P&T Committee Meeting Minutes
Medicaid
May 19, 2020

Present: All voting done electronically.	**Absent: All voting done electronically.**

Call to Order:
Voting was held electronically from Tuesday, May 19, 2020 to May 22, 2020

Review and Approval of Minutes, Reviews, Fast Facts, and Updates:
Approved based on approval from 20 (out of 35 members), no members voted to reject.

DRUG REVIEWS

The following quantity limits were presented and approved:

Drug	**Dosage Form and Strength**	**Formulary Therapeutic Recommendation**
Ability Mycite	Tablet	Add QL of 1/day
Secuado	Patch	Add QL of 1/day
Consensi	Tablet	Add QL of 1/day
Talicia	Capsule	Add QL of 168 per 14 days
Koselugo	Capsule	Add QL: 10 mg cap: 8 per day, 25 mg cap: 4 per day

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

Recarbrio (imipenem/cilastatin/relebactam)

Review: Recarbrio is a combination of imipenem (a carbapenem beta lactam antibiotic), cilastatin (prevents renal metabolism of imipenem), and relebactam indicated in adult patients with complicated urinary tract infection (cUTI) or complicated intra-abdominal infection (cIAI) causes by susceptible gram-negative pathogens. Relebactam is a β-lactamase inhibitor with no intrinsic antibacterial activity but which prevents the degradation of imipenem by certain β-lactamases. An efficacy evaluation relies in part on previous findings of efficacy of imipenem in the treatment of cUTI and cIAI. Carbapenems, including imipenem, are often used as last resort for serious infections with multi-drug resistant gram negative organisms but have increasing incidences of resistance due in part to carbapenemase, a β-lactamase with the capability of cleaving β-lactam amide bonds. By inhibiting β-lactamase, it is thought that relebactam in combination with imipenem may increase its effectiveness against carbapenem-resistant pathogens.

The efficacy of Recarbrio in the treatment of cUTI was investigated in a randomized, double-blind, non-inferiority trial in 302 adult patients with cUTI or acute pyelonephritis. Patients were randomized 1:1:1 to one of two doses of relebactam (250 mg or 125 mg) or placebo in combination with imipenem/cilastatin. The primary

efficacy endpoint which evaluated rate of favorable microbiological response at discontinuation of IV therapy (DCIV) found both doses of relebactam in combination with imipenem/cilastatin to be non-inferior to the group receiving imipenem/cilastatin alone. Secondary endpoints investigating microbiological response at early and late follow up and clinical response at all three time points found comparable results between all three treatment groups.

A second randomized, double-blind controlled trial investigated the efficacy of Recarbrio in 351 adult patients with clinically suspected or bacteriologically documented cIAI requiring hospitalization and treatment with IV antibiotics. Patients were randomized 1:1:1 to one of two doses of relebactam (250 mg or 125 mg) or placebo in combination with imipenem/cilastatin. The primary efficacy endpoint which evaluated rate of favorable clinical response at discontinuation of IV therapy (DCIV) found both doses of relebactam in combination with imipenem/cilastatin to be non-inferior to the group receiving imipenem/cilastatin alone.

No new safety concerns were identified related to relebactam alone or to the combination of imipenem with relebactam compared to imipenem alone. Warnings and precautions were consistent the known warning and precautions of imipenem and other antibiotic therapies. In clinical trials of Recarbrio the adverse events that occurred more frequently than in patients treated with imipenem/cilastatin alone included nausea, vomiting, and diarrhea, infusion site reactions, headache, and increased transaminases.

Outcome: Recarbrio is a medical benefit that will be managed by GHP and should not be added to the GHP Family pharmacy formulary. The following prior authorization criteria should apply:

- Prescription is written by or in consultation with Infectious Disease **AND**
- Medical record documentation that the member is greater than or equal to 18 years of age **AND**
- Medical record documentation of one of the following:
    - Diagnosis of Complicated Urinary Tract Infection (including Pyelonephritis) (cUTI) caused by the following susceptible gram-negative microorganisms: *Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa*.
    - Diagnosis of Complicated Intra-abdominal Infection (cIAI) caused by the following susceptible gram-negative microorganisms: *Bacteroides caccae, Bacteroides fragilis, Bacteroides ovatus, Bacteroides stercoris, Bacteroides thetaiotaomicron, Bacteroides uniformis*, *Bacteroides vulgatus, Citrobacter freundii*, *Enterobacter cloacae*, *Escherichia coli*, *Fusobacterium nucleatum*, *Klebsiella aerogenes, Klebsiella oxytoca*, *Klebsiella pneumoniae, Parabacteroides distasonis,* and *Pseudomonas aeruginosa*.

AND

- Medical record documentation of a culture and sensitivity showing the patient's infection is not susceptible to preferred alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to three (3) preferred alternative antibiotics shown to be susceptible on the culture and sensitivity **AND**
- Medical record documentation of a therapeutic failure on imipenem/cilastatin OR medical rationale of why imipenem/cilastatin cannot be used.

AUTHORIZATION DURATION: up to 14 days

QUANITY LIMITS: 4 vials/day, FACETS Rx count: 7000 units

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

Givlaari (givosiran)

Review: Givlaari is a double-stranded small interfering RNA (siRNA) indicated for the treatment of adult patients with acute hepatic porphyria (AHP). It causes degradation of ALAS1 mRNA in hepatocytes through RNA interference, reducing the elevated levels of ALAS1 which in turn reduces neurotoxic heme intermediates (ALA and PBG) which are associated with acute porphyria attacks and disease manifestations. Givlaari is the only treatment option FDA approved to treat AHP chronically to reduce the number of acute attacks.

The efficacy of Givlaari was investigated in ENVISION, a double-blind, placebo controlled study in 94 patients with a diagnosis of any acute hepatic porphyria who had at least two porphyria attacks requiring hospitalization, urgent healthcare visit, or IV hemin treatment at home within the 6 months prior to screening. Patients were randomized 1:1 to receive Givlaari 2.5 mg/kg once monthly or placebo during a 6-month double-blind period. Eligible patients included 89 with acute intermittent porphyria, 2 patients with variegate porphyria (VP), and 1 patient with hereditary coproporphyria (HCP).

The primary efficacy endpoint was measures as the rate of porphyria attacks requiring hospitalization, urgent healthcare visits, or intravenous hemin administration at home in patients with acute intermittent porphyria (the most common type of AHP). Givlaari met this primary endpoint with a 70% reduction in the rate of porphyria attacks compared to placebo (1.9 compared to 6.5). In a subgroup of patients with no prior hemin use and a low annualized attack rate, patients treated with Givlaari experienced only 1 fewer attack during the 6 month double-blind period. Secondary endpoints showed the Givlaari treatment group had a statistically significant response for the secondary endpoints measuring hemin use, porphyria attack rate in all AHP patients, change from baseline in Physician Component Summary of the 12-item Short Form Health Survey (PCS SF-12, and level of neurotoxic heme intermediates (ALA and PBG). An exploratory endpoint investigating analgesic use (opioid and non-opioid) showed that patients treated with Givlaari had a lower median proportion of days with analgesic use.

