P&T Committee Meeting Minutes
Commercial/Marketplace/GHP Kids E-vote
August 27, 2020

DRUG REVIEWS

NEXLETOL (bempedoic acid) and NEXLIZET (bempedoic acid/ezetimibe)

Review: Nexletol (bempedoic acid) and Nexlizet (bempedoic acid plus ezetimibe) are two new treatment options for patients who are unable to meet cholesterol goals with maximally tolerated stating therapy, with or without ezetimibe or a PCSK9 inhibitor. Bempedoic acid inhibits adenosine triphosphate-citrate lyase (ACL) which results in upregulation of LDL receptors and increases the clearance of LDL-C by the liver and reduces blood LDL-C levels.

The efficacy of Nexletol was investigated in 5 phase 3 studies, CLEAR Wisdom, CLEAR Harmony, CLEAR Harmony OLE, CLEAR Serenity, CLEAR Tranquility. CLEAR Wisdom, a 52-week, randomized, double blind, placebo-controlled study in patients with ASCVD and/or HeFH and persistent hypercholesterolemia despite maximally tolerated statins, showed a -17% difference in LDL-C change from baseline to week 12 between Nexletol and placebo. Exploratory endpoints evaluating High-density lipoprotein (HDL) and triglycerides (TG) showed a -6% difference in HDL change and a -2% difference in TG between Nexletol and placebo from baseline to Week 12. CLEAR Harmony, a 52-week, randomized, double blind, placebo-controlled study in patients with ASCVD and/or HeFH and persistent hypercholesterolemia despite maximally tolerated statins, showed a -18% difference in LDL-C change from baseline to week 12 between Nexletol and placebo. Exploratory endpoints evaluating HDL and TG showed a -6% difference in HDL change and a +3% difference in TG between Nexletol and placebo from baseline to Week 12. CLEAR Serenity and CLEAR tranquility were 24-week and 12-week randomized, double-blind, placebo controlled trial in statin-intolerant patients that showed reductions in LDL-C that were comparable to the clinical trials performed in patients on maximally tolerated statins.

Nexlizet was investigated in fixed combination drug product study which compared a combination of bempedoic acid and ezetimibe with each individual component as well as placebo. Treatment with Nexlizet resulted in significantly greater reductions in LDL-C from baseline compared to bempedoic acid alone, ezetimibe alone, and placebo (-36 vs. -17, -23, and +2 respectively). Exploratory endpoints evaluating HDL and TG showed a -38% difference in HDL change and a -11% difference in TG between Nexlizet and placebo from baseline to Week 12.

Nexletol and Nexlizet have warnings for increased in uric acid levels and gout and increased risk of tendon rupture or injury. In clinical trials of Nexletol, adverse reactions led to discontinuation of treatment of Nexletol in 11% of patients, most commonly from muscle spasms, diarrhea, and pain in extremity. Other adverse reactions which occurred in more than 2% of patients treated with Nexletol were upper respiratory tract infection, back pain, abdominal pain, bronchitis, anemia, and elevated liver enzymes. In clinical trials of Nexlizet, adverse reactions led to discontinuation in 8% of patients on Nexlizet, 5% of patients on placebo, 10% of patients on Nexletol, and 12% of patients on ezetimibe. The most common reason for Nexlizet treatment discontinuation was oral discomfort. The most commonly reported adverse reactions reported with Nexlizet, but not observed in clinical trials of Nexletol or ezetimibe were urinary tract infection, nasopharyngitis, and constipation.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Nexletol is a pharmacy benefit and will be added to the Brand Preferred tier of the Commercial, Exchange, and CHIP pharmacy formularies. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of:
    - Clinical atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes (a history of myocardial infarction or unstable angina), coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin **OR**
    - Heterozygous familial hypercholesterolemia (HeFH) **AND** either:
        - Genetic testing to confirm a mutation in the low-density lipoprotein (LDL) receptor, PCSK9, or ApoB gene **OR**
        - Medical record documentation of definite heterozygous familial hypercholesterolemia (HeFH) (score greater than 8) on the diagnostic criteria scoring system (Table 1) as defined by the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines and the World Health Organization **AND**
- Medical record documentation that Nexletol is prescribed by a cardiologist or lipidologist **AND**
- Medical record documentation of a baseline low-density lipoprotein (LDL) drawn within 3 months of the start of Nexletol therapy with one of the following:
    - Low-density lipoprotein (LDL) greater than 100 if the patient has a diagnosis of heterozygous familial hypercholesterolemia (HeFH) and is using Nexletol for primary prevention **OR**
    - Low-density lipoprotein (LDL) greater than 70 if the patient has a diagnosis of atherosclerotic cardiovascular disease (ASCVD) or either heterozygous familial hypercholesterolemia (HeFH) and is using Nexletol for secondary prevention **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that patient is currently on and is adherent to (taking at least 90% of prescribed doses over the past three months) maximally tolerated dose of atorvastatin or rosuvastatin or has documented therapeutic failure on, intolerance to, or contraindication to atorvastatin and rosuvastatin **AND**
- Medical record documentation that non-pharmacologic therapies are in place including cholesterol lowering diet, exercise, and weight management strategies **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to ezetimibe

