P&T Committee Meeting Minutes
Commercial/Marketplace/GHP Kids E-vote
May 14, 2020

Review and Approval of Minutes:
The March 17, 2020 and April 15, 2020 minutes were approved as written by a unanimous vote. None were opposed.

DRUG REVIEWS

ABILIFY MYCITE (aripirazole)

Review: Abilify Mycite is a drug-device combination which consists of an aripiprazole tablet which is embedded with an Ingestible Event Marker (IEM) sensor, a MYCITE® patch which detects the IEM sensor signal and sends the data to a smart phone, and the MYCITE® smartphone application. In order to detect ingestion, patients need to download the app onto a compatible smart phone which is powered on and Bluetooth®-enabled. Physicians can access the data through a web-based portal which receives data from the smartphone application.

The patch may detect most ingestions within 30 minutes, but it may take up to two hours for the smartphone app and web portal to detect ingestion and in some cases, ingestion may not be detected. Because of this lag time, Abilify Mycite should not be used in emergency situations.

The ability of Abilify Mycite to improve patient compliance and adjust aripiprazole dosage has not been established.

No new safety concerns were identified during the development of Abilify Mycite. In the simulated-use human factor patient interface validation study, rash at the site of patch placement occurred in 12.4% of 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: Abilify Mycite is a pharmacy benefit that will not be added to the formulary. The following prior authorization criteria will apply:

- Medical record documentation of one of the following:
    - Diagnosis of schizophrenia **OR**
    - Diagnosis of use for acute treatment of manic and mixed episodes or maintenance treatment of Bipolar I disorder as monotherapy or as adjunct to lithium or valproate **OR**
    - Diagnosis of use as adjunctive treatment of major depressive disorder

AND

- Medical record documentation of age 18 years or older **AND**

- Medical record documentation of a history of poor adherence to oral medications and documentation that education to improve adherence has been attempted **AND**
- Medical record documentation of access to a compatible smart phone **AND**
- Medical record documentation of one of the following:
    - For schizophrenia and bipolar I disorder:
        - Medical record documentation of reason why aripiprazole oral tablets **AND** Abilify Maintena cannot be used

    OR
    - For major depressive disorder (MDD)
        - Medical record documentation of reason why aripiprazole oral tablets cannot be used

AUTHORIZATION DURATION: Initial authorizations for Abilify Mycite will be approved for a period of 12 months. Reauthorizations will be for a period of 12 months each provided the following criteria are met:

- Claims history and attestation from the provider showing the patient is adherent to Abilify Mycite **OR** continued need to monitor drug ingestion.

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.

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.

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: Adakveo is a medical benefit that will be covered with the following prior authorization 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.

CONSENSI (amlodipine and celecoxib)

Review: Consensi is a new combination product consisting of amlodipine and celecoxib, indicated for use in patients with hypertension and osteoarthritis. Consensi is only available in a celecoxib strength of 200mg and is only to be administered once a day. If analgesic therapy is no longer needed, Consensi should be discontinued and a different antihypertensive medication should be initiated.

The approval of Consensi was based on the clinical trials of the individual drug components rather than a new clinical trial. A pharmacokinetic study of Consensi found that combing amlodipine with celecoxib provided similar blood pressure reductions as compared to amlodipine monotherapy. The listed safety considerations are consistent with the safety considerations of the individual products. No new safety considerations were added with the approval of Consensi.

Consensi is not recommended to be used for short term therapy; however, Consensi is to be used at the lowest dose and shortest duration as possible to decrease the risk of cardiovascular related events. This suggests that Consensi is only appropriate for patients requiring regular NSAID therapy, but the treatment should be limited as clinically appropriate. Consensi utilization is dependent on when the individual

agents are used in their respective disease states. Since Consensi does not offer any advantages in efficacy or safety, the main benefit of Consensi is reducing pill burden for patients but carries limitations in the flexibility of dose escalation and de-escalation.

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: Consensi is a pharmacy benefit that will not be added to the formulary. The following prior authorization criteria will apply:

- Medical record documentation of a therapeutic failure or intolerance to an adequate trial of 3 combinations of formulary NSAID **AND** Calcium-Channel Blocker therapies, one of which MUST be amlodipine and celecoxib used in combination

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.

ESPEROCT (antihemophilic factor (recombinant) glycopegylated-exei)

Review: Esperoct is a coagulation Factor VIII concentrate indicated for use in adults and children with hemophilia A for on-demand treatment and control of bleeding episodes, perioperative management of bleeding, and routine prophylaxis to reduce the frequency of bleeding episodes. Esperoct joins Jivi and Adynovate as a recombinant FVIII concentration that uses PEGylation technology for on-demand treatment, perioperative management, and routine prophylaxis for patients with hemophilia A. Esperoct shares similar indications to Jivi and Adynovate; however, Esperoct and Adynovate are approved for use in children and adults with hemophilia A, whereas Jivi is limited to previously treated adolescents (≥ 12 years) and adults. Adynovate allows for twice weekly dosing in routine prophylaxis. Jivi can be administered twice weekly to every 5 days based on bleeding episodes on the twice weekly dosing. Esperoct is administered every 4 days for prophylaxis in patients 12 years and older and twice weekly in patients < 12 years.

The safety and efficacy of Esperoct have been evaluated in five multinational, open-label trials in male subjects with severe hemophilia A (<1% endogenous Factor VIII activity). All subjects were previously treated. There were a total of 1506 bleeds reported across the clinical trials. For patients on-demand therapy, 88.4% of bleeds were successfully treated with a single dose. In patients receiving prophylaxis, 76.4% were treated with a single dose. For severe bleeds, 80% required more than one dose. In pediatric patients receiving prophylaxis, 63% of mild to moderate were treated with a single injection. In perioperative management, the hemostatic effect was rated as excellent or good in 95.6% of surgeries. For routine prophylaxis with every 4 day dosing in adult and adolescent population, the median ABR was 1.2 and the mean ABR was 3.2 for all bleeds (treated and untreated). For routine prophylaxis in pediatric patients (0 to < 12 years) with twice weekly dosing, the median ABR was 2 and the mean ABR was 4.4 for all bleeds.

Esperoct is contraindicated in patients who have known hypersensitivity to Esperoct or its components, including hamster proteins. Esperoct has warnings for hypersensitivity reactions (including anaphylaxis) and development of neutralizing antibodies (inhibitors). The most common adverse reactions (≥ 1%) were rash, redness, itching and injection site reactions.

