determine if patients 65 years and older respond differently to younger patients. Of the 851 patients with tumor types including nasopharyngeal carcinoma or other types of tumors from the safety pool who were treated with Loqtorzi as a single agent, 171 (20%) were 65 years or older and 13 (1.5%) were 75 years and older. No overall differences in safety were observed between elderly and younger patients.

Loqtorzi has a completed clinical study and ongoing clinical studies in multiple cancer types, including NSCLC and triple-negative breast cancer (TNBC). A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

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

- Medical record documentation that Loqtorzi is prescribed by an 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 that Loqtorzi is being given as first-line treatment in combination with cisplatin and gemcitabine AND documentation of a diagnosis of metastatic or recurrent locally advanced nasopharyngeal carcinoma (NPC)

  OR
    - Medical record documentation that Loqtorzi is being used as a single agent AND documentation of a diagnosis of recurrent unresectable or metastatic NPC with disease progression on or after a platinum-containing chemotherapy

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 patient experiences toxicity or worsening of disease.

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: yes

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

OGSIVEO (nirogacestat)

Review: Ogsiveo is a gamma secretase inhibitor indicated for adult patients with progressing desmoid tumors who require systemic treatment. Ogsiveo blocks proteolytic activation of the Notch receptor, which can activate pathways that contribute to tumor growth when dysregulated.

The recommended dosage of Ogsiveo is 150 mg administered orally twice daily until disease progression or unacceptable toxicity. In the event of certain Grade 3 or 4 adverse reactions (diarrhea ≥ 3 days, hypophosphatemia ≥ 3 days, and hypokalemia) Ogsiveo may be restarted at a dose of 100 mg twice daily once symptoms are resolved to Grade ≤ 1 or baseline. In the event of Grade 2 increased ALT or AST, Ogsiveo can be restarted at 100 mg twice daily until levels are resolved to < 3 ULN or baseline. If Grade 3 or 4 increases in ALT or AST are seen, Ogsiveo should be permanently discontinued. Ogsiveo is supplied as 50 mg tablets.

The efficacy of Ogsiveo was evaluated in DeFi, a randomized, double-blind, placebo-controlled trial in 142 adult patients with progressing desmoid tumors not amenable to surgery. Patients with progressing desmoid tumors that would result in immediate risk to the patient were not eligible. Patients were randomized 1:1 to receive Ogsiveo 150 mg or placebo orally twice daily until **disease progression or** unacceptable toxicity. Patients were stratified by primary tumor location (intra-abdominal verses extra-abdominal). The major efficacy outcome was progression-free survival (PFS) based on RECIST v1.1 as assessed by blinded independent central review or on clinical progression by the investigator (confirmed by independent review). Clinical progression required worsening symptoms resulting in global deterioration of health status and initiation of emergent treatment (e.g. radiotherapy, surgery, or systemic therapy including chemotherapy or kinase inhibitors). Additional outcomes measures included Objective response rate (ORR).

Twenty-three percent of patients had intra-abdominal disease or both intra- and extra-abdominal disease, and 77% had only extra-abdominal disease. Twenty-three percent of patients had received no prior therapy, and 44% received ≥ 3 prior lines of therapy, including surgery, radiotherapy, and systemic therapy. Thirty-three percent of patients were previously treated with a tyrosine kinase inhibitor and 36% were previously treated with chemotherapy.

Results demonstrated a statistically significant 71% reduction in the risk of disease progression or death compared to placebo.

Warnings and Precautions include diarrhea, ovarian toxicity, hepatotoxicity, non-melanoma skin cancers, electrolyte abnormalities, and embryo-fetal toxicity. Serious adverse reactions occurred in 20% of patients who received Ogsiveo, including ovarian toxicity. Permanent discontinuation occurred in 20% of patients, most commonly due to diarrhea, ovarian toxicity, and increased ALT and AST. Dosage interruptions and dose reductions occurred in 51% and 42% of patients, respectively. The most common adverse reactions occurring with Ogsiveo were diarrhea, ovarian toxicity, rash, nausea, fatigue, stomatitis, headache, abdominal pain, cough, alopecia, upper respiratory tract infection, and dyspnea.

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

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

- Medical record documentation that Ogsiveo is prescribed by a hematologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of desmoid tumor(s) with documentation of progression **AND**
- Medical record documentation the desmoid tumor(s) are not amenable to surgery AND require systemic treatment

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

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

QUANTITY LIMIT: 6 tablets per day, 30 day supply per fill

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: yes

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

FAST FACTS

BALVERSA (erdafitinib)

Clinical Summary: Balversa (erdafitinib) is now approved for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (mUC) with susceptible FGFR3 genetic alterations, as determined by an FDA-approved companion diagnostic test, whose disease has progressed on or after at least one line of prior systemic therapy. This approval amends the indication previously granted under accelerated approval for adult patients with mUC with susceptible FGFR3 or FGFR2 genetic alterations whose disease has progressed during or following at least one prior platinum-containing chemotherapy.

No changes to dosing or current quantity limits. The recommended dosage of Balversa for metastatic urothelial carcinoma is 8 mg once daily initially, then increase to 9 mg once daily based on tolerability; continue until disease progression or unacceptable toxicity occurs.

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

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

- Medical record documentation that Balversa is prescribed by an oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of locally advanced or metastatic urothelial carcinoma **AND**
- Medical record documentation of an FGFR3 ~~or FGFR2~~ genetic alteration determined using a Food and Drug Administration (FDA) approved test AND
- Medical record documentation of therapeutic failure ~~on platinum-containing chemotherapy or~~ after at least one line of prior systemic therapy

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

COSENTYX (secukinumab)

Clinical Summary: Cosentyx is now approved for the treatment of adults with moderate to severe hidradenitis suppurativa (HS). The other FDA approved indications of Cosentyx include the treatment of:

- moderate to severe plaque psoriasis (PP) in patients 6 years and older who are candidates for systemic therapy or phototherapy
- active psoriatic arthritis (PsA) in patients 2 years of age and older
- adults with active ankylosing spondylitis (AS)
- adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation
- active enthesitis-related arthritis (ERA) in pediatric patients 4 years of age and older

Cosentyx is now also available for intravenous (IV) use as a 125mg/5mL vial. Intravenous infusion is only for use by a healthcare professional in a healthcare setting. Cosentyx IV infusion is prepared by diluting Cosentyx injection in vial(s) and administering based on patient body weight. Intravenous infusion may be administered only in adults with PsA, AS, and nr-axSpA.