Nexlizet is a pharmacy benefit and should be added to the Brand Preferred tier of the Commercial, Exchange, and CHIP pharmacy formularies. The following prior authorization criteria should apply:

- Medical record documentation of a diagnosis of:
    - Clinical atherosclerotic cardiovascular disease (ASCVD), including acute coronary syndromes (a history of myocardial infarction or unstable angina), coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease presumed to be of atherosclerotic origin **OR**
    - Heterozygous familial hypercholesterolemia (HeFH) **AND** either:
        - Genetic testing to confirm a mutation in the low-density lipoprotein (LDL) receptor, PCSK9, or ApoB gene **OR**
        - Medical record documentation of definite heterozygous familial hypercholesterolemia (HeFH) (score greater than 8) on the diagnostic criteria scoring system (Table 1) as defined by the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines and the World Health Organization **AND**
- Medical record documentation that Nexlizet is prescribed by a cardiologist or lipidologist **AND**

- Medical record documentation of a baseline low-density lipoprotein (LDL) drawn within 3 months of the start of Nexlizet therapy with one of the following:
    - Low-density lipoprotein (LDL) greater than 100 if the patient has a diagnosis of heterozygous familial hypercholesterolemia (HeFH) and is using Nexlizet for primary prevention **OR**
    - Low-density lipoprotein (LDL) greater than 70 if the patient has a diagnosis of atherosclerotic cardiovascular disease (ASCVD) or either heterozygous familial hypercholesterolemia (HeFH) and is using Nexlizet for secondary prevention **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that patient is currently on and is adherent to (taking at least 90% of prescribed doses over the past three months) maximally tolerated dose of atorvastatin or rosuvastatin or has documented therapeutic failure on, intolerance to, or contraindication to atorvastatin and rosuvastatin **AND**
- Medical record documentation that non-pharmacologic therapies are in place including cholesterol lowering diet, exercise, and weight management strategies **AND**
- Medical record documentation of a therapeutic failure on ezetimibe alone.

NOTE:

- Therapeutic failure is defined as an inability to reach target LDL goals (<100 mg/dL for patients with HeFH in primary prevention or < 70 mg/dL for ASCVD or for patients with HeFH using Nexlizet as secondary prevention) despite a > 3 month trial.
- Intolerance to statins is defined as increased LFTs, intolerable myalgia (muscle symptoms without creatinine kinase [CK] elevations) or myopathy (muscle symptoms with CK elevations), or myositis (elevations in CK without muscle symptoms), which persist after two retrials with a different dose or different dosing strategy (i.e. every other day administration) of alternative moderate- or high-intensity statin.
- Contraindications to statins are defined as active liver disease, previous history of rhabdomyolysis, or hypersensitivity

QUANTITY LIMIT: 1 tablet per day

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

SCENESSE (afamelanotide)

Review: Scenesse is indicated to increase pain free light exposure in adult patients with a history of phototoxic reactions from erythropoietic protoporphyria. As a first-in-class melanocortin-1 receptor agonist, Scenesse works by reducing free radical formation and cytokine production, and increasing skin pigmentation by promoting eumelanin production. By stimulating eumelanin, Scenesse decreases the penetration of light through the skin, thus reducing painful phototoxic reactions.