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: Esperoct is a pharmacy or medical benefit. Esperoct will be added to the pharmacy formulary on the specialty tier or the brand non-preferred tier for members with a three tier benefit. Esperoct will be added to the existing pharmacy policy – Antihemophilic Agents for Hemophilia A (514.0):

- Medical record documentation of a diagnosis of hemophilia A (a documented Factor VIII deficiency) **AND**
- Medical record documentation that the antihemophilic agent will be for outpatient use **AND**
- Medical record documentation that the antihemophilic agent will be used appropriate for routine prophylaxis, on-demand treatment/control of bleeding episodes, OR perioperative management of bleeding **AND**
- If request is for Jivi, the following criteria must be met:
    - Member is ≥ 12 years of age **AND**
    - Medical record documentation that the member has previously received treatment for hemophilia A with a Factor VIII product

	Routine Prophylaxis	**On-Demand/ Perioperative**
Advate	X	X
Adynovate	X	X
Afstyla	X	X
Eloctate	X	X
Esperoct	X	X
Helixate FS	X	X
Hemofil M		X
Jivi	X	X
Koate/Koate-DVI		X
Kogenate FS	X	X
Kovaltry	X	X
Monoclate-P		X
Novoeight	X	X
Nuwiq	X	X
Obizur		X
Recombinate		X
Xyntha/Xyntha Solofuse		X

Note: Obizur is indicated for adult patients with acquired hemophilia A.

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.

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: Givlaari is a medical benefit that will be covered with the following prior authorization criteria:

- 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.

KOSELUGO (selumetinib)

Review: Koselugo is a kinase inhibitor indicated for the treatment of pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN). Koselugo, a kinase inhibitor, is the first agent approved by the Food & Drug Administration (FDA) for neurofibromatosis type 1 (NF1), a rare, debilitating autosomal dominant genetic condition. For patients with FN1 with PNs, surgery and pain management are often the mainstay of treatment, noting that when surgical removal of these tumors is not feasible, the quality of life in pediatric patients is severely impacted. The recommended dosage of Koselugo is 25 mg/m2 orally twice daily (approximately every 12 hours) until disease progression or unacceptable toxicity. There are dose adjustments recommended for adverse reactions, hepatic impairment, and use with strong/moderate CYP3A4 inhibitors/fluconazole.

The efficacy of Koselugo was assessed in SPRINT Phase II Stratum 1, an open-label, multicenter, single arm trial. Eligible patients were required to have NF1 with inoperable PN. Patients were also required to have significant morbidity related to the target PN. Patients received Koselugo 25 mg/m2 orally twice daily until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall response rate (ORR), defined as the percentage of patients with complete response (defined as disappearance of the target PN) or confirmed partial response (defined as $\geq$ 20% reduction in PN volume confirmed at a subsequent tumor assessment within 3-6 months). Sixty-six percent of patients had an overall response rate (all partial responses). There was no complete response. Eighty-two percent of

patients had a duration of response ≥ 12 months. The median onset to response was 7.2 months (range: 3.3 months to 1.6 years).

Koselugo has no boxed warnings or contraindications, but does have warnings and precautions for cardiomyopathy, ocular toxicity, gastrointestinal toxicity/diarrhea, skin toxicity, increased creatinine phosphokinase, and embryo-fetal toxicity. Additionally, vitamin E intake must be monitored since Koselugo may increase the risk of bleeding because the capsules contain vitamin E as the excipient, Dalpha-tocopheryl polyethylene glycol 1000 succinate (TPGS). The most common adverse reactions (≥ 40%) were vomiting, rash (all), abdominal pain, diarrhea, nausea, dry skin, fatigue, musculoskeletal pain, pyrexia, acneiform rash, stomatitis, headache, paronychia, and pruritus. The safety and effectiveness only was studied in patients ≥ 2 years to < 18 years.

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: Koselugo is a pharmacy benefit that will be added to the formulary on the OralOncBrandNP tier. The following prior authorization criteria will apply:

- Medical record documentation of prescription written by or in consultation with at least one of the following:
    - A pediatric oncologist
    - A pediatric neurologist
    - A pediatric geneticist **AND**
- Medical record documentation of age ≥ 2 years **AND**
- Medical record documentation of neurofibromatosis type 1 as defined by:
    - Two of the following*:*
        - Six or more brown oval/circular spots on the skin called café-au-lait macules (> 5 mm diameter in prepubertal individuals and > 15 mm in post-pubertal individuals)
        - Freckling in axillary or inguinal regions
        - Two or more neurofibromas of any type, or one plexiform neurofibroma
        - A tumor of the nerve to the eye called optic glioma
        - Two or more Lisch nodules (iris hamartomas)
        - A distinctive osseous lesion (sphenoid dysplasia or tibial pseudarthrosis)
        - A first degree relative with NF1

          OR
    - A positive *NF1* mutation

  AND
- Medical record documentation of symptomatic, inoperable* plexiform neurofibromas (PN).

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.

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).

- 10 mg capsules: 8 capsules per day
- 25 mg capsules: 4 capsules per day

NOTE: In clinical trials, inoperable PN was defined as a PN that could not be completely removed without risk for substantial morbidity due to encasement of, or close proximity to, vital structures, invasiveness, or high vascularity of the PN.

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.

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: Oxbryta is a pharmacy benefit that will not be added to the formulary. The following prior authorization criteria will 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.

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.

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: Oxervate is a pharmacy benefit that will be added to the formulary on the specialty tier or the brand non-preferred tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- 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 Restasis or Xiidra

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: 56 vials per 28 days
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).

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.

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: Recarbrio is a medical benefit that will be covered with the following prior authorization criteria:

- 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* **OR**
    - 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

QUANTITY LIMIT: 4 vials/day, FACETS Rx count: 7000 units

AUTHORIZATION DURATION: up to 14 days

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.
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: Sarclisa is a medical benefit that will be covered with the following prior authorization criteria:

- 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.

SECUADO (asenapine)

Review: Secuado is a once-daily transdermal patch containing asenapine which is approved for the treatment of adult patients with schizophrenia. Asenapine is also the active ingredient in Saphris, an ODT formulation which is approved for adults with schizophrenia and for bipolar disorder in patients 10 years of age and older. Secuado was shown in studies to have similar bioavailability to Saphris and offers a more convenient once-daily dosing as well as eliminates the mouth and tongue reactions that can occur with the ODT formulation.

The approval for Secuado is supported by studies comparing the bioavailability to Saphris as well as a 6-week, randomized, double-blind, placebo-controlled fixed dose efficacy study in 614 inpatient adult patients. Patients included in the trial met the DSM-5 criteria for schizophrenia and currently had an acute exacerbation of schizophrenic symptoms with a current episode duration of eight weeks or less and hospital stay length of 21 days or less. Following a 3- to 14- day screening/run in period, patients were randomized 1:1:1 to receive one Secuado TDS + one placebo TDS, two Secuado TDS, or two placebo TDS. The primary endpoint measuring change from baseline to week 6 in Positive and Negative Syndrome Scale (PANSS) and the secondary endpoint measuring change from baseline to week 6 in Clinical Global Impressions-Severity (CGI-S) both showed statistically significant improvement for both Secuado treatment groups for the symptoms of schizophrenia and overall clinical state.

The most prominent safety concern identified during clinical trials of Secuado were application site reactions, most commonly erythema and mostly mild to moderate in severity. Other than the increase in application site reactions, the overall safety findings were consistent the known safety profile of Saphris and other antipsychotics.

