P&T Committee Meeting Minutes
Commercial/Marketplace/GHP Kids
May 17, 2022

Present (via Teams):	**Absent:**
Megan Ammon, Pharm.D.	Bret Yarczower, MD, MBA – Chair
Emily Antosh, Pharm.D.	Holly Bones, Pharm.D.
Kristen Bender, Pharm.D.	Kim Castelnovo
Jeremy Bennett, MD	Dean Christian, MD
Alyssa Cilia, RPh	Michael Evans, RPh
Kimberly Clark, Pharm.D.	Jason Howay, Pharm.D.
Rajneel Farley, Pharm.D.	Jonas Pearson, RPh
Kelly Faust Pharm.D.	William Seavey, Pharm.D.
Tricia Heitzman, Pharm.D.	Michael Shepherd, MD
Nichole Hossler, MD	Richard Silbert, MD
Emily Hughes, Pharm.D.	Robert Strony, MD MBA
Keith Hunsicker, Pharm.D.	Amanda Taylor, MD
Kelli Hunsicker, Pharm.D.	
Derek Hunt, Pharm.D.	
Philip Krebs, R.EEG T	
Briana LeBeau, Pharm.D.	
Ted Marines, Pharm.D.	
Lisa Mazonkey, RPh	
Tyreese McCrea, Pharm.D.	
Perry Meadows, MD	
Jamie Miller, RPh	
Mark Mowery, Pharm.D.	
Austin Paisley, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Renn, Pharm.D.	
Melissa Sartori, Pharm.D.	
Angela Scarantino	
Kristen Scheib, Pharm.D.	
Leslie Shumlas, Pharm.D.	
Aubrielle Smith Pharm.D.	
Michael Spishock, RPh	
Todd Sponenberg, Pharm.D.	
Jill Stone, Pharm.D.	
Kevin Szczecina, RPh	
Ariana Wendoloski, Pharm.D.	
Brandon Whiteash, Pharm.D.	
Margaret Whiteash, Pharm.D.	
Travis Baughn (non-voting participant)	
MeiLing Montross, Pharm.D. (Pharmacy Resident)	
Rachel Nguyen (Pharmacy Student)	

Call to Order:
Kimberly Clark called the meeting to order at 1:03 p.m., Tuesday, May 17, 2022.

Review and Approval of Minutes:

Kimberly Clark asked for a motion or approval to accept the March 15, 2022 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

OPDUALAG (nivolumab and relatlimab-rmbw)

Review: Opdualag is a fixed-dose combination of Opdivo (nivolumab), a programmed death receptor-1 (PD-1) blocking antibody, and relatlimab, a lymphocyte activation gene-3 (LAG-3) blocking antibody. It is indicated for the treatment of adult and pediatric patients 12 years and older with unresectable or metastatic melanoma. Opdualag is a first-in-class combination PD-1 inhibitor/LAG-3 inhibitor and the first LAG-3 inhibitor to demonstrate benefit in a Phase 3 study. NCCN added recommendations for Opdualag as a preferred first-line systemic therapy option for metastatic or unresectable disease (Category 2A; Figure 1). It is also being studied in several other cancer types, including hepatocellular carcinoma, soft tissue sarcoma, lymphoma, head and neck cancer, non-small cell lung cancer, and ovarian cancer.

The efficacy of Opdualag was investigated in RELATIVITY-047, a randomized, double-blind trial in 714 patients with previously untreated metastatic or unresectable Stage III or IV melanoma. Patients were randomized to receive Opdualag (480 mg-160 mg) by intravenous infusion every four weeks or Opdivo (nivolumab alone) 480 mg intravenous infusion every 4 weeks until disease progression or unacceptable toxicity. The major efficacy outcome evaluating progression-free survival showed that patients treated with Opdualag had a statistically significant improvement in PFS compared to nivolumab alone. A secondary endpoint evaluating overall survival was not statistically significant.

There are no black box warnings for Opdualag. Warnings and precautions are consistent with Opdivo monotherapy and include the risk of severe or fatal immune-mediated adverse reactions (IMARS), infusion related reactions, complications of allogeneic HSCT, and embryo-fetal toxicity. In the RELATIVITY-047 trial, serious adverse reactions occurred in 36% of patients treated with Opdualag, most frequently adrenal insufficiency, anemia, colitis, pneumonia, acute myocardial infarction, back pain, diarrhea, myocarditis, and pneumonitis. The most common adverse reactions that occurred were musculoskeletal pain, fatigue, rash, pruritis, and diarrhea. The most common laboratory abnormalities were decreased hemoglobin, lymphocytes, and sodium and increased AST and ALT.

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: Opdualag is a medical benefit and will be added to the medical benefit cost share list. If processed at a specialty pharmacy, Opdualag will process at the Specialty tier or Brand Non-Preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation that Opdualag is written by a hematologist or oncologist **AND**
- Medical record documentation that patients is greater than or equal to 12 years of age **AND**

- For patients greater than or equal to 12 years and less than 18 years:
    - Medical record documentation of weight greater than or equal to 40 kg

AND

- Medical record documentation of a diagnosis of unresectable or metastatic melanoma

QUANTITY LIMIT: 2 vials (40 mL) per 28 days

AUTHORIZATION DURATION: Initial approval will be for **12 months**. Subsequent approvals will be for an additional **12 months** and will require medical record documentation of continued disease improvement or lack of disease progression. The medication will no longer be covered if patient experiences toxicity or worsening of disease.

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

ADBRY (tralokinumab-ldrm)

Review: Adbry is a monoclonal antibody that inhibits interleukin-13 and is indicated for the treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical therapies or when those therapies are not advisable. Adbry is supplied as a 150 mg/mL solution in a prefilled syringe for subcutaneous injection and is dosed initially 600 mg (4 syringes) followed by 300 mg (2 syringes) every other week. The maintenance dose can be decreased to 300 mg (2 syringes) every four weeks for patients below 100 kg who achieve clear or almost clear skin after 16 weeks of treatment. Adbry may be given with or without topical corticosteroids.

In clinical trials, Adbry significantly improved disease severity and decreased lesion size when compared to placebo. In addition, the medication demonstrated significant clinical improvement when compared to topical corticosteroids as the standard of care. Hypersensitivity, conjunctivitis and keratitis, and helminth infections are listed on the label under warnings and precautions. Side effects include upper respiratory tract infections, conjunctivitis, injection site reactions, and eosinophilia.

Adbry is the second systemic therapy FDA approved for moderate-to-severe atopic dermatitis. Its comparator, Dupixent, showed similar efficacy/safety outcomes though there are no direct head-to-head trials comparing the two medications. The biggest differences between Adbry and Dupixent are that Dupixent has additional indications for asthma and chronic rhinosinusitis with nasal polyposis (both conditions commonly present in patients with atopic dermatitis) as well as decreased number of syringes used for maintenance dose administration (1 syringe every two weeks for Dupixent versus 2 syringes every 2 weeks for Adbry).

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: Adbry is a pharmacy benefit that will be added to the Commercial, Marketplace, and GHP Kids formularies at the Specialty tier or Brand Non-Preferred tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of moderate to severe atopic dermatitis **AND**
- Medical record documentation that Adbry is prescribed by or in consultation with an allergist, dermatologist, or immunologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) **AND**
- Medical record documentation of one of the following:
    - Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid **OR**
    - For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable, therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor.

QUANTITY LIMIT:

Initial Approval – Two authorizations must be entered.

- 600mg once, followed by 300mg every other week
    1. In Darwin: Add PA, OQL, DS, enter 1 in max number of claims authorized, max quantity of 6, minimum day supply 28, and maximum day supply 28 with a duration of 2 weeks.
    2. In PA Hub: Add PA, OQL, and max quantity 4 with a start date 1 day after the loading dose for remainder of the authorization.
        - QL FOR LETTER: Loading Dose: 6 mL per 28 days; Maintenance Dose: 4 mL per 28 days

Renewal

- 300mg every other week
    1. In PA Hub: Add PA, OQL, and max quantity 4.
        - QL FOR LETTER: 4 mL per 28 days
- 300mg every 4 weeks
    2. In PA Hub: Add PA, OQL, and max quantity 2.
        - QL FOR LETTER: 2 mL per 28 days

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals for the medication will be for 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 patient experiences toxicity or worsening of disease.

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

CARVYKTI (ciltacabtagene autoleucel)

Review: Carvykti is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult patients with relapsed or

refractory multiple myeloma after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. Carvykti is an intravenous infusion supplied as a suspension of chimeric antigen receptor (CAR)-positive viable T-cells prepared from the patient's own peripheral blood mononuclear cells obtained via standard leukapheresis. The anti-BCMA CAR-T cells are infused back into the patient where they promote T cell activation, expansion and elimination of BCMA-expressing target cells. In addition to T cells, Carvykti may contain Natural Killer (NK) cells.

The efficacy of Carvykti was evaluated in CARTITUDE-1, an open-label, single-arm trial in adult patients with relapsed or refractory multiple myeloma, who previously received at least prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-C38 monoclonal antibody. The median number of prior lines of therapy was 6, with 82% of patients receiving 4 or more prior lines of therapy, 90% had received prior autologous stem cell transplantation. Ninety-nine percent were refractor to their last line of prior therapy and 88% were refractory to a proteasome inhibitor, immunomodulatory agent, and an anti-CD38 antibody.

Ninety-seven patients were in the efficacy evaluable population, including 17 patients with manufacturing failures. Efficacy was based on overall response rate, complete response rate, and duration of response assessed by Independent Review Committee (IRC) using International Myeloma Working Group (IMWG) criteria. The median time to first response was 1 month. Ninety-five (97.9) patients demonstrated a response following Carvykti administration, with 76% of patients having a stringent complete response. The median duration of response was 21.8 months.
Like other CAR-T therapies, Carvykti has black box warnings for Cytokine release syndrome, neurologic toxicities, Hemophagocytic lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), and prolonged and recurrent cytopenias. Cytokine release syndrome occurred in 95% of patients treated with Carvykti. Grade 3 or higher CRS occurred in 5% of patients with Grade 5 CRS reported in 1 patient. The median time to CRS onset was 7 days and median duration of CRS was 4 days in all but one patient who had a duration of CRS of 97 days and a subsequent fatal outcome (HLH). The most common manifestations of CRS included pyrexia, hypotension, increased AST and ALT, chills, and sinus tachycardia.

During clinical trials, the most common Grade 3 or 4 reactions included infections, pneumonia, febrile neutropenia, and hypotension. The most common all Grade adverse reactions were pyrexia, cytokine release syndrome, hypogammaglobulinemia, hypotension, musculoskeletal pain, fatigue, infections of unspecified pathogen, cough, chills, diarrhea, nausea, encephalopathy, decreased appetite, upper respiratory tract infection, headache, tachycardia, dizziness, dyspnea, edema, viral infections, coagulopathy, constipation, and vomiting. Serious adverse reactions occurred in 55% of patients, most commonly CRS, sepsis, encephalopathy, and pneumonia. Fatal adverse reactions occurred in 9% of patients.

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: Carvykti is a medical benefit and will be added to the medical benefit cost share list and will require prior authorization. The following prior authorization criteria will apply:

- Medical record documentation that Carvykti is prescribed by a hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of relapsed or refractory multiple myeloma **AND**
- Medical record documentation of at least four prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

AUTHORIZATION DURATION: One-time authorization for one administration of Carvykti

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

DHIVY (carbidopa and levodopa)

Review: FDA Approved Indication: DHIVY is a combination of carbidopa (an aromatic amino acid decarboxylation inhibitor) and levodopa (an aromatic amino acid) indicated for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and symptomatic parkinsonism that may follow carbon monoxide intoxication or manganese intoxication

Dosing/How Supplied: Tablet Form: Carbidopa and levodopa 25 mg/100 mg, functionally scored. Each DHIVY tablet has 3 functional scores with each containing 6.25 mg of carbidopa and 25 mg of levodopa. Recommended dosing is one 25/100mg tablet orally three times daily. Max dose is 8 tablets per day. The scoring helps with dosage adjustment. Patients should be prescribed at least 70mg to 100mg of carbidopa per day (maximum dose is 200mg of carbidopa per day). Tapering is required when starting and with discontinuation.

Place in therapy: The treatment of Parkinson's Disease (PD) is usually initiated when the symptoms interfere with the patient's quality of life and functioning. There are 4 general classes for the initial treatment with PD agents, and they include MAO B inhibitors (selegiline, rasagiline, Xadago), amantadine, dopamine agonists (pramipexole, ropinirole, and Neupro), and levodopa. One agent is not preferred over the next but is usually determined by the characteristics of the patient and disease. A trial-and-error approach is recommended. MAO B inhibitors and amantadine are well tolerated, but they only have a modest effect. Levodopa is the most effective agents for control of motor symptoms, but many patients exhibit a "wearing off" effect that occurs over time. Levodopa changes to dopamine in the brain and helps control movement. The carbidopa component prevents the breakdown of levodopa so more of the levodopa can enter the brain. It can also help to lessen GI side effects. Dopamine agonists have been known to improve motor function but can cause somnolence and hallucinations and are usually not recommended in older individuals. Other dopamine agents such as cabergoline and bromocriptine have fallen out of favor due to severe complications.

Summary of Clinical Trials: The efficacy of Dhivy is based on previous findings of efficacy of carbidopa/levodopa in Parkinson's Disease and by comparing the bioavailability of Dhivy to an immediate-release tablet of carbidopa/levodopa 25mg/100mg.

Summary of Safety Considerations: Dhivy is contraindicated in patients taking nonselective monoamine oxidase (MAO) inhibitors (phenelzine, linezolid, tranylcypromine) or in patients who have taken one within 2 weeks (can cause hypertension). An additional contraindication of carbidopa/levodopa is narrow-angle glaucoma. There is a drug interaction with selective MAO-B inhibitors (rasagiline or selegiline) but can be used concomitantly with monitoring.

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

- Medical record documentation of a diagnosis of Parkinson's disease, post-encephalitis parkinsonism, **OR** parkinsonism which may follow carbon monoxide intoxication or manganese intoxication **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives, one of which must be immediate release carbidopa/levodopa

QUANTITY LIMIT: 8 tablets per day (max dose)

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

LIVTENCITY (maribavir)

Review: Livtencity, a CMV pUL97 kinase inhibitor, is an oral antiviral agent that is the first FDA approved drug approved specifically for the treatment of refractory CMV. It is currently approved to treat adult and pediatric patients (12 years of age and older and weighing at least 35 kg) with post-transplant CMV infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir, or foscarnet. Livtencity works by preventing the phosphorylation of proteins and viral DNA replication, encapsidation, and nuclear egress. Because its mechanism of action is different than conventional antivirals used for CMV, Livtencity retains some activity against CMV that is resistant to some conventional agents.

In the Phase 3 SOLSTICE trial, Livtencity achieved viremia clearance in 56% of patients compared with 24% of patients receiving traditional treatment.

The safety profile for Livtencity is favorable compared to conventional CMV antivirals, likely resulting in lower risk of neutropenia compared to ganciclovir and valganciclovir, and potentially a lower risk of renal impairment compared with cidofovir and foscarnet. The most common adverse reactions are taste disturbance, nausea, diarrhea, vomiting and fatigue.

Livtencity will initially be used to treat resistant CMV disease in organ transplant recipients; however, Takeda is investigating maribavir in an ongoing Phase 3 clinical trial (NCT02927067) as a first-line treatment for CMV in HSCT recipients. Livtencity is not FDA-approved in patients with human immunodeficiency virus (HIV) or other nontransplant populations, nor is it approved for prophylaxis of CMV infection. Livtencity previously failed Phase 3 trials for the prevention of CMV in transplant patients.

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

Clinical Discussion: Tricia recommended an additional note to address requests for durations longer than 8 weeks. No additional 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: Livtencity is a pharmacy benefit. Livtencity will be added to the Commercial/Exchange/CHIP formularies at the Specialty Tier or BrandNP tier for members with a 3 Tier benefit. The following prior authorization criteria will apply:

- Medical record documentation that Livtencity is prescribed by a transplant surgeon, infectious disease specialist, or hematologist/oncologist **AND**
- Medical record documentation of age greater than or equal to 12 years of age and weighs over 35 kg **AND**
- Medical record documentation that patient has received a hematopoietic stem cell transplant (HSCT), or solid organ transplant (SOT) **AND**
- Medical record documentation of a diagnosis of post-transplant cytomegalovirus (CMV) infection **AND**
- Medical record documentation that the members CMV infection is refractory to previous treatment with ganciclovir, valganciclovir, cidofovir, or foscarnet **AND**
- Medical record documentation that medication will not be used in combination with another CMV antiviral **AND**
- If request is above 400mg twice daily dosing, medical record documentation of one of the following:
    - For requests of 800mg twice daily dosing: Medical record documentation that member is concurrently receiving carbamazepine **OR**
    - For requests of 1200mg twice daily dosing: Medical record documentation that member is concurrently receiving phenytoin or phenobarbital

QUANTITY LIMIT: 4 tablets/day (coded quantity limit)

- 400 mg twice daily (given as two 200mg tablets twice daily): No QLs need to be entered within the authorization unless the requested quantity exceeds the QL. QL FOR LETTER ONLY: 4 tablets per day
- 800 mg twice daily (given as four 200mg tablets twice daily): Only enter PA, OQL, max daily dose 8. QL FOR LETTER: 8 tablets per day
- 1200mg twice daily (given as six 200mg tablets twice daily): Only enter PA, OQL, max daily dose 12. QL FOR LETTER: 12 tablets per day

MEDISPAN AUTHORIZATION LEVEL: GPI-12

AUTHORIZATION DURATION: 8 weeks

NOTE: Livtencity has not been studied in clinical trials for longer than 8 weeks and should only be used for treatment of active infection. Livtencity is not approved for prophylaxis of CMV infections.

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

PEMFEXY (pemetrexed)

Review: Pemfexy is a folate analog metabolic inhibitor indicated:

- In combination with cisplatin for the initial treatment of patients with locally advanced or metastatic non-squamous, non-small cell lung cancer (NSCLC)

- As a single agent for the maintenance treatment of patients with locally advanced or metastatic non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy
- As a single agent for the treatment of patients with recurrent, metastatic, non-squamous NSCLC after prior chemotherapy

Limitations of Use: Pemfexy is not indicated for the treatment of patients with squamous cell non-small cell lung cancer.

- In combination with cisplatin for the initial treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

The recommended dosage of Pemfexy is 500 mg/m2 intravenous infusion over 10 minutes on Day 1 of each 21 day cycle. When administered with cisplatin for initial treatment of locally advanced or metastatic NSCLC, this is continued for up to 6 cycles, disease progression, or unacceptable toxicity. For maintenance treatment of NSCLC, Pemfexy is initiated after four cycles of platinum-based first-line chemotherapy and is continued until disease progression or unacceptable toxicity. For patients with recurrent NSCLC and patients with mesothelioma, Pemfexy is continued until disease progression or unacceptable toxicity. All Pemfexy dosing recommendations are for patients with a creatinine clearance of 45 mL/min or greater. There is no recommended dose for patients with a CrCl less than 45 mL/min. Patients should also receive folic acid, vitamin B12, and corticosteroids to mitigate toxicity. Pemfexy is supplied as a single dose vial containing 500 mg pemetrexed per 20 mL (25 mg/mL).

Pemfexy efficacy is based on results of clinical trials from the reference product Alimta and in vivo bioavailability studies that demonstrated bioequivalence. The therapeutic active moiety and route of administration are the same, but the products differ in salt form (disodium vs. diacid), excipients, dosage form, and solution for dilution. Prior to administration, Pemfexy is diluted in 5% Dextrose in Water while Alimta is diluted with 0.9% Sodium Chloride. No new clinical safety or efficacy trials were conducted. Pemfexy was approved for the same indications as Alimta intravenous.

The use in specific populations is also based on the previous submitted clinical trial information for Alimta. The safety and efficacy have not been established in pediatric patients. For geriatric patients, there were no overall differences observed for efficacy between older and younger patients. In Alimta clinical trials, the incidences of Grade 3-4 anemia, fatigue, thrombocytopenia, hypertension, and neutropenia were higher in patients 65 years and older compared to younger patients.

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: Pemfexy is a medical benefit and will be added to the medical benefit cost share list. If processed at a specialty pharmacy, Pemfexy will process at the Specialty tier or Brand Non-Preferred tier for members with a three tier benefit.

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

RECORLEV (levoketoconazole)

Review: Recorlev is indicated for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome (CS) for whom surgery is not an option or has not been curative. Recorlev is not indicated for the treatment of fungal infections. The safety and effectiveness of Recorlev for the treatment of fungal infections have not been established.

Initiate dosage at 150mg orally twice daily, with or without food. Titrate dosage by 150mg daily, no more frequently than every 2-3 weeks. Maximum recommended dosage is 1200mg daily, administered as 600mg twice daily. The dosage of Recorlev may be reduced to 150mg once daily if needed for reasons of tolerability.

Recorlev was evaluated in 2 studies, Study 1 and Study 2. In Study 1, the number and percent of patients who had normal mUFC at the end of the randomized withdrawal phase was 11/21 (52.4%) in Recorlev group and 1/18 (5.6%) in placebo group, and the treatment difference (CI) was 46.8% (16.5%, 70.2%). In Study 2, the primary efficacy endpoint was the proportion of patients with normalization of mUFC, defined as mUFC at or below the ULN without requiring a dose increase during the maintenance phase, at the end of the 6-month maintenance phase. 29 of 94 patients [30.9%, 95% CI (21.7%, 41.2%)] met the primary endpoint.

Recorlev has a black box warning for hepatotoxicity and QT prolongation. Recorlev is contraindicated in patients: With cirrhosis, acute liver disease or poorly controlled chronic liver disease, baseline AST or ALT greater than 3 times the upper limit of normal, recurrent symptomatic cholelithiasis, a prior history of drug induced liver injury due to ketoconazole or any azole antifungal therapy that required discontinuation of treatment, or extensive metastatic liver disease; Taking drugs that cause QT prolongation associated with ventricular arrhythmias, including torsades de pointes; With a prolonged QTcF interval of greater than 470 msec at baseline, history of torsades de pointes, ventricular tachycardia, ventricular fibrillation, or long QT syndrome (including first-degree family history); With known hypersensitivity to levoketoconazole, ketoconazole, or any excipient in Recorlev; Taking certain drugs that are sensitive substrates of CYP3A4 or CYP3A4 and P-gP.

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: Recorlev will not be added to the Commercial/Exchange/CHIP formularies. The following prior authorization criteria will apply:

- Medical record documentation of endogenous hypercortisolemia associated with Cushing's syndrome **AND**

- Medical record documentation of age 18 years or older **AND**
- Medical record documentation that Recorlev is being prescribed by or in consultation with an endocrinologist **AND**
- Medical record documentation that pituitary surgery is not an option or has not been curative **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) of the following: ketoconazole, Metopirone, Signifor, Signifor LAR

QUANTITY LIMIT: 8 tablets per day

AUTHORIZATION DURATION: 12 months. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically appropriate. Reauthorization requires medical record documentation of improvement in urinary free cortisol levels compared to baseline.

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

RYPLAZIM (plasminogen, human-tvmh)

Review: Ryplazim is a human-derived plasminogen indicated for the treatment of patients with plasminogen deficiency type 1 (hypoplasminogenemia). Ryplazim treatment temporarily increases plasminogen levels in the blood leading to a reduction or resolution of extravascular fibrinous lesions. Ryplazim is the first and only therapy approved for PLGD Type I.

The efficacy of Ryplazim was evaluated in RYPLAZIM Trial 2, an open-label, single-arm clinical trial in 15 pediatric and adult patients with PLGD Type 1. All patients enrolled had a baseline plasminogen activity level between < 5% and 45% of normal, and biallelic mutations in the plasminogen (PLG) gene. Patients received Ryplazim 6.6 mg/kg every 2 to 4 days for 48 weeks to achieve at least a 10% increase above baseline in individual trough plasminogen activity and to treat clinical manifestations of the disease.

Efficacy was based on overall rate of clinical success at 48 weeks, defined as 50% with visible or other measurable non-visible lesions achieving at least 50% improvement in lesion number or size, or functionality impact from baseline. Results showed that all patients with any lesion at baseline had at least 50% improvement in the number/size of their lesions. Twenty-five of 32 external lesions were resolved by the end of Week 48. Nine of 12 internal lesions were resolved by Week 48. No recurrent or new internal or external lesions occurred in any patient through Week 48. Spirometry was the only organ function test used during the trial. One patient with a history of ligneous airway disease had abnormal spirometry at baseline (FEV1 46.7% of predicted normal) prior to treatment that corrected to normal after 12 weeks of treatment (FEV1 89.3% of predicted normal).

There are no black box warnings for Ryplazim. Warnings include increased risk of bleeding from active mucosal disease-related lesions and worsening of active bleeding not related to disease lesions, tissue sloughing at mucosal sights, including those in the respiratory, gastrointestinal, and genitourinary systems, risk of transmission of infections agents, and hypersensitivity reactions, including anaphylaxis.

During clinical trials, the most frequent reported adverse reactions were abdominal pain, bloating, nausea, fatigue, extremity pain, hemorrhage, constipation, dry mouth, headache, dizziness, arthralgia, and back pain.

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: Ryplazim is a medical benefit and will require a prior authorization. It will be added to the medical benefit cost share list. If processed at a specialty pharmacy, Ryplazim will process at the Specialty tier or Brand Non-Preferred tier for members with a three tier benefit. The following prior authorization will be required:

- Medical record documentation of use for a Food and Drug Administration (FDA) approved indication **AND**
- Medical record documentation of a diagnosis of plasminogen deficiency type 1 (hypoplasminogenemia) confirmed by medical record documentation of all of the following:
    - Documentation of a plasminogen activity level less than or equal to 45% **AND**
    - Documentation of a history of external and/or internal lesions and symptoms consistent with a diagnosis of congenital plasminogen deficiency type 1 (PLGD) **AND**
    - Documentation of the presence of biallelic mutations in the plasminogen (PLG) gene

AUTHORIZATION DURATION: Approval will be given for an initial duration of three (3) months or less if the reviewing provider feels it is medically appropriate. After the initial three (3) month approval, subsequent approvals will be for a duration of six (6) months or less if the reviewing provider feels it is medically appropriate, requiring medical record documentation of:

- Medical record documentation of resolution or improvement in documented lesions **AND** medical record documentation of no new or recurrent lesions **OR**
- Medical record documentation of trough plasminogen level greater than or equal to 10% above baseline trough plasminogen level

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

- Medical record documentation of continued positive response to Ryplazim therapy including no new or recurrent lesions **OR**
- Medical record documentation of trough plasminogen level greater than or equal to 10% above baseline trough plasminogen level

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

SOOANZ (torsemide)

Review: Soaanz is a loop diuretic indicated in adults for the treatment of edema associated with heart failure or renal disease.