The recommended dosage for Cosentyx for HS is 300mg administered by subcutaneous injection at Weeks 0, 1, 2, 3 and 4 and every 4 weeks thereafter. If a patient does not adequately respond, consider increasing the dosage to 300 mg every 2 weeks.

The recommended dosage for Cosentyx for IV use for adults with PsA, AS, and nr-axSpA can be given with or without a loading dose. With a loading dose, the dose is 6 mg/kg loading dose given at Week 0, followed by 1.75 mg/kg every 4 weeks thereafter (maintenance dosage). Without a loading dose, the dose is 1.75mg/kg every 4 weeks. The dose is to be infused over a period of 30 minutes. Total doses exceeding 300 mg per infusion are not recommended for the 1.75 mg/kg maintenance dose.

The efficacy and safety of Cosentyx in the treatment of adult patients with moderate to severe hidradenitis suppurativa (HS) was assessed in two randomized, double-blind, placebo-controlled 52-week Phase 3 trials. In both trials, subjects were randomized to placebo or Cosentyx 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3 and 4, followed by 300 mg every 2 weeks or every 4 weeks. At Week 16, subjects who were randomized to placebo were reassigned to receive Cosentyx 300 mg at Weeks 16, 17, 18, 19, and 20 followed by either Cosentyx 300 mg every 2 weeks or Cosentyx 300 mg every 4 weeks. The primary endpoint in both trials was the proportion of subjects who achieved a Hidradenitis Suppurativa Clinical Response (HiSCR50) defined as at least a 50% decrease in abscesses and inflammatory nodules (AN) count with no increase in the number of abscesses and/or in the number of draining fistulae relative to baseline at Week 16. In HS Trial 1 and HS Trial 2, a statistically significantly higher proportion of subjects treated with Cosentyx 300 mg every 2 weeks (after the first four weeks) achieved a HiSCR50 response at Week 16 compared to patients treated with placebo. In both HS trials, a higher proportion of subjects treated with Cosentyx 300 mg every 4 weeks (after the first four weeks) achieved HiSCR50 at Week 16 compared to subjects treated with placebo, where statistical significance was reached in HS Trial 2. In both trials, the onset of action of Cosentyx occurred as early as Week 2 and the efficacy progressively increased up to Week 16. For the primary endpoint, HiSCR50, subjects who received any rescue medication or lesion intervention were considered treatment failures and handled as non-responders (n=20 in Placebo, 11 in Q4W, and 8 in Q2W in HS Trial 1; n=23 in Placebo, 17 in Q4W, and 13 in Q2W in HS Trial 2). Improvements were seen for the primary endpoint in HS subjects regardless of previous or concomitant antibiotic treatment or previous biologic exposure.

The effectiveness of intravenous Cosentyx in the treatment of adult patients with active PsA was extrapolated from the established effectiveness of subcutaneous Cosentyx in adult patients with active PsA based on pharmacokinetic exposure. The effectiveness of intravenous Cosentyx in the treatment of adult patients with active AS was extrapolated from the established effectiveness of subcutaneous Cosentyx in adult patients with active AS based on pharmacokinetic exposure. The effectiveness of intravenous Cosentyx in the treatment of adult patients with active nr-axSpA was extrapolated from the established effectiveness of subcutaneous Cosentyx in adult patients with active nr-axSpA based on pharmacokinetic exposure.

The warnings and precautions have been updated to include eczematous eruptions as cases of severe eczematous eruptions have occurred in patients receiving Cosentyx. The Inflammatory Bowel Disease (IBD) warning has been updated to include that the incidence of IBD was higher in patients with HS who received Cosentyx 300mg every 2 weeks.

Current Formulary Status: Cosentyx is currently a pharmacy benefit on the brand tier for CHIP and Commercial Traditional. It is on the brand non preferred tier for members with a 3-tier benefit. Cosentyx is on the specialty tier for Marketplace and for members with a 4 tier benefit. It requires prior authorization with a quantity limit.

Recommendation: No changes recommended to the formulary placement of Cosentyx syringes at this time. However, it is recommended to update policy 379.0 to include the following changes. It is recommended that Cosentyx vials be covered as a medical benefit. It is recommended to reactivate Cosentyx policy MBP 131.0 and update it to include the following changes. It is recommended that Cosentyx be added to the site of care policy and Cosentyx be added to the medical benefit cost share list. If processing at a specialty pharmacy, Cosentyx IV should be added to the specialty tier or brand non preferred tier for members with a 3-tier benefit.

Policy 379.0 Cosentyx

For Hidradenitis Suppurativa

- Medical record documentation of a diagnosis of moderate to severe hidradenitis suppurativa (HS), defined as Stage II or III on the Hurley staging system* **AND**
- Medical record documentation that Cosentyx is prescribed by a dermatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of at least 3 abscesses or inflammatory nodules **AND**
- Medical record documentation of concomitant use of oral or systemic antibiotics **AND**
- Medical record documentation that the member has received counseling on weight management (if overweight) and smoking cessation (if the member is an active smoker) **AND**
- Medical record documentation that Cosentyx is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- If requesting a dose of 300 mg every 2 weeks, medical record documentation that the member has been compliant with every 4 week administration of Cosentyx **AND**
- If requesting a dose of 300 mg every 2 weeks, medical record documentation of therapeutic failure on every 4 week administration of Cosentyx

*Hurley staging system:

- Stage I: A single lesion without sinus tract formation.
- Stage II: More than one lesion or area, but with limited tunneling.
- Stage III: Multiple lesions, with more extensive sinus tracts and scarring.

MEDISPAN AUTHORIZATION LEVEL: GPI-10

QUANTITY LIMIT

- **300 mg every 4 weeks**
    1. Add PA, OQL, number of claims authorized 1, max quantity dispensed 8 with a duration of one-month.
        - **QL FOR LETTER:** Loading dose: 8 mL per 28 days; Maintenance dose: 2 mL per 28 days
- **300 mg every 2 weeks**
    1. Add PA, OQL
        - **QL FOR LETTER:** Maintenance dose: 4 mL per 28 days

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

Policy: MBP 131.0

For commercial, exchange, and CHIP lines of business, Cosentyx (secukinumab) vials will be considered medically necessary when all of the following criteria are met:

~~**1. Plaque Psoriasis:**~~

- ~~Prescription must be written by a dermatologist **AND**~~
- ~~Member must be 18 years of age or older **AND**~~
- ~~Medical record documentation of a diagnosis of moderate to severe plaque psoriasis characterized by ≥ 5% of body surface area involved or disease involving crucial body areas such as the hands, feet, face, or genitals. **AND**~~
- ~~Medical record documentation that Cosentyx is not being used concurrently with a TNF blocker or other biologic agent **AND**~~