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: Secuado is a pharmacy benefit that will be added to the brand non-preferred tier of the formulary. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of schizophrenia **AND**
- Medical record documentation of a therapeutic failure on, intolerance to or contraindication to asenapine (Saphris) sublingual tablets **AND** two additional formulary alternatives

QUANTITY LIMIT: 1 patch per day

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

TALICIA (omeprazole magnesium, amoxicillin, and rifabutin)

Review: Talicia is a delayed release capsule containing Omeprazole 10mg (10.3mg omeprazole magnesium), amoxicillin 250mg, and rifabutin 12.5mg that is indicated for the treatment of *Helicobacter pylori* infection in adults. Talicia is taken at a dose of 4 tablets every 8 hours with food for a period of 14 days. Treatment for *H. pylori* consists of combinations of 2-3 antibiotics along with a PPI (concomitantly or sequentially) given for 3 to 14 days. Approximately 20 percent of patients fail the initial attempt at *H. pylori* eradication and therefore require salvage therapy. Rifabutin triple-therapy is recommended by Up To Date and the American College of Gastroenterology as a salvage regimen for patients who have failed initial antibiotic therapy. Rifabutin therapy presents a risk of myelotoxicity (usually reversible) and concerns for inducing resistance among *Mycobacterium tuberculosis* strains.

The effectiveness of Talicia was demonstrated in two clinical trials of *H.pylori* positive, treatment naive patients who were treated for 14 days. In study 1 (ERADICATE-Hp), patients taking Talicia achieved an eradication rate of 76.6% versus 2.4% for the placebo treated group. In study 2 (ERADICATE-Hp2), patients taking Talicia achieved an eradication rate of 83.8% versus 57.7% in the comparator group, who were treated with a total daily dose of amoxicillin 3000mg and omeprazole 120mg. Patients with negative ^{13}C urea breath tests or fecal antigen at 28 days post-therapy were considered treatment successes.

Talicia is contraindicated in patients with a history of hypersensitivity to any of the individual components and when given in combination with rilprivine, delavirdine, or voriconzole containing products. Adverse reactions seen in $\geq$ 1% of patients receiving Talicia in the clinical trials noted above include: diarrhea, headache, nausea, abdominal pain, chromaturia, rash, dyspepsia, vomiting, oropharyngeal pain, and vulvovaginal candidiasis. The safety in effectiveness of Talicia has not been established in patients under 18 years of age and the drug should not be given to patients with severe renal impairment or any degree of hepatic impairment (including Child Pugh A, B, or C).

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: Talicia is a pharmacy benefit that will not be added to the formulary. The following prior authorization criteria will apply:

- Medical record documentation of a confirmed *Helicobacter pylori* infection **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one prior therapy for *H. pylori* infection **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a formulary proton pump inhibitor (omeprazole, pantoprazole, lansoprazole, rabeprazole) + amoxicillin + rifabutin

QUANTITY LIMIT: 168 tablets per 14 days

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.

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: Ubrelvy is a pharmacy benefit that will not be added to the formulary. The following prior authorization criteria will apply:

- 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) formulary triptans

QUANTITY LIMIT: 16 tablets per 30 days
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).

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: 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.

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: Vyondys 53 is a medical benefit that will be covered 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 **AND**
- Medical record documentation that the patient is ambulatory (e.g. able to walk with assistance, not wheelchair bound, does not have full-time dependence on motorized wheelchairs or scooters for mobility) as proven by documentation of a 6-Minute Walk Test Distance (6MWT) within the past 3 months of initiation of Vyondys 53 **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)

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 **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) **AND**
- Medical record documentation that the patient remains ambulatory (e.g. able to walk with assistance, not wheelchair bound, does not have full-time dependence on motorized wheelchairs or scooters for mobility) as proven by documentation of a follow-up 6-Minute Walk Test Distance (6MWT) within the past 6 months

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.

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

CLASS REVIEW

HERCEPTIN BIOSIMILAR CLASS REVIEW

Trade Name	Generic Name	FDA Approved Indication
New FDA Approvals		**For Herceptin and all FDA approved Herceptin biosimilars:** **Adjuvant Breast Cancer** Herceptin and all biosimilars are indicated for adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature) breast cancer • as part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel • as part of a treatment regimen with docetaxel and carboplatin • as a single agent following multi-modality anthracycline based therapy. **Metastatic Breast Cancer** Herceptin and all biosimilars are indicated: • In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer • As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease. **Metastatic Gastric Cancer** Herceptin and all biosimilars are indicated, in combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma who have not received prior treatment for metastatic disease.
Herzuma	**trastuzumab-pkrb**	
Ontruzant	**trastuzumab-dttb**	
Trazimera	**trastuzumab-qyyp**	
Previously Approved		
Ogivri	**trastuzumab-dkst**	
Kanjinti	**trastuzumab-anns**	
Herceptin	**trastuzumab**	

Pharmacology/Place in Therapy: Herzuma, Ontruzant, and Trazimera are three newly approved biosimilars for Herceptin. 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. In order to demonstrate biosimilarity, proposed products must meet both parts of Public Health and Service Act (PHS Act) which defines a biosimilar as "highly similar to the reference product not withstanding minor differences in clinically inactive components" with "no clinically meaningful differences between the proposed biosimilar and the reference product in terms of safety, purity and potency of the product".

Like Herceptin, all trastuzumab biosimilars are humanized monoclonal antibody that preferentially target the extracellular domain of HER2, a proto-oncogene structurally related to epidermal growth factor,

resulting in the inhibition of proliferation of human tumor cells overexpressing HER2. Trastuzumab products 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.

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

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:
Herzuma will be covered as a medical benefit that does not require prior authorization.

Ontruzant will be covered as a medical benefit that does not require prior authorization.

Trazimera will be covered as a medical benefit that does not require 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

BRAFTOVI (encorafenib)

Updated Indication: Braftovi is now indicated for use in combination with cetuximab for the treatment of adult patients with metastatic colorectal cancer, with BRAF V600E mutation (as detected by an FDA approved test), after prior therapy.

Updated Dosing for New Indication:[1] 300mg (four 75mg capsules) once daily in combination with cetuximab

Current formulary status: OralOncBrandNP tier requiring a prior authorization

Recommendation: No changes are recomended to formulary placement at this time. However, it is recommended that the prior authorization criteria be updated to include the following:

- Medical record documentation that Braftovi is prescribed by a hematologist, oncologist, or dermatologist **AND**
- Medical record documentation of a diagnosis of metastatic colorectal cancer **AND**
- Medical record documentation of a BRAF V600E mutation as detected by a Food and Drug Administration (FDA)-approved test **AND**
- Medical record documentation that member has had progression on at least one prior therapy **AND**
- Medical record documentation that Braftovi is being prescribed in combination with cetuximab

QUANTITY LIMIT (for metastatic CRC): 75 mg: 4 tablets per day, 30 day supply per fill
Existing QLs will apply to unresectable/metastatic melanoma indication only

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.

FIASP (insulin aspart injection)

Updated Indication: Fiasp is a rapid-acting human insulin analog indicated to improve glycemic control in adult and pediatric patients with diabetes mellitus.

Previously, Fiasp was only indicated in adult patients with diabetes mellitus.