During clinical trials, the most commonly occurring adverse reactions reported with Givlaari were nausea (27%) and injections site reactions (25%), including erythema, pain, pruritis, rash, discoloration, or swelling at injection site. Elevated transaminase levels at least 3 times the upper limit of normal, increases in serum creatinine, and decreased estimated glomerular filtration rate have also occurred with Givlaari treatment.

Outcome: Givlaari will be covered as a medical benefit managed by GHP and should not be added to the GHP Family pharmacy formulary. The following prior authorization criteria should apply:

- Medical record documentation that Givlaari is prescribed by a specialist with experience managing porphyrias (including but not limited to a hematologist, hepatologist, or gastroenterologist) **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of acute hepatic porphyria (AHP) [including acute intermittent porphyria (AIP), hereditary coproporphyria (HCP), variegate porphyria (VP), and aminolevulinic acid dehydratase (ALAD) porphyria (ADP)] by at least one of the following:
    - Elevated urinary or plasma aminolevulinic acid (ALA) **OR**
    - Elevated urinary or plasma porphobilinogen (PBG) **OR**
    - Genetic testing confirming a mutation associated with acute hepatic porphyria (AHP)

  AND
- Medical record documentation of the baseline number of porphyria attacks requiring hospitalization, urgent healthcare visit, or IV hemin treatment within the previous 6 months **AND**
- Medical record documentation of active disease with at least two documented porphyria attacks within the previous 6 months.

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

will be for a **duration of twelve (12) months** or less if the reviewing provider feels it is medically appropriate, and will require:

- Medical record documentation of a clinically significant positive response to Givlaari treatment as evidenced by:
    - a reduction in the number of porphyria attacks requiring hospitalization, urgent healthcare visit, or IV hemin treatment within the previous 6 months from baseline **OR**
    - decreased severity in the symptoms of acute hepatic porphyria **OR**
    - a reduction in the baseline levels of urinary or plasma aminolevulinic acid (ALA) **OR** urinary or plasma porphobilinogen (PBG)

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

Oxbryta (voxelotor)

Review: Oxbryta is a hemoglobin S polymerization inhibitor indicated for the treatment of sickle cell disease in adults and pediatric patients 12 years of age and older. Preventative therapies for SCD complications currently include blood transfusions, hydroxyurea, Endari, Adakveo, and now Oxbryta.

Like Endari and Adakveo, Oxbryta may be used as monotherapy or in conjunction with hydroxyurea. Oxbryta was approved by the FDA under accelerated approval based on the increase in hemoglobin seen in the preliminary results (24 weeks) of a single phase 3 clinical trial. It is currently unknown whether Oxbryta improves patient reported outcomes associated with anemia, or whether it will have a favorable clinical impact on other SCD long-term complications, such as vasoocclusive crisis (VOC). Until those trials are completed, Oxbryta will likely adopt a place in therapy second line to hydroxyurea, similar to Endari and Adakveo.

The recommended dosage of Oxbryta is 1,500 mg taken orally once daily with or without food. There are dose adjustments recommended for patients with severe hepatic impairment, strong/moderate CYP3A4 inducers, strong CYP3A4 inhibitors, or fluconazole.

The efficacy and safety of Oxbryta in SCD was evaluated in HOPE, a randomized, double-blind, placebo-controlled, multicenter trial. In this study, 274 patients were randomized to daily oral administration of Oxbryta 1,500 mg, Oxbryta 900 mg, or placebo. Efficacy was based on Hb response rate defined as a Hb increase of >1 g/dL from baseline to Week 24 in patients treated with Oxbryta 1,500 mg versus placebo. The response rate for Oxbryta 1,500 mg was 51.1% compared to 6.5% in the placebo group ($p < 0.001$). The number of VOCs per person per year was not statistically significant compared to placebo. Also, the percentage of patients who underwent RBC transfusions during the study were similar in all three groups.

Like Endari and Adakveo, there are no black box warnings associated with Oxbryta. Oxbryta is contraindicated in patients with a history of serious drug hypersensitivity reaction to voxelotor or excipients. Oxbryta carries the following warnings for hypersensitivity reactions and laboratory test interference. The most common adverse reactions (incidence ≥ 10%) are headache, diarrhea, abdominal pain, nausea, fatigue, rash, and pyrexia. The safety and effectiveness of Oxbryta in pediatric patients below the age of 12 years have not been established.

Outcome: Oxbryta is a pharmacy benefit. It is recommended that Oxbryta not be added to the GHP Family formulary. The following prior authorization should apply.

- Prescription written by or in consultation with a hematologist AND.
- Medical record documentation of the member being ≥ 12 years of age AND
- Medical record documentation of diagnosis of sickle cell disease AND
- Medical record documentation of baseline hemoglobin AND
- If the requested dose is 2,500 mg daily: Medical record documentation that the patient is using Oxbryta in combination with a strong or moderate CYP3A4 inducer, including but not limited to apalutamide, bosentan, carbamazepine, efavirenz, etravirine, enzalutamide, mitotane, phenobarbital, phenytoin, primidone, rifampin, St. John's Wort AND
- Medical record documentation of intolerance to, or contraindication to, or therapeutic failure on a minimum 3 month trial of generic hydroxyurea AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Endari.

Authorization Duration: Each treatment period will be defined as 12 months. Re-review will occur every 12 months. The following criteria is recommended for reauthorization:

- Medical record documentation of an increase in hemoglobin from baseline or an improvement in complications of sickle cell disease (e.g. decrease in vasoocclusive crisis related emergencies) AND
- If the requested dose is 2,500 mg daily: Medical record documentation that the patient is using Oxbryta in combination with a strong or moderate CYP3A4 inducer, including but not limited to apalutamide, bosentan, carbamazepine, efavirenz, etravirine, enzalutamide, mitotane, phenobarbital, phenytoin, primidone, rifampin, St. John's Wort

Quantity Limit: Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).
90 tablets per 30 days

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

Vyondys 53 (golodirsen)

Review: Vyondys 53 is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping. Vyondys 53 was approved under the accelerated approval process based on an increase in dystrophin production in skeletal muscle and for continued approval for this indication, Vyondys 53 requires verification of clinical benefit in confirmatory trials. DMD occurs when there are deletions within the DMD gene causing the production of non-functional dystrophin. Vyondys 53 works by binding exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing (exon 53 skipping) and ultimately allows for the production of a truncated and partially functional dystrophin protein. Vyondys 53 is dosed 30mg/kg IV given every week as a maintenance medication. Due to possible renal effects of oligonucleotide treatment, renal monitoring in the form of 24-hour urine collection (due to muscle breakdown in this patient population) is recommended before and during treatment.