- ~~A therapeutic failure on, intolerance to, or contraindication to topical corticosteroids **AND** at least two to three months of systemic therapy (including but not limited to methotrexate and/or cyclosporine) or phototherapy **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy.~~

~~2.~~**1. Psoriatic Arthritis:**

- Medical record documentation of a diagnosis of moderately to severely active psoriatic arthritis which must include the following:
  - Documentation of either active psoriatic lesions or a documented history of psoriasis **AND**
- Prescription must be written by a rheumatologist or dermatologist **AND**
- Member must be at least 18 years of age **AND**
- Medical record documentation that Cosentyx is not being used concurrently with a TNF blocker or other biologic agent **AND**
- **For peripheral disease**: Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on methotrexate **AND** an adequate trial of at least two (2) formulary NSAIDs **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy **OR**
- **For axial disease**: Medical record documentation of an intolerance to, contraindication to, or therapeutic failure to an adequate trial of at least two (2) formulary NSAIDs **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy **AND**
- Medical record documentation that the prescribed dosing is appropriate for member's weight AND does not exceed 300mg per infusion

~~3.~~**2. Ankylosing Spondylitis:**

- Medical record documentation of a diagnosis of ankylosing spondylitis **AND**
- Prescription must be written by a rheumatologist **AND**
- Member must be at least 18 years of age **AND**
- Medical record documentation that Cosentyx is not being used concurrently with a TNF blocker or other biologic agent **AND**
- A therapeutic failure on, contraindication to, or intolerance to an adequate trial of at least two (2) NSAIDs OR a therapeutic failure on or intolerance to prior biologic therapy **AND**
- ~~Medical record documentation that the medication is being dosed as 150 mg every 4 weeks with or without a loading dose of 150 mg at Weeks 0, 1, 2, 3, and 4.~~ Medical record documentation that the prescribed dosing is appropriate for member's weight AND does not exceed 300mg per infusion

3. Non-radiographic Axial Spondylarthritis:

- Medical record documentation of a diagnosis of non-radiographic axial spondylarthritis **AND**
- Prescription must be written by a rheumatologist **AND**
- Member must be at least 18 years of age **AND**
- Medical record documentation that Cosentyx is not being used concurrently with a TNF blocker or other biologic agent **AND**
- Medical record documentation of at least one of the following:
  - C-reactive protein (CRP) level above the upper limit of normal (10 mg/dL) OR
  - Sacroiliitis on magnetic resonance imaging (MRI)
- A therapeutic failure on, contraindication to, or intolerance to an adequate trial of at least two (2) NSAIDs OR a therapeutic failure on or intolerance to prior biologic therapy **AND**
- Medical record documentation that the prescribed dosing is appropriate for member's weight AND does not exceed 300mg per infusion

Note: The recommended dosing for PsA, AS, and nr-axSpA is listed below.

- With loading dose:
  - 6 mg/kg given at Week 0 as a loading dose, followed by 1.75 mg/kg every 4 weeks thereafter (max. maintenance dose 300 mg per infusion).

- Without loading dose:
    - 1.75 mg/kg every 4 weeks (max. maintenance dose 300 mg per infusion).

AUTHORIZATION DURATION: Approval will be given for an initial duration of ~~six (6) months~~ one (1) year. ~~For continuation of coverage, medical record documentation of clinical improvement or lack of progression in the signs and symptoms of the treated indication on six (6) months of Cosentyx therapy is required.~~

~~After the initial six (6) month approval~~, subsequent approvals will be for a duration of one (1) year, requiring medical record documentation of continued or sustained improvement in signs and symptoms of the treated indication while on Cosentyx therapy.

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

ENBREL (etanercept)

Clinical Summary: Enbrel received an updated indication in October 2023 for the treatment of active juvenile psoriatic arthritis in pediatric patients 2 years of age and older. The safety and effectiveness of Enbrel have been established in pediatric patients 2 years to 17 years old with JPsA. Use of Enbrel in JPsA is supported by evidence from adequate and well controlled studies of Enbrel in adults with PsA; pharmacokinetic data from adult patients with PsA, RA, and PsO; and pharmacokinetic data from pediatric patients with active JIA and PsO. Safety of Enbrel in JPsA is supported by a clinical study in 69 pediatric patients with moderately to severely active JIA aged 2 to 17 years; a clinical study in 211 pediatric patients with moderate to severe PsO aged 4 to 17 years; and an open-label extension study in 182 pediatric patients with moderate to severe PsO aged 4 to 17 years.

The evidence indicates comparable trough concentrations between adults with RA and PsA and pediatric patients with active JIA. Similarly, trough concentrations were comparable between adults and pediatric patients with psoriasis. Therefore, the PK exposure is expected to be comparable between adults and pediatric patients with JPsA. The most common adverse reactions reported with etanercept treatment include infections and injection site reactions. The safety and effectiveness in pediatric patients below the age of 2 years have not been established in JPsA.

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 41.0 Enbrel

For Juvenile Psoriatic Arthritis:

- Medical record documentation of a diagnosis of moderate to severe juvenile psoriatic arthritis **AND**
  Rationale for not requiring evidence of active psoriatic lesions or history of psoriasis : the classic skin rash is absent at presentation in approximately half of children with psJIA, sometimes lagging 10 years or more behind onset of joint symptoms. In addition, psoriasis in the young child may be subtle, atypical, and transient and is often initially misdiagnosed as eczema
- Medical record documentation that Enbrel is prescribed by a rheumatologist or dermatologist **AND**
- Medical record documentation of age greater than or equal to 2 years **AND**
- Medical record documentation that Enbrel is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- For peripheral disease: Medical record documentation of therapeutic failure on, intolerance to, or contraindication to methotrexate AND an adequate trial of at least two (2) formulary nonsteroidal

anti-inflammatory drugs (NSAIDs) **OR** medical record documentation of therapeutic failure on or intolerance to prior biologic therapy **OR**

- For axial disease: Medical record documentation of therapeutic failure on, intolerance to, or contraindication to an adequate trial of at least two (2) formulary nonsteroidal anti-inflammatory drugs (NSAIDs) **OR** medical record documentation of therapeutic failure on or intolerance to prior biologic therapy **AND**
- Medical record documentation that the prescribed dosing is appropriate for member's weight

RE-AUTHORIZATION CRITERIA: Enbrel is configured as a prior authorization for new starts only. Enbrel 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-10, 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:

- 50 mg syringe/pen: 4 mL per 28 days
- 25 mg syringe: 4 mL per 28 days
- 5 mg vial: 8 vials per 28 days