Current formulary status: Non-formulary

Recommendation: There are no changes recommended to formulary status at this time. However, it is recommended to update the Commercial/Exchange/CHIP policy to remove the age restriction since Fiasp is indicated for both pediatric and adult patients. The prior authorization criteria will be as follows for Commercial/Exchange/CHIP:

- Medical record documentation of a therapeutic failure on, contraindication to, or intolerance to Novolog

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.

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).

There is no change to the previous indications for Imfinzi of urothelial carcinoma and unresectable stage III NSCLC.

Updated Dosing for New Indication[1]: The dose for Imfinzi in ES-SCLC is 1500 mg in combination with chemotherapy every 3 weeks (21 days) for 4 cycles followed by 1500 mg every 4 weeks as a single agent until disease progression or unacceptable toxicity. Patients with a body weight of 30 kg or less must receive weight based dosing of Imfinzi 20 mg/kg in combination with chemotherapy every 3 weeks (21 days) for 4 cycles, followed by 20 mg/kg every 4 weeks as a single agent until weight increases to greater than 30 kg. Imfinzi is administered prior to chemotherapy on the same day.

Current formulary status: Medical Benefit requiring a prior authorization

Recommendation: No changes are recommended to the formulary placement of Imfinizi. It is recommended to add the following prior authorization criteria and authorization duration to Medical Benefit Policy 156.0 to incorporate the new indication:

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.

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.

MYCAMINE (micafungin for injection)

Updated Indication: Mycamine is indicated in adult and pediatric patients for:

- Treatment of Candidemia, Acute Disseminated Candidiasis, *Candida* Peritonitis and Abscesses in adult and pediatric patients 4 months of age and older.
- 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.
- Treatment of Esophageal Candidiasis in adult and pediatric patients 4 months of age and older.
- Prophylaxis of *Candida* Infections in adult and pediatric patients 4 months of age and older undergoing Hematopoietic Stem Cell Transplantation (HSCT).

Limitations of Use:

- The safety and effectiveness of Mycamine have not been established for the treatment of candidemia **with** meningoencephalitis and/or ocular dissemination in pediatric patients younger than 4 months of age as a higher dose may be needed.
- Mycamine has not been adequately studied in patients with endocarditis, osteomyelitis or meningoencephalitis due to *Candida.*
- The efficacy of Mycamine against infections caused by fungi other than *Candida* has not been established.

Note: Mycamine was previously indicated in adult and pediatric patients 4 months and older for the treatment of Candidemia, Acute Disseminated Candidiasis, Candida Peritonitis and Abscesses, Esophageal Candidiasis, and prophylaxis of Candida Infections in patients undergoing HSCT.
Updated Dosing for New Indication[1]: There are no changes to the dose recommendations for adult and pediatric patients 4 months and older. However, there are dose recommendations for pediatric patients younger than 4 months of age.

For pediatric patients younger than 4 months of age for the treatment of Candidemia, Acute Disseminated Candidiasis, *Candida* Peritonitis and Abscesses **without** meningoencephalitis and/or ocular dissemination the recommended dosage is 4 mg/kg once daily.

Current formulary status: Mycamine is a medical benefit 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.

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.

NERLYNX (neratinib)

Updated Indication: Nerlynx is now indicated in combination with capecitabine, for the treatment of adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 based regimens in the metastatic setting.

Previously: Nerlynx was only indicated for the extended adjuvant treatment of adult patients with early stage HER2-positive breast cancer after trastuzumab-based therapy.

Updated Dosing for New Indication[1]:

- Advanced or metastatic breast cancer: Nerlynx 240 mg (6 tablets) orally once daily with food on Days 1-21 (of a 21-day cycle) plus capecitabine 750mg/m^2 orally twice daily on Days 1-14 (of a 21-day cycle) until disease progression or unacceptable toxicities

Previously:

- Extended Adjuvant Treatment of Early Stage Breast Cancer: Nerlynx 240 mg (6 tablets) orally once daily, with food, continuously until disease recurrence for up to one year.

Current formulary status: Pharmacy benefit on the OralOncBrandNP tier requiring PA (QL applies)

Recommendation: No changes are recommended to the formulary placement of Nerlynx at his time. It is recommended that the GHP Nerlynx policy criteria and authorization duration are updated to include the new indication as outlined below:

- Medical record documentation that Nerlynx is prescribed by an oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- One of the following:
  - Medical record documentation of a diagnosis of early stage (stages I-IIIA) breast cancer **AND**
  - Medical record documentation of HER-2 overexpression/amplification **AND**
  - Medical record documentation of prior treatment with trastuzumab-based therapy

OR

  - Medical record documentation of advanced or metastatic HER2-positive breast cancer **AND**
  - Medical record documentation of two or more prior anti-HER2 based regimens given in the metastatic setting **AND**
  - Medical record documentation that Nerlynx will be used in combination with capecitabine

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

AUTHORIZATION DURATION:

- Early Stage Breast Cancer: One time, 12 month authorization

- Advanced or Metatstatic Breast Cancer: 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.

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.

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.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Previously the indication for Opdivo in Hepatocellular Carcinoma was for use as a single agent only.

Updated Dosing for New Indication[1,2]: The recommended dosage of Opdivo in combination with Yervoy (ipilimumab) for 4 doses is 1 mg/kg every three weeks (30-minute intravenous infusion) with Yervoy 3 mg/kg intravenously over 30 minutes on the same day. After completing 4 doses of combination therapy, Opdivo is administered as a single agent until disease progression or unacceptable toxicity at a dose of 240 mg every 2 weeks or 480 mg every 4 weeks.

Current formulary status: Medical benefit requiring prior authorization

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 to Medical Benefit Policy 126.0:

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)

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.

OZEMPIC (semaglutide)

Updated Indication: Ozempic is now indicated to reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus (T2DM) and established cardiovascular disease. This new indication expands upon the previous indication of as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

Current formulary status: Pharmacy benefit on the Brand Preferred Tier NOT requiring PA (QL applies)

Recommendation: No changes are recommended to the formulary placement or policies of Ozempic at this time. No recommendations to add prior authorization criteria or alter quantity limits at this time.

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.

SYMTUZA (cobicistat/darunavir/emtricitabine/tenofovir)

Updated Indication: Symtuza is now indicated for the treatment of HIV-1 infection in pediatric patients weighting at least 40kg who are treatment naïve or virologically suppressed (< 50 copies/mL) on a stable antiretroviral regimen for at least 6 months. Patients should have no known substitutions associated with resistance to darunavir or tenofovir.

Updated Dosing for New Indication[1]: 40mg once daily with food

Current formulary status: Brand preferred tier with a quantity limit of 1 tablet per day

Recommendation: No changes are recommended to formulary status or prior authorization requirements for Symtuza at this time.

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.

XELJANZ XR (tofacitinib citrate)

Updated Indication: Xeljanz XR is now indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have an inadequate response or who are intolerant to TNF blockers.

Previously Xeljanz XR was only indicated for rheumatoid arthritis and psoriatic arthritis while Xeljanz was indicated for all three indications, rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis.