In clinical trial, Vyondys 53 was found to increase dystrophin expression in skeletal muscle of treated patients. The Western Blot percent normal dystrophin change from baseline ranged from 0.01 to 3.99 depending on the patient. Dystrophin production did not appear to be dependent on Vyondys 53 dose. Patient-oriented clinical outcomes have not yet been reported for Vyondys 53 and clinical benefit has not been confirmed. Vyondys 53 is currently undergoing an open-label confirmatory trial evaluating 6-minute walk test (6MWT) at week 144 as a primary endpoint and pulmonary function testing as a secondary endpoint. Results are expected in 2 to 3 years.

Few treatment emergent adverse events were seen in clinical trials. Renal toxicity with Vyondys 53 was observed in pre-clinical trials in animals. Although it was not observed in clinical studies, renal toxicity (including potentially fatal glomerulonephritis) has been observed after administration of other antisense oligonucleotides (Exondys 51). Adverse reactions of Vyondys 53 include headache, pyrexia, fall, abdominal pain, nasopharyngitis, cough, vomiting, and nausea.

Vyondys 53 joins Exondys 51, which was controversially approved by the FDA in 2016, as a second in class antisense oligonucleotide. Exondys 51, like Vyondys 53, has not been proven to have a clinical benefit to date, and confirmatory trials have not yet been published. Vyondys 53 may be administered in clinic, or in home by an authorized home infusion company (Orsini or Option Care). Due to lack of other available treatments, utilization of Vyondys 53 for eligible patients is expected to be high.

Outcome: Vyondys 53 will be a medical benefit that is GHP managed for GHP Family members. Vyondys 53 should not be added to the GHP Family pharmacy formulary at this time. Vyondys 53 should require prior authorization with the following prior authorization criteria.

- Medical record documentation of interdisciplinary team involvement including, at a minimum, neurology, cardiology, pulmonology, and a genetic specialist (e.g. geneticist, genetic counselor, etc.) **AND**
- Medical record documentation of Duchenne's Muscular Dystrophy (DMD) confirmed by genetic testing **AND**
- Medical record documentation that the member has a confirmed mutation of the DMD gene that is amenable to exon 53 skipping confirmed by a genetic counselor **AND**
- Medical record documentation of a baseline evaluation, including a standardized assessment of motor function by a neurologist with experience treating Duchenne muscular dystrophy **AND**
- Medical record documentation that Vyondys 53 is being given concurrently with oral corticosteroids unless intolerant or contraindicated **AND**
- Medical record documentation that patient has stable pulmonary and cardiac function **AND**
- Medical record documentation that patient will receive a dose consistent with the FDA approved labeling (maximum dose of 30mg/kg infused once weekly)

Note: Exon Deletions* on the Duchenne Muscular Dystrophy Gene Theoretically Amenable to Exon 53 Skipping

3-52	4-52	5-52	6-52	9-52					
10-52	11-52	13-52	14-52	15-52	16-52	17-52	19-52		
21-52	23-52	24-52	25-52	26-52	27-52	28-52	29-52		
30-52	31-52	32-52	33-52	34-52	35-52	36-52	37-52	38-52	39-52
40-52	41-52	42-52	43-52	45-52	47-52	48-52	49-52		
50-52	52	54-58	54-61	54-63	54-64	54-66	54-76	54-77	

*The first number represents the first exon deleted. The last number is the last exon deleted. The dash (-) represents all exons in between the first and last exon deleted.

Authorization Duration: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of the following:

- Medical record documentation that the member continues to benefit from treatment with golodirsen **AND**
- Medical record documentation of an annual evaluation, including an assessment of motor function ability, by a neurologist with experience treating Duchenne muscular dystrophy **AND**
- Medical record documentation that Vyondys 53 continues to be given concurrently with oral corticosteroids unless intolerant or contraindicated **AND**
- Medical record documentation that patient continues to have stable pulmonary and cardiac function **AND**
- Medical record documentation that the patient will continue to receive a dose consistent with the FDA approved labeling (maximum dose of 30mg/kg infused once weekly)

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

Adakveo (crizanlizumab-tmca)

Review: Adakveo is indicated to reduce the frequency of vasoocclusive crises in adults and pediatric patients aged 16 years and older with sickle cell disease. Adakveo (crizanlizumab-tmca) is the third unique molecular entity approved for the management of the chronic complications associated with sickle cell disease (SCD), following hydroxyurea (Siklos, Droxia) and Endari (l-glutamine). Oxbryta received approval after Adakveo.

Adakveo is recommended to be dosed at 5 mg/kg by intravenous infusion over a period of 30 minutes at week 0, week 2, and every 4 weeks thereafter. It may be given with or without hydroxyurea and should be prepared and administered by a healthcare professional.

The efficacy of Adakveo was evaluated in patients with SCD in SUSTAIN, a 52-week, randomized, multicenter, placebo-controlled, double-blind study. A total of 198 patients with SCD and a history of 2 to 10 VOCs in the previous 12 months were eligible for inclusion. Patients were randomized 1:1:1 to Adakveo 5 mg/kg, Adakveo 2.5 mg/kg, or placebo administered over a period of 30 minutes by intravenous infusion on Week 0, Week 2, and every 4 weeks thereafter for a treatment duration of 52 weeks. Patients with SCD who received Adakveo 5 mg/kg had a lower median annual rate of VOC compared to patients who received placebo (1.63 vs. 2.98) which was statistically significant ($p = 0.010$). Reductions in the frequency of VOCs were observed among patients regardless of SCD genotype and/or hydroxyurea use.

There are no black box warnings or contraindications associated with Adakveo. Adakveo has warnings for infusion-related reactions and interference with automated platelet counts (platelet clumping). The most common adverse reactions (incidence > 10%) are nausea, arthralgia, back pain, and pyrexia. Based on animal studies, Adakveo may cause fetal harm when administered to a pregnant woman. The safety and efficacy in pediatric patients below age of 16 years have not been established.

Outcome: Adakveo is not managed by the PDL and will be covered as a medical benefit for GHP family members. Adakveo will require a prior authorization with the following criteria.

- Prescription written by or in consultation with a hematologist AND
- Medical record documentation of the member being ≥ 16 years of age AND
- Medical record documentation of diagnosis of sickle cell disease AND
- Medical record documentation of number of vasoocclusive crises in the previous 12 months AND

- Medical record documentation of intolerance to, or contraindication to, or therapeutic failure on a minimum 3 month trial of generic hydroxyurea AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Endari.