How Supplied/Dosing: Available as a 20 mg, 40 mg and 60 mg tablets.

Initial dosage is 20 mg once daily and the dose may be increased gradually by doubling the dose until the desired diuretic response is obtained; doses greater than 200 mg/day have not been adequately studied.

Place in therapy: When a patient has edema from heart failure or renal disease, diuretics are typically the first pharmacological treatment option utilized to help induce diuresis.

The manufacturer website has three major benefits of Soaanz listed: Increased duration of action (6-8 hours), may help with incidences of hypokalemia, and may reduce excessive urination. However, there are no clinical studies that compare Soaanz to generic Torsemide or even additional clinical studies on Soaanz alone. These benefits outlined by the manufacturer will be discussed further below.

Summary of Clinical Trials: There were no new individual clinical trials performed for Soaanz. Approval for Soaanz was based on existing Torsemide clinical data as well as pharmacokinetic/pharmacodynamic data on Soaanz.

According to the package insert generic Torsemide has an onset of diuresis within 1-hour, peak effect during 1st or 2nd hour, and diuresis lasts about 6-8 hours. Soaanz has the same onset of diuresis within 1 hour and diuresis lasts about 6-8 hours. However, for Soaanz the package insert states peak effect occurs within the first 4 hours. Based on this information it appears the duration of action is the same, but peak effect window is extended with Soaanz

In regard to the statement that Soaanz may help with incidences of hypokalemia the prescribing information available does not show a clear picture of that. Based on the information available around potassium excretion both Soaanz and Torsemide show similar potassium excretion but studies taking into account specific time frames post dose have not been completed.

The manufacture states that Soaanz may reduce excessive urination due to the extended duration of peak effect (1-2 hours for generic Torsemide and 1-4 hours for Soaanz) however due to the lack of head-to-head clinical trials and clinical relevancy of extending peak effect windows this benefit cannot be confirmed.

Summary of Safety Considerations:
There are no black box warnings for Soaanz. Contraindications include: hypersensitivity to Soaanz, patients who are anuric (lack of urine production), and patients with hepatic coma. The warnings and precautions include: hypotension and worsening renal function, electrolyte and metabolic abnormalities, and ototoxicity.

Adverse Reactions: seen in post marketing experience include but are not limited to-abdominal pain, pancreatitis, confusion, visual impairment, loss of appetite, anemia, thrombocytopenia, increase in liver transaminases, thiamine deficiency, pruritus, Stevens-Johnson syndrome

Pediatrics: Safety and efficacy have not been established
Geriatrics: No dosage adjustment necessary
Renal Impairment: No dosage adjustment necessary, higher doses may be required to achieve diuretic response. Watch for electrolyte and metabolic abnormalities.
Hepatic Impairment: Use with caution in patients with hepatic impairment-keeping a close on electrolyte and acid/base imbalances.

Please refer to the package insert for a complete list of drug interactions. Of note, Soaanz is a substrate of CYP2C9 and concomitant use of CYP2C9 inhibitors can decrease torsemide clearance and increase torsemide plasma concentrations. Concomitant use of CYP2C9 inducers can increase torsemide clearance and decrease plasma torsemide concentrations.

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

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Soaanz will be used for the treatment of edema associated with heart failure OR renal disease **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives, one of which must be generic Torsemide

QUANTITY LIMIT:

- 20 mg tablets: 1 tablet per day
- 40 mg tablets: 2 tablets per day
- 60 mg tablets: 3 tablets per day

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

TEZSPIRE (Tezepelumab-ekko)

Review: Tezspire is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. Tezspire is a first-in-class monoclonal antibody that blocks the action of TSLP and the only biologic approved for severe asthma with no phenotype (e.g. eosinophilic or allergic) or biomarker limitation within its approved label. There are 5 other biologics on the market to treat severe asthma, however Tezspire is the first to demonstrate a clinically significant reduction in asthma exacerbations in patients with low blood eosinophils (i.e. < 150 cells/microL), also known as non-eosinophilic asthma. However, similar to other biologics, Tezspire efficacy improves as eosinophil levels increase.

Tezspire is available as a single dose-vial and single-dose pre-filled syringe that contains 210 mg/1.91 mL. The recommended dosage of Tezspire is 210 mg administered subcutaneously once every 4 weeks. Tezspire is intended for administration by a healthcare provider.

The efficacy of Tezspire was evaluated in two randomized double-blind, parallel group, placebo-controlled clinical trials of 52 weeks duration. Both trials enrolled a total of 1609 patients 12 years of age and older with severe asthma. Patients were required to have been on treatment with medium or high-dose inhaled corticosteroids and at least one additional asthma controller, with or without OCS. Patients continued background asthma therapy throughout the trial. In both trials, patients were enrolled without requiring a minimum baseline level of blood eosinophils or FeNO. The primary endpoint was the rate of clinically significant asthma exacerbations measured over 52 weeks. In both trials, patients receiving Tezspire had significant reductions in the annualized rate of asthma exacerbations compared to placebo. There were also fewer exacerbations requiring emergency room visits and/or hospitalization in patients treated with Tezspire compared with placebo. An additional trial looked at the effect of Tezspire (210 mg every 4 weeks) on reducing the use of maintenance OCS. Tezspire did not demonstrate a statistically significant reduction in maintenance OCS dose compared with placebo. In the subgroup analysis, those with baseline levels of blood eosinophils ≥150 cells/microL or ≥300 cells/microL, Tezspire significantly reduced the OCS daily dose. Results were not significant in <300 cells/microL and 150 cells/microL subgroups.

Tezspire is contraindicated in patients who have a known hypersensitivity to Tezepelumab-ekko or any of its excipients. Tezspire has warnings and precautions for hypersensitivity reactions, not for use to treat acute asthma symptoms/exacerbations, risks for systemic withdrawal symptoms and/or unmask conditions that may have been suppressed with corticosteroid therapy associated with abrupt reduction of corticosteroid dose, known parasitic (helminth) infections, and avoid live attenuated vaccines. The most common adverse reactions (incidence ≥ 3% and greater than placebo) include pharyngitis, arthralgia, and back pain. In clinical trials there were no meaningful differences in safety results between the tezepelumab and placebo groups.

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: Tezspire is a medical benefit. Tezspire will be added to the medical benefit cost share list when processed through the medical benefit. If processed at a specialty pharmacy, Tezspire will process at the Specialty tier or Brand Non-Preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Prescription written by or in consultation with an allergist, immunologist, or pulmonologist **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation of severe asthma **AND**
- Medical record documentation that Tezspire will be used as an add-on maintenance treatment **AND**
- Medical record documentation of one of the following:
    - Poor control or intolerance, despite a 3 month trial of: medium –high dose inhaled corticosteroids and another controller medication (long-acting beta agonists, long-acting muscarinic antagonist, or leukotriene receptor antagonists) with or without oral corticosteroids **OR**
    - Two or more asthma exacerbations requiring systemic corticosteroid treatment or one asthma exacerbation resulting in hospitalization in the past 12 months despite current therapy to medium- high inhaled corticosteroids and another controller medication (long-acting beta agonists, long-acting muscarinic antagonist, or leukotriene receptor antagonists) **AND**
- Medical record documentation that Tezspire will not be used in combination with another biologic medication indicated for asthma treatment (e.g. Xolair, Nucala, Fasenra, Dupixent, Cinqair)

QUANTITY LIMIT: 1.19 mL (210 mg) every 28 days

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

Other Recommendations: All the asthma biologic policies for Commercial and Medicare currently have criteria that states one biologic cannot be used in combination with another biologic for the treatment of asthma, however some of the new products are missing from that section of the policies. To increase consistency, it is recommended to update the duplicate therapy criteria in the policies to the following:

- "Medical record documentation that the medication will not be used in combination with another biologic medication indicated for asthma treatment (e.g. list examples)"

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

VONJO (pacritinib)

Review: Vonjo is an oral kinase inhibitor that is indicated for the treatment of adult patients with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocytopenia) myelofibrosis with a platelet count below 50 x 109/L. This was approved

under an accelerated approval based on spleen volume reduction. Continued approval is contingent upon a confirmatory trial. Vonjo has inhibitor activity against wild-type Janus associated kinase 2 (JAK2), mutant JAK2, and FMS-like tyrosine kinase 2 (FLT3), which contribute to cytokine signaling and hematopoiesis and immune function growth factors. It does not inhibit JAK1 at clinically relevant concentrations, so lower rates of myelosuppression are expected. This is the first FDA approved therapy for MF that specifically addresses patients with severe thrombocytopenia (platelet count below 50 x 109/L).

The efficacy of Vonjo was evaluated in the PERSIST-2 trial, a randomized controlled study evaluating Vonjo compared to Best Available Therapy (BAT) in 311 patients with primary or secondary myelofibrosis, palpable splenomegaly, and a platelet count ≤ 100 x 109/L. Patients were randomized 1:1:1 to received Vonjo 400 mg once daily (n=104), Vonjo 200 mg twice daily (n=107), or BAT (n=100). BAT agents could be used alone, in combination, sequentially or intermittently as indicated by standards of care and included any physician-selected treatment such as Jakafi, hydroxyurea, glucocorticoids, erythropoietic agents, immunomodulatory agents, mercaptopurine, danazol, interferons, cytarabine, and/or melphalan. BAT could also include no treatment or symptom-directed treatment without MF-specific treatment.

Efficacy was established in patients treated with Vonjo 200 mg twice daily with a platelet count < 50 × 109/L (n=31). The most common agents used in the BAT treatment arm in patients with a platelet count < 50 × 109/L (n=32) were Jakafi (39%), watchful waiting (32%), and hydroxyurea (26%). Results showed a significantly higher proportion of patients with severe thrombocytopenia treated with Vonjo achieved a 35% reduction in spleen volume from baseline compared to placebo (29% vs. 3%). The median spleen reduction in spleen volume for patients with a platelet count < 50 × 109/L was 27.3% for patients treated with Vonjo compared to 0.9% for the BAT group. A higher proportion of patients treated with Vonjo achieved a 50% reduction in symptoms scores compared to placebo (23% vs 13%).

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: Vonjo is a pharmacy benefit and will be added to the Oral Oncology Brand Non-preferred tier ($0 copay) of the Commercial, Marketplace, and GHP Kids formulary. The following prior authorization criteria will be required:

- Medical record documentation that Vonjo is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis or post-essential thrombocythemia myelofibrosis **AND**
- Medical record documentation of severe thrombocytopenia with platelet count less than or equal to 50 x 109/L **AND**
- Medical record documentation of splenomegaly as measured by computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound **AND**

- Medical record documentation of baseline total symptom score as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF) **AND**
- Medical record documentation that Vonjo will not be used concurrently with other kinase inhibitors

NOTE: Intermediate or High-Risk Myelofibrosis is defined by having at least 2 of the following factors:

- ✓ Age > 65 years
- ✓ WBC > 25 x 109/L
- ✓ Hemoglobin < 10 g/dL
- ✓ Blood Blasts ≥ 1%
- ✓ Presence of Constitutional Symptoms (weight loss, fever, excessive sweats, etc.)
- ✓ Transfusion dependency
- ✓ Platelets less than 100 X 109/L
- ✓ Unfavorable karyotype

QUANTITY LIMIT: 4 capsules per day, 30 day supply per fill

AUTHORIZATION DURATION: Each treatment period will be defined as six (6) months. Re-review with occur every six (6) months. Vonjo will no longer be covered if medical record documentation does not show:

- Medical record documentation of platelet count less than or equal to 50 x 109/L **AND**
- The member has achieved a reduction from pretreatment baseline of at least 35% in spleen volume as measured by computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound **OR**
- The member has achieved a 50% or greater reduction in the Total Symptom Score from baseline as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF)

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

VOXZOGO (vosoritide)

Review: Voxzogo is a C type natriuretic peptide (CNP) analog indicated to increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses. It is the only FDA approved treatment for improving growth in patients with achondroplasia. Achondroplasia is the most common bone dysplasia in humans, occurring in approximately 1 in 20,00- live births, and is caused by a gain of function mutation in FGFR3. FGFR3 belongs to a family of proteins that plays a role in many cellular processes, such as regulation of cell grown and division, determination or cell type, formation of blood vessels, wound healing, and embryo development. The most noticeable clinical features in a patient with achondroplasia include disproportioned short stature (adult height is approximately 4 feet), long-bone shortening predominantly in the proximal upper and lower extremities and macrocephaly.

Voxzogo is a once daily, subcutaneous injection, that is dosed based on patient's actual body weight. The efficacy of Voxzogo was demonstrated in a multi-center, randomized, double-blind, placebo-controlled, phase 3 study in which 121 patients aged 5.1-14.9 years with a confirmed diagnosis of achondroplasia, were randomized to Voxzogo 15mcg/kg daily or placebo. Voxzogo

resulted in a treatment difference in the change from baseline in AGV of 1.57cm/year after 52 weeks of treatment.

The most notable adverse event seen with Voxzogo is a transient decrease in blood pressure, therefore patients should be well hydrated and have adequate food intake prior to administration to decrease this risk. Voxzogo is not recommended for patients with eGFR < 60ml/min/1.73m^2.

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: Voxzogo is a pharmacy benefit and will be added to the Commercial/Exchange/CHIP formularies at the Specialty Tier or BrandNP tier for members with a 3 Tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of achondroplasia with genetic testing confirming a mutation of FGFR3 **AND**
- Medical record documentation that Voxzogo is prescribed by a pediatric endocrinologist **AND**
- Medical record documentation that member is 5 to 18 years of age **AND**
- Medical record documentation of evidence that patient has open epiphyses **AND**
- Medical record patient has not received (within the past 18 months) or plans to receive limb-lengthening surgery **AND**
- Medical record documentation that Voxzogo will not be used in combination with human growth hormone products **AND**
- Medical record documentation of GFR > 60ml/min/1.73m2 **AND**
- Medical record documentation of patient's current weight **AND**
- Medical record documentation that prescribed dose is appropriate for patient's current weight **AND**
- Medical record documentation of baseline annualized growth velocity (AGV), calculated based on standing height measured over the course of 6 months prior to request

QUANTITY LIMIT: 1 vial per day

AUTHORIZATION DURATION: 6 months, Reauthorization will require the following documentation:

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

- Medical record documentation that prescribed dose is appropriate for patient's current weight

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

VYVGART (efgartigimod alfa-fcab)

Review: Myasthenia Gravis is a chronic autoimmune disease While most patients with MG initially present with the ocular form of MG which is limited to the eyelids and extraocular muscles, up to 85% of patients will progress to the generalized form of MG, which causes weakness in ocular muscles and bulbar, limb, and respiratory muscles. Muscle weakness associated with MG is due to an antibody-mediated immunologic attacks directed at 3 postsynaptic proteins in the neuromuscular junction membrane: acetylcholine receptor (AChR), muscle-specific kinase (MuSK), and low-density lipoprotein receptor-related protein 4 (LRP4).

Vyvgart is a human immunoglobulin G1 (IgG1)-derived Fc fragment indicated for the treatment of adult patients with anti-acetylcholine receptor antibody positive gMG. It binds to the neonatal Fc receptor, resulting in the reduction of circulating IgG, including abnormal AChR antibodies that are present in about 85% of patients with gMG. It is administered

There is no cure for gMG, but there are treatments available for symptom management. Acetylcholinesterase inhibitors such as pyridostigmine increase acetylcholine at the neuromuscular junction and are usually started as initial therapy in patients with mild or moderate gMG. Chronic immunosuppressive therapies such as glucocorticoids or non-steroidal immunosuppressants may also be used. For patients with severe disease or myasthenic crisis, rapid immunomodulatory therapies such as IVIG or plasma exchange may be necessary. Surgical removal of the thymus gland may be used as treatment but would typically be reserved for patients with a thymoma (10-15%) or patients over 60 years of age without thymoma with AChR antibodies. Around 10 to 30% of patients will not respond to conventional immunosuppressive therapy and may require management with Soliris or off-label rituximab.

Prior to the approval of Vyvgart, Soliris was the only FDA-approved treatment of gMG. Vyvgart offers a more flexible dosing schedule as well as a less expensive treatment option compared to Soliris. There are some additional pipeline agents that are likely to be approved for gMG over the next few years, including some subcutaneous products as well as additional intravenous products.

Vyvgart is also being evaluated for the treatment of primary immune thrombocytopenia, pemphigus vulgaris, and chronic inflammatory demyelinating polyneuropathy.

The efficacy and safety of Vyvgart in gMG was evaluated in the ADAPT trial, a 26-week randomized, double-blind, placebo-controlled study conducted in adult patients with Class II to IV gMG. The trial included patients with a Myasthenia Gravis Activities of Daily Living (MG-ADL) score (assesses the impact of gMG on daily functions) of at least 5 (50% non-ocular) who were on a stable dose of at least one treatment for gMG (including acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone). The modified intent-to-treat population included AChR antibody-positive patients who had a valid MG-ADL assessment and at least 1 post-baseline MG-ADL assessment. Patients were randomized 1:1 to Vyvgart (10 mg/kg) or matching placebo

administered as 4 infusions per cycle (1 per week), repeated as needed depending on clinical response and no sooner than 8 weeks after initiation of the previous cycle.

The primary efficacy endpoint was the percentage of MG-ADL responders (at least a 2 point reduction in the MG-ADL score compared to baseline for at least 4 consecutive weeks) during the first treatment cycle between treatment groups in the AChR-Ab positive population. Results showed a statistically significant difference favoring Vyvgart during the first treatment cycle (67.7% responder rate for Vyvgart vs. 29.7% for placebo). A secondary endpoint measured the percentage of responders using the Quantitative Myasthenia Gravis (QMG) total score which assesses muscle weakness. There was a statistically significant difference favoring Vyvgart compared to placebo during the first treatment cycle in the percentage of responders (3-point or greater reduction in QMG for at least 4 consecutive weeks) (63.1% responder rate for Vyvgart vs. 14.1% for placebo).

There are no black box warnings for Vyvgart. Safety concerns for Vyvgart include risk of infection, most commonly urinary tract infections and respiratory infections. Hematologic abnormalities were also reported during trials, with decreases in white blood cells, lymphocytes, and neutrophils. The majority of infections and hematologic abnormalities were mild to moderate in severity. Hypersensitivity reactions, including rash, angioedema, and dyspnea have also been observed in Vyvgart-treated patients. Reactions were mostly mild to moderate in severity, occurred within 1 to 3 hours after administration, and did not lead to treatment discontinuation.

The safety of Vyvgart with live or live-attenuated vaccines and the response to immunizations with any vaccine are unknown. Because Vyvgart reduces IgG levels, vaccination with live-attenuated or live-vaccines are not recommended during treatment with Vyvgart. Patients should be evaluated for age-appropriate vaccines before initiation of a new treatment cycle with Vyvgart.

During clinical trials, the most common adverse reactions reported were respiratory tract infection, headache, and urinary tract infection. Paresthesia and myalgia were also reported in a higher percentage of patients treated with Vyvgart compared to placebo. There is also potential for immunogenicity. During the clinical trial, 6 out of 83 patients developed neutralizing antibodies and due to the small number, the data is too limited to draw definitive conclusions regarding immunogenicity and the effect on pharmacokinetics, safety, or efficacy.

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: Vyvgart is a medical benefit and will be added to the medical benefit cost share list. If processed at a specialty pharmacy, Vyvgart will process at the Specialty tier or Brand Non-Preferred tier for members with a three tier benefit. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Vyvgart is prescribed by or in consultation with a neurologist **AND**

- Medical record documentation of a diagnosis of generalized myasthenia gravis (gMG) that is anti-acetylcholine receptor (AChR) antibody positive **AND**
- Medical record documentation of Myasthenia Gravis Foundation of America Clinical Classification (MGFA) Class II to IV **AND***
- Medical record documentation of a baseline Myasthenia Gravis-Activities of Daily Living (MG-ADL) score of 5 or more **AND****
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to cholinesterase inhibitors **AND**
- Medical record documentation of therapeutic failure on intolerance to, or contraindication to at least two (2) non-steroidal immunosuppressive therapies OR has failed at least one (1) immunosuppressive therapy and required chronic plasmapheresis or plasma exchange (PE) **AND**
- Medical record documentation of failure on intolerance to, or contraindication to rituximab or rituximab biosimilar **AND**
- Medical record documentation of failure on intolerance to, or contraindication to intravenous immunoglobulin (IVIG)

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

- Medical record documentation of continued disease improvement or lack of disease progression **AND**
- Medical record documentation that the member is responding positively to therapy as evidenced by a 3-point reduction from baseline in Myasthenia Gravis-Activities of Daily Living (MG-ADL) total score**

The medication will no longer be covered if patient experiences toxicity or worsening of disease.

**Note: Class I Myasthenia gravis is indicated by any eye muscle weakness, possible ptosis (drooping or falling of the upper eyelid) and no other evidence of muscle weakness elsewhere, Class II to IV include muscle weakness in areas of the body beyond the eye.*

Note: Corticosteroids: betamethasone, dexamethasone, methylprednisolone, prednisone
Cholinesterase inhibitors: pyridostigmine, neostigmine
Immunosuppressants: azathioprine, mycophenolate, cyclosporine, Rituxan

MG Activities of Daily Living (MG-ADL)**

Grade	0	1	2	3	Score
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal, but can be understood	Difficult to understand speech	
Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube	
Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube	
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence	
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions	
Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance	
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant	
Eyelid droop	None	Occurs, but not daily	Daily, but not constant	Constant	

Total score _____

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

XIPERE (triamcinolone acetonide injectable suspension)

Review: FDA Approved Indication

- Xipere is a corticosteroid indicated for the treatment of macular edema associated with uveitis.

Dosing/How Supplied

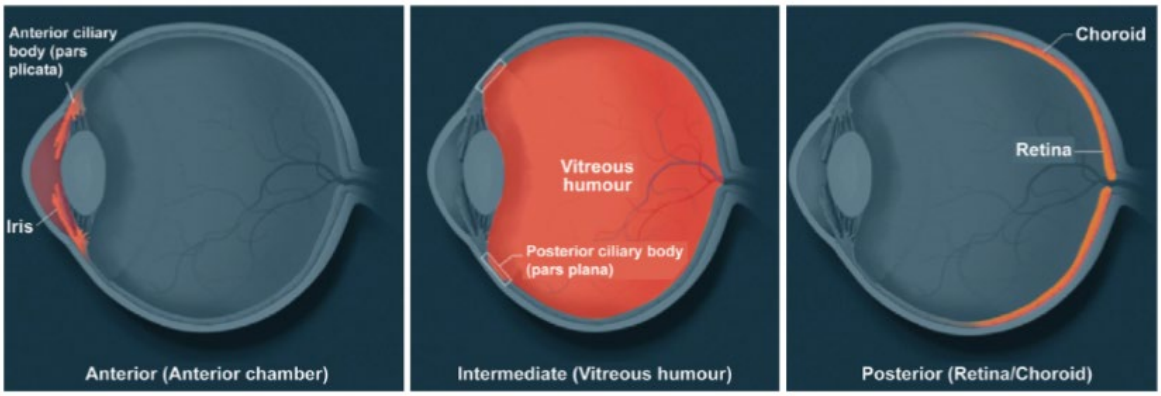
- Xipere is given at a dose of 4 mg (0.1 mL of the 40 mg/mL injectable suspension) for suprachoroidal injection using the SCS Microinjector®.
- Xipere is supplied in a Tyvek covered tray, with the following sterile components for administration:
  - One SCS Microinjector® syringe with vial adapter attached
  - One 30-G x 900-µm needle
  - One 30-G x 1100-µm needle
  - One single-dose vial of triamcinolone acetonide injectable suspension 40 mg/mL (NDC 71565-040-25)

Background of Disease State

- Uveitis is a diverse group of intraocular inflammatory diseases of the uvea (ie. the iris, ciliary body and choroid) and adjacent structures. Uveitis is one of the leading causes of preventable blindness in the United States, and accounts for 15% of the causes of total blindness in Western countries. Uveitis can be classified based on the primary anatomical site of inflammation (i.e. anterior, intermediate, posterior or panuveitis) and/or by the etiologic origin (i.e. infectious, noninfectious or masquerade). Figure 1 summarizes classification of uveitis by site of inflammation.
- Anterior uveitis is the most common form of uveitis, with 81% of all noninfectious uveitis (NIU) cases consisting of anterior NIU. Patients with NIU are at risk for glaucoma, macular edema and cataracts, with recurring flares increasing the risk of impaired vision or blindness as a result of cumulative eye damage. NIU has a

prevalence of 121 cases per 100,000 in adults and 29 cases per 100,000 in children. Infectious uveitis can be caused by bacteria, viruses, spirochetes and parasites. Infectious uveitis is less common than NIU in developed countries like the United States, and accounts for 10%-20% of uveitis cases overall.