Updated Dosing for New Indication: The dosage of Xeljanz XR for the treatment of ulcerative colitis recommends an induction period of Xeljanz XR 22 mg for at least 8 weeks after which patients should be evaluated for transition to maintenance therapy. Patients may continue the induction period for a maximum of 16 weeks if needed, after which the patient should be transition to the maintenance dosage of 11 mg once daily or Xeljanz XR should be discontinued if adequate therapeutic response is not achieved. For patients who have a loss of response during maintenance treatment, 22 mg once daily may be considered and limited to the shortest duration, with careful consideration of the risks versus the benefits.

Xeljanz has similar induction and maintenance periods recommended for ulcerative colitis (10 mg twice daily for 8-16 weeks for induction, then 5 mg twice daily for maintenance). Patients treated with Xeljanz 5 mg twice daily may be switched to Xeljanz XR 11 mg once daily following the last dose of Xeljanz 5 mg. Patients treated with Xeljanz 10 mg twice daily may be switched to Xeljanz XR 22 mg once daily following the last dose of Xeljanz 10 mg.

The dosage of Xeljanz 10 mg twice daily or Xeljanz XR 22 mg once daily is not recommended for the treatment of rheumatoid arthritis and psoriatic arthritis.

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

Recommendation: There are no changes to the formulary placement or the authorization duration of Xeljanz XR. It is recommended to update the prior authorization criteria and quantity limits for ulcerative colitis in the for Xeljanz and Xeljanz XR as follows:

For treatment of rheumatoid arthritis
An exception for coverage of Xeljanz or Xeljanz XR may be made for members who meet the following criteria:

- Medical record documentation of a diagnosis of moderate to severe rheumatoid arthritis (made in accordance with the American College of Rheumatology Criteria for the Classification and Diagnosis of Rheumatoid Arthritis) **AND**
- Medical record documentation that Xeljanz or Xeljanz XR is prescribed by a rheumatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of an inadequate response to a minimum 3 month trial of methotrexate or other disease modifying anti-rheumatic drug (DMARD) if methotrexate is not tolerated or contraindicated **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy **AND**

- Medical record documentation that Xeljanz or Xeljanz XR is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent

QUANTITY LIMIT:
Pharmacist note to CSR: *Authorization should be entered by GPID and only checking the Formulary PA required box (no QLs need to be entered within the authorization).*
- Xeljanz 5 mg: 2 tablets per day, 30 day supply per fill.
- Xeljanz XR 11 mg: 1 tablet per day, 30 day supply per fill

For treatment of psoriatic arthritis
An exception for coverage of Xeljanz or Xeljanz XR may be made for members who meet the following criteria:
- Medical record documentation of a diagnosis of moderately to severely active psoriatic arthritis which must include the following: o Documentation of either active psoriatic lesions or a documented history of psoriasis **AND**
- Medical record documentation of an inadequate response to or intolerance to a 3-month trial of methotrexate or another disease-modifying antirheumatic drug (DMARD) **AND**
- Medical record documentation that Xeljanz or Xeljanz XR is prescribed by a rheumatologist or dermatologist **AND**
- Medical record documentation that Xeljanz or Xeljanz XR is being prescribed in combination with non-biologic disease modifying antirheumatic drug (DMARD) therapy (including but not limited to methotrexate, sulfasalazine, and/or leflunomide) **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of Humira* **AND** Cosentyx* **AND**
- Medical record documentation that Xeljanz or Xeljanz XR is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent

QUANTITY LIMIT:
Pharmacist note to CSR: *Authorization should be entered by GPID and only checking the Formulary PA required box (no QLs need to be entered within the authorization).*
- Xeljanz 5 mg: 2 tablets per day, 30 day supply per fill.
- Xeljanz XR 11 mg: 1 tablet per day, 30 day supply per fill

For treatment of ulcerative colitis
An exception for coverage of Xeljanz may be made for members who meet the following criteria:
- Medical record documentation of a diagnosis of moderate to severe ulcerative colitis **AND**
- ~~Medical record documentation that request is for Xeljanz (NOTE: Xeljanz XR is not Food and Drug Administration approved for this indication) **AND**~~
- Medical record documentation that Xeljanz or Xeljanz XR is prescribed by a gastroenterologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of Humira* **AND**
- Medical record documentation that Xeljanz is not being used concurrently with a tumor necrosis factor (TNF) blocker, potent immunosuppressant (e.g. azathioprine and cyclosporine), or other biologic agent

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).*

- Xeljanz 5 mg or 10 mg*: 2 tablets per day, 30 day supply per fill
- Xeljanz XR 11 mg or 22 mg*: 1 tablet per day, 30 day supply per fill

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.

YERVOY (ipilimumab)

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

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

There are no changes to the previous indications of Yervoy for the treatment of unresectable or metastatic melanoma, cutaneous melanoma, advanced renal cell carcinoma, and metastatic colorectal cancer.

Updated Dosing for New Indication[1,2]: The dosing regimen of Opdivo and Yervoy for the treatment of hepatocellular carcinoma is Opdivo 1 mg/kg followed by Yervoy 3 mg/kg on the same day every 3 weeks for 4 doses, then Opdivo 240 mg every 2 weeks or 480 mg every 4 weeks as a single agent.

Current formulary status: Medical benefit requiring prior authorization

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 to Medical Benefit Policy 91.0:

- 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

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.

UPDATES

MAY 2020 P&T DUR/ADHERENCE 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 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.
  - See below for letters sent:
    - For GHS01: **91**
    - For GHS25: **36**
    - For GT023: **54**
    - For GT036: **12**
    - For GT041: **15**
    - For GT046: **100**
    - For GT062: **100**
    - For GT065: **100**
    - For GT088**: 18**
    - For GT095: **100**
    - For GT107: **14**
    - For GT140: **31**
    - For GT210: **22**
    - For GT260: **30**
    - For GT400: **100**
    - For GHS05: **87**
    - For GHS90: **100**
    - For GT033: **32**
    - For GT038: **14**
    - For GT045: **100**
    - For GT056: **43**
    - For GT064: **14**
    - For GT070: **27**
    - For GT089: **74**
    - For GT106**: 23**
    - For GT108: **14**
    - For GT180: **13**
    - For GT230: **65**
    - For GT310: **28**
    - For GT900: **100**

- 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 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.
  - See below for letters sent:
    - For GHS01: **93**
    - For GHS25: **14**
    - For GT023: **8**
    - For GT038: **3**
    - For GT045: **34**
    - For GT056: **6**
    - For GT064: **2**
    - For GT072: **7**
    - For GT075**: 1**
    - For GT089: **14**
    - For GHS05: **91**
    - For GHS90: **98**
    - For GT036: **1**
    - For GT039: **1**
    - For GT046: **31**
    - For GT062: **98**
    - For GT065: **90**
    - For GT074: **1**
    - For GT088: **4**
    - For GT093**: 4**