FORMULARY ALTERNATIVES for psJIA:
Methotrexate, celecoxib, diclofenac, diclofenac extended release, ibuprofen, etodolac extended release (Children ≥6 years weighing at least 20 kg), indomethacin, indomethacin sustained release (adolescents ≥15 years), ketorolac, meclofenamate (Adolescents ≥14 years), meloxicam, naproxen, naproxen sodium, naproxen EC, oxaprozin (children ≥6 years), piroxicam, sulindac, tolmetin

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

JARDIANCE (empagliflozin)

Clinical Summary: Jardiance is now indicated:

- To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure.
- To reduce the risk of sustained decline in eGFR, end-stage kidney disease, cardiovascular death, and hospitalization in adults with chronic kidney disease at risk of progression.
  - Limitation of Use: Jardiance is not recommended for the treatment of CKD in patients with polycystic kidney disease or patients requiring or with a recent history of intravenous immunosuppressive therapy or greater than 45 mg of prednisone or equivalent for kidney disease. Jardiance is expected to not be effective in these populations.
- To reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.
- As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.
-

Assess renal function before initiating and as clinically indicated. Assess volume status and correct volume depletion before initiating. Recommended dosage is 10 mg orally once daily in the morning, taken with or without food. Withhold Jardiance for at least 3 days, if possible, prior to major surgery or procedures associated with prolonged fasting.

The safety and efficacy of Empagliflozin for use in Chronic Kidney Disease (CKD) was studied in the EMPA-KIDNEY (NCT03594110) trial. This was a randomized, double blind, placebo-controlled trial conducted in adults with CKD being defined as eGFR ≥ 20 to < 45 mL/min/1.73m2; or eGFR ≥ 45 to < 90 mL/min/1.73m2 with urine albumin to creatinine ≥ 200 mg/g. Patients were excluded if they had polycystic kidney disease or required IV immunosuppressive therapy in the preceding three months or >45 mg of prednisone (or 3 Geisinger Health Plan Jardiance (Empagliflozin) Fast Facts equivalent) at the time of screening. The primary objective of this trial was to determine the effectiveness of empagliflozin as an adjunct to standard of care therapy, including RAS-inhibitor therapy when appropriate, on time to kidney disease progression or cardiovascular death.

The patient population included 6,609 patient who were equally randomized to Jardiance 10 mg or placebo and were followed for a median of 24 months. 85% of patients were treated with an ACE inhibitor or ARB, 64% with statins, and 34% with antiplatelet agents at baseline. The study concluded that Jardiance was superior to placebo in reducing the risk of the primary composite outcome of sustained ≥ 40% eGFR decline, sustained eGFR < 10 mL/min/1.73m2, progression to end stage kidney disease, or CV or renal death. It was also shown that Jardiance reduced the risk of first and recurrent hospitalization.

Section 5.7 was added to address Lower Limb Amputations. It was shown that in some clinical studies with SGLT2 inhibitors an imbalance in the incidence of lower limb amputation has been observed. In the long-term cardio-renal outcome trial in patients with chronic kidney disease the occurrence of lower limb amputations was reported with event rates of 2.9 and 4.3 events per 1000 patient years in the placebo and Jardiance 10 mg treatment groups respectively. The most frequent amputations occurred in the toe and mid-foot along with some patients requiring multiple amputations. The most common causes of these events were peripheral artery disease and diabetic foot infection. The risk of amputation was highest in patients with a history of diabetic foot, peripheral artery disease or diabetes. It is recommended to counsel patients on the importance of preventative foot care and to monitor for signs and symptoms of infection, new pain or other potential indicators.

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.

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

JAYPIRCA (pirtobrutinib)

Clinical Summary: Jaypirca is now indicated for adult patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor. This indication is approved under accelerated approval based on response rate.

There is no change to the dosage of Jaypirca for the new indication. The recommended dosage for all indications is 200 mg orally once daily until disease progression or unacceptable toxicity.

The efficacy of Jaypirca in patients with CLL/SLL is supported by results of BRUIN, an open-label, single arm, multi-cohort study evaluating Jaypirca as monotherapy. Efficacy was based on 108 patients with CLL/SLL treated with Jaypirca had previously been treated with at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor. Efficacy was based on overall response rate (ORR) and duration of response (DOR) as assessed by an independent review committee (IRC) using 2018 iwCLL criteria. Median time to response was 3.7 months.

There are no new safety signals identified with the new indication of Jaypirca and the adverse reactions observed in CLL/SLL are consistent with the known safety profile of Jaypirca.

NCCN recommends Jaypirca as second line or third line therapy (useful in certain circumstances for resistance or intolerance to prior covalent BTKi) or for relapsed or refractory disease after prior BTKi and venetoclax-based regimens (if not previously given) (Category 2A).

Current Formulary Status: Oral Oncology Brand NP tier, PA NSO, QL: 100 mg tablet: 60 per 30 days, 50 mg: 30 mg per 30 days, 30 day supply per fill

Recommendation: There are no changes recommended for the formulary placement, authorization duration, or quantity limits for Jaypirca. It is recommended that the following prior authorization criteria be added to Commercial Policy 748.0 to incorporate the new indications:

CLL/SLL

- Medical record documentation that Jaypirca 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 chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) **AND**
- Medical record documentation of at least two lines of systemic therapy, including a BTK inhibitor and a BCL-2 inhibitor

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 received approval for the expansion of the indication for urothelial cancer to the following: Keytruda in combination with enfortumab vedotin for the treatment of adult patients with locally advanced or metastatic urothelial cancer. Previously this indication was an accelerated approval limited to patients who were not eligible for cisplatin-containing chemotherapy.

Keytruda also received a new indication in combination with chemoradiotherapy, for the treatment of patients with FIGO 2014 Stage III-IVA cervical cancer.
There are no changes to the recommended dosage of Keytruda for the expanded urothelial cancer and remains 200 mg every 3 weeks or 400 mg every 6 weeks until disease progression, unacceptable toxicity, or up to 24 months.

The recommended dosage for adult patients with cervical cancer is 200 mg every 3 weeks or 400 mg every 6 weeks. Keytruda is administered prior to chemoradiotherapy when administered on the same day. Keytruda treatment is continued until disease progression, unacceptable toxicity, or up to 24 months.

Keytruda in combination with Padcev was evaluated in EV-302, an open-label, randomized trial in 886 patients with locally advanced or metastatic urothelial cancer who received no prior systemic therapy for locally advanced or metastatic disease. Patients were randomized to receive Padcev followed by Keytruda or gemcitabine with cisplatin or carboplatin. The major efficacy outcome measures were overall survival (OS) and progression free survival (PFS) as assessed by blinded independent central review (BICR) according to RECIST v1.1. Additional outcome measures included objective response rate (ORR) as assessed by BICR. Results demonstrated a statistically significant improvement in OS, PFS, and ORR (Table 1).