Figure 1. Classification of Uveitis by inflammation site[3]



Place in therapy

- Triamcinolone acetonide is a corticosteroid hormone receptor agonist with immunosuppressive and anti-inflammatory activity. Xipere is the only medication approved for use via suprachoroidal injection and is supplied with a patented suprachoroidal space (SCS) Microinjector®, which delivers medication to the choroid and retina located at the back of the eye.
- Other corticosteroid-containing products for NIU include intravitreal injection Triesence (triamcinolone acetonide injectable suspension), intravitreal implants Retisert (fluocinolone acetonide), Yutiq (fluocinolone acetonide), and Ozurdex (dexamethasone), and topicals Pred Forte (prednisolone acetate) and Durezol (difluprednate). Topical corticosteroids are the mainstay of treatment for anterior uveitis, however topical corticosteroids generally do not penetrate the uvea sufficiently to be effective in treating intermediate or posterior uveitis. Additional options for posterior uveitis include intravitreal corticosteroid injections and intraocular corticosteroid implant. The implants are generally reserved for patients who require frequent local corticosteroid injections or when systemic therapies may not be appropriate.
- Other systemic therapies used for NIU include immunosuppressive agents such as antimetabolites (azathioprine, methotrexate, mycophenolate mofetil), T-cell inhibitors (cyclosporine, tacrolimus) and alkylating agents (cyclophosphamide, chlorambucil) and are used to attain complete remission and/or to reduce corticosteroid doses to avoid adverse effects. Anti-tumor necrosis factor (TNF) agents provide an alternative or concurrent option to immunomodulators as corticosteroid-sparing therapies for NIU. Humira is FDA approved for treatment of noninfectious intermediate, posterior and panuveitis uveitis in adults and pediatric patients 2 years of age and older.
- Intravitreal injection Opsiria (sirolimus) is currently in Phase 3 development with study results expected in June 2022 and would provide an alternative to steroid therapy and Humira.

Summary of Clinical Trials

- The efficacy of Xipere in comparison to sham treatment was evaluated in a 6-month, randomized, multicenter, double-masked, sham-controlled study in 160 patients with macular edema associated with noninfectious anterior-, intermediate-, posterior-, or pan-uveitis. Patients were required to have a best-corrected visual acuity (BCVA) between 5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters read and 70 ETDRS letters read (Snellen equivalent 20/800 to 20/40) in the study eye. Key exclusion criteria was any active ocular disease or infection in the study eye, intraocular pressure (IOP) more than 22 mmHg, or uncontrolled glaucoma. Up to 2 IOP-lowering medications were allowed to be taken if IOP was ≤ 22 mmHg. Mean BCVA in the study eye was 55 and 54 ETDRS letters read (approximate Snellen equivalent 20/80) in treatment and control arms, respectively. Overall distribution of anatomic subtypes was: anterior (26%), intermediate (36%), posterior (22%) and panuveitis (32%).
- Patients were randomized 3:2 to receive suprachoroidally injected Xipere or sham treatment administered at day 0 and week 12. Oral prednisone (or equivalent corticosteroids) less than or equal to 20 mg/day, systemic immunomodulatory therapies, or both were allowed to be taken. Rescue therapy could be introduced if certain criteria were met in the study eye or if a patient was not improving starting week 4.
- The primary efficacy endpoint was the proportion of patients in whom BCVA had improved by ≥ 15 letters from baseline after 24 weeks of follow-up. A statistically significant greater proportion of patients treated with Xipere achieved a ≥ 15-letter improvement in BCVA than control patients ($p<0.01$) at week 24. Results are summarized in Table 1 and Figure 2. In addition, central subfield thickness was reduced from baseline in Xipere patients by 153 µm compared with a reduction of 18 µm in the control group at week 24, a difference of 135 µm ($P <0.001$). At week 24, 13.5% (13/96) of patients in the Xipere arm and 72% (46/64) patients in the control arm required rescue therapy.

Summary of Safety Considerations

- Safety considerations of Xipere (triamcinolone acetonide injectable suspension) differ from safety considerations of Triesence (triamcinolone acetonide injectable suspension). Contraindications for Xipere are significant for ocular or periocular infections including most viral diseases of the cornea and conjunctiva (active dendritic keratitis, vaccinia, varicella, mycobacterial infections and fungal disease), and known hypersensitivity to triamcinolone acetonide or any other components of the product. Warnings and precautions are significant for potential corticosteroid-related effects including cataracts, increased intraocular pressure, glaucoma and enhancement of established secondary ocular infections, and alterations in endocrine function including Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and hyperglycemia with chronic use. Table 2 summarizes the most common ocular and non-ocular adverse reactions in patients during clinical trial.
- Geriatric use: No overall differences in safety or effectiveness have been observed between elderly and younger patients with Xipere.

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: Xipere is a medical benefit. Xipere will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Xipere will process at the Specialty tier or the Brand Non-preferred tier for members with a three tier benefit. No prior authorization will apply.

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

CLASS REVIEWS

CROHN'S DISEASE

Biologic Agents for Crohn's Disease			
Brand Name	**Generic**	**Generic Available?**	**Manufacturer**
Tumor Necrosis Factor (TNF) Inhibitors			
Cimzia	certolizumab pegol	No	UCB, Inc.
Humira	adalimumab	No	AbbVie
Remicade	infliximab	Yes	Janssen Biotech
Anti-Integrin Agents			
Entyvio	vedolizumab	No	Takeda Pharmaceuticals
Tysabri	natalizumab	No	Biogen Inc.
Interleukin-12 and -23 (IL-12/IL-23) Antagonist			
Stelara	ustekinumab	No	Janssen Biotech

Background of Disease State: Crohn's Disease – chronic inflammation in the gastrointestinal tract, most often the distal ileum and/or colon

- Mild to Moderate Severity:
  - Crohn's Disease Activity Score (CDAI) score 150-220, able to eat and move, ulcers <2 cm
  - Treatment Options:
    - Budesonide 9 mg/day
      - Can add prednisone 40-60 mg/day if remission not reached
      - Taper dose off when clinical response achieved
    - Sulfasalazine 3-6 g/day if colonic or ileocolonic (not isolated small bowel disease)
- Moderate to Severe:
  - CDAI score 220-450, fever, significant weight lossy, abdominal pain, intermittent nausea and vomiting without obstruction, moderate-to-severe endoscopic activity
  - Treatment Options:
    - Corticosteroids for short-term alleviation (2-4 weeks)
      - Can add once weekly methotrexate
    - Azathioprine or 6-mercaptopurine
    - Anti-Tumor Necrosis Factor (TNF) therapy if patients do not respond to the above
      - Can combine with thiopurine
        - Infliximab + thiopurine = more effective than monotherapy
    - Vedolizumab +/- immunomodulator if no response to corticosteroids, thiopurines, methotrexate, or anti-TNF
    - Ustekinumab if no response to corticosteroids, thiopurines, methotrexate, or anti-TNF; OR no prior exposure to anti-TNF
    - Natalizumab can be used, but risk of PML caused by JC virus
- Severe or Fulminant:
  - CDAI score >450, fever, persistent vomiting, intestinal obstruction, abscess, cachexia
  - Treatment options:
    - Anti-TNF agents
      - Consider infliximab for fulminant Crohn's

Pharmacology/Place in Therapy: American Gastroenterological Association (AGA) Clinical Practice Guidelines 2021:
For Adult Outpatient Therapy for Moderate to Severe Crohn's Disease:
For Induction and Maintenance of Remission

- Biologic drug monotherapy recommended over thiopurine monotherapy (Strong recommendation, Moderate Certainty) with early introduction of the biologic preferred over delaying therapy after failure of 5-aminosalicylates and/or corticosteroids (Conditional Recommendation, Low Certainty)
- Anti-TNF treatment is recommended over no treatment (Strong Recommendation)
    - Moderate Certainty - infliximab and adalimumab
    - Low Certainty – certolizumab pegol
- Interleukin 12/23 Antagonist recommended over no treatment (Strong Recommendation)
    - Moderate Certainty - ustekinumab
- Anti-Integrin vedolizumab treatment is recommended over no treatment (Conditional Recommendation)
    - Low Certainty for induction, Moderate Certainty for maintenance
- Anti-Integrin natalizumab treatment NOT recommended over no treatment (Conditional Recommendation)
    - Moderate Certainty due to post-marketing harm

For Patients Naïve to Biologic Drugs for Induction of Remission:

- Infliximab, adalimumab, or ustekinumab recommended over certolizumab pegol (Strong Recommendation, Moderate Certainty)
    - Infliximab + thiopurines (ex. methotrexate) suggested over infliximab monotherapy (Conditional Recommendation, Moderate Certainty)
    - Adalimumab + thiopurines (ex. methotrexate) suggested over adalimumab monotherapy (Conditional Recommendation, Very Low Certainty)
    - No recommendation of using ustekinumab +/- thiopurine due to knowledge gap
- Vedolizumab suggested over certolizumab pegol (Conditional Recommendation, Low Certainty)
    - No recommendation for using +/- thiopurines due to knowledge gap

For Patients Who Never Responded to Anti-TNF Treatment (Primary Nonresponse) For Induction of Remission:

- Ustekinumab recommended over no treatment (Strong Recommendation, Moderate Certainty)
- Vedolizumab suggested over no treatment (Conditional Recommendation, Low Certainty)

For Patients Who Previously Responded to Infliximab (Secondary Nonresponse) For Induction of Remission:

- Adalimumab or ustekinumab recommended over no treatment (Strong Recommendation, Moderate Certainty)
- Vedolizumab suggested over no treatment (Conditional Recommendation, Low Certainty)

For Patients with Crohn's Disease and Active Perianal Fistula for Induction of Maintenance of Fistula Remission

- Biologic drug recommended in combination with antibiotic over biologic drug alone (Strong Recommendation, Moderate Certainty)
    - Infliximab recommended over no treatment (Strong Recommendation, Moderate Certainty)
    - Adalimumab, ustekinumab, or vedolizumab recommended over no treatment (Conditional Recommendation, Low Certainty)
    - Certolizumab pegol NOT suggested due to inefficacy (Conditional Recommendation, Low Certainty)

Recommendations:

Medication	Current Formulary Status/Policy	Recommendations

Remicade (infliximab) Avsola (infliximab-axxq) Inflectra (infliximab-dyyb) Renflexis (infliximab-abda)	Commercial: Brand NP, PA, QL, SP Exchange: Specialty, PA, QL, SP CHIP: Brand, PA, QL, SP Current Medical Policy MBP 5.0 • Must be 6 years of age or older; AND • Prescription is written by a gastroenterologist AND • Medical record documentation of a diagnosis of moderate to severe Crohn's disease AND • Medical record documentation that the infliximab product is not being used concurrently with a TNF blocker or other biologic agent AND • One of the following: o Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to Humira* OR o Physician documentation of Crohn's disease with actively draining fistulas. AND • One of the following: o For infliximab biosimilar requests other than Avsola (e.g. Renflexis, Inflectra), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to infliximab-axxq (Avsola) OR o For infliximab reference product requests (i.e. Remicade), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to infliximab-axxq (Avsola) AND infliximab-abda (Renflexis), AND infliximab-dyyb (Inflectra).	No changes recommended based on clinical review at this time *Rationale: Clinically, there is no reason to make criteria more restrictive at this time.*
Humira (adalimumab)	Commercial: Brand NP, PA-NSO, QL, SP Exchange: Specialty, PA-NSO, QL, SP CHIP: Brand, PA-NSO, QL, SP Current Pharmacy Policy 84.0 Biweekly Dosing: • Medical record documentation that Humira is prescribed by a gastroenterologist AND • Medical record documentation of age greater than or equal to 6 years AND • Medical record documentation of a diagnosis of moderately or severely active Crohn's disease AND	No changes recommended based on clinical review at this time *Rationale: Clinically, there is no reason to make criteria more restrictive at this time.*

	• Medical record documentation of one of the following:
	  ○ Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids AND immunomodulators (e.g. azathioprine and 6-mercaptopurine) OR medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy OR
	  ○ Medical record documentation of moderate/high risk patient as defined by age at initial diagnosis less than 30 years, extensive anatomic involvement, perianal and/or severe rectal disease, deep ulcers, prior surgical resection, and structuring and/or penetrating behavior AND
	• Medical record documentation that Humira is <u>not</u> being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent
	
	Weekly Dosing:
	• Medical record documentation that Humira is prescribed by a gastroenterologist AND
	• Medical record documentation of age greater than or equal to 6 years AND
	• Medical record documentation of a diagnosis of moderately or severely active Crohn's disease AND
	• Medical record documentation of one of the following:
	  ○ Medical record documentation of therapeutic failure on, intolerance to, or contraindication to corticosteroids AND immunomodulators (e.g. azathioprine and 6-mercaptopurine) OR medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy OR
	  ○ Medical record documentation of moderate/high risk patient as defined by age at initial diagnosis less than 30 years, extensive anatomic involvement, perianal and/or severe rectal disease, deep ulcers, prior surgical	

	resection, and structuring and/or penetrating behavior AND • Medical record documentation that Humira is <u>not</u> being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent AND • Medical record documentation of a contraindication to, intolerance to, or therapeutic failure on BIWEEKLY (every other week) administration of Humira AND • Medical record documentation that the member has been compliant with BIWEEKLY administration of Humira AND • Medical record documentation of inadequate drug trough level (less than 7.5mcg/mL) to support weekly dosing, per American Gastroenterological Association (AGA) guidelines	
Cimzia (certolizumab pegol)	Commercial: Brand NP, PA-NSO, QL, SP Exchange: Specialty, PA-NSO, QL, SP CHIP: Brand, PA-NSO, QL, SP Current Medical Policy MBP 74.0 • Physician documentation for a diagnosis of moderate to severe Crohn's disease AND • Prescription written by a gastroenterologist AND • Insured individual is 18 years of age or older AND • Medical record documentation that Cimzia is not being used concurrently with a TNF blocker or other biologic agent AND • Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on Humira* (*requires prior authorization)	No changes recommended based on clinical review at this time *Rationale: Clinically, there is no reason to make criteria more restrictive at this time.*
Entyvio (vedolizumab)	Commercial: Brand NP, PA, QL, SP Exchange: Specialty, PA, QL, SP CHIP: Brand, PA, QL, SP Current Medical Policy MBP 118.0 • Prescription written by a gastroenterologist AND • Medical record documentation of age >18 years AND	Update Policy to: • 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* or infliximab*

	• 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*	*Rationale: Infliximab is a preferred medication.*
Tysabri (natalizumab)	Commercial: Brand NP, PA, QL, SP Exchange: Specialty, PA, QL, SP CHIP: Brand, PA, QL, SP Current Medical Policy MBP 57.0 Tysabri® is considered medically necessary as a second line therapy after conventional therapy and TNF inhibitors, when the following criteria are met: The insured individual • Must be 18 years of age or older; AND • Has had a formal consultation with a gastroenterologist and recommendation for treatment with natalizumab; AND • Has a diagnosis of active Crohn's disease considered to be moderate or severe based on clinical signs and symptoms and documented contraindication to, intolerance to, or failure on adequate conventional therapy; (corticosteroids, 5-aminosalicylates, and/or 6-mercaptopurine/azathioprine, methotrexate) and an inadequate response to, contraindication to, or failure on 12 weeks of adalimumab (Humira) therapy and 12 weeks of infliximab (Remicade) therapy; AND • is enrolled in a risk-minimization program, called the TOUCH™ Prescribing Program	No changes recommended based on clinical review at this time *Rationale: Clinically, there is no reason to make criteria more restrictive at this time.*
Stelara (ustekinumab)	Commercial: Brand NP, PA-NSO, QL, SP Exchange: Specialty, PA-NSO, QL, SP CHIP: Brand, PA-NSO, QL, SP Current Medical Policy MBP 75.0 • Prescription must be written by a gastroenterologist AND • Member must be at least 18 years of age AND • Medical record documentation of moderately to severely active Crohn's disease AND • Medical record documentation that Stelara is not being used concurrently	No changes recommended based on clinical review at this time *Rationale: Clinically, there is no reason to make criteria more restrictive at this time.*

	with a TNF blocker or other biologic agent AND • Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3-month trial of three (3) of the following medications: Humira*, Cimzia*, Entyvio*, infliximab (or biosimilar) *, or Tysabri* AND • Medical record documentation of Stelara 130mg vials as IV infusion (for induction therapy) OR Stelara 90mg syringes (for maintenance therapy) being prescribed. Current Pharmacy Policy 318.0 • Medical record documentation that Stelara is prescribed by a gastroenterologist AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of a diagnosis of moderately to severely active Crohn's disease AND • Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of three (3) of the following medications: Humira*, Cimzia*, Entyvio*, infliximab*, or Tysabri* AND • Medical record documentation of Stelara 130 mg vials as IV infusion (for induction therapy) OR Stelara 90 mg syringes (for maintenance therapy) being prescribed AND • Medical record documentation that Stelara is <u>not</u> being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	

No changes to formulary or PA status based on cost at this time.

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.

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

RHEUMATOID ARTHRITIS

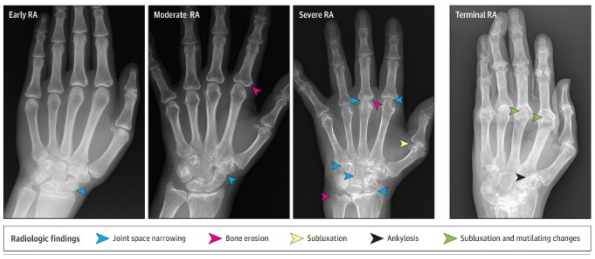
Biologic Disease-Modifying Antirheumatic Drugs (bDMARDs)			
Brand Name	**Generic**	**Generic Available?**	**Manufacturer**
Tumor Necrosis Factor (TNF) Inhibitors			
Humira (± MTX)	adalimumab	No	AbbVie
Enbrel (± MTX)	etanercept	No	Amgen
Simponi (+ MTX)	golimumab	No	Janssen Biotech
Cimzia (± MTX)	certolizumab Pegol	No	UCB
Remicade (+ MTX)	infliximab	Yes	Janssen Biotech
Janus Kinase (JAK) Inhibitors			
Xeljanz	tofacitinib	No	Pfizer
Olumiant	baricitinib	No	Eli Lilly and Company
Rinvoq	upadacitinib	No	AbbVie
Selective T-Cell Co-stimulation Blocker			
Orencia (± MTX)	abatacept	No	Bristol-Myers Squibb
Interleukin-6 (IL-6) Receptor Antagonists			
Actemra (in patients who failed DMARD therapy)	Tocilizumab	No	Roche
Kevzara (in patients who failed DMARD therapy)	Sarilumab	No	Sanofi-Aventis and Regeneron
Interleukin-1 (IL-1) Receptor Antagonist			
Kineret (in patients who failed DMARD therapy)	Anakinra	No	Sobi
Monoclonal Antibody			
Rituxan, Ruxience, Truxima (+ MTX)	Rituximab	No	Genentech

Background of Disease State: Rheumatoid arthritis (RA) is a chronic and systemic inflammatory disease of the joints. Being the most common inflammatory arthritis, its worldwide prevalence is about 5 per 1000 adults. It is more common in women than men and onset is generally between 30 and 60 years of age, however it has the ability to occur at any age. Risk factors can be genetic and environmental. In the past, an RA diagnosis led to the inability to work as well as decreased mortality. However, there have been many recent breakthroughs in terms of treatment and the understanding of the RA pathophysiology. This has led to the development of better outcomes and therapies.

RA is a polyarticular symmetric disease. It generally involves the hands, wrists, and feet and presents bilaterally. Typical presentation includes pain and swelling of the joints that leads to functional impairment. The swelling is most commonly in the wrists and metacarpophalangeal, metatarsophalangeal, and proximal interphalangeal joints. Patients are generally stiff in the mornings and this can last more than 30 minutes and up to several hours. The autoimmune response in RA is thought to be triggered by an environmental exposure to a genetically susceptible individual. RA can be further classified into major subtypes based on the presence of anti-citrullinated protein antibodies, or ACPAs. These develop as a result of abnormal antibody responses to a variety of citrullinated proteins. About two-thirds of RA patients are ACPA positive. This can be a useful diagnostic reference as these patients may have a less effective response to methotrexate or rituximab.

There are multiple stages of RA progression. First is the triggering stage as mentioned above where a gene-environmental interaction can influence the reactivity of autoantibodies to citrullinated antigens. Next is the maturation state. This is initiated at secondary site of lymphoid tissues or bone marrow. Self-antigens are released and lead to the development of immune responses to endogenous epitopes. Both of these stages happen prior to joint symptom onset. Next is the targeting stage. At this age joint swelling

occurs due to synovial membrane inflammation. The normal synovial compartment is now infiltrated by leukocytes and the fluid contains pro-inflammatory mediators, resulting in a inflammatory cascade. At the fulminant stage, there is hyperplastic synovium, cartilage damage, bone erosion, and other systemic consequences. Hyperplastic synovium causes an absence of joint lubrication leading to a decrease in function.



If RA is left to be untreated, extra-articular manifestations may develop. Most frequently this results in rheumatoid nodules, or firm subcutaneous lumps near bony prominences. As described above, RA is a dynamic disease that continues to cause increasing damage to an increasing number of joints over time. In early disease, bone and cartilage damage is minimal. In severe and established RA, damage progresses and spreads to multiple joints. There can be cartilage damage, or joint space narrowing, as well as bone damage or erosions.

When diagnosing patients, the goal is to identify patients with rheumatoid arthritis as early as possible in order to begin treatment before erosive change have started to take place. Patients with suspected rheumatoid arthritis should be referred to a rheumatologist as soon as possible to initiate blood testing and imaging. Blood tests should include autoantibodies such as rheumatoid factor (RF) and anticyclic citrullinated peptide (anti-CCP) antibodies, acute phase reactants such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), as well as a CBC and complete metabolic panel.

According to the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 criteria for diagnosis, 1 or more joints with definite clinical synovitis not explained by another disease must be present as well as 1 or more of the following:

Aletaha D, Smolen JS. Diagnosis and Management of Rheumatoid Arthritis: A Review. *JAMA*. 2018;320(13):1360-1372. doi:10.1001/jama.2018.13103

- presence of long-standing disease previously satisfying classification criteria
- presence of ≥ 2 typical periarticular erosions
- score ≥ 6 on following criteria
    - joint involvement (0-5)
        - 1 medium-to-large joint – 0
        - 2-10 medium-to-large joints – 1
        - 1-3 small joints (large joints not counted) – 2
        - 4-10 small joints (large joints not counted) – 3
        - > 10 joints (≥ 1 small joint) – 5
    - autoantibody serology (0-3)
        - negative rheumatoid factor (RF) and anticitrullinated protein antibody (ACPA) – 0
        - low positive RF or low positive ACPA – 2
        - high positive RF or high positive ACPA – 3
    - acute phase reactants (0-1)
        - normal C-reactive protein and normal erythrocyte sedimentation rate (ESR) – 0
        - abnormal C-reactive protein or abnormal ESR – 1
    - duration of symptoms (0-1)
        - < 6 weeks – 0
        - ≥ 6 weeks - 1

Although RA remains to be incurable, many treatment advances have allowed for significant disease control. This is done through the use of disease-modifying antirheumatic drugs, or DMARDs. These medications interfere with signs and symptoms of RA, have the ability to improve physical function, and stop the progression of joint damage. Nonsteroidal anti-inflammatory drugs, or NSAIDs, as well as pain medications do not have this same ability. They do not prevent damage progression and irreversible disability. Therefore, these are only used as adjunctive treatment and symptomatic therapy.