        - For GT095: **99**
        - For GT017: **3**
        - For GT180: **3**
        - For GT230: **18**
        - For GT260: **2**
        - For GT310: **6**
        - For GT900: 1**3**
        - For GT106**: 3**
        - For GT140: **10**
        - For GT210: **4**
        - For GT231: **1**
        - For GT280: **6**
        - For GT400: **100**
    - Adam K. was able to re-run the data on this population on 3/27/2020 and of the original 871 members that we sent letters to 741 are still active. Of those 741 members, 158 now have a claim for a statin. This equates to 21% of the members

- Asthma DUE
    - This is the 2019 3rd quarter MedImpact DUE for all LOBs
    - From this report, we identified 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.
    - See below for letters sent:
        - For GHS01: **93**
        - For GHS05: **68**
        - For GHS25: **5**
        - For GHS90: **95**
        - For GT023: **3**
        - For GT036: **2**
        - For GT038: **1**
        - For GT045: **6**
        - For GT046: **4**
        - For GT056: **1**
        - For GT062: **9**
        - For GT065: **59**
        - For GT072: **4**
        - For GT086: **3**
        - For GT089: **5**
        - For GT095: **18**
        - For GT140: **2**
        - For GT230: **4**
        - For GT280: **2**
        - For GT400: **95**
        - For GT900: **1**
    - Adam K. was able to re-run the data on this population on 12/13/2019 and of the original 480 members that we sent letters to 424 members are still active. Of those 424 members 34 members now have a claim for an asthma controller medication. This equates to 8% 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 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.

- See below for letters sent:
  - For GHS01: **85**
  - For GHS05: **85**
  - For GHS90: **86**
  - For GT038: **30**
  - For GT065: **71**
  - For GT095: **82**
  - For GT400: **92**
- Adam K. was able to re-run the data on this population on 9/25/2019 and of the original 531 members that we sent letters to 479 members are still active. Of those 479 members 44 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
  - Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - Currently, Kayla Stanishefski runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications for GHP Family
    - As of 1/1/2020, this measure now applies for all LOBs so we will do the same for Commercial/Exchange

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 2020:
    - For GHS01: **1 member** reviewed and **0 interventions** made
    - For GHS05: **2 members** reviewed and **1 intervention** made
    - For GHS90: **4 members** reviewed and **1 intervention** made

        - For GT045: **1 member** reviewed and **0 interventions** made
        - For GT062: **1 member** reviewed and **0 interventions** made
        - For GT065: **2 members** reviewed and **0 interventions** made
        - For GT095: **1 member** reviewed and **0 interventions** made
        - For GT400: **5 members** reviewed and **0 interventions** made
        - For GT900: **1 member** reviewed and **0 interventions** made

- 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 Commercial/Exchange 2020, we have reviewed the Q1 report (9/2019-12/2019) and have not had to make any interventions yet
- Suboxone with an Opioid Report
    - We are getting this report **weekly** for **all LOBs** from Adam Kelchner. 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 Commercial/Exchange and TPAs in 2019, see below for the new members reviewed and those referred to Dr. Meadows
    - For 2020:
        - For GHS01: we have reviewed **2 new members** and **0 members** were referred to Dr. Meadows
        - For GHS90: we have reviewed **2 new members** and **2 members** were referred to Dr. Meadows
        - For GT023: we have reviewed **1 new member** and **0 members** were referred to Dr. Meadows
        - For GT400: we have reviewed **4 new members** and **1 member** was 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 Commercial/Exchange and TPAs in 2020, see below for the number of letters we have sent to members notifying them that we are ending their opioid authorization(s):
        - For GHS90: **2**
        - For GT400: **1**
- 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 Commercial/Exchange and TPAs in 2020, see below for the number of reviewed cases.
        - For GHS90: **1**
- 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 GHS01 in 2020, we have reviewed **18 cases** so far and **corrected 7 claims**, resulting in a **cost savings of $368.76**
        - For GHS05 in 2020, we have reviewed **13 cases** so far and **corrected 9 claims**, resulting in a **cost savings of $763.48**
        - For GHS90 in 2020, we have reviewed **29 cases** so far and **corrected 12 claims**, resulting in a **cost savings of $706.58**
        - For GT038 in 2020, we have reviewed **6 cases** so far and **corrected 3 claims,** resulting in a **cost savings of $36.02**
        - For GT056 in 2020, we have reviewed **1 case** so far and **corrected 1 claim**, resulting in a **cost savings of $32.92**
        - For GT062 in 2020, we have reviewed **7 cases** so far and **corrected 1 claim**, resulting in a **cost savings of $12.03**
        - For GT065 in 2020, we have reviewed **24 cases** so far and **corrected 18 claims**, resulting in a **cost savings of $1,365.78**
        - For GT095 in 2020, we have reviewed **12 cases** so far and **corrected 3 claims**, resulting in a **cost savings of $307.20**
        - For GT180 in 2020, we have reviewed **2 cases** so far and **corrected 2 claims**, resulting in a **cost savings of $1.90**
        - For GT400 in 2020, we have reviewed **19 cases** so far and **corrected 11 claims**, resulting in a **cost savings of $859.23**
- 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 Commercial/Exchange in 2020, we have sent letters to providers on the below members:
        - For GHS01: **7**
        - For GHS05: **3**
        - For GHS90: **9**
        - For GT038: **1**
        - For GT062: **1**
        - For GT065: **4**
        - For GT095: **5**
        - For GT400: **5**
        - For GT900: **1**
- Enbrel Overutilization for Treating Plaque Psoriasis
    - A **monthly** report was created to determine 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 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 Commercial/Exchange in 2020, we have sent letters to the below members:
        - For GHS01: **3**
        - For GHS05: **1**
        - For GHS90: **3**
        - For GT062: **1**
        - For GT065: **4**

        - For GT230: **1**
        - For GT400: **1**
- 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

Completed

- Commercial/Exchange 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
        - Severity Report
        - Duplicate Anticoagulant Report
- Current Member Letters
        - Ending Opioid Authorizations
        - Antidepressant Medication Management-AMM
        - Asthma Medication Ratio-AMR
        - Medication Management for People with Asthma-MMA

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

EMGALITY, AIMOVIG, AND AJOVY UPDATE

Current Formulary Status/PA criteria:

Aimovig is a pharmacy benefit available at the Specialty Tier or on the Brand Non-Preferred Tier for members with a three tier benefit. The following prior authorization criteria should apply.

- Prescription written by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura, based on the ICHD-III diagnostic criteria **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least three (3) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/Sodium Valproate
    - Amitriptyline
    - Venlafaxine

AND

- If the request is for use in combination with Botox, all of the following must be met:
    - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Ajovy is a pharmacy benefit available at the Specialty Tier or on the Brand Non-Preferred Tier for members with a three tier benefit. The following prior authorization criteria should apply.

- Prescription written by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura, based on the ICHD-III diagnostic criteria **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least three (3) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/Sodium Valproate
    - Amitriptyline
    - Venlafaxine

AND

- If the request is for use in combination with Botox, all of the following must be met:
    - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Emgality is a pharmacy benefit available at the Specialty Tier or on the Brand Non-Preferred Tier for members with a three tier benefit. The following prior authorization criteria should apply.