Authorization Duration: Each treatment period will be defined as 12 months. Re-review will occur every 12 months. The following criteria is recommended for reauthorization:
- Medical record documentation of continued or sustained improvement in the acute complications of sickle cell disease (i.e. number of vasooclussive crises, hospitalizations, and number of ACS occurrences)

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

Sarclisa (isatuximab-irfc)

Review: Sarclisa is indicated in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor. It is an IgG1 derived monoclonal antibody which binds a specific epitope on human cell surface antigen CD38 on myeloma cells and causes tumor cell death through multiple mechanisms of action, including antibody dependent cellular-mediated cytotoxicity, antibody dependent cellular phagocytosis and direct induction of apoptosis.

The efficacy of Sarclisa was shown in the ICARIA-MM study, a phase 3, open-label, randomized active control study in 307 patients with relapsed or refractory multiple myeloma who have received at least two previous lines of treatment and had not responded to therapy with lenalidomide and a proteasome inhibitor given alone or in combination. Patients were excluded if they were shown to be refractory to previous anti-CD38 treatments. Patients were randomized 1:1 to receive Sarclisa plus pomalidomide and dexamethasone (Isa-Pd) (n=154) or pomalidomide and dexamethasone (n=153).

The primary efficacy outcome found that Isa-Pd treatment group had a significantly longer median progression free survival compared to the group treated with pomalidomide and dexamethasone, with results consistent across all pre-specified subgroups analyzed (11.53 months vs. 6.47 months, respectively). Secondary endpoints showed a significantly greater overall response rate for the Isa-Pd group with more patients in the Isa-Pd treatment group demonstrating a partial response or a very good partial response compared to those who received only pomalidomide + dexamethasone (overall response rate of 60.4% vs. 35.3%, respectively).

Sarclisa includes warning and precautions for infusion related reactions, neutropenia, second primary malignancies, and risk of fetal harm. The most commonly reported reactions during the ICARIA-MM trial were neutropenia, infusion related reactions, pneumonia, upper respiratory tract infection and diarrhea.

Outcome: Sarclisa is a medical benefit and should not be added to the GHP Family pharmacy formulary. The following prior authorization criteria should apply:
- Medical record documentation that Sarclisa 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 diagnosis of multiple myeloma AND
- Medical record documentation of prior treatment with at least two lines of therapy which included lenalidomide and a proteasome inhibitor (including but not limited to Velcade*, Kyprolis*, or Ninlaro*) AND

- Medical record documentation that Sarclisa will be used in combination with pomalidomide and dexamethasone.

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 the member experiences unacceptable toxicity or worsening of disease.

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

Ubrelvy (ubrogepant)

Review: Ubrelvy is a calcitonin gene-related peptide receptor antagonist indicated for the acute treatment of migraine with or without aura in adults. Ubrelvy is the first oral calcitonin gene-related peptide (CGRP) antagonist indicated for the acute treatment of migraine. For mild to moderate migraine attacks, analgesics (NSAIDs, acetaminophen) are first-choice. For moderate to severe migraine attacks, oral triptans and triptan combinations (e.g. sumatriptan-naproxen) are recommended first-line.

The recommended dose of Ubrelvy 50 mg or 100 mg. If needed a second dose may be taken at least 2 hours after the initial dose. The maximum dose in a 24-hour period is 200 mg. The safety of treating more than 8 migraines in a 30-day period has not been established.

The efficacy of Ubrelvy for acute treatment of migraine was demonstrated in two randomized, double-blind, placebo-controlled trials. Both trials compared Ubrelvy to placebo. Up to 23% of patients taking preventive medications for migraine at baseline. None of these patients were on concomitant preventive medication that act on the CGRP pathway. The primary efficacy analyses were conducted in patients who treated a migraine with moderate to severe pain. The efficacy of Ubrelvy was established by an effect on pain freedom at 2 hours post-dose and most bothersome symptom (MBS) freedom at 2 hours post-dose, compared to placebo. In both studies, the percentage of patients achieving headache pain freedom and MBS freedom 2 hours post-dose was significantly greater among patients receiving Ubrelvy compared to those receiving placebo. The incidence of photophobia and phonophobia was reduced following administration of Ubrelvy at both doses (50 mg and 100 mg) as compared to placebo.

Ubrelvy is contraindicated with concomitant use of strong CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, clarithromycin), due to the increase in exposure of ubrogepant. There are no warnings and precautions listed in the labeling. The most common adverse reactions (2% and greater than placebo) were nausea and somnolence. The safety and effectiveness in pediatric patients have not been established.

Outcome: Ubrelvy is a pharmacy benefit and will not be added to formulary. Ubrelvy will require a prior authorization with the following criteria.

- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation that Ubrelvy will be used for the acute treatment of migraine with or without aura AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to nonsteroidal anti-inflammatory drug (NSAID) therapy AND

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) preferred antimigraine agents, triptans

Quantity Limit: Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).
16 tablets per 30 days

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

Oxervate (cenegermin-bkbj)

Review: Oxervate is indicated for the treatment of neurotrophic keratitis in patients 2 years of age or older. Neurotrophic keratitis (NK) has an estimated prevalence of fewer than five per 10,000 individuals, or about 65,000 people in the US. NK is a degenerative disease of the cornea caused by an impairment of trigeminal innervation. NK is a rare disease of the cornea, management was limited to only supportive care (e.g. artificial tears, antibiotics, and therapeutic contact lenses) and palliative surgical interventions. Oxervate (cenegermin-bkbj) is the first drug approved for neurotrophic keratitis (NK). Oxervate represents the first therapy to address the underlying cause of NK and repair corneal damage to prevent further vision loss, thus providing an alternative to more invasive palliative treatment options.

Oxervate is dosed at 1 drop in the affected eye(s) 6 times per day at 2 hour intervals, continued for a total of 8 weeks. Oxervate is supplied as a Delivery System Kit, with one week supply of 0.002% (20 mcg/mL) strength preservative-free, multi-dose vials closed with a stopper and cap. Each weekly kit contains 7 multi-dose vials in addition to auxiliary supplies: vial adapters, pipettes, disinfectant wipes, and a dose recording card. If both eyes are being treated, patients are required to use a separate vial for each eye.

Oxervate was studied in a total of 151 patients with NK from two 8-week, phase II, multi-centered, randomized, double-blinded, placebo-controlled clinical trials. Both trials compared Oxervate to placebo. The primary endpoint of REPARO (N=156) was the percentage of patients who achieved corneal healing (defined as <0.5 mm lesion staining) at week 4. Both strengths of cenegermin met statistical significance at weeks 4 and 8 in achieving corneal healing compared to placebo. There was a higher percentage of patients with complete corneal healing in the Oxervate arm compared to placebo at week 8 ($p<0.01$ in both studies). Of note, approximately 20% (REPARO) and 14% (NGF0214) of these patients experienced recurrence of corneal lesions. No difference was detected between Oxervate and placebo for the outcome of improving corneal sensitivity.