Pharmacology/Place in Therapy:

2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis[1]:

Guiding Principles	
Conventional Synthetic DMARD (csDMARD)	Hydroxychloroquine, sulfasalazine, methotrexate, leflunomide
Biologic DMARD (bDMARD)	TNF* inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab pegol), T cell costimulatory inhibitor (abatacept), IL-6 receptor inhibitors (tocilizumab, sarilumab), Anti-CD20 antibody (rituximab)
Targeted Synthetic DMARD (tsDMARD)	JAK inhibitors (tofacitinib, baricitinib, upadacitinib)
***TNF = tumor necrosis factor** - **Recommendations referring to bDMARDs exclude rituximab unless patients have had an inadequate response to TNF inhibitors (in order to be consistent with FDA approval) or have a history of lymphoproliferative disorder for which rituximab is an approved therapy** - **Target refers to low disease activity or remission** - **Triple therapy refers to hydroxychloroquine, sulfasalazine, and either methotrexate or leflunomide** - **Anakinra was not included due to infrequent use for patients with RA**	

- Methotrexate monotherapy is strongly recommended over:
    - Hydroxychloroquine or sulfasalazine
        - Certainty of evidence: Very low/low
    - bDMARD or tsDMARD monotherapy
        - Certainty of evidence: Very low/moderate
    - Combination of methotrexate plus a non-TNF inhibitor bDMARD or tsDMARD
        - Certainty of evidence: Low/Very low
- Addition of a bDMARD or tsDMARD is conditionally recommended over triple therapy for patients taking maximally tolerated doses of methotrexate who are not at target
    - Certainty of evidence: Very low
- Switching to a bDMARD or tsDMARD of a different class if conditionally recommended over switching to a bDMARD or tsDMARD belonging to the same class for patients taking a bDMARD or tsDMARD who are not at target
    - Certainty of evidence: Very low

2019 European League Against Rheumatism (EURLAR) Recommendations[2]:

Guiding Principles	
Poor prognostic factors	- Persistently moderate or high disease activity despite csDMARD therapy according to composite measures including joint counts - High acute phase reactant levels - High swollen joint count - Presence of RF and/or ACPA, especially at high levels - Presence of early erosions - Failure of two or more csDMARDs
Synthetic DMARDs	- csDMARDs (methotrexate, leflunomide, sulfasalazine, hydroxychloroquine) - tsDMARDs (baricitinib, tofacitinib, upadacitinib)

bDMARDs	- TNFi (adalimumab, certolizumab, etanercept, golimumab, infliximab) - IL6Ri (sarilumab, tocilizumab) - Co-stimulation-i: (abatacept) - Anti-B cell (CD20) (rituximab) - Biosimilar DMARDs (currently for: adalimumab, etanercept, infliximab, rituximab)
Target	Low disease activity

- Initial treatment strategies
  - Include methotrexate as part of the first treatment strategy in patients with RA (Grade A, Level 1a)
    - Can be used as monotherapy or combined with other agents
  - If methotrexate is contraindicated or not tolerated, consider leflunomide or sulfasalazine as part of first treatment strategy (Grade A, Level 1a)
- Strategies if target is not achieved with first nonbiologic DMARD strategy
  - In patients without poor prognostic factors, consider different nonbiologic DMARD (Grade D; Level 5)
  - In patients with any poor prognostic factor, add biologic or targeted nonbiologic DMARD (Grade A, Level 1b)
- Strategies if not achieved using biologic or targeted nonbiologic DMARDS
  - Use biologic or targeted nonbiologic DMARD in combination with conventional nonbiologic DMARD
  - In patients in whom conventional nonbiologic DMARDs cannot be used as co-medication, interleukin-6 (IL-6) pathway inhibitors and targeted nonbiologic DMARDs may be more advantageous than other biologic DMARDs
- If patient has failed a biologic (Grade A, Level 1b) or targeted nonbiologic DMARD (Grade D, Level 5)
  - Consider treatment using another biologic or targeted nonbiologic DMARD
  - If TNF inhibitor failed, a different TNF inhibitor or an agent with a different mode of action may be considered

Recommendations:

Medication	Current Policy	Recommendations
Humira (adalimumab)	**Commercial:** Brand Preferred, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 84.0** **Biweekly Dosing:** • 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 Humira is prescribed by a rheumatologist AND • Medical record documentation of an inadequate response to a minimum 3 month trial of methotrexate or other	No changes based on clinical review at this time *Rationale: No clinical reason to change criteria at this time*

	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 of age greater than or equal to 18 years AND • Medical record documentation that Humira is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **Weekly Dosing:** • 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 Humira 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 the member has been compliant with BIWEEKLY administration of Humira AND • Medical record documentation of a contraindication to, intolerance to, or therapeutic failure on BIWEEKLY (every other week) administration of Humira AND • Medical record documentation that Humira is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	
Enbrel (etanercept)	**Commercial:** Brand NP, PA-NSO, QL, SP	**Update:** • Medical record documentation of a diagnosis of moderate to severe

	Exchange: Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 41.0** • 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 Enbrel is prescribed by a rheumatologist AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Enbrel is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	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 Enbrel is prescribed by a rheumatologist AND • Medical record documentation of age greater than or equal to 18 years AND • ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* 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 Enbrel is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors.*
Simponi (golimumab)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 198.0** • Medical record documentation that Simponi is prescribed by a rheumatologist AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of a diagnosis of moderate to severe rheumatoid arthritis (made in accordance with the American College of Rheumatology Criteria for	**Update:** • Medical record documentation that Simponi is prescribed by a rheumatologist AND • Medical record documentation of age greater than or equal to 18 years AND • 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 of Diagnosis of Rheumatoid Arthritis) AND • Medical record documentation of concomitant methotrexate use AND • Medical record documentation of therapeutic failure on, intolerance to,

	the Classification of Diagnosis of Rheumatoid Arthritis) AND • Medical record documentation of concomitant methotrexate use AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Simponi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	or contraindication to a minimum 3 month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND • Medical record documentation that Simponi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred.*
Cimzia (certolizumab pegol)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 197.0** • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation that Cimzia is prescribed by a rheumatologist AND • 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 of Diagnosis of Rheumatoid Arthritis) AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Cimzia is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	**Update:** • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation that Cimzia is prescribed by a rheumatologist AND • 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 of Diagnosis of Rheumatoid Arthritis) AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND • Medical record documentation that Cimzia is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*
Remicade (infliximab)	**Commercial:** Brand NP, PA, QL, SP **Exchange:** Specialty, PA, QL, SP **CHIP:** Brand, PA, QL, SP	**Update:** • Must be 18 years of age or greater AND

Avsola (infliximab-axxq) **Inflectra (infliximab-dyyb)** **Renflexis (infliximab-abda)**	**Current Medical Policy MBP 5.0** • Must be 18 years of age or greater AND • Requesting provider must be a rheumatologist AND • Diagnosis of moderate to severe rheumatoid arthritis according the American College of Rheumatology Criteria for the Classification and Diagnosis of Rheumatoid Arthritis AND • Medical record documentation that the infliximab product is not being used concurrently with a TNF blocker or other biologic agent AND • Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Continuation of effective dose of methotrexate during infliximab therapy AND • One of the following: ○ For infliximab biosimilar requests other than Avsola (e.g. Renflexis, Inflectra), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to infliximab-axxq (Avsola) OR ○ For infliximab reference product requests (i.e. Remicade), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to infliximab-axxq (Avsola) AND infliximab-abda (Renflexis), AND infliximab-dyyb (Inflectra).	• Requesting provider must be a rheumatologist AND • Diagnosis of moderate to severe rheumatoid arthritis according the American College of Rheumatology Criteria for the Classification and Diagnosis of Rheumatoid Arthritis AND • Medical record documentation that the infliximab product is not being used concurrently with a TNF blocker or other biologic agent AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND • Continuation of effective dose of methotrexate during infliximab therapy AND • One of the following: ○ For infliximab biosimilar requests other than Avsola (e.g. Renflexis, Inflectra), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to infliximab-axxq (Avsola) OR ○ For infliximab reference product requests (i.e. Remicade), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to infliximab-axxq (Avsola) AND infliximab-abda (Renflexis), AND infliximab-dyyb (Inflectra). *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*
Xeljanz (tofacitinib)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 273.0**	**Update:** • 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 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 AND • Medical record documentation that Xeljanz or Xeljanz XR is being dosed consistent with Food and Drug Administration (FDA)-approved labeling	• 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 AND • Medical record documentation that Xeljanz or Xeljanz XR is being dosed consistent with Food and Drug Administration (FDA)-approved labeling AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira* OR Enbrel* *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, specifically Rinvoq and Xeljanz.*
Olumiant (baricitinib)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 530.0** • 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 Olumiant is prescribed by a rheumatologist AND	**Update:** • 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 Olumiant is prescribed by a rheumatologist AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3

	• Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Olumiant is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND • Medical record documentation that Olumiant is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*
Rinvoq (upadacitinib)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 605.0** • Medical record documentation that Rinvoq is prescribed by a rheumatologist AND • Medical record documentation of age greater than or equal to 18 years AND • 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 Rinvoq is not being used concurrently with a TNF blocker or other biologic agent AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to methotrexate	**Update:** • Medical record documentation that Rinvoq is prescribed by a rheumatologist AND • Medical record documentation of age greater than or equal to 18 years AND • 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 Rinvoq is not being used concurrently with a TNF blocker or other biologic agent AND ~~• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to methotrexate AND~~ • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira* OR Enbrel* *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, specifically Rinvoq and Xeljanz.*
Orencia (abatacept)	**Commercial:** Brand NP, PA-NSO, QL, SP	**Update:**

	Exchange: Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 253.0** • Medical record documentation that subcutaneous Orencia is prescribed by a rheumatologist AND • 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 of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Orencia is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	• Medical record documentation that subcutaneous Orencia is prescribed by a rheumatologist AND • 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 of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND • Medical record documentation that Orencia is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*
Actemra (tocilizumab)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 321.0** • Medical record documentation that Actemra Self Injectable is prescribed by a rheumatologist AND • 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 of age greater than or equal to 18 years AND	**Update:** • Medical record documentation that Actemra Self Injectable is prescribed by a rheumatologist AND • 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 of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND

	• Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Actemra is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	• Medical record documentation that Actemra is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*
Kevzara (sarilumab)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP **Current Pharmacy Policy 472.0** • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation that Kevzara is prescribed by a rheumatologist AND • Medical record documentation of a diagnosis of moderate to severe rheumatoid arthritis (RA) made in accordance with the American College of Rheumatology Criteria for the Classification and Diagnosis of RA AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Kevzara is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	**Update:** • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation that Kevzara is prescribed by a rheumatologist AND • Medical record documentation of a diagnosis of moderate to severe rheumatoid arthritis (RA) made in accordance with the American College of Rheumatology Criteria for the Classification and Diagnosis of RA AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND • Medical record documentation that Kevzara is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*
Kineret (anakinra)	**Commercial:** Brand NP, PA-NSO, QL, SP **Exchange:** Specialty, PA-NSO, QL, SP **CHIP:** Brand, PA-NSO, QL, SP	**Update:** • Medical record documentation of a diagnosis of moderate to severe rheumatoid arthritis made in accordance with the American College of Rheumatology Criteria for

	Current Pharmacy Policy 71.0 • 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 of age greater than or equal to 18 years AND • Medical record documentation that Kineret is prescribed by a rheumatologist AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of Humira*, Rinvoq*, OR Xeljanz* AND • Medical record documentation that Kineret is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent	the Classification and Diagnosis of Rheumatoid Arthritis AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation that Kineret is prescribed by a rheumatologist AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to a minimum 3 month trial of two (2) preferred biologic agents indicated for rheumatoid arthritis (Humira*, Enbrel*, Rinvoq*, Xeljanz*) AND • Medical record documentation that Kineret is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent *Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*
Rituxan (rituximab) **Truxima (rituximab-abbs)**	**Commercial:** Brand NP, PA, QL, SP **Exchange:** Specialty, PA, QL, SP **CHIP:** Brand, PA, QL, SP **Current Medical Policy MBP 48.0** All of the following criteria must be met: • Physician documentation of a diagnosis of moderate to severe rheumatoid arthritis in accordance with the American College of Rheumatology Criteria for the Classification and Diagnosis of Rheumatoid Arthritis; AND • At least 18 years of age or older; AND • Prescription written by a rheumatologist; AND • Medical record documentation that an effective dose of methotrexate will be continued during rituximab therapy; AND • Medical record documentation that Rituxan is not being used concurrently with a TNF blocker AND	**Update:** All of the following criteria must be met: • Physician documentation of a diagnosis of moderate to severe rheumatoid arthritis in accordance with the American College of Rheumatology Criteria for the Classification and Diagnosis of Rheumatoid Arthritis; AND • At least 18 years of age or older; AND • Prescription written by a rheumatologist; AND • Medical record documentation that an effective dose of methotrexate will be continued during rituximab therapy; AND • Medical record documentation that Rituxan is not being used concurrently with a TNF blocker AND • Physician documentation of an inadequate response to 12 weeks of therapy with two (2) of the following: Humira*, Enbrel*, Rinvoq*, or Xeljanz*

	• Physician documentation of an inadequate response to 12 weeks of therapy with Humira*, Rinvoq*, OR Xeljanz	*Rationale: New safety data poses updated risks and warnings in regard to JAK inhibitors. Recent guidelines do not prefer one class of agents over the other. Due to safety risks, additional TNF inhibitors should be preferred over the JAK inhibitors, Rinvoq and Xeljanz.*

Recommend removing the following non-preferred products from formulary to align with preferred rebating opportunities:

- Kineret
- Olumiant
- Orencia
- Kevzara

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.

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

FAST FACTS

KEYTRUDA (pembrolizumab)

Clinical Summary: Keytruda has two changes recently approved by the FDA. The first is the withdrawal of the third line gastric cancer indication, which was previously approved under accelerated approval. The second change is a new indication, as a single agent, for the treatment of patients with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

The withdrawal of the gastric cancer indication follows results of a phase III study of Keytruda as monotherapy for third-line treatment that did not meet its primary endpoint of overall survival benefit in this population. Other gastric cancer indications for Keytruda remain unchanged.

The new indication for Keytruda in the treatment of advanced MSI-H or dMMR endometrial cancer is supported by results of KEYNOTE-158, a non-randomized, open-label, multi-cohort trial in 90 patients with unresectable or metastatic MSI-H or dMMR endometrial cancer (cohorts D and K). The recommended dosage of Keytruda is similar to the recommended dose in patients with other MSI-H or dMMR carcinomas and is given as 200 mg every 3 weeks or 400 mg every 6 weeks until disease progression, unacceptable toxicity, or up to 24 months. Patients in KEYNOTE-158 were treated with Keytruda 200 mg intravenously every 3 weeks until unacceptable toxicity or disease progression. The major efficacy outcomes measures were objective response rate and duration of response, assessed by BICR according to RECIST v 1.1. Efficacy results showed an objective response rate of 46%, with 12% of patients achieving a complete response and 33% achieving a partial response. Median duration of response was not reached at the time of analysis, and 68% of patients had a response lasting at least 12 months and 44% of patients had a response lasting at least 24 months.

No new safety concerns were observed in KEYNOTE-158 and adverse reactions occurring in patients were consistent with those in previously trials in patients with melanoma or NSCLC treated with Keytruda as a single agent.

Current formulary status: Medical Benefit, requiring a prior authorization; When processed at a specialty pharmacy: Specialty tier or Brand NP tier.

Recommendation: No changes are recommended to the formulary placement or authorization duration of Keytruda. The following changes are recommended to Medical Benefit Policy 119.0 to incorporate the new changes to Keytruda indications:

7. Gastric Cancer
   - Prescription written by a hematologist/oncologist AND
   - ~~Medical record documentation of one of the following:~~
     - ~~Medical record documentation of a diagnosis of recurrent locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma AND~~
     - ~~Medical record documentation that tumors express PD-L1 (combined positive score [CPS] greater than or equal to 1) as determined by an FDA-approved test AND \~~
     - ~~Medical record documentation of disease progression on or after two or more prior lines of therapy (including fluoropyrimidine- and platinum-containing chemotherapy)* AND~~
     - ~~If patient has HER2-positive disease, medical record documentation of disease progression on or after HER2/neu-targeted therapy (including but not limited to trastuzumab (Herceptin)*~~

~~OR~~

- Medical record documentation of a diagnosis of locally advanced unresectable or metastatic HER-2 positive gastric or gastroesophageal junction adenocarcinoma AND
- Medical record documentation that Keytruda will be used as first-line treatment AND
- Medical record documentation that Keytruda will be used in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy

~~*Note to reviewer: Current recommendations intend Keytruda to be used as third-line treatment (i.e. patient is to have 2 prior lines of therapy, one of which must include HER2/neu-targeted therapy if the patient has HER-2 positive disease)~~

14. Endometrial Carcinoma
    - Prescription written by a hematologist/oncologist AND
    - Medical record documentation of a diagnosis of advanced endometrial carcinoma AND
    - Medical record documentation of disease progression following at least one prior systemic therapy AND
    - Medical record documentation that patient is not a candidate for curative surgery or radiation AND
    - Medical record documentation of one of the following:
        - Medical record documentation that tumors are not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) AND
        - Medical record documentation that Keytruda will be given in combination with lenvatinib (Lenvima)

    OR

        - Medical record documentation that Keytruda will be used as a single agent for treatment of tumors that are microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR)

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.

COSENTYX (secukinumab)

Clinical Summary: The indications of Cosentyx have been updated to include the treatment of active psoriatic arthritis (PsA) in patients 2 years of age and older and for the treatment of active enthesitis-related arthritis (ERA) in patients 4 years of age and older. Cosentyx was previously indicated for the following:

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

The updated dosing for the new indications for Cosentyx is as follows:

- Psoriatic arthritis (PsA) for pediatric patients 2 years and older:

    - For patients weighing ≥ 15 kg and < 50 kg: Inject 75 mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
    - For patients weighing ≥ 50 kg: Inject 150mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
- Enthesitis-related arthritis (ERA):
    - For patients weighing ≥ 15 kg and < 50 kg: Inject 75 mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
    - For patients weighing ≥ 50 kg: Inject 150mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter

The efficacy and safety of Cosentyx was evaluated in a two year, 3-part, double-blind, placebo-controlled, event-driven, randomized, Phase 3 study (NCT03031782) in 86 patients 2 to less than 18 years of age with active ERA or juvenile psoriatic arthritis (JPsA). The study consisted of an open-label portion (Part 1) followed by randomized withdrawal (Part 2) followed by open-label treatment (Part 3). The JIA patient subtypes at study entry were: 60.5% ERA and 39.5% JPsA. In the study 67.6% of patients with JPsA, and 63.5% of patients with ERA, were treated concomitantly with MTX. Patients were given a dose of 75 mg if weighing less than 50 kg or 150 mg if weighing greater than or equal to 50 kg. The primary endpoint was time to flare in Part 2, which was defined as a greater than or equal to 30% worsening in at least three of the six JIA ACR response criteria and greater than or equal to 30% improvement in not more than one of the six JIA ACR response criteria and a minimum of two active joints. In open-label Part 1, all patients received Cosentyx until Week 12. Patients classified as responders (achieving JIA ACR30 response) at Week 12 entered into the Part 2 double-blind phase and were randomized 1:1 to continue treatment with Cosentyx or begin treatment with placebo. Similar responses were seen in each JIA subtype (JPsA and ERA). The results for each indication during Part 2 are as follows:

- Juvenile Psoriatic Arthritis (JPsA): Eleven JPsA patients in the placebo group experienced a flare event compared with 4 JPsA patients in the Cosentyx group. The risk of flare was reduced by 85% for patients on Cosentyx compared with patients on placebo.
- Enthesitis-Related Arthritis (ERA): Ten ERA patients in the placebo group experienced a flare event compared with 6 ERA patients in the Cosentyx group. The risk of flare was reduced by 53% for patients on Cosentyx compared with patients on placebo.

There are no updated safety considerations for Cosentyx with this update.

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

Recommendation: No changes recommended to the formulary placement of Cosentyx at this time. However, it is recommended to update policy 379.0 to include the following criteria:

For Psoriatic Arthritis

- Medical record documentation of a diagnosis of moderately to severely active psoriatic arthritis which must include the following:
- Documentation of either active psoriatic lesions or a documentation history of psoriasis **AND**

- Medical record documentation that Cosentyx is prescribed by a rheumatologist or dermatologist **AND**
- Medical record documentation of age greater than or equal to ~~18 years~~ 2 years **AND**
- Medical record documentation that Cosentyx is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- For peripheral disease: Medical record documentation of therapeutic failure on, intolerance to, or contraindication to methotrexate **AND** an adequate trial of at least two (2) formulary nonsteroidal anti-inflammatory drugs (NSAIDs) **OR** medical record documentation of therapeutic failure on or intolerance to prior biologic therapy **OR**
- For axial disease: Medical record documentation of therapeutic failure on, intolerance to, or contraindication to an adequate trial of at least two (2) formulary nonsteroidal anti-inflammatory drugs (NSAIDs) **OR** medical record documentation of therapeutic failure on or intolerance to prior biologic therapy **AND**
- If the request is for a pediatric patient, medical record documentation that the prescribed dosing is appropriate for patient's weight

NOTE:
For pediatric patients weighing ≥ 15 kg and < 50 kg: Inject 75 mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
For pediatric patients weighing ≥ 50 kg: Inject 150mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter

MEDISPAN AUTHORIZATION LEVEL: GPI-10

QUANTITY LIMIT

- 75 mg every 4 weeks
    1. In Darwin: Add PA, OQL, number of claims authorized 1, max quantity dispensed 2 with a duration of one month.
        - QL FOR LETTER: Loading dose: 2 mL per 28 days; Maintenance dose: 0.5 mL per 28 days
- 150 mg every 4 weeks
    1. In Darwin: Add PA, OQL, number of claims authorized 1, max quantity dispensed 4 with a duration of 3 weeks.
    2. In PA Hub: Add OUP, DS, Max Days Supply 56. Start date of this authorization is one-day after loading dose ends.
        - QL FOR LETTER: Loading dose: 4 mL per 28 days; Maintenance dose: 2 mL per 56 days
- 300 mg every 4 weeks
    1. In PA Hub: Add PA, OQL, number of claims authorized 1, max quantity dispensed 8 with a duration of one-month.
        - QL FOR LETTER: Loading dose: 8 mL per 28 days; Maintenance dose: 2 mL per 28 days

For Enthesitis-Related Arthritis

- Medical record documentation of a diagnosis of enthesitis-related arthritis **AND**
- Medical record documentation that Cosentyx is prescribed by a rheumatologist **AND**
- Medical record documentation of age greater than or equal to 4 years **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to an adequate trial of at least two (2) formulary nonsteroidal anti-inflammatory drugs (NSAIDs) **AND**
- Medical record documentation that Cosentyx is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- Medical record documentation that the prescribed dosing is appropriate for patient's weight

NOTE:
For patients weighing ≥ 15 kg and < 50 kg: Inject 75 mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
For patients weighing ≥ 50 kg: Inject 150mg subcutaneously at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter

MEDISPAN AUTHORIZATION LEVEL: GPI-10

QUANTITY LIMIT

- 75 mg every 4 weeks
    1. In Darwin: Add PA, OQL, number of claims authorized 1, max quantity dispensed 2 with a duration of one month.
        - QL FOR LETTER: Loading dose: 2 mL per 28 days; Maintenance dose: 0.5 mL per 28 days

- 150 mg every 4 weeks
    1. In Darwin: Add PA, OQL, number of claims authorized 1, max quantity dispensed 4 with a duration of 3 weeks.
    2. In PA Hub: Add OUP, DS, Max Days Supply 56. Start date of this authorization is one-day after loading dose ends.
        - QL FOR LETTER: Loading dose: 4 mL per 28 days; Maintenance dose: 2 mL 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.

FINTEPLA (fenfluramine)

Clinical Summary: Fintepla is indicated for the treatment of seizures associated with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients 2 years of age and older. Previously, it was only indicated for seizures associated with DS in patients 2 years of age and older.

The recommended dosing for patients with LGS is similar to DS. The initial starting dose is 0.1 mg/kg twice daily, which should be increased weekly. The titration scheduled is showed in Table

1. Patients who are not on concomitant stiripentol who are tolerating Fintepla should be titrated to the recommended maintenance dose of 0.35 mg/kg twice daily (maximum dose of 26 mg). For those who are taking concomitant stiripentol plus clobazam who are tolerating Fintepla should be titrated to the recommended maintenance dose of 0.2 mg/kg twice daily (maximum daily dosage of 17 mg). For patients (both DS and LGS) with concomitant use of Fintepla with a strong CYP1A2 or CYP2D6 inhibitor or for patients with severe renal impairment, a maximum total daily dose of 20 mg without concomitant stiripentol and 17 mg with concomitant stiripentol plus clobazam is recommended.

Table 1: Fintepla Recommended Titration Schedule

	Without concomitant stiripentol*		**With concomitant stiripentol plus clobazam**	
	Weight-based Dosage	**Maximum Total Daily Dosage±**	**Weight-based Dosage**	**Maximum Total Daily Dosage±**
Initial Dosage+	0.1 mg/kg twice daily	26 mg	0.1 mg/kg twice daily	17 mg
Day 7	0.2 mg/kg twice daily	26 mg	0.15 mg/kg twice daily	17 mg
Day 14**	0.35 mg/kg twice daily	26 mg	0.2 mg/kg twice daily	17 mg

* *For patients not on concomitant stiripentol in whom a more rapid titration is warranted, the dose may be increased every 4 days.*

\+ For patients with Dravet Syndrome, dosage may be increased based on clinical response to the maximum recommended dosage, as needed.

** For patients with Lennox-Gastaut syndrome, dosage should be increased as tolerated to the recommended maintenance dosage (i.e., Day 14).

± For maximum dosage with concomitant use of strong CYP1A2 or CYP2D6 inhibitors or in patients with severe renal impairment see Dosage and Administration 2.3, 2.4.

The effectiveness of Fintepla for the treatment of seizures associated with LGS in patients 2 years of age and older was established in a randomized, double-blind, placebo-controlled study in 263 patients 2 to 35 years of age. The trial compared Fintepla 0.7 mg/kg/day and Fintepla 0.2 mg/kg/day with placebo. Patients included in the trial had a diagnosis of LGS and were inadequately controlled on at least one AED, with or without vagal nerve stimulation and/or ketogenic diet. The study had a 4-week baseline period, during which patients were required to have a minimum of 8 drop seizures while on stable AED therapy. Drop seizures were generalized tonic-clonic, secondarily generalized tonic-clonic, tonic, atonic, or tonic-atonic seizures that were confirmed to result in drops. The baseline period was followed by randomization into a 2-week titration period and a subsequent 12-week maintenance period, where the dose of Fintepla remained stable. In the trial, 99% of patients were taking between 1 and 4 concomitant AEDs. The most frequently used concomitant AEDs were clobazam (45%), lamotrigine (34%), and valproate (56%). The primary endpoint was the median percent change from baseline in the frequency of drop seizures per 28 days during the combined 14-week titration and maintenance periods (i.e. treatment period). The proportion of patients who achieve improvement (minimally, much, or very much improved) in the Clinical Global Impression of Change (CGI-I) as assessed by Principal Investigator was a secondary endpoint. The median percent change from baseline (reduction) in the frequency of drop seizures per 28 days was significantly greater for the 0.7 mg/kg/day dose group of Fintepla compared with placebo. A reduction in drop seizures was observed within 2 weeks of initiating treatment with Fintepla, and the effect remained generally consistent over the 14-week treatment period. The median percent reduction from baseline in drop seizure frequency per 28 days for the lower dose of Fintepla (0.2 mg/kg/day) did not reach statistical significance compared to placebo, see Table 2. Numerically greater improvements on the CGI-I by Investigator were observed in patients treated with Fintepla compared with placebo.

Change in Drop Seizure Frequency During the Treatment Period

Drop Seizure Frequency (per 28 days)	Placebo	FINTEPLA 0.2 mg/kg/day	FINTEPLA 0.7 mg/kg/day
Study 3	**N=85***	**N=86***	**N=83***
Baseline Period Median Seizure Frequency	55.0	77.8	80.0
Median Percentage Change from Baseline During Treatment	-8.7%	-13.2%	-23.7%
p-value compared to placebo		0.1917#	0.0037

*The total number of patients upon which the efficacy analysis was based is less than the total number randomized in the double-blind, placebo-controlled study because patients with missing data were excluded from the efficacy analysis.
Not statistically significant

The most common adverse reactions (≥ 10%) in patients with Lennox-Gastaut syndrome were diarrhea, decreased appetite, fatigue, somnolence, and vomiting.

Current formulary status: Fintepla is pharmacy benefit available at the Specialty tier or the Brand Non-Preferred tier for members with a three tier benefit. Fintepla requires a prior authorization.