The efficacy of Keytruda in combination with chemoradiotherapy (CRT), was evaluated in KEYNOTE-A18, a randomized, double-blind, placebo-controlled study in 1060 patients with cervical cancer who had no previously received any definitive surgery, radiation, or systemic therapy for cervical cancer. There were 596 patients with FIGO 2014 Stage III to IVA (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) with either node-positive or node-negative disease and 462 patients with FIGO 2014 Stage IB2-

IIB (tumor lesions > 4 cm or clinically visible lesions that have spread beyond the uterus but have not extended onto the pelvic wall or to the lower third of the vagina). Two patients had FIGO 2014 Stage IVB disease. Patients were randomized to receive one of the following:

- Keytruda 200 mg IV every 3 weeks (5 cycles) concurrent with cisplatin 40 mg/m2 IV weekly (5 cycles, an optional sixth infusion could be administered per local practice) and radiotherapy (EBRT followed by BT), followed by Keytruda 400 mg IV every 6 weeks (15 cycles)
- Placebo IV every 3 weeks (5 cycles) concurrent with cisplatin 40 mg/m2 IV weekly (5 cycles, an optional sixth infusion could be administered per local practice), and radiotherapy (EBRT followed by BT), followed by placebo IV every 6 weeks (15 cycles)

Treatment continued until RECIST v1.1-defined progression of disease as determined by investigator or unacceptable toxicity. The trial demonstrated a statistically significant improvement in PFS in the overall population. In an exploratory subgroup analysis for the 462 patients with FIGO 2014 Stage IB2-IIB disease, the PFS HR estimate was 0.91 indicating that the PFS improvement in the overall population was primary attributed to results seen in the subgroup of patients with FIGO 2014 Stage III-IVA disease. Overall survival data was not mature at the time of analysis.

There are no new safety signals identified when Keytruda is administered in combination with Padcev. Adverse reactions reported were consistent with the known safety profile of the individual treatments.

When Keytruda was given in combination with CRT, fatal adverse reactions occurred in 1.4% of patients, including 1 case of each of large intestinal perforation, urosepsis, sepsis, and vaginal hemorrhage. Serious adverse reactions occurred in 30% of patients including urinary tract infection, urosepsis, and sepsis. The most common adverse reactions reported in patients receiving Keytruda in combination with chemoradiotherapy include nausea, diarrhea, vomiting, constipation, abdominal pain, urinary tract infection, fatigue, pyrexia, hypothyroidism, hyperthyroidism, decreased appetite, weight loss, dysuria, rash, and pelvic pain.

Current Formulary Status: Medical Benefit, PA required, Auth duration: 6 months initial, 12 months continuation, When processed at a specialty pharmacy, processes as Specialty tier or Brand NP tier for members with a 3-tier benefit, MBP 119.0

Recommendation: There are no changes recommended to the authorization duration. The following changes are recommended for Medical Benefit Policy 119.0 to incorporate the expanded urothelial carcinoma indication and the new cervical cancer indication:

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
    - 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

- ~~Patient is not eligible for cisplatin-containing chemotherapy **AND**~~
- Keytruda is being used in combination with Padcev

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

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

ORENCIA SC SYRINGES (abatacept)

Clinical Summary: Orencia SC syringes are now indicated for the treatment of patients 2 years and older with active psoriatic arthritis. Orencia SC was previously indicated for the treatment of adults with PsA, pediatric and adult patients with pJIA, and adults with RA.

No new studies were done. Use of Orencia in this age group is supported by well-controlled studies of Orencia in adults with PsA, pharmacokinetic data from adults with RA, adults with PsA, and pediatric patients with pJIA and safety data from clinical studies in pediatric patients with pJIA.

Current Formulary Status: Orencia SC syringes are non-formulary.

Recommendation: No formulary placement changes recommended but it is recommended to update the PA criteria.

Psoriatic Arthritis

- Medical record documentation of age greater than or equal to 2 years **AND**
- Medical record documentation of a diagnosis of moderately to severely active psoriatic arthritis which must include documentation of either active psoriatic lesions or a documented history of psoriasis **AND**
- Medical record documentation that subcutaneous Orencia is prescribed by a rheumatologist or dermatologist **AND**
- Medical record documentation that Orencia is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent
- If Orencia ClickJect autoinjector is prescribed: Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of an inadequate response to, contraindication to, or failure on at least 3 months of two (2) preferred formulary biologics for the treatment of psoriatic arthritis

Formulary Alternatives:

Adults with PsA: Cosentyx*, Humira*, Enbrel*, Otezla*, Skyrizi*, Tremfya*, Rinvoq*, Xeljanz/XR*
Pediatrics with PsA: Cosentyx*, Enbrel*

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

PADCEV (enfortumab vedotin-ejfv)

Clinical Summary: Padcev received approval for the expansion of the indication for urothelial cancer to the following: Padcev in combination with pembrolizumab for the treatment of adult patients with locally advanced or metastatic urothelial cancer. Previously this indication was an accelerated approval limited to patients who were not eligible for cisplatin-containing chemotherapy. There are no changes for the indications where Padcev is given as a single agent.

There are no changes to the recommended dosage of Padcev for the change in indication. The recommended dosage of Padcev when given in combination with Keytruda is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥ 100 kg) administered as an intravenous infusion on Days 1 and 8 of a 21 day cycle until disease progression or unacceptable toxicity.

The efficacy of Padcev in combination with pembrolizumab was evaluated in EV-302, an open-label, randomized trial in 886 patients with locally advanced or metastatic urothelial cancer who received no prior systemic therapy for locally advanced or metastatic disease. Patients were randomized to receive Padcev followed by pembrolizumab or gemcitabine with cisplatin or carboplatin. The major efficacy outcome measures were overall survival (OS) and progression free survival (PFS) as assessed by blinded independent central review (BICR) according to RECIST v1.1. Additional outcome measures included objective response rate (ORR) as assessed by BICR. Results demonstrated a statistically significant improvement in OS, PFS, and ORR (Table 1).

There are no updated adverse reactions reported in the new clinical trials of Padcev and the adverse reactions observed in EV-302 were consistent with the known safety profile of Padcev when given in combination with pembrolizumab.