EPP is a rare, inherited autosomal recessive disorder resulting from mutations in the ferrochelatase gene (FECH). A reduction in ferrochelatase activity causes an accumulation of protoporphyrin IX (PPIX). When excess PPIX in the skin is exposed to the sun, it becomes photoactivated, generating free radicals that cause tissue damage and painful photosensitivity. Symptoms of burning, stinging, and tingling usually present in early infancy or childhood upon first exposure to the sun. The diagnosis of EPP is made by demonstrating an increased total erythrocyte protoporphyrin (usually 300-8000 mcg/dL; normal <80 mcg/dL) and an increased percentage of erythrocyte metal-free protoporphyrin. Differentiating between EPP and the X-linked form of EPP using molecular testing (FECH,

ALAS2) is not necessary for therapy or diagnosis but may be important for testing family members and for genetic counseling.

A single Scenesse 16 mg implant should be inserted subcutaneously above the anterior supra-iliac crest every 2 months by a trained health care professional. Sun and light protection measures should be maintained during treatment with Scenesse to prevent phototoxic reactions related to EPP.

The efficacy of Scenesse was assessed in two multicenter, randomized, double-blind, vehicle-controlled trials. Patients were included if they were at least 18 years of age with confirmed EPP, and without clinically significant hepatic or other organ dysfunction, skin cancer, premalignant lesions, or photodermatoses. Ninety-three patients in the United States (Study CUV039) and 74 patients (Study CUV029) in Europe were randomly assigned, in a 1:1 ratio, to receive a subcutaneous implant of Scenesse or vehicle every 2 months and followed for a total of 180 days (Study CUV039) or 270 days (Study CUV029). In study CUV039, the primary endpoint was the total number of hours over 180 days spent in direct sunlight between 10 am and 6 pm on days with no pain. The median total number of hours over 180 days spent in direct sunlight between 10 am and 6 pm on days with no pain was 64.1 hours for subjects receiving Scenesse and 40.5 hours for subjects receiving vehicle. In study CUV029, the primary endpoint was the total number of hours over 270 days spent outdoors between 10 am and 3 pm on days with no pain for which "most of the day" was spent in direct sunlight. The median total number of hours over 270 days spent outdoors between 10 am and 3 pm on days with no pain for which "most of the day" was spent in direct sunlight was 6.0 hours for subjects in the Scenesse group vs. 0.75 hours for subjects in the vehicle group.

Scenesse bears no black box warnings or contraindications, but it does carry a warning and precaution for increased skin pigmentation and darkening of pre-existing nevi and ephelides. It is recommended to perform a full body examination twice yearly to monitor pre-existing and new pigmentary skin lesions. The most common adverse reactions (incidence >2%) are implant site reaction, nausea, oropharyngeal pain, cough, fatigue, dizziness, skin hyperpigmentation, somnolence, melanocytic nevus, respiratory tract infection, non-acute porphyria, and skin irritation. The safety and effectiveness of Scenesse have not been established in pediatric patients.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Scenesse will be a medical benefit for Commercial/Exchange/CHIP members. The following prior authorization criteria will apply:

- Prescription written by a dermatologist **AND**
- Medical record documentation of the member being ≥ 18 years of age **AND**
- Medical record documentation of a diagnosis of erythropoietic protoporphyria (EPP) as confirmed by elevated total erythrocyte protoporphyrin* **AND**
- Medical record documentation of one of the following:
    - Erythrocyte fractionation showing a greater percentage of metal-free protoporphyrin compared to zinc protoporphyrin** **OR**
    - Gene sequencing showing an FECH or ALAS2 mutation **AND**
- Medical record documentation of a history of phototoxic reaction (e.g. pain, stinging, redness, swelling) **AND**

- Medical record documentation that sun and light protection measures will be maintained during treatment with Scenesse

  ***NOTE TO REVIEWER:** Increased total erythrocyte protoporphyrin with EPP is usually 300-8000 mcg/dL; (normal <80 mcg/dL).

  ****NOTE TO REVIEWER:** In patients with EPP due to FECH defects, the excess protoporphyrin is almost always > 85% metal-free protoporphyrin and < 15% zinc protoporphyrin. Patients with X-linked form of EPP have 50-85% of porphyrins as metal-free protoporphyrin. Laboratories that measure free protoporphyrin and zinc protoporphyrin include: Porphyria Laboratory and Center, University of Texas Medical Branch at Galveston and Mayo Medical Laboratories.

  AUTHORIZATION DURATION: Initial approval will be for 6 months and subsequent approvals will be for 6 months.

  REAUTHORIZATION CRITERIA:
    - Medical record documentation of reduction in pain associated with light exposure or an increase in light exposure tolerance AND
    - Medical record documentation that the member received a full skin examination by a dermatologist within the last six months AND
    - Medical record documentation that sun and light protection measures will be maintained during treatment with Scenesse.