Recommendation: There are no changes to formulary status or quantity limits at this time. However, it is recommended to update the criteria to the following:

- Medical record documentation that Fintepla is prescribed by a neurologist **AND**
- Medical record documentation of age greater than or equal to 2 years **AND**
- Medical record documentation of one of the following:
  - A diagnosis of Dravet Syndrome **OR**
  - A diagnosis of Lennox-Gastaut syndrome **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to two (2) formulary alternatives appropriate for diagnosis

Dravet Syndrome: Divalproex, divalproex ER, levetiracetam, levetiracetam ER, topiramate, topiramate ER*, valproic acid, clobazam, Epidiolex*, Diacomit*

Lennox Gastaut syndrome: clonazepam, felbamate, lamotrigine, topiramate, topiramate ER*, rufinamide*, clobazam, Epidiolex*, Sympazan*

*Prior authorization required

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)

Clinical Summary: Opdivo is now indicated in combination with platinum-doublet chemotherapy, for neoadjuvant treatment of adult patients with resectable (tumors ≥ 4 cm or node positive) non-small cell lung cancer. The dosing for the new indications is 360 mg intravenously every 3 weeks with platinum-doublet chemotherapy on the same day every 3 weeks. Treatment is continued for 3 cycles.

Support for the new indication comes from results of the CHECKMATE-816 trial, a randomized, open-label trial in patients with resectable histologically confirmed Stage IB, II, or IIIA NSCLC. The trial excluded patients with unresectable or metastatic NSCLC, known EGFR mutations or ALK translocations, Grade 2 or higher peripheral neuropathy, active autoimmune disease, or medical conditions required immunosuppression. Patients were randomized 1:1 to receive Opdivo + platinum-doublet chemotherapy every 3 weeks for 3 cycles (n=179), or platinum-doublet chemotherapy alone every 3 weeks for 3 cycles (n=179). Platinum-doublet chemotherapy consisted of paclitaxel + carboplatin; pemetrexed + cisplatin; or gemcitabine + cisplatin. The platinum-doublet chemotherapy arm had two additional treatment options, vinorelbine + cisplatin or docetaxel + cisplatin. Randomization was stratified by tumor PD-L1 expression level (< 1% or ≥ 1%), disease stage (IB/II or IIIA), and sex (male or female). Surgery was planned to occur within 6 weeks after the completion of neoadjuvant treatment. The major efficacy outcome measures evaluated event free-survival (EFS) based on BICR assessment and pathologic complete response (pCR). Results are shown events in 64 (35.8%) patients treated with Opdivo + chemotherapy compared to 87 (48.6) patients treated with chemotherapy (p=0.0052). A pCR was achieved in 43 (24.0%) patients treated with Opdivo compared to 4 (2.2%) patients treated with chemotherapy (p<0.0001).

No new safety concerns were identified during the CHECKMATE-816 trial. Serious adverse reactions occurred in 30% of patients and at least 30% of patients had at least one treatment withheld for an adverse reaction. The most common adverse reactions reported were nausea, constipation, fatigue, decreased appetite, and rash.

Current formulary status: Medical Benefit, requiring a prior authorization; When processed at a specialty pharmacy: Specialty tier or Brand NP tier.

Recommendation: No changes are recommended to the formulary placement of Opdivo. It is recommended that the following prior authorization criteria and auth duration criteria be added to Medical Benefit Policy 126.0 for Opdivo to incorporate the new indication.

2. *Non-Small Cell Lung Cancer (NSCLC)*

If the request is for metastatic NSCLC with progression after platinum-based chemotherapy:

- Medical record documentation of a diagnosis of metastatic non-small cell lung cancer (NSCLC) with disease progression while on or after platinum-based chemotherapy **AND**
- Medical record documentation that Opdivo is not being used in combination with any other agents for the treatment of metastatic non-small cell lung cancer (NSCLC)

OR

If the request is for first-line treatment of metastatic NSCLC expressing PD-L1 (≥ 1%):

- Medical record documentation of a diagnosis of metastatic non-small cell lung cancer (NSCLC) **AND**
- Medical record documentation of PD-L1 ≥ 1% as determined by an FDA-approved test **AND**
- Medical record documentation of no EGFR or ALK genomic tumor aberrations **AND**
- Medical record documentation that Opdivo will be used for first-line treatment in combination with Yervoy

OR

If the request is for first-line treatment metastatic or recurrent NSCLC:

- Medical record documentation of a diagnosis of metastatic or recurrent non-small cell lung cancer (NSCLC) **AND**
- Medical record documentation of no EGFR or ALK genomic tumor aberrations **AND**
- Medical record documentation that Opdivo will be used for first-line treatment in combination with Yervoy and 2 cycles of platinum-doublet chemotherapy

OR

If the request is for neoadjuvant treatment of resectable NSCLC:

1. Medical record documentation of resectable (tumor size greater than or equal to 4 centimeters or node-positive) non-small cell lung cancer (NSCLC) AND
2. Medical record documentation that Opdivo will be used for neoadjuvant treatment in combination with platinum-doublet chemotherapy.

AUTHORIZATION DURATION:

Neoadjuvant NSCLC: One approval will be given for up to 3 cycles for a total duration of 6 months.

Authorization of Opdivo for the neoadjuvant treatment of NSCLC should not exceed the FDA-approved treatment duration of 3 cycles. For requests exceeding the above limit, medical record documentation of the following is required:

- Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration

Discussion: No comments or questions.

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

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

ORENCIA (abatacept)

Clinical Summary: Orenica is now indicated for the prophylaxis of acute graft versus host disease (aGVHD), in combination with a calcineurin inhibitor and methotrexate, in adult and pediatric patients 2 years of age and older undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor. Orencia previously was only indicated for adult rheumatoid arthritis, polyarticular juvenile idiopathic arthritis in patients 2 years of age and older, and adult psoriatic arthritis.

The intravenous dosing regimen is the only regimen recommended for aGVHD. Before administering Orencia, antiviral prophylactic treatment for Epstein-Barr Virus (EBV) reactivation should be administered and continued for 6 months following HSCT. Also, prophylactic antivirals for Cytomegalovirus (CMV) infection/reactivation during treatment and for six months following HSCT should be considered. For patients 6 years and older, Orencia 10 mg/kg (maximum dose of 1,000 mg) is recommended as an intravenous infusion over 60 minutes on the day before transplantation (Day -1), followed by administration on Days 5, 14, and 28 after transplantation. For patients 2 to less than 6 years old, Orencia 15 mg/kg is recommended as an intravenous infusion over 60 minutes on the day before the transplantation (Day -1), followed by 12 mg/kg as an intravenous infusion over 60 minutes on Days 5, 14, and 28 after transplantation.

The efficacy of Orencia in combination with a calcineurin inhibitor (CNI) and methotrexate (MTX) for the prophylaxis of aGVHD was evaluated in a multicenter, two cohort clinical study in patients aged 6 years and older who underwent HSCT from a matched or 1 allele-mismatched unrelated donor. The two cohorts included: 1) an open-label, single arm study of 43 patients who underwent a 7 of 8 Human Leukocyte Antigen (HLA)- matched HSCT (7 of 8 cohort); and 2) a randomized (1:1), double-blind, placebo-controlled study of patients who underwent an 8 of 8 HLA-matched HSCT who received Orencia or placebo in combination with a CNI and MTX (8 of 8 cohort). In both the cohorts, Orencia was administered at a dose of 10 mg/kg (1,000 mg maximum dose) as an intravenous infusion over 60 minutes, beginning on the day before transplantation (Day-1), followed by administration on Days 5, 14, and 28 after transplantation. Efficacy was established based on overall survival (OS) and grade II-IV aGVHD free survival (GFS) results assessed at Day 180 post-transplantation. Orenica + CNI and MTX did not significantly improve grade III-IV GFS versus placebo + CNI and MTX at Day 180 post-transplantation. The results of the 8 of 8 cohort are shown in Table 1.

Table 1: Efficacy Results in 8 of 8 Cohort in Study GVHD-1 at Day 180 Post-transplantation[1]

Endpoint	ORENCIA (+CNI and MTX) n=73	Placebo (+CNI and MTX) n=69
Gr III-IV aGVHD Free Survival[a] Rate (95% CI)	87% (77%, 93%)	75% (63%, 84%)
Hazard Ratio (95% CI)	0.55 (0.26, 1.18)	
Gr II-IV aGVHD Free Survival[b] Rate (95% CI)	50% (38%, 61%)	32% (21%, 43%)
Hazard Ratio (95% CI)	0.54 (0.35, 0.83)	
Overall Survival Rate (95% CI)	97% (89%, 99%)	84% (73%, 91%)
Hazard Ratio (95% CI)	0.33 (0.12, 0.93)	

[a] Gr III-IV aGVHD Free Survival was measured from the date of transplantation until the onset of documented Grade III-IV aGVHD, or death by any cause up to Day 180 post-transplantation.

[b] Gr II-IV aGVHD Free Survival was measured from the date of transplantation until the onset of documented Grade II-IV aGVHD, or death by any cause up to Day 180 post-transplantation.

GVHD-2 was a clinical study that used data from the Center of International Blood and Marrow Transplant Research (CIBMTR). The study analyzed the outcomes of Orencia in combination with a CNI and MTX, versus a CNI and MTX alone, for the prophylaxis of aGVHD, in patients 6 years and older who underwent HSCT from a 1 allele-mismatched unrelated donor between 2011 and 2018. The Orencia group (n=54) included 42 patients from GVHD-1 in addition to 12 patients treated with Orencia outside of GVHD-1. The comparator group (n=162) was randomly selected in a 3:1 ratio to the Orencia- treated group from the CIBMTR registry from patients who had not received Orencia during the study period. Efficacy was based on Overall Survival (OS) at Day 180 post-HSCT. The OS rate at Day 180 in the Orencia in combination with CNI and MTX group was 98% (95% CI: 78, 100) and the OS rate at Day 180 in the CNI and MTX group was 75% (95% CI: 67, 82).

There was an updated warning added for Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV) Reactivation in aGVHD Prophylaxis after Hematopoietic Stem Cell Transplant. Patients should be monitored for EBV reactivation. Prophylaxis for EBV injection should be provided for 6 months post-transplantation to prevent EBV-associated PTLD. Patients should also be monitored for CMV infection/reactivation for 6 months post-transplant regardless of donor or recipient pre-transplant CMV serology. Prophylaxis for CMV infection/reactivation should be considered.

In the aGVHD clinical trials, the most common adverse reactions (≥ 10%) were anemia, hypertension, CMV reactivation/CMV infection, pyrexia, pneumonia, epistaxis, CD4 lymphocytes decreased, hypermagnesemia, and acute kidney injury. Serious adverse reactions reported in > 5% of patients included pyrexia, pneumonia, acute kidney injury, diarrhea, hypoxia, and nausea.

Per UpToDate, aGVHD presents early post-transplantation (e.g. first 100 days) but it can present later. Clinical symptoms primarily affect the skin, GI tract, and liver. Even though routine prophylaxis is given, aGVHD develops in up to one-half of transplant recipients, especially when the donor and recipient have greater differences. The mainstay of pharmacologic GVHD prophylaxis is a combination of calcineurin inhibitor (i.e. cyclosporine, tacrolimus) plus an antimetabolite (e.g. methotrexate or mycophenolate mofetil). For HCT with a HLA-matched sibling/related donor, it is recommended to use methotrexate plus either tacrolimus or cyclosporine. For HCT using a matched unrelated donor (i.e. ≥ 9/10 or ≥7/8 HLA alleles), it is recommended to add antithymocyte globulin (ATG) to methotrexate plus a calcineurin inhibitor. In clinical trials, survival was similar with or without ATG, but patients who received ATG had a lower incidence of cGVHD and required less immunosuppressive therapy.

Current formulary status: Orencia vial is a medical benefit and requires a prior authorization. If Orencia vial processes through a specialty pharmacy, it will process at the Specialty tier or the Brand Non-Preferred tier for members with a three tier benefit.

Recommendation: There are no changes to formulary status. However, it is recommended to update the criteria to include the new indication. The following will be added to the current MBP 040 policy:

4. Prophylaxis of Acute Graft Versus Host Disease:
    - Prescription written by a hematologist, oncologist, or transplant specialist **AND**

- Medical record documentation that the patient is 2 years of age and older **AND**
- Medical record documentation that patient is undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor **AND**
- Medical record documentation Orencia will be used in combination with a calcineurin inhibitor (i.e. cyclosporine, tacrolimus) and methotrexate **AND**
- Medical record documentation that the member is receiving an FDA approved dose*

*Note: The FDA approved dose for prophylaxis of acute graft versus host disease:

- For patients 2 years to less than 6 years old: 15 mg/kg IV on the day before transplantation (Day -1), followed by 12mg/kg IV on Days 5, 14, and 28 after transplantation
- For patients 6 years and older: 10 mg/kg (maximum of 1,000 mg) IV on the day before transplantation (Day -1), followed by administration on Days 5, 14, and 28 days after transplantation

Authorization Duration: Authorization for prophylaxis of Acute Graft Versus Host Disease should not exceed the FDA-approved treatment duration of 28 days after transplantation. For requests exceeding 1 month auth duration, medical record documentation of the following is required:

- Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

Discussion: No comments or questions

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

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

SKYRIZI (risankizumab-rzaa)

Clinical Summary: Skyrizi is now indicated for the treatment of active psoriatic arthritis in adults. Previously, Skyrizi was only indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. In patients with psoriatic arthritis, Skyrizi can be administered alone or in combination with non-biologic disease-modifying antirheumatic drugs (DMARDs).

Dosing for Psoriatic Arthritis: 150mg administered by subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter.

Summary of Updated Clinical Studies: The safety and efficacy of Skyrizi were assessed in 2 randomized, double-blind, placebo-controlled studies.

- Population: 1407 patients aged 18 years and older with active psoriatic arthritis (PsA). 964 patients were enrolled in PsA-1 and 443 patients were enrolled in PsA-2. In PsA-1, all patients had a previous inadequate response or intolerance to non-biologic DMARD therapy and were biologic naïve. In PsA-2, 53.5% of patients had a previous inadequate response or intolerance to non-biologic DMARD therapy and 46.5% of patients had a previous inadequate response or intolerance to biologic therapy.

- Intervention/Comparison: Patients were randomized to receive Skyrizi 150mg or placebo at Weeks 0, 4, and 16. Starting from Week 28, all patients received Skyrizi every 12 weeks.
- Outcome: The primary endpoint was the proportion of patients who achieved an American College of Rheumatology (ACR) 20 response at Week 24. In both studies, treatment with Skyrizi resulted in significant improvement in measures of disease activity compared with placebo at Week 24. Similar responses were seen regardless of concomitant non-biologic DMARD use and number of prior non-biologic DMARDs. In PSA-2, responses were seen regardless of prior biologic therapy.

Efficacy Results in Study PsA-1			
Endpoint	**Placebo Response Rate N=481**	**Skyrizi Response Rate N=483**	**Difference from Placebo (95% CI)**
ACR20 Response*			
Week 16	33.4%	56.3%[a]	23.1% (16.8, 29.4)
Week 24	33.5%	57.3%[a]	24.0% (18.0, 30.0)
ACR50 Response*			
Week 16	11.1%	26.4%	15.4% (10.6, 20.2)
Week 24	11.3%	33.4%	22.2% (17.3, 27.2)
ACR70 Response*			
Week 16	2.7%	11.8%	9.2% (6.1, 12.4)
Week 24	4.7%	15.3%	10.5% (6.9, 14.2)

[a] Multiplicity-controlled p≤0.001, Skyrizi vs. placebo comparison
*A subject was considered as a non-responder after initiation of rescue medication or concomitant medications for PsA that could meaningfully impact efficacy assessment.

Efficacy Results in Study PsA-2			
Endpoint	**Placebo Response Rate N=219**	**Skyrizi Response Rate N=224**	**Difference from Placebo (95% CI)**
ACR20 Response*			
Week 16	25.3%	48.3%[a]	22.6% (13.9, 31.2)
Week 24	26.5%	51.3%[a]	24.5% (15.9, 33.0)
ACR50 Response*			
Week 16	6.8%	20.3%	13.5% (7.3, 19.7)
Week 24	9.3%	26.3%	16.6% (9.7, 23.6)
ACR70 Response*			
Week 16	3.4%	11.2%	7.8% (3.0, 12.6)
Week 24	5.9%	12.0%	6.0% (0.8, 11.3)

[a] Multiplicity-controlled p≤0.001, Skyrizi vs. placebo comparison
*A subject was considered as a non-responder after initiation of rescue medication or concomitant medications for PsA that could meaningfully impact efficacy assessment.

Summary of Update Safety Considerations: Skyrizi is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab-rzaa or any of the excipients. Skyrizi also has a warning/precaution for hypersensitivity reactions: serious hypersensitivity reactions, including anaphylaxis, may occur.

Current formulary status: Skyrizi is a pharmacy benefit on the Brand Non-Preferred Tier for Commercial and CHIP requiring prior authorization. Skyrizi is non-formulary for Marketplace.

Recommendation: No changes recommended to the formulary placement of Skyrizi at this time. It is recommended to update the following policies to reflect the new indication for PsA.

Plaque Psoriasis:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Skyrizi is prescribed by a dermatologist **AND**
- Medical record documentation of a diagnosis of moderate to severe plaque psoriasis with greater than or equal to 5% body surface area involved **OR** disease involving crucial areas of the body such as hands, feet, face, and/or genitals **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Cosentyx* **AND** Humira* **AND**
- Medical record documentation that Skyrizi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent

Psoriatic Arthritis:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Skyrizi is prescribed by a rheumatologist or dermatologist **AND**
- Medical record documentation of active psoriatic arthritis (PsA) which must include the following:
  - Documentation of either active psoriatic lesions or a documented history of psoriasis **AND**
- Medical record documentation that Skyrizi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Cosentyx* **AND** Humira*

2023 updates: Recommend addition of Skyrizi to the Marketplace formulary for 2023, at the Specialty Tier.

Plaque Psoriasis:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Skyrizi is prescribed by a dermatologist **AND**
- Medical record documentation of a diagnosis of moderate to severe plaque psoriasis with greater than or equal to 5% body surface area involved **OR** disease involving crucial areas of the body such as hands, feet, face, and/or genitals **AND**
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Cosentyx* **AND** Humira* **AND**~~
- Medical record documentation that Skyrizi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to topical corticosteroids **AND** at least two to three months of systemic therapy (including but not limited to methotrexate and/or cyclosporine) or phototherapy **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy

Psoriatic Arthritis:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Skyrizi is prescribed by a rheumatologist or dermatologist **AND**

- Medical record documentation of active psoriatic arthritis (PsA) which must include the following:
  - Documentation of either active psoriatic lesions or a documented history of psoriasis **AND**
- Medical record documentation that Skyrizi is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- **For peripheral disease**: Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on methotrexate **AND** an adequate trial of at least two (2) formulary nonsteroidal anti-inflammatory drugs (NSAIDs) **OR** medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy **OR**
- **For axial disease:** Medical record documentation of an intolerance to, contraindication to, or therapeutic failure to an adequate trial of at least two (2) formulary nonsteroidal anti-inflammatory drugs (NSAIDs) OR medical record documentation of a therapeutic failure on or intolerance to prior biologic therapy
- ~~Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Cosentyx* **AND** Humira*~~

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.

OTEZLA (apremilast)

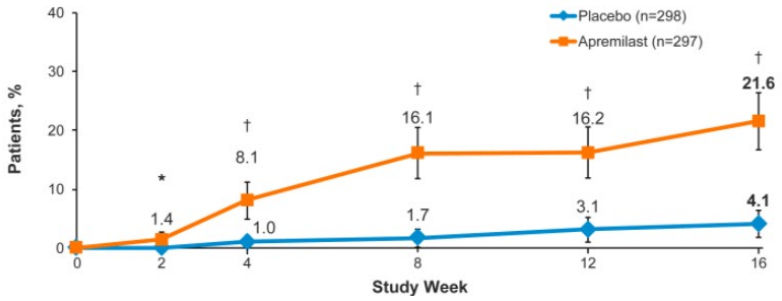
Clinical Summary: Updated Indication: Otezla is now indicated for the treatment of mild-moderate plaque psoriasis in adult patients. Previously, Otezla was indicated for the treatment of moderate-severe plaque psoriasis, psoriatic arthritis, and oral ulcers associated with Beçhet's Disease in adult patients.

Updated Dosing for New indication: no dosing updates

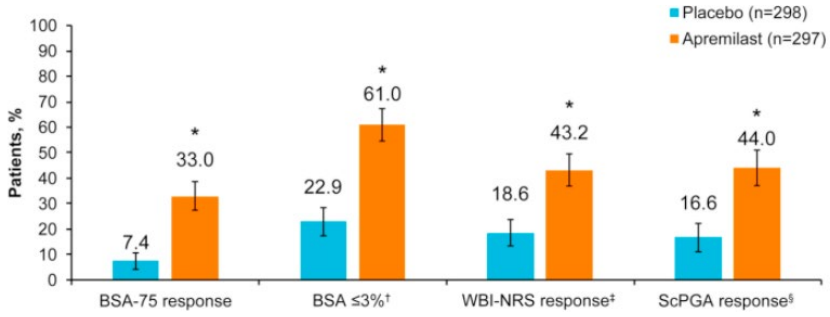
Summary of Updated Clinical Studies: Safety and efficacy assessed in a multicenter, randomized, double-blind, placebo-controlled trial that was conducted in 595 adult patients aged 18-85 with mild to moderate plaque psoriasis (BSA involvement of 2-15%, sPGA score of 2-3 [mild or moderate disease], and PASI score of 2-15]. Subjects were randomized 1:1 to receive either Otezla 30mg twice daily or placebo twice daily for 16 weeks. At week 16, the placebo group switched to receive Otezla and the Otezla group continued drug through week 32.

The primary endpoint was the proportion of subjects who achieved an sPGA response by week 16 which was defined as sPGA score of clear [0] or almost clear [1] with at least a 2-point reduction from baseline. Secondary endpoints included the achievement of ≥75% improvement in BSA, proportion of subjects with a Whole Body Itch NRS response (defined as a ≥4 point reduction from baseline) at week 16 among subjects with a baseline Whole Body Itch NRS ≥4, and the proportion of subjects with an ScPGA response (defined as ScPGA score of clear [0] or almost clear [1] with at least a 2-point reduction from baseline) at week 16 among subjects with a baseline ScPGA score of ≥2.

The primary endpoint was met with statistically significantly greater and clinically meaningful achievement of sPGA scores at week 16 as shown in Graph 1. The secondary endpoints were also met with at week 16 as shown in Graph 2.
Graph 1:



Graph 2:



Summary of Updated Safety Considerations: No new safety considerations

Current formulary status: Otezla is a pharmacy benefit available at the Specialty Tier or Brand Non-Preferred Tier for members with a three-tier benefit. Otezla requires prior authorization.

Recommendation: There are no changes to formulary status or quantity limits at this time. However, it is recommended to update the prior authorization criteria to the following:

For Plaque Psoriasis:

- Medical record documentation that Otezla is prescribed by a dermatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- For mild disease:
    - Medical record documentation of a diagnosis of mild to moderate plaque psoriasis characterized by less than 5% of body surface area involved **AND**
    - Medical record documentation of an intolerance to, contraindication to, or therapeutic failure of 2 topical therapies (one of which is a corticosteroid of at least medium potency) **AND**
    - Medical record documentation of an intolerance to, contraindication to, or therapeutic failure of phototherapy.
- For moderate-severe disease:
    - Medical record documentation of a diagnosis of moderate to severe plaque psoriasis characterized by greater than 5% of body surface area involved or disease involving crucial body areas such as the hands, feet, face, or genitals **AND**
    - Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of Cosentyx* **AND** Humira*

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.

OXBRYTA (voxelotor)

Updated Indication: Oxbryta is a hemoglobin S polymerization inhibitor that is now indicated for the treatment of sickle cell disease in adults and pediatric patients 4 years of age and older. Previously Oxbryta was indicated in pediatric patients 12 years and older.

For pediatric patients 4 years to less than 12 years of age, the dose is based on the patient's ability to swallow tablets and patient weight. The recommended dose for patients aged 4-12 is shown in Table 1 and the recommended dose in patients aged 4-12 when used with concomitant strong or moderate CYP3A4 inducers is listed in Table 2. Oxbryta is now supplied as oral tablets for suspension. These tablets should be dispersed in room temperature clear liquid and then administered immediately after. The tablets for oral suspension should not be swallowed whole, cut, crush, or chewed.

Table 1. Recommended OXBRYTA Dosage in Pediatric Patients 4 Years to Less Than 12 Years[1]

Body Weight	Recommended Dose (once daily)
40 kg or greater	1,000 mg (two 500 mg tablets) or 900 mg (three 300 mg tablets for oral suspension)
20 kg to less than 40 kg	600 mg
10 kg to less than 20 kg	300 mg

Table 2. OXBRYTA Recommended Dosage for Pediatric Patients 4 Years to Less Than 12 Years When Used with Concomitant Strong or Moderate CYP3A4 Inducers[1]

Body Weight	Recommended Dose (once daily)	
	Concomitant Use of Strong CYP3A4 Inducers	Concomitant Use of Moderate CYP3A4 Inducers
40 kg or greater	2,500 mg (five 500 mg tablets) or 2,400 mg (eight 300 mg tablets for oral suspension)	2,000 mg (four 500 mg tablets) or 2,100 mg (seven 300 mg tablets for oral suspension)
20 kg to less than 40 kg	1,500 mg	1,200 mg
10 kg to less than 20 kg	900 mg	900 mg

For patients 12 years and older who have difficulty swallowing tablets, the tablets for oral suspension can be substituted to achieve the recommended dosage of 1500 mg once daily.

The efficacy and safety of Oxbryta was evaluated in 45 pediatric patients 4 to < 12 years of age with sickle cell disease in an open-label, phase 2 trial. Patients received Oxbryta based on body weight at baseline. Most patients (80%) were receiving hydroxyurea and were allowed to continue if they had been on stable doses for at least 90 days. Efficacy evaluating hemoglobin (Hb) response rate (> 1 g/dL from baseline to week 24) showed a 36% response rate in patients aged 4 to less than 12 who took at least one dose of Oxbryta. The overall safety profile of Oxbryta in pediatric patients 4 to < 12 years was similar to that seen in adults and pediatric patients 12 years and older.