There are no black block warnings or contraindications for Oxervate. There is a warning that patients should remove contact lenses before applying Oxervate and wait 15 minutes after instillation of the dose before reinsertion. Also, there is a warning that Oxervate may cause mild to moderate eye discomfort such as eye pain during treatment.

The most common adverse effect (AE) in the Oxervate clinical trials was eye pain (16%). Other AEs occurring more frequently in Oxervate than placebo and at rates of 1-10%: corneal deposits, foreign body sensation, ocular hyperemia (enlarged blood vessels in the white of the eyes), ocular inflammation, and tearing.

For Oxervate, Dr. Upton requires patients to fail OTC tears/ointment and prescription treatment (Restasis, Xiidra, Cequa, serum tears) or punctal plug/ cautery

Outcome: Oxervate is a pharmacy benefit and it is not managed by the PDL. Oxervate will not be added to the GHP Family formulary and it will require a prior authorization with the following criteria.

- Prescription written by an ophthalmologist AND
- Medical record documentation of age greater than or equal to 2 years AND
- Medical record documentation of diagnosis of neurotrophic keratitis (NK) as confirmed by a decrease or loss in corneal sensitivity AND one of the following:
    - Superficial keratopathy
    - Persistent epithelial defects
    - Corneal ulcers

AND

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one conventional non-surgical treatment for neurotrophic keratitis (NK) (e.g. preservative-free artificial tears, gels/ointments; discontinuation of preserved topical drops and medications that can decrease corneal sensitivity; therapeutic contact lenses) AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to the preferred ophthalmics, immunomodulators (e.g. Restasis Droperette)

Authorization Duration: 8 weeks.
Reauthorization Criteria: For requests beyond the FDA-approved treatment duration (8 weeks), documentation of medical or scientific literature to support the use of this agent beyond the FDA-approved treatment duration is required.
Quantity Limit: Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization). **56 vials per 28 days**

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

HERCEPTIN BIOSIMILAR CLASS REVIEW

Review: Herzuma, Ontruzant, and Trazimera are three recently approved Herceptin biosimilars. They are the third, fourth, and fifth Herceptin biosimilars available in the US following Kanjinti and Ogivri and all five biosimilars share all indications of Herceptin in the treatment of adjuvant and metastatic breast cancer and metastatic gastric cancer. Trastuzumab products, including biosimilars, combined with chemotherapy in patients with HER2 positive metastatic breast and gastric cancer has significantly improved response rates, progression free survival, and overall survival as well as improved survival in early HER2 positive breast cancer.

In clinical trials, Herzuma, Ontruzant, and Trazimera demonstrated bioequivalence in the treatment of neoadjuvant/adjuvant (Herzuma and Ontruzant) and metastatic (Trazimera) breast cancer with comparable rates of objective responses as well as key secondary endpoints, including progression free survival and overall survival.

There were no significant differences in the incidence of reported adverse events between Herzuma, Ontruzant, and Trazimera and Herceptin and the safety profile of all three biosimilars were consistent with the known safety profile of Herceptin. All three biosimilars all had similar incidences and titers of anti-drug antibodies, indicated that there would be no increased risk of immunogenicity compared to Herceptin.

NCCN recommends all trastuzumab biosimilars as appropriate substitutes for Herceptin. It currently does not recommend one specific biosimilar product over another

Outcome:
Herzuma will be covered as a medical benefit and will not be added to the GHP Family pharmacy formulary. It will be managed by GHP and will not require a prior authorization.

Ontruzant will be covered as a medical benefit and will not be added to the GHP Family pharmacy formulary. It will be managed by GHP and will not require a prior authorization.

Trazimera will be covered as a medical benefit and will not be added to the GHP Family pharmacy formulary. It will be managed by GHP and will not require a prior authorization.

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

FAST FACTS

Mycamine (micafungin for injection)

Updated Indication: Treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses without meningoencephalitis and/or ocular dissemination in pediatric patients younger than 4 months of age.

Current formulary status: Mycamine is not managed by the PDL and is a medical benfit and does not require a prior authorization.

Recommendation: Based on the updated indication, there is no change recommended to formulary status or utilization management at this time

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

Yervoy (ipilimumab)

Updated Indication: Yervoy is now indicated for patients with hepatocellular carcinoma who have been previously treated with sorafenib, in combination with nivolumab.

Current formulary status: Medical benefit requiring prior authorization, managed by GHP

Recommendation: There are no changes recommended to the formulary placement of Yervoy. It is recommended to add the following prior authorization criteria and authorization duration:

- Prescription written by a hematologist/oncologist AND
- Medical record documentation of hepatocellular carcinoma AND
- Medical record documentation of a therapeutic failure on or intolerance to sorafenib (Nexavar)
- Medical record documentation that Yervoy will be used in combination with nivolumab (Opdivo)

Authorization Duration
Approval will be for one (1) 6-month authorization for the FDA-approved maximum of up to four (4) doses of Yervoy. Requests for authorization exceeding these limits will require the following:

- Medical record documentation of continued disease improvement or lack of disease progression AND

- Medical record documentation of 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

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

Opdivo (nivolumab)

Updated Indication: Opdivo is a programmed death receptor-1 (PD-1) blocking antibody indicated for the treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib, as a single agent or in combination with ipilimumab.

Current formulary status: Medical benefit requiring prior authorization, managed by GHP

Recommendation: There are no changes recommended to the formulary placement or the authorization duration of Opdivo for hepatocellular carcinoma. It is recommended to add the following prior authorization criteria:

For Hepatocellular Carcinoma

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation of hepatocellular carcinoma **AND**
- Medical record documentation of a therapeutic failure on or intolerance to sorafenib (Nexavar) **AND**
- Medical record documentation that Opdivo will be used as a single-agent or in combination with ipilimumab (Yervoy)

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

Imfinzi (durvalumab)

Updated Indication: Imfinzi is now indicated in combination with etoposide and either carboplatin or cisplatin, as first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).

Current formulary status: Medical benefit requiring prior authorization, managed by GHP

Recommendation: No changes are recommended to the formulary placement of Imfinizi. It is recommended to add the following prior authorization criteria and authorization duration:

Extensive-Stage Small Cell Lung Cancer

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is greater than or equal to 18 years of age **AND**
- Medical record documentation of extensive-stage small cell lung cancer (ES-SCLC)***AND**
- Medical record documentation that Imfinzi will be used as first-line treatment **AND**
- Medical record documentation that Imfinzi will be used in combination with etoposide and either carboplatin or cisplatin

*Note: NCCN defines small cell lung cancer as consisting of two stages:
Limited Stage: Stage I-III (T any, N any, M0) that can be safely treated with definitive radiation doses. Excludes T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan.