  QUANTITY LIMIT: Medaccess: 1 implant every 60 days; max qty supply: 1; min and max day supply: 60.

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

FAST FACTS

CRYSVITA (burosumab-twza)

Updated Indication: Crysvita is a fibroblast growth factor 23 (FGF23) blocking antibody now indicated for the treatment of FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized in adult and pediatric patients 2 years of age and older.

Updated Dosing for New Indication: The dosage of Crysvita for the new indication for pediatric patients age 2 to less than 18 years old is a starting dose of 0.4 mg/kg body weight administered every 2 weeks, rounded to the nearest 10 mg , up to 2 mg/kg (not to exceed 180 mg) every 2 weeks. After initiation, serum phosphorous should be assessed monthly for the first three months, starting 2 weeks post dose. If serum phosphorous is within range, the patient should be maintained on that dose. If the phosphorous is below range, it can be adjusted following the titration schedule in the package insert (Table 1). Crysvita should not be adjusted more frequently than every 4 weeks.

Table 1. Tumor Induced Osteomalacia Schedule for Dose Increase for Pediatric Patients Weighing 10 kg or more

Body Weight (kg)	Starting Dose (mg)	First Dose Increase to (mg)	Second Dose Increase to (mg)	Third Dose[a] Increase to (mg)
10 – 14	5	10	15	20
15 – 18	5	10	20	25
19 – 31	10	20	25	30
32 – 43	10	30	40	50
44 – 56	20	40	50	70
57 – 68	20	50	70	90
69 – 80	30	60	80	100
81 – 93	30	70	100	120
94 – 105	40	80	110	140
106 and greater	40	90	130	160

[a] The table shows a dose increase up to 1.5 mg/kg. Further dose increases to a maximum of 2 mg/kg not to exceed 180 mg, administered every 2 weeks should be calculated by the physician.

The recommended dosage of Crysvita for adult patients is a starting dose of 0.5 mg/kg body weight administered every 4 weeks, rounded to the nearest 10 mg, up to a maximum of 2 mg/kg not to exceed 180 mg administered every 2 weeks. Serum phosphorous should be assessed once monthly for the first three months, starting two weeks after Crysvita initiation. If serum phosphorous is within range, the patient should be maintained on that dose. If the phosphorous is below range, it can be adjusted following the titration schedule in the package insert (Table 2). Crysvita should not be adjusted more frequently than every 4 weeks. For patients not reaching a serum phosphorous greater than the lower limit of the normal range, the total dose administered every four weeks may be divided in half and administered every two weeks.

Table 2. Tumor Induced Osteomalacia Schedule for Dose Increase for Adult Patients

	Starting Dose	First Dose Increase***	Second Dose Increase***	Third Dose Increase***	Fourth Dose Increase	Fifth Dose Increase (maximum dose)
If serum phosphorus 2 weeks post-dose adjustment is below lower limit of normal	0.5 mg/kg every 4 weeks	Increase to: 1 mg/kg every 4 weeks OR 0.5 mg/kg every 2 weeks	Increase to: 1.5 mg/kg every 4 weeks**** OR 0.75 mg/kg every 2 weeks	Increase to: 2 mg/kg every 4 weeks**** OR 1 mg/kg every 2 weeks	Increase to: 1.5 mg/kg not to exceed 180 mg every 2 weeks	Increase to: 2 mg/kg not to exceed 180 mg every 2 weeks

*Rounded to the nearest 10 mg.
**Do not adjust CRYSVITA more frequently than every 4 weeks.
*** For those individuals not reaching a serum phosphorus greater than the lower limit of the normal range, physicians may consider dividing total dose administered every 4 weeks and administering every 2 weeks.
**** In patients with high body weight, if the calculated dose is greater than 180 mg every 4 weeks, move to a divided dose every 2 weeks.