Current formulary status: NF, requires PA, QL

Recommendation: There are no changes recommended to the formulary placement of the Oxbryta 500 mg tablets. The Oxbryta 300 mg oral soluble tablets will be placed to match the Oxbryta 500 mg tablets (Non-formulary for Commercial. Oxbryta 300 mg tablets will be included in Commercial Policy 622.0 and the following changes will be made to the prior authorization criteria and Quantity Limits to incorporate the new population, dosage, and formulation:

- Medical record documentation that Oxbryta is prescribed by or in consultation with a hematologist **AND**
- Medical record documentation of age greater than or equal to ~~12 years~~ 4 years **AND**
- Medical record documentation of a diagnosis of sickle cell disease **AND**
- Medical record documentation of baseline hemoglobin **AND**
- Medical record documentation of one of the following:
    - For patients 5 years of age and older: documentation of therapeutic failure on, intolerance to, or contraindication to a minimum three (3) month trial of generic hydroxyurea **AND** Endari **OR**
    - For patients less than 5 years of age: documentation of therapeutic failure on, intolerance to, or contraindication to a minimum three (3) month trial of generic hydroxyurea

AND

- If the requested ~~dose is 2,500 mg daily~~ quantity exceeds three tablets per day of Oxbryta 500 mg or five tablets per day of Oxbryta 300 mg: 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

MEDISPAN AUTHORIZATION LEVEL: GPI-12

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

QL FOR LETTER ONLY:

- Oxbryta 500 mg tablets: 3 tablets per day, 30 day supply per fill
- Oxbryta 300 mg oral soluble tablets: 5 tablets per day, 30 day supply per fill

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 vaso-occlusive crisis related emergencies) **AND**
- If the requested ~~dose is 2,500 mg daily~~ quantity exceeds three tablets per day of Oxbryta 500 mg or five tablets per day of Oxbryta 300 mg: 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

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.

RINVOQ (upadacitinib)

Clinical Summary: Rinvoq is a Janus Kinase (JAK) Inhibitor that is now indicated for the treatment of adults with active psoriatic arthritis (PsA) who have had an inadequate response or intolerance to one or more TNF blockers, for the treatment of adult and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic medications including biologics or when use of those therapies should be avoided, for the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to one or more TNF blockers, and for the treatment of adult patients with active ankylosing spondylitis who have had inadequate response or intolerance to one or more TNF blockers.

Previously, Rinvoq was only indicated for the treatment of adults with moderately to severely rheumatoid arthritis (RA) who have had an inadequate response to one or more TNF blockers.

The dosing for Rinvoq in the setting of psoriatic arthritis and ankylosing spondylitis is the same as for rheumatoid arthritis, 15 mg once daily. For patients with ulcerative colitis, there is an induction dose of 45 mg once daily for 8 weeks, then 15 mg once daily as the maintenance dosing. Providers can consider increasing the maintenance dosing to 30 mg once daily for patients with refractory, severe, or extensive ulcerative colitis, although Rinvoq should be discontinued if an adequate therapeutic response is not achieved with 30 mg dosage. Dosing of Rinvoq for atopic dermatitis is separated by age: For pediatric patients 12 years of age and older weighing at least 40 kg, and adult patients under the age of 65 years, treatment should be initiated at 15 mg once daily and if inadequate response is shown, may increase to 30 mg once daily. Adults over the age of 65 years, and patients with severe renal impairment, are both recommended to be treated with 15 mg once daily.

The safety and efficacy of Rinvoq in patients with psoriatic arthritis were assessed in two Phase 3 randomized, double-blind, multicenter, placebo-controlled studies in patients 18 years of age and older with moderately to severely active psoriatic arthritis. All patients included in the study had active psoriatic arthritis for at least 6 months as defined by the Classification Criteria for Psoriatic Arthritis (CASPAR), at least 3 tender joints and at least 3 swollen joints, and active

plaque psoriasis or a history of plaque psoriasis. Study PsA-I (NCT03104400) was a 24-week trial that included 1705 patients who had an inadequate response to at least one non-biologic DMARD. Patients were randomized to receive Rinvoq 15 mg, 30 mg, adalimumab, or placebo, alone or in combination with background non-biologic DMARDs. At week 24, all patients taking placebo were switched to Rinvoq 15 mg or 30 mg in a blinded manner. The primary endpoint achieved a statistically significant proportion of patients who achieved American College of Rheumatology ≥20% improvement (ACR20) response at Week 12. Study PsA-II (NCT03104374) was nearly identical to PsA-I, but this study included 642 patients who had an inadequate response to at least one biologic DMARD. This study supported the findings of PsA-I, with statistical significance in the proportion of patients who achieved an ACR20 response at week 20.

The safety and efficacy of Rinvoq for the treatment of atopic dermatitis were assessed in three Phase 3 randomized, double-blind, multicenter trials (AD-1, AD-2, AD-3; NCT03569293, NCT03607422, and NCT03568318). In total, 2584 patients were included, with 344 being pediatric patients 12 years of age and older, and 2240 being adult patients, all with moderate to severe atopic dermatitis not adequately controlled by topical medications. Baseline disease severity was determined by a validated Investigator's Global Assessment score ≥3 in the overall assessment of AD (vIGA-AD) on a severity scale of 0 to 4, an Eczema Area and Severity Index (EASI) score ≥16, a minimum body surface area (BSA) of ≥10%, and weekly average Worst Pruritus Numerical Rating Scale (NRS) score ≥4. Patients in all 3 trials were randomized to receive Rinvoq 15 mg, 30 mg, or placebo for 16 weeks. Patients enrolled in Trial AD-3 received concomitant topical corticosteroids in addition to Rinvoq or placebo for 16 weeks. The co-primary endpoints in these studies were the proportion of patients with a vIGA-AD score of 0 (clear) or 1 (almost clear) with at least a 2-point improvement, and the proportion of patients with EASI-75 (improvement of EASI score from baseline) at Week 16. Secondary endpoints included EASI-90 at Week 16, EASI-100 at Week 16, and the proportion of patients with reduction in itch (≥4-point improvement from baseline in the Worst Pruritus NRS) at weeks 1, 4, and 16. Trials AD-1 and AD-2 also included the secondary endpoint of reduction in pain (≥4-point improvement in the Atopic Dermatitis Symptom Scale [ADerm-ss] Skin Pain NRS) from baseline to Week 16. All of these outcomes proved to be statistically significant, this is the case for the adult patients as well as for the pediatric patients.

The safety and efficacy of Rinvoq in patients with ulcerative colitis were assessed in two identical induction trials (UC-1, UC-2; NCT02809635, NCT03653026). A total of 998 patients were randomized 2:1 to receive either Rinvoq 45 mg once daily or placebo for 8 weeks. The patients in these two studies were adults with moderately to severely active ulcerative colitis who had an inadequate response, loss of response, or intolerance to oral aminosalicylates, corticosteroids, immunosuppressants, or biologic therapy. Patients were allowed to remain on stable doses of aminosalicylates, methotrexate, UC-related antibiotics, and/or oral corticosteroids. Disease severity was assessed using modified Mayo score (mMS), a 3-component Mayo score (0-9) which consists of the following subscores (0 to 3 for each subscore): stool frequency (SFS), rectal bleeding (RBS), and findings on centrally read endoscopy score (ES). The primary endpoint was clinical remission using the mMS at Week 8 while secondary endpoints included clinical response, endoscopic improvement, and histologic endoscopic mucosal improvement. All primary and secondary endpoints were statistically significant. A third trial (UC-3; NCT02819635) studied the safety and efficacy of Rinvoq used as maintenance therapy. A total of 451 patients that were previously enrolled in UC-1, UC-2, or UC-4 and had received Rinvoq 45 mg once daily were rerandomized to receive Rinvoq 15 mg, 30 mg, or placebo once daily for up to 52 weeks. The primary endpoint was clinical remission defined using mMS at Week 52 while secondary endpoints included corticosteroid-free clinical

remission, endoscopic improvement, and histologic endoscopic mucosal improvement. All primary and secondary endpoints of this study were statistically significant.
The safety and efficacy of Rinvoq in patients with active ankylosing spondylitis were evaluated in two randomized, double-blind, multicenter, placebo-controlled trials. Patients in the study were at least 18 years of age with active ankylosing spondylitis as defined by the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 and Patient's Assessment of Total Back Pain score ≥4. Both trials were 14 weeks in length with a primary endpoint being the proportion of patients achieving an Assessment of SpondyloArthritis international Society 40 (ASAS40) response at Week 14. In Trial AS-I (NCT 03178487), patients were enrolled that had an inadequate response to, intolerance to, or contraindication to at least two nonsteroidal anti-inflammatory drugs (NSAIDs) and had no previous exposure to biologic DMARDs. In Trial AS-II (NCT04169373), patients were enrolled that had an inadequate response to one or two biologic DMARDs. In both studies, at Week 14, all patients randomized to placebo were switched to Rinvoq 15 mg once daily. Both studies saw a statistically significant proportion of patients achieving an ASAS40 response in those taking Rinvoq 15 mg as compared to those taking placebo at Week 14.

Several new safety concerns and adverse reactions were identified through the studies for the new indications. Adverse reactions are now separated by indication in the package insert. Newly identified adverse reactions occurring in ≥1% of patients with rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis include: herpes zoster, herpes simplex, bronchitis, acne, and headache. For patients treating atopic dermatitis adverse reactions include the same reactions for RA, PsA, and AS as well as the following newly identified reactions occurring in ≥1% of patients: increased blood creatine phosphokinase, hypersensitivity, folliculitis, abdominal pain, increased weight, influenza, fatigue, neutropenia, myalgia, and influenza like illness. Adverse reactions occurring in 5% of patients using Rinvoq to treat ulcerative colitis include: upper respiratory tract infections, increased blood creatine phosphokinase, acne, neutropenia, elevated liver enzymes, and rash. A new warning was added for serious hypersensitivity reactions in addition to a new contraindication, known hypersensitivity to Rinvoq or any of the excipients.

Current formulary status: Pharmacy benefit on the specialty tier or the brand non-preferred tier for members with a 3-tier benefit. Prior authorization required.

Recommendation: No changes are recommended to the formulary placement of Rinvoq. It is recommended that the Rinvoq 30 mg tablet and 45 mg tablet be added to the formulary at the same tier as the 15 mg tablet, with the 30 mg tablet having a quantity limit of 1 tablet per day, and the 45 mg tablet having a quantity limit of 56 tablets per 180 days. It is also recommended that the following prior authorization criteria and auth duration criteria be added to Commercial Policy 605.0 to incorporate the new indications:

For treatment of Rheumatoid Arthritis (RA)

- Medical record documentation that Rinvoq is prescribed by a rheumatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- 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 Rinvoq is not being used concurrently with a TNF blocker or other biologic agent **AND**

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

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

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

- QL FOR LETTER ONLY: 1 tablet per day, 30 day supply per fill

For treatment of Psoriatic Arthritis (PsA)

- Medical record documentation of a diagnosis of psoriatic arthritis **AND**
- Medical record documentation that Rinvoq is prescribed by a rheumatologist or dermatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of either active psoriatic arthritis which must include the following:
  - Documentation of either active psoriatic lesions or a documented history of psoriasis **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to
- at least 3 months of therapy with Cosentyx* **AND** Humira* **AND**
- Medical record documentation that Rinvoq is not being used concurrently with a TNF blocker or
- other biologic agent

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

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

- QL FOR LETTER ONLY: 1 tablet per day, 30 day supply per fill

For treatment of Ankylosing Spondylitis (AS)

- Medical record documentation of a diagnosis of ankylosing spondylitis **AND**
- Medical record documentation that Rinvoq is prescribed by a rheumatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least 3 months of therapy with Cosentyx* **AND** Humira* **AND**
- Medical record documentation that Rinvoq is not being used concurrently with a TNF blocker or other biologic agent

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

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

- QL FOR LETTER ONLY: 1 tablet per day, 30 day supply per fill

For treatment of Atopic Dermatitis

- Medical record documentation of a diagnosis of moderate to severe atopic dermatitis **AND**
- Medical record documentation that Rinvoq is prescribed by an allergist, dermatologist, or
- immunologist **AND**
- Medical record documentation of age greater than or equal to 12 years **AND**
- Medical record documentation of one of the following:
    - Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid **OR**
    - For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable (use on sensitive areas, age between 2 and 15 years): Therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) **AND**
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure to Dupixent

MEDISPAN AUTHORIZATION LEVEL: GPI-12, number of claims authorized = 1, enter for the remainder of the calendar year

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

- QL FOR LETTER ONLY: 1 tablet per day, 30 day supply per fill

For treatment of Ulcerative Colitis (UC)

- Medical record documentation of a diagnosis of moderate to severe ulcerative colitis **AND**
- Medical record documentation that Rinvoq is prescribed by a gastroenterologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least 3 months of therapy of Humira* **AND**
- Medical record documentation that Rinvoq is not being used concurrently with a TNF blocker or other biologic agent

MEDISPAN AUTHORIZATION LEVEL: GPI-12

QUANTITY LIMIT:

- 45 mg once daily for 8 weeks
    1. In PA Hub: Add PA, OQL, number of claims authorized 1, max quantity dispensed 56 with a duration of 8 weeks
        - QL FOR LETTER: Loading dose : 56 tablets per 180 days; Maintenance dose: 1 tablet per day

Discussion: No comments or questions.

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

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

LYNPARZA (olaparib)

Updated Indication: Lynparza is now indicated for the adjuvant treatment of adult patients with deleterious or suspected deleterious gBRCAm human epidermal growth factor receptor 2 (HER2)-negative high risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Patients should be selected based on FDA-approved companion diagnostic for Lynparza.

Previously Lynparza was indicated for the treatment of patients with germline BRCA-mutated HER2-negative metastatic breast cancer as well as indications in prostate cancer, pancreatic cancer, an ovarian cancer.
There is no change to the recommended dosage of Lynparza for the new indication. It is 300 mg twice daily with or without food. For the adjuvant treatment of high risk early breast cancer, treatment with Lynparza is continued for a total of 1 year, or until disease recurrence or unacceptable toxicity, whichever occurs first. Patients with hormone receptor positive HER2-negatvie breast cancer should continue concurrent treatment with endocrine therapy according to current clinical practice guidelines.

Support of the new indication comes from results of the OlympiA trial, a randomized, double-blind, placebo-controlled study in patients with gBRCAm HER2-negative high risk early breast cancer who had completed definitive local treatment and neoadjuvant or adjuvant chemotherapy. Patients were randomized to receive Lynparza 300 mg twice daily or placebo for up to 1 year, until disease recurrence, or unacceptable toxicity. Patients included in the trial had completed at least 6 cycles of neoadjuvant or adjuvant chemotherapy with anthracyclines, taxanes, or both. Prior platinum therapy for previous cancer (e.g., ovarian) or as adjuvant or neoadjuvant treatment for breast cancer was allowed. The major efficacy endpoint was invasive disease free survival (IDFS), defined as time from randomization to date of first recurrence (invasive loco-regional, distant recurrence, contralateral invasive breast cancer, new cancer, or death from any cause). Overall survival was also evaluated. A statistically significant improvement in IDFS and OS were demonstrated in patients in the Lynparza arm compared to placebo arm (Table 1).

Table 1. Efficacy Results from OlympiA

	Lynparza tablets (N=921)	Placebo (N=915)
Invasive Disease Free Survival (IDFS)*		
Number of events (%)	106 (12)	178 (20)
Hazard Ratio (95% CI)†	0.58 (0.46, 0.74)	
p-value (2-sided)‡	< 0.0001	
3-year event-free rate, % (95% CI)§	86 (82.8, 88.4)	77 (73.7, 80.1)
Overall Survival¶		
Number of events (%)	75 (8)	109 (12)
HR (95% CI)†	0.68 (0.50, 0.91)	
p-value (2-sided)‡	0.0091	
3-year event-free rate, % (95% CI)§	93 (90.8, 94.4)	89 (86.7, 91)

* Data from the pre-specified interim analysis (86% of the number of events for the planned final analysis).
† Based on the stratified Cox's Proportional Hazards Model.
‡ p-value from a stratified log-rank test. Compared with the allocated alpha of 0.005 for IDFS and 0.015 for OS.
§ Percentage are calculated using Kaplan-Meier estimates.
¶ Data from the pre-specified second interim analysis of OS (at ~330 IDFS events).
CI = confidence interval.

No new safety concerns were identified during the OlympiA trial and observed side effects were consistent with the known profile of Lynparza.

Current formulary status: Oral Onc Brand NP tier ($0 copay), PA required, QL: 4 tablets per day, 30 day supply per fill

Recommendation: There are no changes recommended for the formulary placement or quantity limit of Lynparza. It is recommended that the following prior authorization criteria and changes to the authorization duration be made to Commercial Policy 362.0 to incorporate the new indication for Lynparza.

For Adjuvant Treatment of High Risk Early Breast Cancer

- Medical record documentation that Lynparza is prescribed by an oncologist or hematologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of deleterious or suspected deleterious *gBRCA*m, HER2-negative high risk early breast cancer* **AND**
- Medical record documentation that member has been previously treated with chemotherapy in the neoadjuvant or adjuvant setting

*In the OlympiA trial, high risk was defined as follows:

- Prior Neoadjuvant Chemotherapy:
    - Triple Negative Breast Cancer (TNBC) or Hormone Receptor Positive Breast cancer must have had residual invasive cancer in the breast and/or the resected lymph nodes (non-pathologic complete response) at the time of surgery.
    - Hormone Receptor Positive Breast Cancer must also have had a score of ≥3 based on pre-treatment clinical and post-treatment pathologic stage (CPS), estrogen receptor (ER) status, and histologic grade as shown in the Table 1 below.

Table 1. Early Breast Cancer Stage, Receptor Status, and Grade Scoring Requirements for Study Enrollment

Stage/feature		Points
Clinical Stage (pre-treatment)	I/IIA	0
	IIB/IIIA	1
	IIIB/IIIC	2
Pathologic Stage (post-treatment)	0/I	0
	IIA/IIB/IIIA/IIIB	1
	IIIC	2
Receptor status	ER positive	0
	ER negative	1
Nuclear grade	Nuclear grade 1-2	0
	Nuclear grade 3	1

- Prior Adjuvant Chemotherapy:
    - TNBC must have had node positive disease or node negative disease with a ≥2cm primary tumor
    - Hormone Receptor Positive, HER2-negative breast cancer must have had ≥4 pathologically confirmed positive lymph nodes.

AUTHORIZATION DURATION (Commercial Policy 362.0):
For adjuvant treatment of high-risk early breast cancer
One time authorization for 12 months or less if the reviewing provider feels it is medically appropriate.

Authorization of Lynparza for the adjuvant treatment of high-risk early breast cancer should not exceed the FDA-approved treatment duration of 1 year (12 months). For requests exceeding the above limit, medical record documentation of the following is required:

- Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration

For first-line maintenance of BRCA-mutated advanced ovarian cancer (failure on first-line platinum-based chemotherapy) and for first-line maintenance of HRD-positive advanced ovarian cancer in combination with bevacizumab:
Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. One subsequent approval for Lynparza will be granted for up to an additional 12 months (total of two years of therapy) 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

For members requesting approval of treatment beyond two (2) years, medical record documentation will be required showing patient has continued evidence of disease and treating healthcare provider believes member can derive further benefit from continuous treatment. Each additional approval will be for a period of 12 months. Members with complete response at two years, will not be granted additional treatment, per the package labeling.

For all other indications:
Initial approval will be for 12 months or less if the reviewing provider feels it is medical 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.

SIKLOS (hydroxyurea)

Clinical Summary: Siklos is now indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions in adult and pediatric patients, 2 years of age and older, with sickle cell anemia with recurrent moderate to severe painful crises. Previously Siklos was only indicated for use in pediatric patients.

Current formulary status: Tier 5 w/PA (Exchange), Tier 2 w/PA (CHIP, Commercial Traditional), Tier 3 w/PA (Commercial 4-Tier Plans and Triple Choice)

Recommendation: There are no changes recommended.

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.

XARELTO FOR ORAL SUSPENSION (rivaroxaban)

Clinical Summary: Xarelto (rivaroxaban) for oral suspension is indicated for treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years and for thromboprophylaxis in pediatric patients 2 years and older with congenital heart disease after the Fontan procedure.

The dosing for Xarelto suspension is based on body weight (see tables 2 and 3).

Treatment of Venous Thromboembolism and Reduction in Risk of Recurrent Venous Thromboembolism in Pediatric Patients

Table 2: Recommended Dosage in Pediatric Patients Birth to Less than 18 Years for Treatment of and Reduction in Risk of Recurrent VTE*,†

Dosage Form	Body Weight	1 mg XARELTO = 1 mL Suspension			
		Dosage			Total Daily Dose‡
		Once a Day§	2 Times a Day§	3 Times a Day§	
Oral Suspension Only	2.6 kg to 2.9 kg			0.8 mg	2.4 mg
	3 kg to 3.9 kg			0.9 mg	2.7 mg
	4 kg to 4.9 kg			1.4 mg	4.2 mg
	5 kg to 6.9 kg			1.6 mg	4.8 mg
	7 kg to 7.9 kg			1.8 mg	5.4 mg
	8 kg to 8.9 kg			2.4 mg	7.2 mg
	9 kg to 9.9 kg			2.8 mg	8.4 mg
	10 kg to 11.9 kg			3 mg	9 mg
	12 kg to 29.9 kg		5 mg		10 mg
Oral Suspension or Tablets	30 kg to 49.9 kg	15 mg			15 mg
	≥50 kg	20 mg			20 mg

* Initiate XARELTO treatment following at least 5 days of initial parenteral anticoagulation therapy.

† Patients <6 months of age should meet the following criteria: at birth were at least 37 weeks of gestation, have had at least 10 days of oral feeding, and weigh ≥2.6 kg at the time of dosing.

‡ All doses should be taken with feeding or with food since exposures match that of 20 mg daily dose in adults.

§ Once a day: approximately 24 hours apart; 2 times a day: approximately 12 hours apart; 3 times a day: approximately 8 hours apart

Dosing of XARELTO was not studied and therefore dosing cannot be reliably determined in the following patient populations. Its use is therefore not recommended in children less than 6 months of age with any of the following:

- Less than 37 weeks of gestation at birth
- Less than 10 days of oral feeding
- Body weight of less than 2.6 kg.

To increase absorption, all doses should be taken with feeding or with food. Monitor the child's weight and review the dose regularly, especially for children below 12 kg. This is to ensure a therapeutic dose is maintained.

Thromboprophylaxis in Pediatric Patients with Congenital Heart Disease after the Fontan Procedure

Table 3: Recommended Dosage for Thromboprophylaxis in Pediatric Patients with Congenital Heart Disease

Dosage Form	Body Weight	1 mg XARELTO = 1 mL Suspension		
		Dosage		Total Daily Dose*
		Once a Day†	2 Times a Day†	
Oral Suspension Only	7 kg to 7.9 kg		1.1 mg	2.2 mg
	8 kg to 9.9 kg		1.6 mg	3.2 mg
	10 kg to 11.9 kg		1.7 mg	3.4 mg
	12 kg to 19.9 kg		2 mg	4 mg
	20 kg to 29.9 kg		2.5 mg	5 mg
	30 kg to 49.9 kg	7.5 mg		7.5 mg
Oral Suspension or Tablets	≥50 kg	10 mg		10 mg

* All doses can be taken with or without food since exposures match that of 10 mg daily dose in adults.

† Once a day: approximately 24 hours apart; 2 times a day: approximately 12 hours apart.

XARELTO for the treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE was evaluated in the EINSTEIN Junior Phase 3 study [NCT02234843], a multicenter, open-label, active-controlled, randomized study in 500 pediatric patients from birth to less than 18 years with confirmed VTE. There were 276 children aged 12 to <18 years, 101 children aged 6 to <12 years, 69 children aged 2 to <6 years, and 54 children aged <2 years. Patients <6 months of age were excluded from enrollment if they were <37 weeks of gestation at birth, or had <10 days of oral feeding, or had a body weight of <2.6 kg.

Index VTE was classified as either central venous catheter-related VTE (CVC-VTE), cerebral vein and sinus thrombosis (CVST), and all other VTE including DVT and PE (non-CVC-VTE).

Patients received initial treatment with therapeutic dosages of unfractionated heparin (UFH), low molecular weight heparin (LMWH), or fondaparinux for at least 5 days, and were randomized 2:1 to receive either body weight-adjusted doses of XARELTO (exposures to match that of 20 mg daily dose in adults) or comparator group (UFH, LMWH, fondaparinux or VKA) for a main study treatment period of 3 months (or 1 month for children <2 years with CVC-VTE). A diagnostic imaging test was obtained at baseline and at the end of the main study treatment. When clinically necessary, treatment was extended up to 12 months in total (or up to 3 months in total for children <2 years with CVC-VTE).

Table 28 displays the primary and secondary efficacy results.

Table 28: Efficacy Results in EINSTEIN Junior Study – Full Analysis Set

Event	XARELTO* N=335 n (%) (95% CI)†	Comparator Group‡ N=165 n (%) (95% CI)†	XARELTO vs. Comparator Group Risk Difference (95% CI)§	XARELTO vs. Comparator Group Hazard Ratio (95% CI)
Primary efficacy outcome: Symptomatic recurrent VTE	4 (1.2) (0.4%, 3.0%)	5 (3.0) (1.2%, 6.6%)	-1.8% (-6.0%, 0.6%)	0.40 (0.11, 1.41)
Secondary efficacy outcome: Symptomatic recurrent VTE or asymptomatic deterioration on repeat imaging	5 (1.5) (0.6%, 3.4%)	6 (3.6) (1.6%, 7.6%)	-2.1% (-6.5%, 0.6%)	

* Treatment schedule: body weight-adjusted doses of XARELTO (exposures to match that of 20 mg daily dose in adults); randomized 2:1 (XARELTO: Comparator).
† Confidence intervals for incidence proportion were calculated by applying the method of Blyth-Still-Casella.
‡ Unfractionated heparin (UFH), low molecular weight heparin (LMWH), fondaparinux or VKA.
§ Confidence intervals for difference in incidence proportions were calculated by unstratified exact method according to Agresti-Min using the standardized test statistic and inverting a two-sided test.