Extensive Stage: Stage IV (T any, N any, M1a/b), or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan

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

DUR UPDATE

Drug Use Evaluations (DUEs)

- Coronary Artery Disease DUE
    - This is the 2020 1st quarter MedImpact DUE for all LOBs
    - From this report, we identified 90 members age 40-75 years who are not on a statin drug therapy in a 3-month timeframe and who have at least one of the following cardiovascular disease (CVD) risk factors: diabetes, hypertension, or smoking.
    - Brandy P. is completed the mail merge and sent out letters to the member's providers on 2/21/2020.
    - We will have Adam K. re-run this data in June 2020 to show us the effectiveness of the letter.
- Statin Use in Persons with Diabetes DUE
    - This is the 2019 4th quarter MedImpact DUE for Commercial/Exchange and GHP Family
    - From this report, we identified 89 members whose medication history was suggestive of the presence of diabetes and who were not receiving a statin drug during the previous three-month period.
    - Brandy P. completed the mail merge and sent out the letters to the member's providers on 12/5/2019.
    - Adam K. was able to re-run the data on this population on 3/27/2020 and of the original 89 members that we sent letters to 81 are still active. Of those 81 members, 18 now have a claim for a statin. This equates to 22% of the members.
- Asthma DUE
    - This is the 2019 3rd quarter MedImpact DUE for all LOBs
    - From this report, we identified 90 members who received 4 or more prescriptions for an asthma medication over a 12-month period but did not receive an asthma controller medication in that same 12-month period.
    - Brandy P. completed the mail merge and sent out the letters to the member's providers on 8/26/2019.
    - Adam K. was able to re-run the data on this population on 12/13/2019 and of the original 90 members that we sent letters to 81 members are still active. Of those 81 members 6 members now have a claim for an ACEI or ARB medication. This equates to 7.4% of the members.
- Congestive Heart Failure DUE
    - This is the 2019 2nd quarter MedImpact DUE for Commercial/Exchange and GHP Family
    - From this report, we identified 90 members who have a presumed diagnosis of heart failure taking metoprolol succinate, carvedilol, or bisoprolol, and who were not taking an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) drug therapy in a 3-month timeframe.

- Adam K. was able to re-run the data on this population on 9/25/2019 and of the original 90 members that we sent letters to 76 members are still active. Of those 76 members 7 members now have a claim for an ACEI or ARB medication. This equates to 9.2% of the members.

In Progress

- STENT Adherence Report
  - Currently in the process of functionalizing an adherence report to replace the current STENT program
  - We will identify members on an antiplatelet medication and then flag for betablocker and statin medication claims
    - We will assess adherence to all 3 medications and outreach to members with PDC <80% via letter and/or telephonic outreach
- HEDIS Reports
  - Statin Therapy for Patients with Diabetes (SPD)
    - In the process of functionalizing a report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
      - We will reach out to providers to initiate therapy and members to encourage adherence via letter
  - Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - In the process of functionalizing a report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
      - We will reach out to providers to initiate therapy and members to encourage adherence via letter

Ongoing

- DUR Duplicate Anticoagulant Report
  - We get this report weekly for all LOBs flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/pharmacy of the flagged members to confirm proper medication therapy.
    - For GHS30 in 2020, we have reviewed 9 members and have made interventions for 3 members
- Duplicate Specialty Therapy
  - We run an in-house retrospective report quarterly for all LOBs with help from Adam Kelchner and Aubrielle Prater. These members are identified and written up and sent to a medical director if follow up is needed.
    - For GHS30 in 2020, we have reviewed the Q1 report (9/2019-12/2019) and have discussed 1 patient with Dr. Yarczower for intervention
- Duplicate Buprenorphine Therapy
  - We are getting this report quarterly with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows for further outreach.
    - For GHS30 in 2020, we have reviewed 14 members and 4 members were referred to Dr. Meadows
- Suboxone with an Opioid Report
  - We are getting this report weekly for all LOBs from Adam Kelchner and we are writing up each member that flags on the report. These members are being forwarded to Dr. Meadows, and he is looking into whether it is appropriate to end the opioid authorizations still in place
    - For GHS30 in 2020, we have reviewed 35 new members, and 5 members were referred to Dr. Meadows
- Ending Opioid Authorizations

- We are working on identifying members who have active opioid authorizations in place but have since started Buprenorphine therapy. The letter is sent to the members notifying them the opioid authorization has been ended due to the start of buprenorphine therapy.
    - For GHS30 in 2020, we have sent 4 members letters notifying them of the end of their opioid authorization

- Medicaid Opioid Overutilization Report
    - We are getting this report monthly from MedImpact and we are writing up each member that flags on the report. We have been monitoring the members that are continuously showing up on the report by any change in their MED. For those members we deem appropriate we will send a letter to their PCP.
        - For GHS30 in 2020, we have reviewed 1 case so far, have not referred any patients to Dr. Meadows, and did not send any prescriber letters
- FWA Reports
    - We are getting this report weekly for all LOBs from Marie Strausser. We prepare this report by determining which claims need to be verified, and the Wilkes pharmacy students/GHP technicians have been making the calls to pharmacies.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For GHS30 in 2020, we have reviewed 169 cases so far and corrected 112 claims, resulting in a cost savings of $9,237.03
- Severity Report
    - This is a monthly report for all LOBs on members who have filled a medication that has a level one interaction with another medication they have a claim for
        - For GHS30 in 2020, we have sent letters to providers on 42 GHP Family members
- Duplicate Antipsychotics
    - Adam Kelchner runs this report quarterly, and we send letters to the PCPs to address potential duplicate therapy issues.
        - For GHS30 in 2020, we have sent letters to 70 providers so far concerning patients on multiple antipsychotics.
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - Kayla Stanishefski runs this report monthly, and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
    - HEDIS Specifications: The percentage of members 19-64 years of age during the measurement year with schizophrenia or schizoaffective disorder who were dispensed and remained on an antipsychotic medication for at least 80% of their treatment period.
        - Currently working on the mail merge for the first release of proactive HEDIS data
- Enbrel Overutilization for Treating Plaque Psoriasis
    - A monthly report was created to identify members who have been overutilizing Enbrel twice weekly dosing as outlined by the FDA approved dose.
        - We put in place QLs for Enbrel, so we should not be seeing these cases moving forward for new starts or for re-authorization
            - For GHS30 in 2020 we have not identified any members
- Tobacco Cessation Program
    - We are getting this report monthly to identify members on prolonged tobacco cessation treatment. We send a letter and resource pamphlet to provide additional behavioral health support through Geisinger Health and Wellness.
        - For GHS30 in 2020, we have sent letters to 58 members so far.
- Antidepressant Medication Management
    - Kayla Stanishefski runs this proactive HEDIS report monthly, and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
        - Currently working on the mail merge for the first release of proactive HEDIS data