Current formulary status: Medical Benefit requiring a prior authorization

Recommendation: There are no changes recommended to the formulary placement for Crysvita. It is recommended to add the following prior authorization and update the authorization duration as follows for Medical Benefit Policy 182.0 to incorporate the new indication:

FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO)

- Medical record documentation that the patient is at least 2 years of age or older **AND**
- Medical record documentation that Crysvita is being prescribed by, or in consultation with, an endocrinologist, nephrologist, geneticist, or oncologist **AND**
- Medical record documentation of a diagnosis of FGF23-related hypophosphatemia in tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors **AND**
- Medical record documentation of a serum level of FGF23 greater than or equal to 100 pg/mL determined by Kainos assay **AND**
- Medical record documentation that tumors cannot be curatively resected or localized **AND**
- Medical record documentation that the patient is not concurrently using vitamin D analogs or phosphate supplements.

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate and the following criteria are met:

- Medical record documentation that patient is being followed regularly by and receiving medication from an endocrinologist, nephrologist, geneticist or oncologist **AND**
- Medical record documentation that Crysvita is improving patient's disease as evidenced by normalized or improved serum phosphorus levels **AND**
- Medical record documentation that the patient is not concurrently using Vitamin D analogs or phosphate supplements.

Discussion: No comments or questions.

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

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

CYRAMZA (ramucirumab)

Updated Indication: Cyramza is a human vascular endothelial growth factor receptor 2 (VEGFR2) antagonist now indicated in combination with erlotinib, for first line treatment of metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations.

Updated Dosing for New Indication: The recommended dosage for Cyramza given in combination with erlotinib in NSCLC with EGFR exon 19 deletions (ex19del)or exon 21 (L858R) substitution mutations is 10 mg/kg every 2 weeks administered by intravenous infusion over 60 minutes for the first infusion and over 30 minutes for subsequent infusions. Cyramza is continued until disease progression or unacceptable toxicity.

Current formulary status: Medical Benefit, requiring a prior authorization

Recommendation: No changes are recommended to the formulary placement or authorization duration of Cyramza. The following changes are recommended for Medical Benefit Policy 115.0 to incorporate the new indication:

2. NSCLC:

- Prescription is written by an oncologist **AND**
- Medical Record documentation of one of the following:
    - Medical record documentation of metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) mutations **AND**
    - Medical record documentation that Cyramza will be used as first-line treatment in combination with erlotinib

OR

- Medical record documentation of metastatic non-small cell lung cancer with disease progression on or after platinum-based chemotherapy **AND**
- Patients with EGFR or ALK genomic tumor aberrations must provide medical record documentation of disease progression on FDA-approved therapy for these aberrations prior to receiving Cyramza **AND**
- Medical record documentation of use in combination with docetaxel

Discussion: No comments or questions.

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

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

DUPIXENT (dupilumab)

Updated Indication: Dupixent is an interleukin-4 receptor alpha antagonist now indicated for the treatment of patients age 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Previously this indication was for patients 12 years and older. There are no changes to the other indications for Dupixent for moderate-to-severe asthma and chronic rhinosinusitis with nasal polyposis.

Updated Dosing for New Indication: For pediatric patients aged 6 to 17 years, the recommended dosage based on weight is listed in Table 1. Per the package insert, the Dupixent pre-filled pen is only for use in adults and adolescents aged 12 years and older. For patients 6-11 years, Dupixent pre-filled syringe should be given by a caregiver. Dupixent can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used but should be reserved for problem areas such as face, neck, and genital areas.

Table 1. Dupixent Dose in Pediatric Patients (Subcutaneous Administration)

Body Weight	Initial Dose	Subsequent Doses
15 to less than 30 kg	600 mg (two 300 mg injections)	300 mg every 4 weeks
30 to less than 60 kg	400 mg(two 300 mg injections)	200 mg every other week
60 kg or more	600 mg (two 300 mg injections)	300 mg every other week

Current formulary status: Specialty tier or Brand Non-Preferred tier for patients with a 3 tier benefit, requiring a prior authorization

Recommendation: No changes are recommended to the formulary placement or authorization duration of Dupixent. It is recommended that the following changes be made to the prior authorization criteria and quantity limits for Dupixent for atopic dermatitis in Commercial Policy 457.0 to incorporate the new patient population and recommended dosage:

Atopic Dermatitis

- Medical record documentation that Dupixent is prescribed by or in consultation with an allergist, dermatologist, or immunologist **AND**
- Medical record documentation of one of the following:
  - If the request is for Dupixent pre-filled pen: documentation of age greater than or equal to 12 years **OR**
  - If the request is for Dupixent pre-filled syringe: documentation of age greater than or equal to ~~12 years~~ 6 years