- Prescription written by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura, based on the ICHD-III diagnostic criteria **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least three (3) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/Sodium Valproate
    - Amitriptyline
    - Venlafaxine

AND

- If the request is for use in combination with Botox, all of the following must be met:
    - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Recommendations:
It is recommended to move Emgality and Aimovig to a Brand Preferred tier. For Emgality and Aimovig, we will change the number of preventive agents a patient needs to fail from 3 to 2. Ajovy will be non-preferred. Approval of Ajovy will require failure on Emgality and Aimovig.

Aimovig is a pharmacy benefit and will be added to the Brand Preferred tier. The following prior authorization criteria should apply.

- Prescription written by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura, based on the ICHD-III diagnostic criteria **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least two (2) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/Sodium Valproate
    - Amitriptyline
    - Venlafaxine

AND

- If the request is for use in combination with Botox, all of the following must be met:
    - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
    - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Ajovy is a pharmacy benefit available at the Specialty Tier or on the Brand Non-Preferred Tier for members with a three tier benefit. The following prior authorization criteria should apply.

- Prescription written by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura, based on the ICHD-III diagnostic criteria **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least three (3) of the following:
    - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
    - Topiramate
    - Divalproex/Sodium Valproate
    - Amitriptyline
    - Venlafaxine

AND

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Aimovig and Emgality **AND**
- If the request is for use in combination with Botox, all of the following must be met:

- Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
- Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Emgality is a pharmacy benefit and will be added to the Brand Preferred tier. The following prior authorization criteria should apply.

- Prescription written by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of migraine with or without aura, based on the ICHD-III diagnostic criteria **AND**
- Medical record documentation of number of baseline migraine or headache days per month **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least two (2) of the following:
  - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
  - Topiramate
  - Divalproex/Sodium Valproate
  - Amitriptyline
  - Venlafaxine

AND

- If the request is for use in combination with Botox, all of the following must be met:
  - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
  - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

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.

ENTYVIO POLICY UPDATE

Review:

VARSITY Trial[1]: Vedolizumab vs Adalimumab in Moderate to Severe Active Ulcerative Colitis

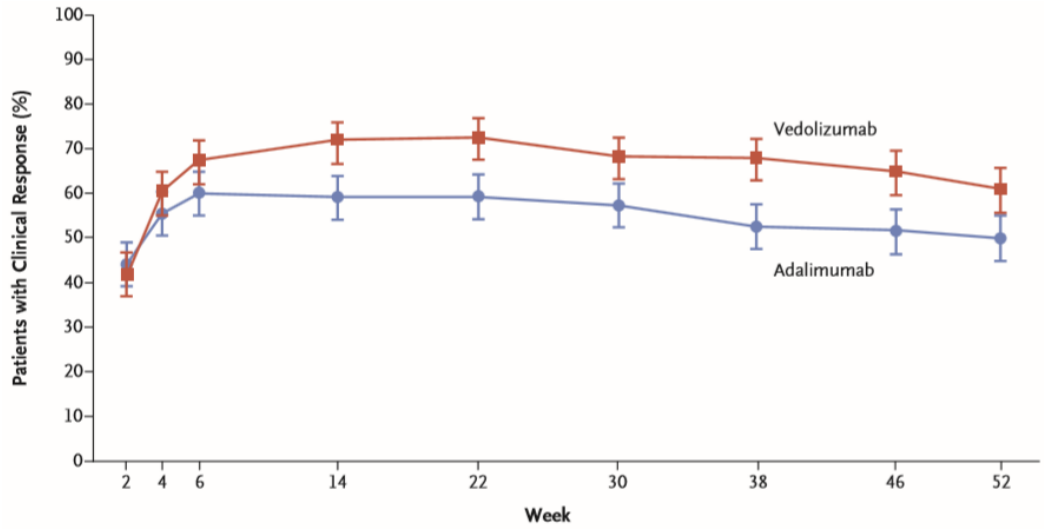
- *Phase IIIb, double blind, double dummy, randomized, active-controlled superiority trail conducted in 245 centers in 34 countries from 2015 – 2019.*
- Population (n = 769)
  - Adults 18 – 85 with a confirmed diagnosis of UC at least 3 months before screening, have colonic involvement of at least 15cm, and have a total score of 6 – 12 on Mayo Scale with a subscore of at least 2 on the endoscopic component of the Mayo Scale
    - Mayo Score range is 0 – 12 (higher scores indicate more severe disease) and subscores of each of the four components range from 0 – 3
  - 25% of patients had previous exposure to an TNFα inhibitor (not adalimumab) and the rest of patients were never tried TNFα inhibitor and had a loss of response to

conventional treatments (ex. aminosalicylates, oral immunomodulators, or corticosteroids). All patients never tried vedolizumab.

- Intervention
  - Vedolizumab Group (n = 383)
    - 300mg IV on day 1 at weeks 2, 6, 14, 22, 30, 38, and 46 (plus placebo SQ)
  - Adalimumab Group (n = 386)
    - 40mg SQ with a total dose of 160 mg at week 1, 80 mg at week2, and 40 mg every 2 weeks thereafter until week 50 (plus placebo IV)
  - Dose escalation not permitted
- Outcomes
  - Clinical remission at week 52 (≤ 2 on Mayo scale and no subscore > 1 on any of the four components)
    - Overall, more patients achieved clinical remission in vedolizumab group than in adalimumab group (31.3% vs 22.5%, p = 0.0006)
  - Additional Efficacy Outcome Analysis
    - Endoscopic Improvement
      - Overall, more patients achieved mucosal healing in vedolizumab group than in adalimumab group (39.7% vs 27.7%, p < 0.001)
    - Corticosteroid Free Remission at week 52
      - Overall, 12.6% (14 out of 111) patients in the vedolizumab group and 21.8% (26 out of 119) in the adalimumab group achieved clinical remission without steroid use (CI: -18.9 – 0.4)
  - See additional exploratory outcomes below
  - Safety

Events	Adalimumab (n = 386)	Vedolizumab (n =383)
Any Adverse Event, n (%)	267 (69.2)	240 (62.7)
Averse Events, excluding UC, n (%)	250 (64.8)	229 (59.8)
Serious Adverse Events, n (%)	53 (13.7)	42 (11.0)
Infections, no. of patients/incidence rate per 100 patient years	124/34.6	103/23.4
Musculoskeletal and connective tissue disorder, no. of patients/incidence rate per 100 patient years	44/12.3	50/11.4
Skin and subcutaneous tissue disorders, no. of patients/incidence rate per 100 patient years	52/14.5	38/8.6

Clinical Response via change in partial Mayo Score



Partial Mayo Score (range o – 9, combines stool frequency, rectal bleeding, and PGA, with the exclusion of endoscopy). Clinical remission was defined as at least 2 point reduction and at least 25% change from baseline, with an accompanying decrease of at least 1 point on the rectal bleeding component of the Mayo scale or rectal bleeding subscore of 0 or 1.