- Asthma Medication Ratio
    - Kayla Stanishefski runs this proactive HEDIS report monthly, and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
        - Currently working on the mail merge for the first release of proactive HEDIS data
- Medication Management for People with Asthma
    - Kayla Stanishefski runs this proactive HEDIS report monthly, and we send letters to the flagged members who appear non-adherent to their asthma controller medications.
        - Currently working on the mail merge for the first release of proactive HEDIS data
- Antipsychotic with Opioid Report
    - This is a quarterly report to identify Medicaid members with an overlap of 8 or more days between an opioid and antipsychotic medication.
    - We send a letter with claims data to both the opioid prescriber and the antipsychotic prescriber to encourage collaboration in medication management.
        - For GHS30 in 2020, we have identified 163 patients and sent 150 letters to opioid prescribers and 136 letters to antipsychotic prescribers.

Completed

- Medicaid DUR/FWA Program Fliers
    - Last updated 02/2020 next update 06/2020
- Current Provider Letters
        - Congestive Heart Failure DUE
        - Coronary Artery Disease DUE
        - Statin Use in Persons with Diabetes DUE
        - Asthma MED Ratio DUE
        - Opioid Overutilization
        - Duplicate Antipsychotics
        - Severity Report
        - Duplicate Anticoagulant Report
        - Antipsychotic with Opioid Report
- Current Member Letters
        - Ending Opioid Authorizations
        - Adherence to Antipsychotics-SAA
        - Antidepressant Medication Management-AMM
        - Asthma Medication Ratio-AMR
        - Medication Management for People with Asthma-MMA

April Electronic Vote

Due to the volume of line extensions that must reviewed by the P&T Committee an additional electronic vote was held from Wednesday April 8, 2020 to April 15, 2020. Responses were received from 24 members (out of 35) and all voted to approve.

The following was approved for GHP Family:

Drug	**Dosage Form and Strength**	**Formulary Therapeutic Recommendation**
Caplyta	Capsule	Add QL of 1/day
Stelara	Vial/Syringe	Add QL for UC: Initial authorization: 104 mL per 56 days, Remainder/Subsequent Authorizations: 1 mL per 56 days

The following vaccines will be allowed to process at pharmacies:

VACCINE	STRENGTH	FDA APPROVED INDICATION	FDA APPROVED AGE RANGE	AGE RESTRICTION RECOMMENDATIONS
ADACEL TDAP (DIPH,PERTUSS(ACELL),TET VAC/PF	2-2.5-5/.5	Active booster immunization against tetanus, diphtheria and pertussis	10 – 64 years	18 years up to and including 64 years
BEXSERO (MENINGOCOCCAL B VACCINE,4-COMP)	50-50/0.5	Active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B	10 – 25 years	18 years up to and including 25 years
BOOSTRIX TDAP (DIPHTH,PERTUSS(ACELL),TET VAC)	2.5-8-5/.5	Active booster immunization against tetanus, diphtheria, and pertussis	10 years and older	18 years and up
ENGERIX-B ADULT (HEPATITIS B VIRUS VACCINE/PF)	20 MCG/ML	Immunization against infection caused by all known subtypes of hepatitis B virus	20 years and older	20 years and up
ENGERIX-B PEDIATRIC-ADOLESCENT (HEPATITIS B VIRUS VACCINE/PF)	10 MCG/0.5	Immunization against infection caused by all known subtypes of hepatitis B virus	Birth – 19 years	18 years up to and including 19 years
GARDASIL 9 (HPV VACCINE 9-VALENT/PF)	0.5 ML	Prevention of diseases caused by Human Papillomavirus (HPV) types 6, 11, 16, 18, 31, 33, 45, 52, and 58	9 – 45 years	18 years up to and including 45 years
HAVRIX (HEPATITIS A VIRUS VACCINE/PF)	1440/ML	Active immunization against disease caused by hepatitis A virus (HAV)	19 years and older	19 years and up
HAVRIX (HEPATITIS A VIRUS VACCINE/PF)	720/0.5ML	Active immunization against disease caused by hepatitis A virus (HAV)	12 months – 18 years	18 years only
HEPLISAV-B (HEPATITIS B VACCINE/CPG1018/PF)	20 MCG/0.5	Prevention of infection caused by all known subtypes of hepatitis B virus	18 years and older	18 years and up
MENACTRA (MENING VAC A,C,Y,W-135 DIP/PF)	4MCG/0.5 ML	Active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135	9 months – 55 years	18 years up to and including 55 years
MENVEO* (MENING VAC A,C,Y,W-135 DIP/PF) *SUPPLIED AS A KIT	10-5/0.5ML	Active immunization to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135	2 months – 55 years	18 years up to and including 55 years
M-M-R II VACCINE (MEASLES,MUMPS,RUBELLA VACC/PF)	12500/0.5	Simultaneous vaccination against measles, mumps, and rubella	12 months and older	18 years and up

PNEUMOVAX 23 (PNEUMOCOCCAL 23-VAL P-SAC VAC)	25MCG/0.5	Active immunization for the prevention of pneumococcal disease caused by the 23 serotypes contained in the vaccine (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F)	50 years of age or older and persons aged ≥2 years who are at increased risk for pneumococcal disease	18 years and up
PREVNAR 13 (PNEUMOC 13-VAL CONJ-DIP CRM/PF)	0.5 ML	In adults 18 years of age and older: active immunization for the prevention of pneumonia and invasive disease caused by *S. pneumoniae*	6 weeks and older	18 years and up
RECOMBIVAX HB (HEPATITIS B VIRUS VACCINE/PF)	10 MCG/ML	Prevention of infection caused by all known subtypes of hepatitis B virus	20 years and older	20 years and older
RECOMBIVAX HB (HEPATITIS B VIRUS VACCINE/PF)	5 MCG/0.5ML	Prevention of infection caused by all known subtypes of hepatitis B virus	Birth – 19 years	18 up to and including 19 years
RECOMBIVAX HB DIALYSIS (HEPATITIS B VIRUS VACCINE/PF)	40 MCG/ML	Prevention of infection caused by all known subtypes of hepatitis B virus	18 years and older	18 years and older
SHINGRIX* (VARICELLA-ZOSTER GE/AS01B/PF) *SUPPLIED AS A KIT	50 MCG/ML	Prevention of herpes zoster (shingles)	50 years and older	50 years and older
TDVAX (TETANUS, DIPHTHERIA TOX,ADULT)	2-2 LF/0.5	Active immunization for the prevention of tetanus and diphtheria	7 years and older	18 years and up
TENIVAC (TETANUS-DIPHTHERIA TOXOIDS/PF)	5-2/0.5ML	Active immunization for the prevention of tetanus and diphtheria	7 years and older	18 years and up