Complete resolution of thrombus on repeat imaging without recurrent VTE occurred in 128 of 335 children (38.2%, 95% CI 33.0%, 43.5%) in the XARELTO group and 43 of 165 children (26.1%, 95% CI 19.8%, 33.0%) in the comparator group. Symptomatic recurrent VTE or major bleeding events occurred in 4 of 335 children (1.2%, 95% CI 0.4%, 3.0%) in the XARELTO group and 7 of 165 children (4.2%, 95% CI 2.0%, 8.4%) in the comparator group.

The efficacy and safety of XARELTO for thromboprophylaxis in pediatric patients with congenital heart disease who have undergone the Fontan procedure was evaluated in the UNIVERSE Phase 3 study [NCT02846532]. UNIVERSE was a prospective, open-label, active controlled, multicenter, 2-part study, designed to evaluate the single- and multiple-dose pharmacokinetic properties of XARELTO (Part A), and to evaluate the safety and efficacy of XARELTO when used for thromboprophylaxis for 12 months compared with aspirin (Part B) in children 2 to 8 years of age with single ventricle physiology who had the Fontan procedure. Patients in Part B were randomized 2:1 to receive either body weight-adjusted doses of XARELTO (exposures to match that of 10 mg daily dose in adults) or aspirin (approximately 5 mg/kg). Patients with eGFR <30 ml/min/1.73 m2 were excluded.

The median time between Fontan procedure and the first dose of XARELTO was 4 (range: 2-61)
days in Part A and 34 (range: 2-124) days in part B. In comparison, the median time to initiating aspirin was 24 (range 2-117) days.

Table 29 displays the primary efficacy results.

Table 29: Efficacy Results in UNIVERSE Study – Full Analysis Set

	Part A*	Part B†		
Event	XARELTO N=12 n (%) (95% CI)‡	XARELTO§ N=64 n (%) (95% CI)‡	Aspirin§ N=34 n (%) (95% CI)‡	XARELTO vs. Aspirin Risk Difference (95% CI)¶
Primary efficacy outcome: any thrombotic event	1 (8.3) (0.4%, 34.9%)	1 (1.6) (0.1%, 7.8%)	3 (8.8) (2.4%, 22.2%)	-7.3% (-21.7%, 1.1%)
Ischemic stroke	0 (0.0%, 23.6%)	0 (0.0%, 5.6%)	1 (2.9) 0.2%, 15.1%)	-2.9% (-16.2%, 2.9%)
Pulmonary embolism	0 (0.0%, 23.6%)	1 (1.6) (0.1%, 7.8%)	0 (0.0%, 9.0%)	1.6% (-9.9%, 8.4%)
Venous thrombosis	1 (8.3) (0.4%, 34.9%)	0 (0.0%, 5.6%)	2 (5.9) (1.1%, 18.8%)	-5.9% (-20.6%, -0.1%)

* Part A: single arm; not randomized
† Part B: randomized 2:1 (XARELTO: Aspirin)
‡ Confidence intervals for incidence proportion were calculated by applying the method of Blyth-Still-Casella.
§ Treatment schedule: body weight-adjusted doses of XARELTO (exposures to match that of 10 mg daily dose in adults) or aspirin (approximately 5 mg/kg)
¶ Confidence intervals for difference in incidence proportions were calculated by unstratified exact method according to Agresti-Min using the standardized test statistic and inverting a two-sided test.

The safety and effectiveness of XARELTO have been established in pediatric patients from birth to less than 18 years for the treatment of VTE and the reduction in risk of recurrent VTE. Use of XARELTO is supported in these age groups by evidence from adequate and well-controlled studies of XARELTO in adults with additional pharmacokinetic, safety and efficacy data from a multicenter, prospective, open-label, active-controlled randomized study in 500 pediatric patients from birth to less than 18 years of age. XARELTO was not studied and therefore dosing cannot be reliably determined or recommended in children less than 6 months who were less than 37 weeks of gestation at birth; had less than 10 days of oral feeding, or had a body weight of less than 2.6 kg.

The safety and effectiveness of XARELTO have been established for use in pediatric patients aged 2 years and older with congenital heart disease who have undergone the Fontan procedure. Use of XARELTO is supported in these age groups by evidence from adequate and well controlled studies of XARELTO in adults with additional data from a multicenter, prospective, open-label, active controlled study in 112 pediatric patients to evaluate the single- and multipledose pharmacokinetic properties of XARELTO and the safety and efficacy of XARELTO when used for thromboprophylaxis for 12 months in children with single ventricle physiology who had the Fontan procedure.

Clinical studies that evaluated safety, efficacy, pharmacokinetic and pharmacodynamic data support the use of XARELTO 10 mg, 15 mg, and 20 mg tablets in pediatric patients. For the XARELTO 2.5 mg tablets, there are no safety, efficacy, pharmacokinetic and pharmacodynamic data to support the use in pediatric patients. Therefore, XARELTO 2.5 mg tablets are not recommended for use in pediatric patients.

Although not all adverse reactions identified in the adult population have been observed in clinical trials of children and adolescent patients, the same warnings and precautions for adults should be considered for children and adolescents.

Current formulary status: Xarelto tablets are currently on the formulary, Brand preferred.

Recommendation: Recommend adding Xarelto suspension to the formulary on the brand preferred tier, no prior authorization required.

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/XELJANZ XR (tofacitinib citrate)

Clinical Summary: Xeljanz/Xeljanz XR are now indicated for the treatment of adult patients with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more tumor necrosis factor (TNF) blockers.

The recommended dosing for AS is Xeljanz 5mg twice daily or Xeljanz XR 11mg once daily.

The safety and efficacy of Xeljanz/Xeljanz XR was established in a placebo-controlled confirmatory trial (Study AS-I). Patients had active disease as defined by both Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and back pain score (BASDAI question 2) of greater or equal to 4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease modifying anti-rheumatic drug (DMARD) therapy. Study AS-I was a randomized, double-blind, placebo-controlled, 48-week clinical trial in 269 adult patients who had an inadequate response (inadequate clinical response or intolerance) to at least 2 NSAIDs. Patients were randomized and treated with XELJANZ 5 mg twice daily or placebo for 16 weeks of blinded treatment and then all received treatment of XELJANZ 5 mg twice daily for additional 32 weeks. The primary endpoint was to evaluate the proportion of patients who achieved an ASAS20 response at Week 16. Approximately 7% and 21% of patients used concomitant methotrexate or sulfasalazine, respectively from baseline to Week 16. Twenty-two percent of patients had an inadequate response to 1 or 2 TNF blockers. Patients treated with XELJANZ 5 mg twice daily achieved greater improvements in ASAS20 and ASAS40 responses compared to placebo at Week 16 (Table 17). Consistent results were observed in the subgroup of patients who had an inadequate response to TNF blockers for both the ASAS20 (primary endpoint) and ASAS40 (secondary endpoint) at Week 16 (Table 17).

Table 17: ASAS20 and ASAS40 Responses at Week 16, Study AS-I

	Placebo	XELJANZ 5mg Twice Daily	Difference from Placebo
All patients (N)	N=136	N=133	
ASAS20 response*, %	29	56	27 (16, 38)†
ASAS40 response*, %	13	41	28 (18, 38)†
TNFi-IR patients (N)	N=30	N=29	
ASAS20 response, %	17	41	25 (2, 47)
ASAS40 response, %	7	28	21 (2, 39)

Abbreviations: CI = confidence interval; TNFi-IR = tumor necrosis factor inhibitor inadequate response.
*type I error-controlled. †p-value <0.0001.

The improvements in the components of the ASAS response and other measures of disease activity were higher in XELJANZ 5 mg twice daily compared to placebo as shown in Table 18.

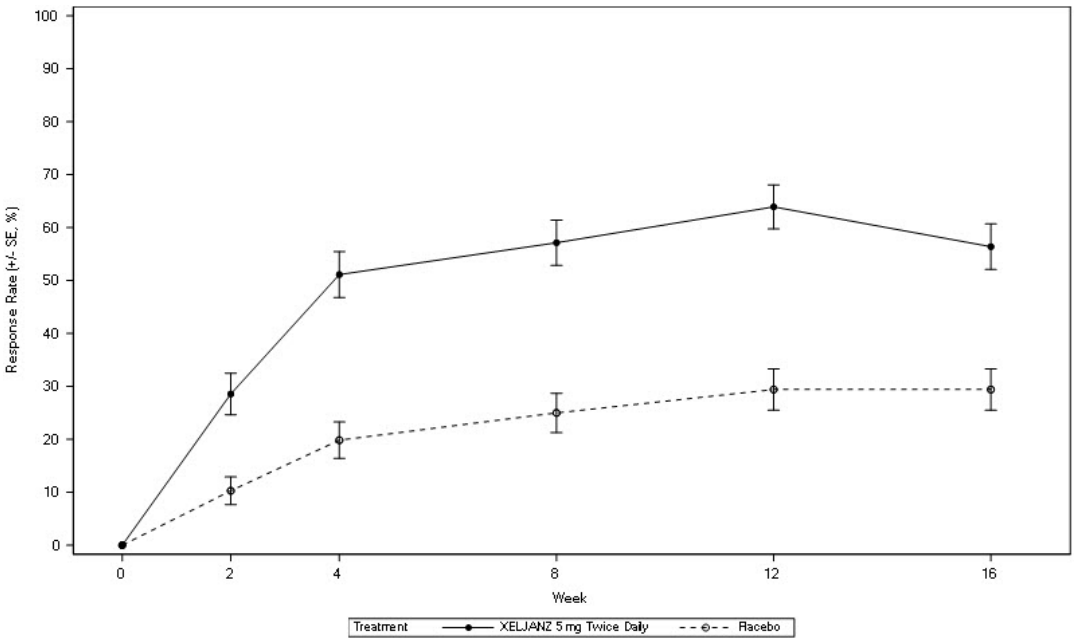
Table 18: ASAS Components and Other Measures of Disease Activity at Week 16, Study AS-I

	Placebo (N=136)		XELJANZ 5mg Twice Daily (N=133)		
	Baseline (mean)	Week 16 (LSM change from Baseline)*	Baseline (mean)	Week 16 (LSM change from Baseline)	Difference from Placebo (95% CI)*
ASAS Components					
- Patient Global Assessment of Disease Activity (0–10)†,‡	7.0	-1.0	6.9	-2.5	-1.5 (-2.00, -0.97)§
- 000000000000Total spinal pain (0–10)†,‡	6.9	-1.1	6.9	-2.6	-1.5 (-2.00, -1.03)§
- BASFI (0–10)¶,‡	5.9	-0.8	5.8	-2.0	-1.2 (-1.64, -0.79)§
- Inflammation (0–10)#,‡	6.8	-1.1	6.6	-2.8	-1.7 (-2.13, -1.18)§
BASDAI ScoreÞ	6.5	-1.2	6.4	-2.6	-1.4 (-1.86, -0.98)§
BASMIß,‡	4.4	-0.1	4.5	-0.6	-0.5 (-0.66, -0.36)§
hsCRPà,‡ (mg/dL)	1.8	-0.1	1.6	-1.1	-0.9 (-1.17, -0.69)§

LSM = least squares mean.
* Estimates are generated based on a mixed model for repeated measures using both on-treatment and off-treatment data.
† Measured on a numerical rating scale with 0 = not active or no pain, 10 = very active or most severe pain.
‡ type I error-controlled.
§ $p < 0.0001$.
¶ Bath Ankylosing Spondylitis Functional Index measured on a numerical rating scale with 0 = easy and 10 = impossible.
# Inflammation is the mean of two patient-reported stiffness self-assessments in BASDAI.
Þ Bath Ankylosing Spondylitis Disease Activity Index total score.
ß Bath Ankylosing Spondylitis Metrology Index.
à High sensitivity C-reactive protein.

The percentage of patients achieving ASAS20 response by visit is shown in Figure 6.

Figure 6: ASAS20 Response Over Time Up to Week 16, Study AS-I



SE=standard error.
Patients with missing data were treated as non-responders.

Patients treated with XELJANZ 5 mg twice daily achieved greater improvements from baseline in Ankylosing Spondylitis Quality of Life (ASQoL) (-4.0 vs -2.0) compared to placebo-treated patients at Week 16.

The safety profile observed in patients with AS treated with XELJANZ was consistent with the safety profile observed in rheumatoid arthritis and psoriatic arthritis patients.

The following indications have also been updated:

- Rheumatoid Arthritis: XELJANZ/XELJANZ XR is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance ~~to methotrexate. It may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs (DMARDs).~~ to one or more TNF blockers.
- Psoriatic Arthritis: XELJANZ/XELJANZ XR is indicated for the treatment of adult patients with active psoriatic arthritis who have had an inadequate response or intolerance ~~to methotrexate or other disease-modifying antirheumatic drugs (DMARDs).~~ to one or more TNF blockers.
- Ulcerative Colitis: XELJANZ/XELJANZ XR is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers.
- Polyarticular Course Juvenile Idiopathic Arthritis: XELJANZ/XELJANZ Oral Solution is indicated for the treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more TNF blockers.

Current formulary status: Xeljanz/Xeljanz XR is a pharmacy benefit available at the Specialty tier or the Brand Non-Preferred tier for members with a three tier benefit and requires a prior authorization.

Recommendation: There are no formulary changes recommended at this time. However, it is recommended that the following prior authorization criteria be added to the Xeljanz policy.

For treatment of ankylosing spondylitis
An exception for coverage of Xeljanz may be made for members who meet the following criteria:

- Medical record documentation of a diagnosis of ankylosing spondylitis **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 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 AND
- Medical record documentation that Xeljanz or Xeljanz XR is being dosed consistent with Food and Drug Administration (FDA)-approved labeling

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 of intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of Humira* **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 **AND**
- Medical record documentation that Xeljanz or Xeljanz XR is being dosed consistent with Food and Drug Administration (FDA)-approved labeling

NOTE: Xeljanz 10 mg twice daily and Xeljanz XR 22 mg once daily are only indicated for the treatment of ulcerative colitis induction treatment and in cases of loss of response to maintenance treatment. The maximum recommended dosage for rheumatoid arthritis and psoriatic arthritis are Xeljanz 5 mg twice daily or Xeljanz XR 11 mg once daily.

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

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

- QL FOR LETTER ONLY:
    - 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

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

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

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.

YESCARTA (axicabtagene ciloleucel)

Clinical Summary: Yescarta is a CD19-directed genetically modified autologous T cell immunotherapy now indicated for the treatment of adult patients with large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy.

Previously, Yescarta was indicated for:

- Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.
- Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

There is no change for the dose for the new indication and the target dose is 2×10^6 CAR-positive viable T cells per kilogram body weight, with a maximum of 2×10^8 CAR-positive viable T cells.

The efficacy of Yescarta was evaluated in a randomized, open-label, multicenter trial in adult patients with relapsed or refractory Large B-Cell Lymphoma (LBCL) after first-line chemoimmunotherapy that included rituximab and anthracycline. Patients were required to have primary refractory disease or relapse within 12 months following completion of first-line therapy, have not received treatment for relapse or refractory lymphoma previously, and be potential candidates for autologous hematopoietic stem cell transplantation (HSCT). Key exclusion criteria was patients with primary mediastinal B-cell lymphoma, any history of central nervous system lymphoma, need for urgent therapy due to tumor mass effect, active or serious infections, and ECOG performance status of 2 or greater. The median age was 59 years (range: 21 to 81 years), and 74% of patients had primary refractory LBCL, while 26% of patients had relapsed disease within 12 months of first-line therapy. Diagnoses included new Diffuse Large B-cell Lymphoma (DLBCL) not otherwise specified (63%), High-Grade B-cell Lymphoma with or without MYC and BCL-2 and/or BCL-6 rearrangements (19%), and large cell transformation of follicular lymphoma (13%).

359 patients were randomized 1:1 to receive single agent Yescarta as a single intravenous infusion at a target dose of 2 x 10^6 CAR-positive viable T cells/kg, or to receive standard second line therapy with 2 or 3 cycles of chemoimmunotherapy followed by high-dose therapy and autologous HSCT in patients who attained complete response (CR) and partial response (PR). Of the 180 patients randomized to receive Yescarta, 178 underwent leukapheresis, and 170 received treatment with Yescarta. 8 patients were not treated with Yescarta following leukapheresis due to progressive disease, serious adverse events or death. The median dose was 2.0 × 10^6 CAR-positive viable T cells/kg. Of the 179 patients randomized to receive standard therapy, 168 received any study treatment and 62 of the 179 (35%) received high-dose therapy and on-protocol HSCT. The most common reason for not receiving HSCT was lack of response to salvage chemotherapy.

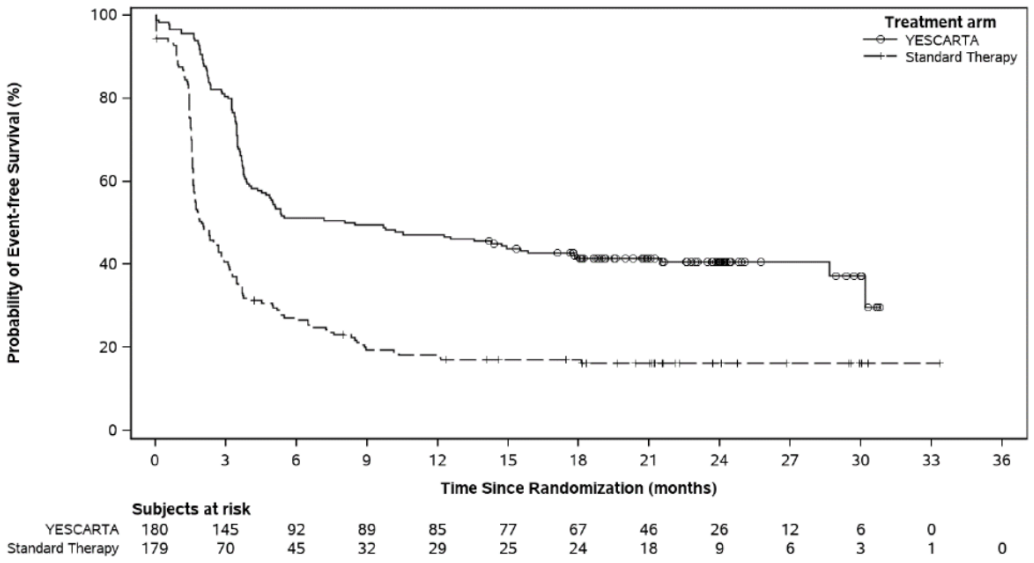
The primary efficacy measure was event-free survival (EFS), with the estimated EFS rate at 18 months being 41.5% [95% CI: 34.2, 48.6] in the Yescarta arm and 17.0% [95% CI: 11.8, 23.0] in the standard therapy arm. The estimated duration of response (DOR) was 28.4 months (95% CI: 26.9, NE) in the Yescarta arm for patients who achieved CR and 1.6 months (95% CI: 1.4, 1.9) in the Yescarta arm for patients who achieved a best response of PR. 55% of patients randomized to the standard therapy arm subsequently received CD19-directed CAR T therapy off protocol. Results are summarized in Table 1 and Figure 1.

Table 1. Efficacy Results for ZUMA-7

Outcome[a]	**Yescarta (N = 180)[e]**	**Standard Therapy (N = 179)**
Event-Free Survival[b]		
Number of events, n (%)	108 (60)	144 (80)
Median, months [95% CI][c]	8.3 [4.5, 15.8]	2.0 [1.6, 2.8]
Stratified hazard ratio [95% CI]	0.40 [0.31, 0.51]	
Stratified log-rank p-value	<0.0001	
Best Objective Response Rate, % [95% CI]	**83 [77, 88]**	**50 [43, 58]**
Difference in ORR, % [95% CI]	33 [23, 42]	
Stratified p-value[d]	<0.0001	
Complete remission rate, % [95% CI]	65 [58, 72]	32 [26, 40]
Partial remission rate, % [95% CI]	18 [13, 25]	18 [13, 24]
Progression-Free Survival		
Number of events, n (%)	93 (52)	81 (45)
Median, months [95% CI][c]	14.9 [7.2, NE]	5.0 [3.4, 8.5]
Stratified hazard ratio [95% CI]	0.56 [0.41, 0.76]	

CI, confidence interval; NE, not estimable.
a. Per the International Working Group Lugano Classification (Cheson 2014), as assessed by the independent review committee.
b. EFS is defined as time from randomization to the earliest date of disease progression or relapse, best response of stable disease up to and including the Day 150 assessment, commencement of new lymphoma therapy, or death from any cause.
c. Kaplan-Meier estimate.
d. Per Cochran-Mantel-Haenszel method. For all stratified analyses, stratification was based on response to first-line therapy (primary refractory, vs relapse within 6 months of first-line therapy vs relapse within > 6 but ≤ 12 months) and second-line age-adjusted International Prognostic Index.
e. Two recipients of non-conformal product are included in the efficacy analysis.

Figure 1. Kaplan-Meier Curve of Event-Free Survival in ZUMA-7



The expected level of high-grade toxic events did occur in the ZUMA-7 trial. Adverse events of grade 3 or higher occurred in 91% of the patients who received Yescarta and in 83% of patients who received standards of care. Grade 3 or higher cytokine release syndrome occurred in 6% of patients receiving Yescarta, and grade 3 or higher neurological events occurred in 21% of Yescarta patients. The most common (>5%) serious adverse reactions included cytokine release syndrome (CRS), fever, encephalopathy, hypotension, infection with unspecified pathogen, and pneumonia. The most common (≥ 10%) Grade 3 or higher non-laboratory adverse reactions included febrile neutropenia, encephalopathy, and hypotension.

Current formulary status: Medical benefit requiring prior authorization

Recommendation: There are no changes recommended to the formulary placement or authorization duration of Yescarta. It is recommended that the following prior authorization criteria be changed to the Medical Benefit Policy 162.0 to incorporate the new indication:

Large B-Cell Lymphoma (second-line)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or older **AND**
- Medical record documentation of large B-cell lymphoma that is refractory to first-line chemoimmunotherapy **OR** that relapses within 12 months of first-line chemoimmunotherapy **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

Large B-Cell Lymphoma (third-line or beyond)

- Prescription written by a hematologist/oncologist **AND**
- Medical record documentation that patient is 18 years of age or older **AND**
- Medical record documentation of one of the following diagnoses:
    - Relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified **OR**
    - Relapsed or refractory primary mediastinal large B-cell lymphoma **OR**
    - Relapsed or refractory high-grade B-cell lymphoma **OR**

    - Relapsed or refractory diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma

AND

- Medical record documentation of a therapeutic failure on two or more previous lines of therapy **AND**
- Medical record documentation that the member has not received prior treatment with CAR-T cell therapy or other genetically modified T cell therapy

Note: Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

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

INTRAVITREAL VEGF INHIBITOR QUANTITY LIMIT UPDATE

Background: Currently, we do not have any quantity limits on the intravitreal VEGF inhibitors. CVS Specialty billed 3 claims for Eylea as 50 mL when it should have been billed as 0.05 mL. We worked with CVS to have the claims adjusted, however we would like to put quantity limits in place to prevent inappropriate billing.

Recommendation: It is recommended to add the following quantity limits.

Beovu: (no quantity limits need to be entered within the authorization)
- For Darwin: 0.1mL per 30 days
- For Facets: J0179 (1 mg): 12 per 30 days

Eylea: (no quantity limits need to be entered within the authorization)
- Far Darwin: 0.1 mL per 30 days
- For Facets: J0178 (1 mg): 4 per 30 days

Lucentis: (no quantity limits need to be entered within the authorization)
- For Darwin: 0.1 mL per 30 days
- For Facets: J2278 (0.1 mg): 10 per 30 days

Vabysmo: (no quantity limits need to be entered within the authorization)
- For Darwin: 0.1 mL per 30 days
- For Facets: 12 mg every 30 days

Susvimo: (no quantity limits need to be entered within the authorization)
- For Darwin:
    - GPI-14 86655060002040: 0.2 mL (2 vials) per 24 weeks
    - GPI-14 86655060002042: 0.2 mL (2 vials) per 24 weeks
    - GPI-14 97604040002340: 2 implants (1 implant per eye) per lifetime
- For Facets:
    - GPI-14 86655060002040: 20 mg (2 vials) per 24 weeks
    - GPI-14 86655060002042: 20 mg (2 vials) per 24 weeks
    - GPI-14 97604040002340: 2 implants (1 implant per eye) per lifetime

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.

DOPTELET (avatrombopag) & TAVALISSE (fostamatinib)

Discussion: It is recommended to update the prior authorization criteria for Doptelet (Commercial Policy 536.0) and Tavalisse (Commercial Policy 524.0) to align policies for the indication of Chronic ITP across all applicable products. It is also recommended to update the list of alternative agents for Tavalisse (Commercial Policy 524.0) to include all available thrombopoietin receptor agonists.

Recommendation:

Commercial Policy 536.0 Doptelet

Chronic Immune Thrombocytopenia

- Medical record documentation that Doptelet is prescribed by or in consultation with a hematologist AND
- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation of a diagnosis of chronic immune thrombocytopenia (cITP) AND
- Medical record documentation of symptomatic ITP with bleeding symptoms and platelet count of less than 30 x 10^9/L OR a documented history of significant bleeding and platelet count less than 30 x 10^9/L OR a platelet count of less than 20 x 10^9/L ~~and an increased risk of bleeding~~ AND
- Medical record documentation that the member is not receiving other thrombopoietin receptor agonists (TPO-Ras) (Nplate/romiplostim, Promacta/eltrombopag) AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) previous treatments, including, but not limited to:
    - Corticosteroids
    - IVIG*
    - Rhogam (if RhD-positive and spleen intact)
    - Rituximab*
    - Splenectomy
    - Promacta*/Nplate*

*prior authorization required

Commercial Policy 524.0 Tavalisse

- Medical record documentation that Tavalisse is prescribed by or in consultation with a hematologist AND
- Medical record documentation of age greater than or equal to 18 years AND
- Medical record documentation of a diagnosis of chronic immune thrombocytopenia (cITP) AND
- Medical record documentation of symptomatic immune thrombocytopenia (ITP) with bleeding symptoms and platelet count less than 30,000/microL OR a documented history of significant bleeding and platelet count less than 30,000/microL OR a platelet count of less than 20,000/microL ~~and an increased risk of bleeding~~ AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) of the following:
    - Corticosteroids
    - Intravenous Immunoglobulin (IVIG)*
    - Rhogam (if RhD-positive and spleen intact)
    - ~~Rituxan~~ Rituximab*
    - Splenectomy
    - Promacta*/Nplate*/Doptelet*

*prior authorization required

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.