	Adalimumab SC 40 mg Q2W (N=386)	Vedolizumab IV 300 mg Q8W (N=383)	Treatment Difference, (95% CI)
Rectal bleeding subscore indicative of mild disease (≤1) at Week 52, n (%)	211 (54.7)	252 (65.8)	11.1 (4.2, 17.9)
PGA subscore indicative of mild disease (≤1) at Week 52, n (%)	189 (49.0)	234 (61.1)	12.1 (5.1, 19.0)
Stool frequency subscore indicative of mild disease (≤1) at Week 52, n (%)	173 (44.8)	223 (58.2)	13.3 (6.4, 20.3)
Clinical remission with rectal bleeding and endoscopy subscore of 0 at Week 52, n (%)	54 (14.0)	85 (22.2)	8.2 (2.8, 13.5)
Endoscopy subscore ≤1, rectal bleeding subscore of 0, and stool frequency subscore of 0 at Week 52, n (%)	75 (19.4)	91 (23.8)	4.3 (-1.5, 10.1)
Endoscopy subscore ≤1, rectal bleeding subscore of 0, and stool frequency subscore ≤1 at Week 52, n (%)	91 (23.6)	127 (33.2)	9.5 (3.2, 15.9)
Quality of life - IBDQ score change of ≥16 points from Baseline to Week 52, n (%)	163 (42.2)	199 (52.0)	9.7 (2.7, 16.7)
Clinical remission based on IBDQ score >170 at Week 52, n (%)	156 (40.4)	192 (50.1)	9.6 (2.8, 16.5)
Major UC-related events, Hazard ratio, 95% CI: • UC-related hospitalizations, n (%) • UC-related bowel resections, n (%) • UC-related procedures, n (%)	 20 (5.2) 3 (0.8) 8 (2.1)	 15 (3.9) 0 7 (1.8)	0.061 (0.035, 0.105)
Histological remission, per Geboes score < 2.0, at week 52, n (%)	12 (3.1)	40 (10.4)	7.3 (3.8, 10.8)
Histological remission, per RHI score < 3, at week 52, n (%)	77 (19.9)	144 (37.6)	17.6 (11.3, 23.8)

Recommendations from National Agencies and Organizations:

American Gastroenterology Association:[2] Moderate to Severe Ulcerative Colitis

- Biologic-naïve patients are recommended to start infliximab or vedolizumab over adalimumab, for remission induction. Adalimumab may be a reasonable first for patients with less severe disease and value the convenience of self-administered subcutaneous injection more than the relative efficacy of medications).
- Ustekinumab or tofacitinib is recommended over vedolizumab or adalimumab for induction of remission in patients with previous infliximab exposure, especially if primary nonresponse.
- The FDA recommends that tofacitinib use is reserved for failure of or intolerance to TNFα antagonists.

American College of Gastroenterology:[3] Moderately to Severe Active Ulcerative Colitis

- TNFα antagonists (Infliximab, adalimumab, and golimumab) demonstrated superiority over placebo, with a trend from various studies suggesting a higher remission rate with Infliximab over adalimumab or golimumab. Evidence also suggested lower corticosteroid use, less all cause hospitalizations, and UC hospitalizations with infliximab when compared to adalimumab.
- Vedolizumab is also an effective choice over placebo and has a targeted mechanism of action, providing a more favorable safety profile with a lower risk of infections. Vedolizumab demonstrated efficacy in patients that failed TNFα antagonists. Tofacitinib is also more effective compared to placebo and demonstrated efficacy after failure of TNFα inhibitor.

Specialist Feedback: Dr. Korta Yuasa, Gastroenterologist at Geisinger Health System, noted that the VARSITY trial confirmed what he has seen in clinical practice – that there are treatments available for UC that are better than Humira. Previously he stated that he did not feel they could position biologic treatments effectively due to lack of head to head data. With the release of this trial data and head to head comparison, he recommends positioning Entyvio as a first line biologic option for UC. He also notes that the two newer biologics (Entyvio and Stelara) have much less risks of complications which have been echoed by many experts over the past 2-3 years.

Current Formulary Status: Entyvio is covered under the medical benefit with the following prior authorization criteria:

Crohn's Disease

- Prescription written by a gastroenterologist **AND**
- Medical record documentation of age >18 years **AND**
- Medical record documentation of a diagnosis of moderate-to-severe Crohn's disease **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Humira*

Ulcerative Colitis

- Prescription written by a gastroenterologist **AND**
- Medical record documentation of age >18 years **AND**
- Medical record documentation of a diagnosis of moderate-to-severe ulcerative colitis **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Humira*.

AUTHORIZATION DURATION: After the initial 6 month approval, subsequent approvals will be for a duration of 12 months. Reevaluation of coverage will be every 12 months requiring documentation of improvement of signs and symptoms while on Entyvio

Recommendations: Entyvio is covered under the medical benefit. Recommend updating the prior authorization criteria as follows:

Crohn's Disease

- Prescription written by a gastroenterologist **AND**
- Medical record documentation of age >18 years **AND**
- Medical record documentation of a diagnosis of moderate-to-severe Crohn's disease **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Humira*

Ulcerative Colitis

- Prescription written by a gastroenterologist **AND**
- Medical record documentation of age >18 years **AND**
- Medical record documentation of a diagnosis of moderate-to-severe ulcerative colitis **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to azathioprine or 6-mercaptopurine (6-MP)
- ~~Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Humira*.~~

AUTHORIZATION DURATION: After the initial 6 month approval, subsequent approvals will be for a duration of 12 months. Reevaluation of coverage will be every 12 months requiring documentation of improvement of signs and symptoms while on Entyvio

FACETS RX COUNT:

Initial Authorization:

- Facets RX Count: 1500 (J3380 – Vedolizumab)
- MedImpact Quantity Limit (for non-Medicare LOB): one-time 1-week authorization of 2 vials per 28 days. Remainder of initial 6 month authorization, 1 vial per 56 days

Subsequent Authorizations:

- Facets RX Count: 2100 (J3380 – Vedolizumab)
- MedImpact Quantity limit (for non-Medicare LOB): 1 vial per 56 days

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.

SIROLIMUS POLICY UPDATE

Update on the use of sirolimus for graft versus host disease prophylaxis in patients undergoing stem-cell transplant.

Clinical Evidence Summary: Sirolimus has demonstrated efficacy in studies with patients undergoing treatment for graft versus host disease prophylaxis. Studies consisted of additive sirolimus to first line therapy (triple therapy) and in comparison to first line immunosuppressive agents such as methotrexate or mycophenolate mofetil.

Recommendations: It is recommended that the following changes be added to the current policy for Sirolimus:

Current:

- Medical record documentation of age greater than or equal to 13 years **AND**
- Medical record documentation of a renal transplant

OR

- Medical record documentation of a diagnosis of lymphangioleiomyomatosis

Updated Language:

Add to current policy:

OR

- Medical record documentation of use for graft versus host disease prophylaxis **AND**
- Treatment with a calcineurin inhibitor **AND** one of the following**:**
    - Documentation of failure on, intolerance to, or a contraindication to methotrexate or mycophenolate mofetil **OR**
    - Use of triple therapy with a calcineurin inhibitor, methotrexate or mycophenolate mofetil, and sirolimus

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.

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.