Current Formulary Status: Medical Benefit, PA, 34 day supply per fill, Auth duration: 12 months, When processed at a specialty pharmacy, processes as Specialty tier or Brand NP tier for members with a 3-tier benefit

Recommendation: There are no changes recommended for the formulary placement or authorization duration of Padcev. The following changes are recommended to Medical Benefit Policy 209.0 to incorporate the expanded indication of Padcev:

- Medical record documentation that prescription is written by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of locally advanced or metastatic urothelial cancer **AND**
- Medical record documentation of one of the following:
    - Medical record documentation that member has received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy **OR**
    - Medical record documentation that member has received at least one prior line of therapy and is ineligible for cisplatin-containing chemotherapy* **OR**
    - Medical record documentation that member is ineligible for cisplatin-containing chemotherapy* AND medical record documentation that Padcev will be prescribed in combination with Keytruda

*Note to reviewer: In clinical trials, patients who were not considered cisplatin-eligible had one or more of the following characteristics: baseline creatinine clearance of 30 – 59 mL/min, ECOG performance status of 2, or Grade 2 or greater hearing loss.

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.

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

PIQRAY (alpelisib)

Clinical Summary: Piqray is now indicated for use in pre and perimenopausal women. Piqray is a kinase inhibitor indicated in combination with fulvestrant for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer as detected by an FDA-approved test following progression on or after an endocrine-based regimen.

Recommended Dose: 300 mg (two 150 mg tablets) taken orally once daily with food. For adverse reactions, consider dose interruption, dose reduction, or discontinuation.

SOLAR-1 (NCT02437318) was a randomized, double-blind, placebo-controlled trial of Piqray plus fulvestrant versus placebo plus fulvestrant in 572 patients with HR-positive, HER2-negative, advanced or metastatic breast cancer whose disease had progressed or recurred on or after an aromatase inhibitor-based treatment (with or without CDK4/6 combination). Patients were excluded if they had inflammatory breast cancer, diabetes mellitus Type 1 or uncontrolled Type 2, or pneumonitis. Randomization was stratified by presence of lung and/or liver metastasis and previous treatment with CDK4/6 inhibitor(s). Overall, 60% of enrolled patients had tumors with one or more PIK3CA mutations in tissue, 50% had liver/lung metastases, and 6% had previously been treated with a CDK4/6 inhibitor.

There were 341 patients enrolled by tumor tissue in the cohort with a PIK3CA mutation and 231 enrolled in the cohort without a PIK3CA mutation. Of the 341 patients in the cohort with a PIK3CA mutation, 336 (99%) patients had one or more PIK3CA mutations confirmed in tumor tissue using the FDA-approved therascreen® PIK3CA RGQ PCR Kit. Out of the 336 patients with PIK3CA mutations confirmed in tumor tissue, 19 patients had no plasma specimen available for testing with the FDA-approved therascreen® PIK3CA RGQ PCR Kit. Of the remaining 317 patients with PIK3CA mutations confirmed in tumor tissue, 177 patients (56%) had PIK3CA mutations identified in plasma specimen, and 140 patients (44%) did not have PIK3CA mutations identified in plasma specimen.

Patients received either Piqray (300 mg) or placebo orally once daily on a continuous basis, plus 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 radiographic disease progression or unacceptable toxicity. Tumor assessments were performed every 8 weeks for the first 18 months and every 12 weeks thereafter.

The median age of patients was 63 years (range, 25 to 92). Most patients were women (99.8%) and most patients were white (66%), followed by Asian (22%), Other/Unknown (10%), black or African American (1.4%), and American Indian or Alaskan Native (0.9%). Baseline ECOG performance status was 0 (68%) or 1 (32%).

Patient demographics for those with PIK3CA-mutated tumors were generally representative of the broader study population. The median duration of exposure to Piqray plus fulvestrant was 8.2 months with 59% of patients exposed for > 6 months.

The majority of patients (98%) received prior hormonal therapy as the last treatment (48% metastatic setting, 52% adjuvant setting). Primary endocrine resistance, defined as relapsed within 24 months on adjuvant endocrine therapy or progression within 6 months on endocrine therapy for advanced disease, was observed in 13% of patients and secondary endocrine resistance, defined as relapsed after 24 months on adjuvant endocrine therapy, relapsed within 12 months of the end of adjuvant endocrine therapy, or progression after 6 months on endocrine therapy for advanced disease, was observed in 72% of patients.

The major efficacy outcome was investigator-assessed progression-free survival (PFS) in the cohort with a PIK3CA mutation per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Additional efficacy outcome measures were overall response rate (ORR) and overall survival (OS) in the cohort with a PIK3CA mutation.

The results from the investigator-assessed PFS and ORR for the cohort with a PIK3CA mutation in tumor tissue are presented in Table 8, and Figure 1. Investigator-assessed PFS results for the cohort with a PIK3CA mutation were supported by consistent results from a blinded independent review committee (BIRC) assessment. Similar results were seen in patients with tissue or plasma PIK3CA mutations. At the pre-specified final OS analysis, there was no significant difference in OS between the PIQRAY plus fulvestrant arm and the placebo plus fulvestrant arm (hazard ratio [HR] = 0.86, 95% CI: 0.64, 1.15).

No benefit was observed in patients whose tumors did not have a PIK3CA tissue mutation (PFS: HR = 0.85, 95% CI: 0.58, 1.25; OS: HR = 0.92, 95% CI: 0.65, 1.29).

No new safety considerations. There is now additional guidance on the management of hyperglycemia and uveitis in now reported as an adverse reaction from post-marketing experience.

Current Formulary Status: Piqray is a pharmacy benefit currently on formulary as a specialty medication with the requiring prior authorization under commercial policy 566.0.

Recommendation: Recommend no changes to the formulary placement, auth duration or quantity limits. Recommend the following changes to the current prior authorization criteria in Commercial Policy 566.0:

- Medical record documentation that Piqray is prescribed by an oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of advanced or metastatic breast cancer that is hormone receptor-positive, HER2-negative (HR+/HER2-) **AND**
- Medical record documentation of a PIK3CA mutation determined using a Food and Drug Administration (FDA) approved test **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to prior endocrine therapy **AND**
- Medical record documentation that Piqray is being prescribed in combination with fulvestrant

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

VELTASSA (patiromer)

Clinical Summary: Veltassa is a potassium binder indicated for the treatment of hyperkalemia in adults and pediatric patients ages 12 years and older. It was previously indicated in patients 18 years of age and older.