INTRAVENOUS IMMUNE GLOBULIN (IVIG)

Background: It is recommended to update the prior authorization criteria for Intravenous Immune Globulin (IVIG) (Medical Benefit Policy 4.0) for the indication of Catastrophic Antiphospholipid Syndrome (CAPS) to reflect classification criteria as outlined by the Catastrophic antiphospholipid syndrome international consensus statement on classification criteria and treatment guidelines.

It is also recommended to rearrange the existing prior authorization criteria to accurately depict the clinical situations in which approval and denial would be recommended in accordance with the classification criteria for definite and probable CAPS as outlined by the Catastrophic antiphospholipid syndrome international consensus statement on classification criteria and treatment guidelines. The rearrangement of the existing prior authorization criteria is expected to result in consistency across all reviews. No clinical recommendations apply at this time.

Recommendation:

- All four criteria are met, except for only two organs, systems and/or sites of tissues involvement **OR**
- ~~All four criteria are met, except for laboratory confirmation **OR**~~
- Criteria 1, 2, and 4 are met **OR**
- Criteria 1,3, and 4 and the development of a third event in more than a week but less than a month, despite anticoagulation

- **Catastrophic Antiphospholipid Syndrome (CAPS) (III/C)**
  All of the following criteria must be met:
  1. Documentation of patient with antiphospholipid syndrome (APS) with multiorgan failure (evidence of involvement of <u>two</u> or more organs, systems, and/or tissues) **AND**
  2. Development of manifestations simultaneously or in less than one week **AND**
  3. Confirmation by histopathology of small vessel occlusion in at least one organ or tissue **AND**
  4. Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, and/or anti-beta2-glycoprotein I antibodies) **AND**
  5. Medical record documentation Intravenous Immunoglobulin (IVIG) will be used in combination with conventional therapies (eg. anticoagulation and corticosteroids).

  OR

  1. Documentation of patient with antiphospholipid syndrome (APS) with multiorgan failure (evidence of involvement of <u>three</u> or more organs, systems, and/or tissues **AND**
  2. Development of manifestations simultaneously or in less than one week **AND**

3. Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, and/or anti-beta2-glycoprotein I antibodies) **AND**
4. Medical record documentation Intravenous Immunoglobulin (IVIG) will be used in combination with conventional therapies (eg. anticoagulation and corticosteroids).

OR

1. Documentation of patient with antiphospholipid syndrome (APS) with multiorgan failure (evidence of involvement of three or more organs, systems, and/or tissues **AND**
2. Confirmation by histopathology of small vessel occlusion in at least one organ or tissue **AND**
3. Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, and/or anti-beta2-glycoprotein I antibodies) **AND**
4. Development of a third event in more than a week but less than a month, despite anticoagulation **AND**
5. Medical record documentation Intravenous Immunoglobulin (IVIG) will be used in combination with conventional therapies (eg. anticoagulation and corticosteroids).

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.

SITE OF CARE POLICY

Background: On October 1st, 2019 Geisinger Health Plan (GHP) implemented a new site of care program for infliximab products and intravenous/subcutaneous immune globulin products, which direct members to the most cost-effective, yet clinically appropriate location to receive drug infusions under the medical benefit. The site of care program is administered as part of the existing prior authorization program which requires clinical approval of the medication as well as approval at hospital based outpatient facilities via the following prior authorization criteria. Since that time, additional drugs have been added to the site of care program in phases.

On July 15, 2022 GHP will implement Phase 11 drugs (Elaprase, Elelyso, Kanuma, Mepsevii, Revcovi, Vpriv and Vimizim) to the site of care program. The current Site of Care Policy (MBP 181.0) will apply in addition to the drugs' respective existing clinical prior authorization program.

Recommendation: It is recommended that the following changes (highlighted in green) be made to MBP 181.0 so that this policy may apply to the Phase 11 drugs (Elaprase, Elelyso, Kanuma, Mepsevii, Revcovi, Vpriv and Vimizim). No changes are recommended to the criteria for self-injected drugs.

1. Abatacept (Orencia IV)
2. Agalsidase Beta (Fabrazyme)
21. Idursulfase (Elaprase)
22. Immune Globulin (IVIG)

3. Alglucosidase Alfa (Lumizyme)
4. Alpha$_1$-Proteinase Inhibitor [Human] products
5. Belimumab (Benlysta IV)
6. Benralizumab (Fasenra)
7. C1 esterase Inhibitor [Human] (Cinryze)
8. Casimersen (Amondys 45)
9. Canakinumab (Ilaris)
10. Certolizumab (Cimzia)
11. Denosumab (Prolia, Xgeva)
12. Eculizumab (Soliris)
13. Edaravone (Radicava)
14. Elapegademase-lvlr (Revcovi)
15. Elosulfase alfa (Vimizim)
16. Eptinezumab (Vyepti)
17. Eteplirsen (Exondys 51)
18. Galsulfase (Naglazyme)
19. Golodirsen (Vyondys 53)
20. Golimumab (Simponi Aria)
23. Imiglucerase (Cerezyme)
24. Inebilizumab (Uplizna)
25. Infliximab & infliximab biosimilar products
26. Laronidase (Aldurazyme)
27. Mepolizumab (Nucala)
28. Omalizumab (Xolair)
29. Patisiran (Onpattro)
30. Ravulizumab (Ultomiris)
31. Sebelipase alfa (Kanuma)
32. Taliglucerase alfa (Elelyso)
33. Tildrakizumab (Ilumya)
34. Tocilizumab (Actemra IV)
35. Ustekinumab (Stelara)
36. Vedolizumab (Entyvio)
37. Velaglucerase alfa (Vpriv)
38. Vestronidase alfa-vjbk (Mepsevii)
39. Viltolarsen (Viltepso)

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.

DULOXETINE 40 MG CAPSULES

Background: Following discussion at the Quarterly Case Audit for 4th Quarter 2021, it has been decided to create a policy for duloxetine 40mg to aid in reviewing prior authorization cases more efficiently and consistently.

MAC prices per the 805 Commercial List February 2022 are listed in the table below.

Drug	MAC Pricing
Duloxetine 20mg (generic Cymbalta)	$0.42
Duloxetine 30mg (generic Cymbalta)	$0.41
Duloxetine 60mg (generic Cymbalta)	$0.40
Duloxetine 40mg (generic Irenka)	$2.50

Recommendation:

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to duloxetine (generic Cymbalta) at the same dose as requested

Discussion: Keith questioned the need for including a pulmonologist in the criteria. No additional 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.

MAY 2022 DUR UPDATE

Drug Use Evaluations (DUEs)

- Asthma Medication Ratio
    - This is our 2022 1st quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, CHIP
    - From this report, we used proactive HEDIS data and identified members aged 5-64 with an AMR<0.5. Pharmacy claims from the prior 6 months (9/2021-3/2022) were pulled into the report.
        - See below for the number of members that were identified with an AMR<0.5
            - For **COMM:** 26
            - For **D6: 49**
        - Letters were sent to the MI attributed PCP of each member with the respective medication fill history to encourage conversation around the importance of controller medications.
    - Letters were mailed out on 4/20/2022
    - We will re-run this data round 7/31/2022 to analyze the impact of the letter
- Use of Opioids from Multiple Providers (UOP) DUE
    - This is our 2021 3rd quarter Geisinger Health Plan DUE for Medicare, Medicaid, Commercial
    - From this report, we identified members 18 years of age and older with a total day supply of all opioid claims to be 15 day or greater based on claims from 1/1/2021 through 9/27/2021:
        - See below for the number of **members** who were identified who were seeing 4 or more providers from different offices for their opioid prescriptions
            - For COMM: **15**
            - For D6: 5
        - See below for the number of **members** who were identified who were seeing 4 or more providers within the same office for their opioid prescriptions
            - For COMM: **0**
            - For D6: **0**
        - We sent letters to the member's MI attributed PCP with the respective medication fill history to encourage medication evaluation of the opioid medications
    - Mitch Kocen completed the mail merge via Quadient on 10/14/2021 and the print shop sent out the letters on 10/18/2021

    - Adam K. re-ran this data on 3/10/2022 to analyze the effectiveness of the letter. Of the 20 members initially addressed, 13 members were still active. Of those members, **all 13 members** showed a decrease in the number of prescribers they were seeing compared to 10/2021
- Statin Use in Persons with Diabetes DUE
    - This is our 2021 2nd quarter Geisinger Health Plan DUE for all LOBs
    - From this report, we identified **1,564 members** age 40 to 75 with at least 2 distinct fills of any diabetic medication(s) without a statin claim. We sent an educational letter to providers to encourage prescribing of a statin to members, if medically appropriate.
    - The Print Shop completed the mail merge and sent out letters to the member's providers on 8/2/2021.
    - Adam K. re-ran this data on 11/19/2021 to analyze the effectiveness of the letter. Of the **1564 members** initially addressed, **1430** are still active. Of those members, **128** now have a claim for a statin medication. This equates to about **9%** of the targeted members.
    - See below for the number of letters sent:
        - For COMM: **613**
        - For D6: **372**
        - For TP23: **4**
        - For TP33: **2**
        - For TP41: **2**
        - For TP45: **34**
        - For TP46: **11**
        - For TP49: **2**
        - For TP50: **11**
        - For TP56: **2**
        - For TP64: **3**
        - For TPA6: **2**
        - For TPA7: **3**
        - For TPB3: **1**
        - For TPD2: **1**
        - For TPE0: **4**
        - For TPF0: **1**
        - For TPF2: **2**
        - For TPH2: **0**
        - For TPI0: **4**
        - For TPI2: **4**
        - For TPL0: **0**
        - For TPM2: **2**
        - For TPN1: **1**
        - For TPU1: **2**
        - For TPW1: **2**
        - For WF89: **11**
        - For EMYD: **0**
        - For SASE: **6**
        - For SAI1: **1**
        - For SASF: **1**
        - For SASN: **55**
        - For SASX: **5**
        - For PM70: **2**
        - For PM71: **1**
        - For TG48/TG51: **397**

In Progress

- We are working on building a report to monitor members on an Immunomodulator or Oral Oncology medications as we have taken off the renewal prior authorization requirement for select medications in these classes.
    - We hope to identify members who have not been seen in the last 15 months by the specialist prescribing one of these medications and outreach to the provider to notify them to set up an appointment with the member.

Ongoing

- Cystic Fibrosis Adherence Report
    - We get this report monthly for all LOBs from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.

        - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence
        - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
        - And for all members we send a letter discussing the importance of medication adherence
        - In 2022, please see below for the number of **members** an adherence letter was sent to:
            - Letters are only sent to members every 6 months
                - For COMM: **2**
                - For D6: **0**
                - For TP48: **1**
                - For WF89: **1**
        - There were no letters sent to Non-GHS pulmonologists
        - Please see below for the number of members referred to the CF coordinators:
                - For COMM: **8**
                - For D6: **9**
                - For TP48: **16**
                - For WF89: **4**
- Duplicate Anticoagulant Report
    - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
    - For 2022:
        - For COMM (Commercial): **3 members** reviewed and **1 intervention** made
        - For D6 (Exchange): **2 members** reviewed and **0 interventions** made
        - For TG48/GH51: **4 members** reviewed and **0 interventions** made
        - For TP45: **0 members** reviewed and **0 interventions** made
        - For TP56: **0 members** reviewed and **0 interventions** made
        - For EMYD: **0 members** reviewed and **0 interventions** made
        - For MT38: **0 members** reviewed and **0 interventions** made
        - For TP74: **0 members** reviewed and **0 interventions** made
        - For SASN: 0 **member** reviewed and **0 interventions** made
        - For SASF: 0 **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 Smith. These members are identified and written up and sent to a medical director if follow up is needed.
        - For Commercial/Exchange/TPA in 2022, we reviewed all 2022 data and **0 members** were referred to Dr. Yarczower for additional follow-up.
- Suboxone with an Opioid Report
    - We get this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each new member that flags on the report. These members are being discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both medical directors look into whether it is appropriate to end the opioid authorizations still in place or if further intervention is required.
    - For Commercial/Exchange/TPA in 2022, see below for the new members reviewed and those referred to the MDs:

        - For COMM: we have reviewed **0 new members** and **0 members** were referred to MDs
        - For D6: we have reviewed **0 new members** and **0 members** were referred to MDs
        - For EMYD: we have reviewed **0 new members** and **0 members** were referred to MDs
        - For TG48: we have reviewed **0 new members** and **0 members** was referred to MDs
        - For SASE: we have reviewed **0 new members** and **0 members** was referred to MDs
        - For TPI2: we have reviewed **1 new member** and **1 member** was referred to MDs
- 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/TPA in 2022, see below for the number of letters we sent to members notifying them that we are ending their opioid authorization(s):
        - For D6: **0**
        - For COMM: **0**
        - For TG48/TG51: **1**
- Opioid Overutilization Report
    - We get this report **monthly** from PerformRx and we write 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/TPA in 2022, see below for the number of reviewed cases.
        - For COMM: we have reviewed **0 patients** and sent **0 cases** to MDs for review
        - For EMYD: we have reviewed **0 patients** and sent **0 cases** to MDs for review
        - For TG48: we have reviewed **0 patients** and sent **0 cases** to MDs for review
- FWA Reports
    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For COMM in 2022, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $387.03**
        - For D6 in 2022, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $659.81**
        - For TPJ0 in 2022, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $29.99**
        - For TPE0 in 2022, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $17.19**
        - For TPN2 in 2022, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $156.32**

        - For EMYD in 2022, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $608.78**
        - For TG48, TG51 in 2022, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $2,293**
        - For SASN in 2022, we reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $800.91**
- Duplicate Antipsychotics
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - We have not sent any provider letters in 2022
- Severity Report
    - We get this report **monthly** 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/TPA in 2022 see below for the number of members identified and had sent letters to their MI attributed PCP:
            - For COMM: **45**
            - For D6: **47**
            - For EMYD: **0**
            - For SASF: **1**
            - For SASN: **4**
            - For SASE: **0**
            - For TG48, TG51: **42**
            - For TPB3: **0**
            - For TPE0: **1**
            - For TPH2: **1**
            - For TPM2: **1**
            - For TP23: **0**
            - For TP45: **2**
            - For TP46: **1**
            - For TP50: **1**
            - For TP56: **0**
            - For TP88: **0**
            - For TPA6: **0**
            - For WF89: **2**
- Tobacco Cessation Program
    - We get 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/TPA in 2022, we sent letters to the below number of members:
        - For COMM: **1**
        - For D6: **1**
        - For EMYD: **3**
        - For SASN: **0**
        - For SASE: **0**
        - For TG48, TG51: **4**
        - For TPB3: **0**
        - For TP23: **0**
        - For TP33: **1**
        - For TP45: **0**

        - For TP46: **0**
        - For TP50: **1**
        - For TP56: **0**
        - For TP88: **0**
        - For TPA6: **0**
        - For WF89: **0**
- STENT Adherence Report
    - We get this report **monthly** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
    - In 2022, we have sent letters encouraging adherence to the below number of members:
        - **Members for Antiplatelet:**
            - COMM: **35**
            - D6: **30**
            - EMYD: **4**
            - SASN: **3**
            - TG48, TG51: **4**
            - TP41: **0**
            - TP23: **0**
            - TP45: **1**
            - TP46: **0**
            - TP50: **2**
            - TP56: **0**
            - TP74: **0**
            - PM71: **1**
            - TP88: **0**
            - TPA6: **0**
            - WF89: **2**
            - TPD2: **0**
            - SASE: **2**
            - SASF: 0
            - TPB3: **0**
            - TPF2: **0**
            - TPI0: **0**
            - TPL0: **0**
            - TPM2: **1**
            - **P**M70: **1**
        - **Members for Beta-Blocker:**
            - COMM: **47**
            - D6: **39**
            - EMYD: **10**
            - SASN: **7**
            - TG48, TG51: **23**
            - TP23: **2**
            - TP45: **1**
            - TP46: **1**
            - TP50: **0**
            - TP56: **0**
            - TP88: **0**
            - TPA6: **0**
            - WF89: **0**
            - TPI0: **1**
            - SASK: **0**
            - TPR1: **1**
            - SASE: **2**
        - **Members for Statin:**
            - COMM: **50**
            - D6: **33**
            - EMYD: **12**
            - SASN: **5**
            - TG48, TG51: **20**
            - TP23: **1**
            - TP45: **2**
            - TP46: **1**
            - TP56: **0**
            - PM71: **0**
            - SASK: **0**
            - SAQ2: **1**
            - TPI0: **0**
            - TPM2: **1**
            - TPR1: **0**
            - TP88: **0**
            - TPA6: **0**
            - WF89: **0**
            - TP50: **1**
            - PM70: **0**
            - TP74: **2**
            - SASE: **1**
            - TPB3: **2**
            - TP41: **1**
        - *member may flag for more than one measure and are included in the count for each measure

- In 2022, we have attempted telephonic outreach to the below number of members non-adherent in all 3 measures and reached the below members to encourage adherence.
  - COMM:
    - Attempted: **1**
    - Reached: **1**
  - D6:
    - Attempted: **1**
    - Reached: **0**

- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR)
  - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
    - For Commercial/Exchange in 2022, see below for the number of letters sent to members:
      - COMM: **0**
      - D6: **0**
- Asthma Medication Ratio (AMR) Member Calls
  - Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. The RPHs call Commercial/Exchange members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication.
  - For Commercial/Exchange in 2022, see below for the number of members we have outreached to and the number of members that have been reached:
    - COMM:
      - Outreached to: **9**
      - Reached: **6**
    - D6:
      - Outreached to: **6**
      - Reached: **3**
- Antidepressant Medication Management (AMM)
  - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
    - For Commercial/Exchange in 2022, see below for the number of letters sent to members:
      - Effective Acute Phase:
        - COMM: **0**
        - D6: **0**
      - Effective Continuation Phase:
        - COMM: **20**
        - D6: **11**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
  - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
    - For Commercial/Exchange in 2022, see below for the number of letters sent to members:
      - COMM: **0**
      - D6: **0**

- Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange in 2022, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **5**
            - D6: **5**
        - For Commercial/Exchange in 2022, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **0**
            - D6: **0**
- Statin Therapy for Patients with Diabetes (SPD)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange in 2022, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **53**
            - D6: **25**
        - For Commercial/Exchange in 2022, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **4**
            - D6: **2**
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)
    - We get this report **monthly** to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For Commercial/Exchange in 2022, see below for the number of letters sent to **members:**
            - COMM: **0**
            - D6: **0**
- Use of Opioids from Multiple Providers (UOP)
    - We get this report quarterly to identify members 18 years of age and older with a total day supply of all opioid claims to be 15 days or greater
        - See below for the number of members that were identified who were seeing 4 or more providers from different offices for their opioid prescriptions
            - **COMM: 8**
            - **D6: 1**
        - See below for the number of members that were identified who were seeing 4 or more providers within the same office for their opioid prescriptions
            - **COMM: 1**
            - **D6: 1**
        - We sent letters to the MI attributed PCP of each member with the respective medication fill history to encourage medication evaluation of the opioid medications

Fliers/Letters

- Commercial/Exchange DUR/FWA Program internal Fliers
  - Last updated 02/2022 next update 08/2022
- Current Provider Letters
  - Cystic Fibrosis Adherence Letter
  - Congestive Heart Failure DUE
  - Coronary Artery Disease DUE
  - Statin Use in Persons with Diabetes DUE
  - Opioid Overutilization
  - Duplicate Antipsychotic medication
  - Severity Report
  - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
  - HEDIS: Statin Therapy for Patients with Diabetes (SPD)
  - HEDIS: Asthma Medication Ratio (AMR)
  - HEDIS: Use of Opioids from multiple providers (UOP)
- Current Member Letters
  - Cystic Fibrosis Adherence Letter
  - Ending Opioid Authorizations
  - Tobacco Cessation Letter
  - STENT Adherence Report
  - HEDIS: Asthma Medication Ratio (AMR)
  - HEDIS: Antidepressant Medication Management (AMM)
  - HEDIS: Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
  - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
  - HEDIS: Statin Therapy for Patients with Diabetes (SPD)
  - HEDIS: Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)

CHIP (CHBQ)

- All of our Medicaid adherence/DUR reports include logic to identify the CHIP population

Drug Use Evaluations (DUEs)

- Asthma Medication Ratio
  - This is our 2022 1st quarter Geisinger Health Plan DUE for Commercial, Exchange, Medicaid, CHIP
  - From this report, we used proactive HEDIS data and identified members aged 5-64 with an AMR<0.5. Pharmacy claims from the prior 6 months (9/2021-3/2022) were pulled into the report.
    - **0 members** were identified with an AMR<0.5
    - Letters were sent to the MI attributed PCP of each member with the respective medication fill history to encourage conversation around the importance of controller medications.
- Statin Use in Persons with Diabetes DUE
  - This is our 2021 2nd quarter Geisinger Health Plan DUE for all LOBs
  - From this report, we identified **0 members** age 40 to 75 with at least 2 distinct fills of any diabetic medication(s) without a statin claim. We sent an educational letter to providers to encourage prescribing of a statin to members, if medically appropriate.

Ongoing

- Cystic Fibrosis Adherence Report
  - We get this report **monthly** for **all LOBs** from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.
    - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence with the member
    - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
    - And for all members we send a letter discussing the importance of medication adherence
    - For CHBQ in 2022, we sent **0 members** an adherence letter
      - Letters are only sent to members every 6 months
      - There were **0 members** who saw a non-GHS pulmonologist and a letter was sent to that pulmonologist
      - There were **0 members** who saw GHS pulmonologists and were sent to the CF coordinators for follow up
- Duplicate Anticoagulant Report
  - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
    - For CHBQ in 2022, we have reviewed **0 members** and have made interventions for **0 members**
- Duplicate Specialty Therapy
  - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Smith. These members are identified and written up and sent to a medical director if follow up is needed.
    - For CHBQ in 2022, we reviewed all 2022 data and **0 members** were referred to Dr. Yarczower for additional follow-up.
- Duplicate Buprenorphine Therapy
  - We get this report **quarterly** with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and

generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows and Dr. Hossler for further outreach.
    - For CHBQ in 2022, we have reviewed **0 members** and **0 members** were referred to MDs
- Suboxone with an Opioid Report
    - We get this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each member that flags on the report. These members are being discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both MDs look into whether it is appropriate to end the opioid authorizations still in place or if further intervention is required.
        - For CHBQ in 2022, we have reviewed **0 new members**, and **0 members** were referred to MDs
- 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 CHBQ in 2022, we sent **0 members** a letter notifying them of the end of their opioid authorization(s).
- 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 CHBQ in 2022, letters have been sent to MI attributed providers of **1 CHIP member**
- FWA Reports
    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For CHBQ in 2022, we have reviewed cases and corrected claims, resulting in a potential **cost savings/avoidance of $1,057.61**
- Tobacco Cessation Program
    - We get 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 CHBQ in 2022, we have not sent any letters
- STENT Adherence Report
    - We get this report **monthly** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
    - For CHBQ in 2022, we have sent letters encouraging adherence to:
        - Members for Antiplatelet:
            - CHBQ: **0**
        - Members for Beta-blocker:
            - CHBQ: **0**
        - Members for Statin:
            - CHBQ: **0**
        - *member may flag for more than one measure and are included in the count for each measure
- Antipsychotic with Opioid Report
    - We get this report **quarterly** to identify **CHIP** members with an overlap of 8 or more days between an opioid and antipsychotic medication.
    - We send a letter with claims data to both the opioid prescriber and the antipsychotic prescriber to encourage collaboration in medication management.

        - For CHBQ in 2022, we sent **0 letters** to **opioid prescribers** and **0 letters** to **antipsychotic prescribers**
- Duplicate Antipsychotics
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - For CHBQ in 2022, we have sent letters to **0 providers**

- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR)
    - Jesse Barsh 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.
        - For CHBQ in 2022, we sent **1 letter** to members
- Asthma Medication Ratio (AMR) Member Calls
    - Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. we send CHIP members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication to the Respiratory Therapists for direct telephonic outreach.
        - For CHBQ in 2022, we have referred **1 member** to the Respiratory Therapists for outreach.
- Antidepressant Medication Management (AMM)
    - Jesse Barsh runs this proactive HEDIS report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
        - For CHBQ in 2022, we sent **0 letters** to members in the **Effective Acute Phase**, and **0 letters** to members in the **Effective Continuation Phase**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
        - For CHBQ in 2022, we have sent **0 letters** to members
- Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ in 2022, we have sent **0 letters** to providers
        - For CHBQ in 2022, we have sent **0 letters** to members
- Statin Therapy for Patients with Diabetes (SPD)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ in 2022, we have sent **0 letters** to providers
        - For CHBQ in 2022, we have sent **0 letters** to members
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH)
    - This is a **monthly** report to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For CHBQ in 2022, we have sent **0 letters** to members

Fliers/Letters

- Current Provider Letters
        - Cystic Fibrosis Adherence Letter
        - Duplicate Antipsychotic medication
        - Severity Report
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - HEDIS: Statin Therapy for Patients with Diabetes (SPD)
        - HEDIS: Asthma Medication Ratio (AMR)
- Current Member Letters
        - Cystic Fibrosis Adherence Letter

- Ending Opioid Authorizations
- Tobacco Cessation Letter
- STENT Adherence Report
- HEDIS: Asthma Medication Ratio (AMR)
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- HEDIS: Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
- HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
- HEDIS: Statin Therapy for Patients with Diabetes (SPD)

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

Meeting adjourned at 5:15 pm

Future Scheduled Meetings

The next bi-monthly scheduled meeting will be held on July 19th, 2022 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.