AND

- Medical record documentation of a diagnosis of moderate to severe atopic dermatitis **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure* on an adequate trial of at least one medium potency** topical corticosteroid unless deemed inadvisable due to potential risks such as (a) use on sensitive skin areas (face, axillae, or groin) or (b) member is between 2 and 15 years of age **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on tacrolimus ointment **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on Eucrisa* **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment)

***NOTE:** Therapeutic failure is defined as an inability to achieve and maintain remission of low to mild disease activity

AUTHORIZATION PARAMETERS:

If requesting a dose of:	Initial – One-time, one-week authorization	Remainder/Subsequent
300 mg every other week	Quantity limit: 8 mL per 42 days Max quantity supply: 8 Min day supply: 42 Max day supply: 42	Quantity limit: 4 mL per 28 days Max quantity supply: 4 Min day supply: 28 Max day supply: 28

200 mg every other week	Quantity limit: 4.56 mL per 42 days Max quantity supply: 4.56 Min day supply: 42 Max day supply: 42	Quantity Limit: 2.28 mL per 28 days Max quantity supply: 2.28 Min day supply: 28 Max day supply: 28
300 mg every 4 weeks	Quantity limit: 8 mL per 42 days Max quantity supply: 8 Min day supply: 42 Max day supply: 42	Quantity Limit: 2 per 28 days Max quantity supply: 2 Min day supply: 28 Max day supply: 28

Discussion: No comments or questions.

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

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

MYLOTARG (gemtuzumab ozogamicin)

Updated Indication: Mylotarg is a CD33-directed antibody and cytotoxic drug conjugate now indicated for treatment of newly-diagnosed CD33-positive acute myeloid leukemia (AML) in adults and pediatric patients 1 month and older. Previously this indication only included the adult population.

There is no change to the indication of Mylotarg in adult and pediatric patients 2 years and older as treatment for relapsed or refractory CD33-positive AML.

Updated Dosing for New Indication: The recommended dose of Mylotarg in pediatric patients 1 month and older is a body surface area (BSA) based dose of 3 mg/m^2 for patients with a body surface area greater than or equal to 0.6 m^2 or a weight based dose of 0.1 mg/kg for patients with a BSA less than 0.6 m^2. Although adult patients have dosing for both combination regimen and single-agent treatment with Mylotarg, pediatric patients should only receive Mylotarg in combination with 5-cycles of standard chemotherapy (two induction cycles and 3 intensification cycles). For induction 1, Mylotarg is given in combination with standard chemotherapy on day 6. No Mylotarg is given in the second induction cycle. No Mylotarg is given in the first and third intensification cycles. For Intensification 2, Mylotarg is given once in combination with standard chemotherapy on Day 7.

Pediatric patients 1 month and older should be premedicated with acetaminophen and diphenhydramine 1 hour prior to Mylotarg dosing and methylprednisolone 30 minutes prior to dosing. Additional doses of acetaminophen and diphenhydramine may be repeated every 4 hours after the initial pretreatment dose if needed. Methylprednisolone or an equivalent corticosteroid should be repeated for any sign of infusion reaction during infusion or within 4 hours afterword.

Current formulary status: Medical Benefit, requiring a prior authorization

Recommendation: No changes are recommended to the formulary placement of Mylotarg. Due to updated dosing which only recommends Mylotarg in combination with standard chemotherapy for pediatric patients, the following changes should be made to Medical Benefit Policy 163.0 to incorporate the new indication:

Newly-diagnosed CD33-positive Acute Myeloid Leukemia

- Prescription written by a hematologist/oncologist **AND**

- Medical record documentation of a diagnosis of newly diagnosed CD33-positive Acute Myeloid Leukemia **AND**
- Medical record documentation of one of the following:
    - Documentation of the member being ≥ 18 years

    OR
    - Documentation of member being ≥ 1 month of age and < 18 years of age **AND**
    - Documentation that Mylotarg will be used in combination with standard chemotherapy.

Relapsed or refractory CD33-positive Acute Myeloid Leukemia
- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of relapsed or refractory CD33-positive Acute Myeloid Leukemia **AND**
- Medical record documentation of the member being ≥ 2 years

AUTHORIZATION DURATION:
For newly-diagnosed CD33 positive Acute Myeloid Leukemia in patients ≥ 1 month of age and < 18 years of age: Maximum of two (2) doses for a six (6) month authorization duration

For all other indications: Maximum of nine (9) cycles for a 12 month authorization duration

For requests exceeding the above limits, medical record documentation of the following is required:
Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration

Discussion: No comments or questions.