TRUMENBA (N.MENINGITIDIS B,LIPID FHBP RC)	120MCG/0.5	Active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B	10 – 25 years	18 up to and including 25 years
TWINRIX (HEPATITIS A AND B VACCINE/PF)	720-20/ML	Active immunization against disease caused by hepatitis A virus and infection by all known subtypes of hepatitis B virus	18 years and older	18 years and up
VAQTA (HEPATITIS A VIRUS VACCINE/PF)	25/0.5ML	Prevention of disease caused by hepatitis A virus (HAV)	12 months – 18 years	18 years only

VAQTA (HEPATITIS A VIRUS VACCINE/PF)	50 UNIT/ML	Prevention of disease caused by hepatitis A virus (HAV)	19 years and older	19 years and up
ZOSTAVAX* (ZOSTER VACCINE LIVE/PF) *SUPPLIED AS A KIT	19400 UNIT	Prevention of herpes zoster (shingles)	50 years and older	50 years and up

Pretomanid (pretomanid) Drug Review
Mylan Laboratories Limited
Pharmacy Benefit

Review: Pretomanid is indicated, as part of a combination regimen with Sirturo (bedaquiline) and linezolid for the treatment of adults with pulmonary extensively drug resistant tuberculosis (XDR-TB) or treatment-intolerant or nonresponsive multidrug-resistant tuberculosis (TI/NR MDR-TB). Pretomanid Tablets are not indicated in patients with the following conditions: Drug-sensitive (DS) tuberculosis, Latent infection due to Mycobacterium tuberculosis, Extra-pulmonary infection due to Mycobacterium tuberculosis, or MDR-TB that is not treatment-intolerant or nonresponsive to standard therapy. The safety and effectiveness of Pretomanid Tablets have not been established for its use in combination with drugs other than Sirturo (bedaquiline) and linezolid.

Pretomanid is the first agent approved in the novel nitroimidazooxazine class, which inhibits mycolic acid biosynthesis & cell wall production. . The indication is limited to patient with one of the following forms of pulmonary tuberculosis TI/NR MDR-TB or XDR-TB. TI/NR MDR-TB are organisms that are resistant to rifampin and isoniazid. In addition, patients with MDR TB may fail or be intolerant to standard of care therapy. The standard of care for MDR TB is a customized regimen of usually 4 anti-tubercular agents to which the organism remains sensitive for a duration of 9 to 18 months or more. Agents may include moxi/levo-floxacin, bedaquiline, linezolid, clofazimine, cycloserine, ethambutol, pyrazinamide, mero/imi-penem, and aminoglycosides (amikacin, streptomycin). XDR-TB organisms meet the MDR criteria but are also resistant to a fluoroquinolone and either an aminoglycoside or capreomycin. Treatment options for XDR are poor, with a five-drug regimen of the previously mentioned agents being recommended, continuing for 6 months beyond sputum culture conversion. The recommended dosage of pretomanid is 200mg (1 tablet) orally once daily for 26 weeks. Dosing of the combination regimen may be extended beyond 26 weeks if necessary.

Pretomanid was approved based on a single, prospective, open-label study in patients with XDR, treatment-intolerant MDR, or non-responsive MDR pulmonary TB. The patients received a combination regimen of pretomanid tablets, bedaquiline, and linezolid for six months (extended to 9 months in two patients) with 24 months of follow-up. Treatment failure was defined as the incidence of bacteriologic failure (reinfection – culture conversion to positive status with different M. tuberculosis strain), bacteriological relapse (culture conversion to positive status with same M. tuberculosis strain), or clinical failure through follow-up until 6 months after the end of treatment. Of the 107 patients assessed, outcomes were classified as success for 95 (89%) patients and failure for 12 (11%) patients. The success rate significantly exceeded the historical success rates for XDR-TB. The outcomes were similar in both HIV negative and HIV positive patients.

There are no black box warnings associated with pretomanid. Several warnings and precautions are included in the pretomanid Prescribing Information. Because the drug was always given in combination with bedaquiline and linezolid in the NIX-TB trial, it is not possible to know what proportion of risk for these adverse events is due to pretomanid, but it appears that pretomanid confers little to no additive risk for the following adverse effects: hepatic adverse effects, myelosuppression, peripheral and optic neuropathy, QT prolongation, and lactic acidosis. One warning/precaution that is unique to pretomanid surround its reproductive effects. Pretomanid caused testicular atrophy and impaired fertility in male rats. The most common adverse reaction (≥ 10%) are peripheral neuropathy, acne, anemia, nausea, vomiting, headache, increased transaminases, dyspepsia, decreased appetite, rash, pruritus, abdominal pain, pleuritic pain, increased gamma-glutamyltransferase, lower respiratory tract infection,

hyperamylasemia, hemoptysis, back pain, cough, visual impairment, hypoglycemia, abnormal loss of weight, and diarrhea. The safety and effectiveness in pediatric patients have not been established.

Outcome: Pretomanid will be a pharmacy benefit. It is recommended that Pretomanid be added to the GHP Family formulary at the Brand tier. Pretomanid will require a prior authorization with the following criteria.

- Prescription written by a physician specializing in infectious disease AND
- Medical record documentation of age greater or equal to 18 years AND
- Medical record documentation of pulmonary infection due to *Mycobacterium tuberculosis* AND
- Medical record documentation of one of the following:
    - Extensively drug resistant tuberculosis (XDR-TB) OR
    - Treatment-intolerant or nonresponsive multidrug-resistant tuberculosis (TI/NR MDR-TB) AND
- Medical record documentation that Pretomanid will be used in combination with Sirturo (bedaquiline) and linezolid

Authorization Duration: 26 weeks
Quantity Limit: Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).
One (1) tablet per day
Note to Reviewer:

- TI/NR MDR-TB (Treatment-Intolerant or Nonresponsive Multi-Drug Resistant TB). MDR-TB organisms are resistant to rifampin and isoniazid and possibly additional agents.
- XDR-TB (Extensively Drug Resistant TB). These organisms are resistant to isoniazid, rifampin, and fluoroquinolones as well as either aminoglycosides and/or capreomycin.

Future Scheduled Meetings

The next bi-monthly scheduled meeting will be held on Tuesday July 21, 2020 at 1:00 HCN3A & 3B Conference room

All of these meetings are scheduled to be held at Geisinger Health Plan, Hughes Center North and South Buildings; 108 Woodbine Lane; Danville, PA 17821.