The potassium-lowering effect of Veltassa was evaluated in an open-label, single-arm study in pediatric patients 12 to 17 years of age with CKD and hyperkalemia. The study included an initial 14-day dose finding phase, followed by an up to 24-week long-term (LT) treatment phase and a 2-week follow-up period. Veltassa was given once daily as a powder for oral suspension. The dose of Veltassa was titrated, as needed, based on the serum potassium level, assessed starting on Day 3 and then at Day 7 and Day 14, with the aim of maintaining serum potassium in the target range (3.8 mEq/L to < 5.0 mEq/L). All 14 patients 12 to 17 years of age completed the dose finding phase.

Approximately 57% were on RAAS inhibitor therapy at baseline. The mean (SD) baseline serum potassium was 5.5 mEq/L (0.3 mEq/L). The mean change in serum potassium from baseline to Day 14 was -0.5 mEq/L (95% CI -0.8, - 0.2). The proportion of patients 12 to 17 years of age with a serum potassium within the normal range was 50% at Day 14. The median dose at Day 14 was 4.2 g/day.

Current Formulary Status: Pharmacy Benefit; Formulary, Prior Authorization required, QL

Recommendation: There are no recommended changes to formulary status, quantity limits, or authorization duration at this time. It is recommended to update policy 414.0 to include the new FDA approved age range.

- Medical record documentation of a diagnosis of mild to moderate hyperkalemia (serum potassium greater than or equal to 5.1 mEq/L and less than 6.5 mEq/L) **AND**
- Medical record documentation of age greater than or equal to 12 ~~18~~ years **AND**
- Medical record documentation that attempt has been made to identify and correct the underlying cause of the patient's hyperkalemia **OR** rationale as to why the underlying cause cannot be corrected **AND**
- For mild hyperkalemia (serum potassium greater than or equal to 5.1 mEq/L and less than 5.5 mEq/L): Medical record documentation that a low potassium diet has been tried and was unsuccessful at controlling the patient's serum potassium level **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to loop diuretic or thiazide diuretic therapy

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: 1 packet per day

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

VOXZOGO (vosoritide)

Clinical Summary: Voxzogo is a C type natriuretic peptide (CNP) analog that was previously approved to increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses. It is now indicated for all pediatric patients.

Voxzogo is a once daily, subcutaneous injection, that is dosed based on patient's actual body weight (as listed in Table 1). It is supplied as a 0.4mg, 0.56mg, or 1.2mg lyophilized powder in a single dose vial for reconstitution.

The safety and effectiveness of Voxzogo have been established in pediatric patients supported by evidence from an adequate and well controlled study in 121 pediatric patients aged 5 to 15 years with achondroplasia, pharmacokinetic data in pediatric patients aged 4.5 months to 15 years, and additional safety data in pediatric patients aged 4.4 months to < 5 years. No clinically significant differences in the vosoritide pharmacokinetics were observed based on age (0.4 to 15 years).

The safety of Voxzogo for pediatric patients less than 5 years of age with achondroplasia was evaluated in a Study 2. Study 2 was a 52-week randomized, double blind, placebo-controlled study including 64 patients from 4.4 months to < 5 years of age. The participants were randomized to receive either a daily vosoritide dose with similar exposure to that characterized to be safe and effective in children with ACH aged greater than 5 years of age, or placebo. An additional 11 patients received open-label treatment as part of this study. Subjects received 30mcg/kg while they were < 2 years of age. The daily dose for subjects was adjusted to 15mcg/kg immediately following their 2nd birthday. The most common adverse reactions reported in pediatric patients < 5 years were injection site reactions and rash. The overall safety profile of Voxzogo in pediatric patients < 5 years was similar to that seen in older pediatric patients.

Current Formulary Status: Voxzogo is a pharmacy benefit on the Specialty Tier or BrandNP tier for members with a 3 tier benefit. Prior authorization is required and quantity limit of 1 vial per day applies.

Recommendation: There are no changes recommended to the formulary placement or auth duration of Voxzogo. The following changes are recommended to the prior authorization criteria in Commercial Policy 707.0:

- Medical record documentation of a diagnosis of achondroplasia with genetic testing confirming a mutation of FGFR3 **AND**
- Medical record documentation that Voxzogo is prescribed by a pediatric endocrinologist **AND**
- Medical record documentation that member is ~~5 to~~ less than 18 years of age **AND**
- Medical record documentation of evidence that patient has open epiphyses **AND**
- Medical record patient has not received (within the past 18 months) or plans to receive limb-lengthening surgery **AND**
- Medical record documentation that Voxzogo will not be used in combination with human growth hormone products **AND**
- Medical record documentation of glomerular filtration rate (GFR) greater than 60ml/min/1.73m^2 **AND**
- Medical record documentation of member's current weight **AND**
- Medical record documentation that prescribed dose is appropriate for member's current weight **AND**
- Medical record documentation of baseline annualized growth velocity (AGV), calculated based on standing height measured over the course of 6 months prior to request

AUTHORIZATION DURATION: 6 months. The following renewal criteria applies:

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

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 adults with advanced renal cell carcinoma (RCC) following a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and a vascular endothelial growth factor tyrosine kinase inhibitor (VEGF-TKI). Previously, this was only indicated in adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated RCC, central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery.

The updated dosage for the new indication is 120 mg orally once daily with or without food. This is the same dosage as was used for the previously approved indication.

The safety and efficacy of Welireg in adult patients with unresectable, locally advanced or metastatic clear cell RCC that progressed following PD-1 or PD-L1 checkpoint inhibitor and VEGF receptor targeted therapies either in sequence or in combination, were assessed in LITESPARK-005 (NCT 04195750), a randomized, active-controlled, open-label study. There were 746 patients included in this study. Patients were allowed to have had up to 3 prior treatment regimens and have measurable disease per RECIST v1.1. Patients in this study were randomized 1:1 to receive either Welireg 120 mg or everolimus 10 mg orally once daily. The efficacy outcomes studied included Progression Free Survival (PFS), Overall Survival (OS), and objective response rate (ORR). The study showed a statistically significant improvement in PFS for patients randomized to Welireg compared with everolimus.

The most common adverse reactions occurring in ≥25% of patients for this patient population included musculoskeletal pain, decreased lymphocytes, increased alanine aminotransferase, decreased sodium, increase potassium, increased aspartate aminotransferase, and the known adverse reactions in adults. No new warnings, contraindications, or black box warnings were identified, only one change was made to the warning for anemia where it previously advised to withhold Welireg until hemoglobin ≥9 g/dL and now it says until hemoglobin ≥8 g/dL.

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 Welireg. The following changes are recommended to incorporate the new indication to the existing policies:

Advanced Renal Cell Carcinoma

- Medical record documentation of a diagnosis of advanced renal cell cancer **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)

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

ZORYVE (roflumilast)

Clinical Summary: Zoryve cream has an updated age for the topical treatment of plaque psoriasis, including intertriginous areas in patients 6 years of age and older. It was previously indicated in patients 12 years of age and older.