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

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

OFEV (nintedanib)

Updated Indication: Ofev is now indicated for treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype.

Previous indications for Ofev include idiopathic pulmonary fibrosis (IPF) and systemic sclerosis-associated interstitial lung disease (SSc-ILD).

Updated Dosing for New Indication: There has been no change to the dosing of Ofev for the new indication. The recommended dosage is 150 mg twice daily approximately 12 hours apart.

Current formulary status:
Commercial/CHIP: Non-formulary
Exchange: Specialty tier, requiring prior authorization

Recommendation: No changes are recommended to the formulary placement or current quantity limits of Ofev. It is recommended to add the following criteria to Commercial Drug Policy 365.0 to incorporate the new indication:

Chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype

- Prescription written by or in consultation with a pulmonologist and/or rheumatologist **AND**
- Medical record documentation of patient age 18 years or older **AND**
- Medical record documentation of a diagnosis of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype* **AND**
- Medical record documentation of chronic interstitial lung disease confirmed by all of the following:
    - ≥ 10% fibrosis on a chest high resolution computer tomography **AND**
    - FVC ≥ 45% of predicted normal **AND**
    - DLCO (diffusion capacity of the lung for carbon monoxide) 30-80% of predicted normal

AND

- Medical record documentation of interstitial lung disease progression despite appropriate management with documentation of one of the following:
    - FVC decline ≥ 10% **OR**
    - FVC decline ≥5% to <10% with documentation of either worsening symptoms OR increasing fibrotic changes on imaging **OR**
    - Documentation of both worsening symptoms AND increasing fibrotic changes on imaging

*NOTE: Chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype includes, but is not limited to:

- Rheumatoid arthritis associated ILD (RA-ILD)
- Mixed connective tissue disease
- Chronic hypersensitivity pneumonitis (HP)
- Idiopathic nonspecific interstitial pneumonia (iNSIP)
- Unclassifiable idiopathic interstitial pneumonia (uIIP)
- Exposure-related ILD
    Sarcoidosis

Discussion: No comments or questions.

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

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

TECENTRIQ (atezolizumab)

Updated Indication: Tecentriq is a programmed death-ligand 1 (PD-L1) blocking antibody with two new indications. It is now indicated:

- for the first-line treatment of adult patients with metastatic NSCLC whose tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]), as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations.
- in combination with cobimetinib and vemurafenib for the treatment of patients with BRAF V600 mutation-positive unresectable or metastatic melanoma.

Updated Dosing for New Indication: The recommended dosage of Tecentriq as a single agent for the treatment of NSCLC is 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks administered intravenously over 60 minutes (30 minutes for subsequent doses) until disease progression or unacceptable toxicity.

For melanoma, prior to initiating Tecentriq patients should receive a 28 day treatment cycle of cobimetinib 60 mg orally once daily (21 days on and 7 days off) and vemurafenib 960 mg orally twice daily from Days 1 to 21 and 720 mg orally twice daily Days 22-28. The recommended dosage of Tecentriq is 840 mg administered intravenously over 60 minutes (30 minutes for subsequent doses) every 2 weeks until disease progression or unacceptable toxicity. This should be administered with cobimetinib 60 mg once daily (21 days on and 7 days off) and vemurafenib 720 mg twice daily.

Current formulary status: Medical Benefit, requiring a prior authorization

Recommendation: There are no changes recommended for the formulary placement or authorization duration of Tecentriq. For NSCLC, it is recommended that the following changes be made to Medical Benefit Policy 144.0 Tecentriq to incorporate the new indication for NSCLC with high PD-L1 expression:

Non-Small Cell Lung Cancer:

- Prescription written by an oncologist AND
- Medical record documentation of a diagnosis of non-small cell lung cancer meeting one of the following situations:
  - Medical record documentation of disease progression during or following platinum-containing chemotherapy

  OR
  - Medical record documentation of disease progression on at least one FDA-approved therapy targeting EGFR or ALK if the patient has EGFR or ALK genomic tumor aberrations (e.g. mutation, deletion, insertion, etc.)

  OR
  - Medical record documentation of a non-squamous histologic subtype AND
  - Medical record documentation that Tecentriq will be given as first-line treatment AND
  - Medical record documentation that Tecentriq will be given in combination with bevacizumab, paclitaxel, AND carboplatin OR paclitaxel protein-bound AND carboplatin
  - Medical record documentation that the patient does not have an EGFR or ALK genomic tumor aberration.

  OR
  - Medical record documentation that Tecentriq will be given as first-line treatment for metastatic disease **AND**
  - Medical record documentation that tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]) as determined by an FDA-approved test **AND**
  - Medical record documentation that the patient does not have an EGFR or ALK genomic tumor aberration.

For melanoma, the following criteria should be added to the Medical Benefit Policy 144.0 Tecentriq and Part D Policy 547.0D to incorporate the new indication.

1. Melanoma
- Medical record documentation of unresectable or metastatic melanoma **AND**
- Medical record documentation of BRAF V600 mutation as determined by an FDA-approved test **AND**

  Medical record documentation that Tecentriq will be given in combination with Cotelliq (cobimetinib) and Zelboraf (vemurafenib)

Discussion: No comments or questions.

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

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

TIVICAY/TIVICAY PD (dolutegravir)

Updated Indication: Tivicay and Tivicay PD (a new formulation of tablets for suspension) are a human immunodeficiency virus type 1 (HIV-1) integrase strand transfer inhibitor (INSTI) indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults (treatment-naïve or -experienced) and in pediatric patients (treatment-naïve or -experienced but INSTI-naïve) aged at least 4 weeks and weighing at least 3 kg.

Previously Tivicay this indication included adults and pediatric patients weighing at least 30 pounds. In addition , Tivicay is indicated in combination with rilpivirine as a complete regimen for the treatment of HIV-1 infection in adults to replace the current antiretroviral regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure or known substitutions associated with resistance to either antiretroviral agent.

Updated Dosing for New Indication: There is no change to the adult dosage of Tivicay in the new patient population. For pediatric patients recommended dosages include Tivicay tablets (10 mg or 50 mg) and the new formulation, Tivicay PD, 5 mg tablets for oral suspension which can be swallowed whole or dispersed into 5-10 mL of drinking water according to package insert directions. The Tivicay tablet and Tivicay PD formulations are not bioequivalent and are not interchangeable on a milligram-per-milligram basis and the dosage should be adjusted when switching from one formulation to another.

The recommended dosage for pediatric patients 4 weeks and older and weighing 3 to 14 kg (treatment-naïve or treatment experienced but naïve to integrase strand transfer inhibitor (INSTI) treatment) is based on body weight and uses Tivicay PD tablets (Table 1). For pediatric patients 4 weeks and older weighing 14 kg or greater (treatment-naïve or treatment experienced but naïve to INSTI treatment), either Tivicay PD tablets for oral suspension or Tivicay tablets can be used with body weight based dosing (Table 2).

Table 1. Recommended Dosage of TIVICAY PD in Pediatric Patients 4 Weeks and Older Weighing 3 to 14 kg

Body Weight	TIVICAY PD Tablets for Oral Suspension	
	Daily Dose	Number of 5-mg tablets
3 kg to less than 6 kg	5 mg once daily	1
6 kg to less than 10 kg	15 mg once daily	2
10 kg to less than 14 kg	20 mg once daily	4

Table 2. Recommended Dosage in Pediatric Patients weighing 14 kg or greater

Body Weight	**TIVICAY PD Tablets for Oral Suspension**	
	Daily Dose	**Number of Tablets**
14 kg to less than 20 kg	25 mg once daily	5
20 kg and greater	30 mg once daily	6
	TIVICAY tablets	
14 kg to less than 20 kg	40 mg once daily	4 x 10 mg
20 kg and greater	50 mg once daily	1 x 50 mg

Current formulary status: Tivicay: Brand Preferred, QL: 2 tablets per day

Recommendation: The formulary placement of Tivicay PD and the quantity limits for Tivicay 10 mg and Tivicay PD should be updated as follows:

- Tivicay 10 mg tablets : QL: 4 tablets per day
- Tivicay PD: add to Brand Preferred tier, QL: 6 tablets per day

Discussion: No comments or questions.

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

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

The clinical portion of the reviews were approved by 21 of 35 voting members. No response was received from the remaining 14 members.

The financial portion of the reviews were approved by 21 of 35 voting members. No response was received from the remaining 14 members.

Future Scheduled Meetings

The next bi-monthly scheduled meeting will be held virtually on Tuesday, September 15, 2020 at 1:00 pm.