The efficacy of Zoryve cream was evaluated in DERMIS-1 and DERMIS-2, two multicenter, randomized, double -blind, vehicle-controlled, trials in 881 adult and pediatric patients with mild to severe plaque psoriasis, body surface area (BSA) of 2%-20% who were randomized 2:1 to receive Zoryve cream or vehicle cream applied topically once daily for 8 weeks.

The primary efficacy endpoint was the proportion of subjects who achieved Investigator Global Assessment (IGA) treatment success at Week 8. IGA success was defined as a score of "Clear" (0) or "Almost Clear" (1), plus a 2-grade improvement from baseline. At baseline, 16% of patients had an IGA score of 2 (mild), 76 % had a score of 3 (moderate) and 8% had a score of 4 (severe). Patients treated with Zoryve cream had a significantly higher rate of IGA success compared to patients who received vehicle cream. Results are listed in table below: 41.5% in Dermis-1 trial and 36.7% in Dermis-2 trial had IGA success with Zoryve as compared to patients who received vehicle cream.

Secondary endpoints included the proportion of subjects that achieved Intertriginous-IGA (I -IGA) success at Week 8 and Worst Itch Numeric Rating Scale (WI-NRS) success sequentially at Weeks 8, 4, and 2 (Figure below). WI-NRS success was defined as a reduction of at least 4 points from baseline in subjects with a baseline WI-NRS score of at least 4. At baseline, 179 subjects had an Intertriginous IGA (I-IGA) score of 2 or higher and 678 subjects had a baseline Worst Itch Numeric Rating Scale score of 4 or higher which was on a scale of 0-10.

The safety and effectiveness specifically in pediatric patients 6 to less than 18 years of age is supported by data from the two 8-week, vehicle-controlled safety and efficacy trials which included 18 pediatric subjects 6 to 17 years of age, of whom 11 received Zoryve cream. The use of Zoryve cream in pediatric patients 6 to less than 12 years of age is also supported by data from one 4-week, open label, safety and pharmacokinetic (PK) study which included 20 pediatric subjects 6 to less than 12 years of age.

The adverse reaction profile in subjects 6 to less than 18 years of age was consistent with that observed in adults. The safety and effectiveness of Zoryve cream in pediatric patients below the age of 6 years have not been established.

Current Formulary Status: Pharmacy Benefit, Formulary, Prior Authorization required, QL

Recommendation: It is recommended to update policy 744.0 to include the new FDA approved age range and trial of the appropriate alternatives based on age.

A formulary exception for coverage of Zoryve may be made for members who meet the following criteria for ages 12 and above:

- Medical record documentation that Zoryve is prescribed by or in consultation with a dermatologist or rheumatologist **AND**
- Medical record documentation of age greater than or equal to 12 years old **AND**
- Medical record documentation of a diagnosis of chronic plaque psoriasis **AND**
- Medical record documentation of BSA involvement less than or equal to 20% **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to at least one of the following:
    - A high- to ultrahigh-potency topical corticosteroid used concurrently with a generic topical calcipotriene product **OR**
    - A generic calcipotriene/betamethasone combination product **OR**
    - A high- to ultrahigh-potency topical corticosteroid used concurrently with generic tazarotene 0.1%

A formulary exception for coverage of Zoryve may be made for members who meet the following criteria for ages 6 to 11:

- Medical record documentation that Zoryve is prescribed by or in consultation with a dermatologist or rheumatologist **AND**
- Medical record documentation of age 6 to 11 years old **AND**

- Medical record documentation of a diagnosis of chronic plaque psoriasis **AND**
- Medical record documentation of BSA involvement less than or equal to 20% **AND**
- Medical record documentation of therapeutic failure, intolerance, or contraindication to a medium to high-potency topical corticosteroid used concurrently with a generic topical calcipotriene product [calcipotriene should be avoided on the face, genitalia, intertriginous areas/flexures]

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

UPDATES

MOUNJARO (tirzepatide)

Background: Mounjaro is a dual agonist of glucose-dependent insulin (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor and is indicated for adults with type 2 diabetes mellitus to improve glycemic control as an adjunct to diet and exercise. Initial dosage is: 2.5 mg subcutaneously (SUBQ) once weekly for 4 weeks, then increase to 5 mg SUBQ once weekly. The lower initial dose (2.5 mg weekly) is intended to reduce gastrointestinal (GI) symptoms; it does not provide effective glycemic control.

The current quantity limit (QL) for GLP-1 agonist, Rybelsus 3 mg, is 30 tablets in 180 days since the 3 mg dose is only indicated for treatment initiation and not for glycemic control. Most of the GLP-1 agonists start with a titration, but it is difficult to limit quantity due to how the product is available as well as the titration instructions.

Recommendation: It is recommended to add a QL of 2 mL per 180 days for the 2.5 mg dose of Mounjaro to Commercial Policy 732.0 (Preferred GLP-1 Agonists and Mounjaro) to ensure titration to appropriate dose for glycemic control. No other recommended changes at this time.

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

OLPRUVA (sodium phenylbutyrate)

Background: Olpruva is available as 2g, 3g, 4g, 5g, 6 g, and 6.67g oral powder packets to be prepared for oral suspension via oral administration only. The recommended dosing of Olpruva is 9.9 to 13 g/m2 per day divided into three to six doses with food. Each dose of Olpruva should be rounded to the nearest available dosage strength.

At November P&T, I recommended the quantity limit by calculating 1 packet per dose. It was brought to my attention that each dose of the medication is supplied in dose envelopes which include active ingredient packets and mix-aid packets. The medication is billed by the total number of packets used, including both active ingredient packets and mix-aid packets. The dose envelope contains either 2 packets (for 2gm and 3gm dose) or 3 packets (for 4gm, 5gm, 6gm and 6.67gm dose).

Recommendation: It is recommended to update the quantity limit to the following:

- For 2gm dose: 20 packets per day (ten 2gm dose envelopes per day)
- For 3gm dose: 12 packets per day (six 3gm dose envelopes per day)
- For 4gm dose: 15 packets per day (five 4gm dose envelopes per day)
- For 5gm dose: 12 packets per day (four 5gm dose envelopes per day)
- For 6gm and 6.67gm dose: 9 packets per day (three 6gm or 6.67gm dose envelopes per day)

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 29 of 50 members. The vote was approved by majority.

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

Meeting will be held virtually via phone/Microsoft Teams.