Geisinger

POLICIES AND PROCEDURE MANUAL

P&T Committee Meeting Minutes
Commercial, Exchange, CHIP
September 17th, 2024

Present (via Teams):	Absent:
Bret Yarczower, MD, MBA – Chair	Alyssa Cilia, RPh
Amir Antonious, Pharm.D.	Keri Donaldson, MD, MSCE
Emily Bednarz, Pharm.D.	Michael Evans, RPh
Kristen Bender, Pharm.D.	Nichole Hossler, MD
Jeremy Bennett, MD	Jonas Pearson, RPh
Kim Castelnovo, RPh	Angela Scarantino
Kimberly Clark, Pharm.D.	William Seavey, Pharm.D.
Bhargavi Degapudi, MD	Michael Shepherd, MD
Michael Dubartell, MD	
Kelly Faust, Pharm.D.	
Tricia Heitzman, Pharm.D.	
Jason Howay, Pharm.D.	
Keith Hunsicker, Pharm.D.	
Kelli Hunsicker, Pharm.D.	
Derek Hunt, Pharm.D.	
Emily Jacobson, Pharm.D.	
Dennis Janozczyk, Pharm.D.	
Alexandra Kempf-Malys, MSW, BSc	
Kerry Ann Kilkenny, MD	
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.	
Andrei Nemoianu, MD	
Austin Paisley, Pharm.D.	
Lauren Pheasant, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Sartori, Pharm.D.	
Kristen Scheib, Pharm.D.	
Leslie Shumlas, Pharm.D.	
Kirsten Smith, Pharm.D.	
Aubrielle Smith-Masri, Pharm.D.	
Michael Spishock, RPh	
Todd Sponenberg, Pharm.D.	
Jill Stone, Pharm.D.	
Luke Sullivan, DO	
Kevin Szczecina, RPh	
Amanda Taylor, MD	
Ariana Wendoloski, Pharm.D.	
Brandon Whiteash, Pharm.D.	
Margaret Whiteash, Pharm.D.	
Benjamin Andrick, Pharm.D. (non-voting participant)	
Birju Bhatt, MD (non-voting participant)	
Shelby Chan (pharmacy student)	
Alfred Denio, MD (non-voting participant)	
Jeremy Garris, Pharm.D. (non-voting participant)	
Macy Meng (pharmacy student)	

Call to Order:

Dr. Bret Yarczower called the meeting to order at 1:02 p.m., Tuesday, September 17, 2024.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the June e-vote and July 16, 2024 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

TECELRA (afamitresgene autoleucel)

Review: Tecelra is a melanoma-associated antigen A4 (MAGE-A4)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are HLA-A*02:01P, -A*02:02P, -A02:03P, or -A02:06P positive and whose tumor expresses the MAGE-A4 antigen as determined by FDA-approved or cleared companion diagnostic devices. This indication is approved under accelerated approval based on overall response rate and duration of response. Tecelra is the first FDA-approved T-cell receptor (TCR) gene therapy. It consists of CD4 and CD8 positive T cells transduced with a self-inactivating lentiviral vector (LV) expressing an affinity-enhanced T-cell receptor (TCR) specific for the human melanoma-associated antigen A4 (MAGE-A4), which is highly expressed in human leukocyte antigen (HLA)-A*02–positive synovial sarcoma and has restricted expression in normal tissues. Antigen-specific activation of Tecelra via TCR-peptide-HLA-A*02 complex results in T-cell proliferation, cytokine secretion, and killing of MAGE-A4/HLA-A*-2 expressing synovial sarcoma cells.

Tecelra is prepared from the patient's peripheral blood mononuclear cells (PBMCs) which are obtained via a standard leukapheresis procedure. The PBMCs are enriched for T cells and are then transduced with replication-incompetent LV contain the MAGE-A4 TCR transgene. The transduced T cells are expanded, washed, formulated into a suspension and cryopreserved. The drug product formulation contains 5% dimethyl sulfoxide (DMSO).

The recommended dose of Tecelra is 2.68 x 109 to 10 x 109 MAGE-A4 T cell receptor (TCR) positive T cells administered as a single intravenous infusion. Tecelra is provided as a single dose for infusion in one or more infusion bag(s).

Prior to the administration of Tecelra, the patient will receive a lymphodepleting chemotherapy regimen of fludarabine 30 mg/m2/day intravenously for 4 days starting on the 7th day before Tecelra infusion (Day 7 to Day 4) and cyclophosphamide 600 mg/m2/day intravenously for 3 days starting the seventh day before Tecelra infusion (Day 7 to Day 5). Patients should be premedicated with an H1-antihistamine and acetaminophen approximately 30 to 60 minutes prior to Tecelra infusion. Prophylactic systemic corticosteroids should be avoided as they may interfere with the activity of Tecelra.

The efficacy of Tecelra was evaluated in a mutli-cohort, single-arm, open-label clinical trial (SPEARHEAD-1, Cohort 1) in HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P, and 383 HLA-A*02:06P allele positive patients with inoperable or metastatic synovial sarcoma who had received prior systemic therapy with either doxorubicin and/or ifosfamide and whose tumor expressed he MAGE-A4 tumor antigen. The study included patients with measurable disease according to RECIST v1.1, ECOG status scores of 0 or 1, and glomerular filtration rate (GFR) ≥ 60 mL/min. The study excluded patients with HLA-A*02:05P in either allele, patients on systemic corticosteroids for at least 14 days prior to leukapheresis and lymphodepletion, and recipients of allogeneic hematopoietic stem cell transplants.

Patients had tumor samples tested for MAGE-A4 expression by immunohistochemistry (IHC) clinical trial assay at a centralized testing site. Patients underwent leukapheresis for collection of autologous cells for processing and manufacture into Tecelra. Risk of manufacturing or delivery failure was 8% (4/52) patients in the clinical trial. Patients underwent lymphodepleting chemotherapy with fludarabine and cyclophosphamide as recommended then received Tecelra administration as a single IV infusion on Day 1. Fifty-two patients were enrolled and underwent leukapheresis, eight of whom did not receive Tecelra due to the following: death (n=3), loss of eligibility prior to lymphodepleting chemotherapy (n=3), withdrawal by the patient (n=1), and investigator decision (n=1). Forty-five patients with synovial sarcoma received lymphodepletion and one patient withdrew consent before receiving Tecelra (n=44).

The median number of prior lines of systemic therapies was three (range: 1 to 12 lines). Prior therapies included ifosfamide (100%), doxorubicin (95%), pazopanib (48%), trabectedin (25%), dacarbazine (11%), and gemcitabine (11%). Between leukapheresis and initiation of lymphodepletion, 16 (36%) of the 44 patients received bridging therapy. The most commonly used bridging therapy was pazopanib (69%). The median dose of Tecelra was 8x10 416 9 MAGE-A4 TCR positive T cells (range: 2.68 x 109 to 9.99 x109 417).

The major efficacy outcome measure was overall response rate (ORR) according to RECIST v1.1 evaluated by independent review committee (IRC). Duration or response was also evaluated.

The median time to response from Tecelra treatment was 4.9 weeks (95% CI: 4.4 weeks, 8 weeks) by Kaplan Meier estimation.

Tecelra is contraindicated in adults who are heterozygous or homozygous for HLA-A*02:05P. There is a black box warning for cytokine release syndrome, including potentially life threatening reactions which have been observed following administration of Tecelra. CRS occurred in 75% of patients, 2% of whom had Grade 3 or greater CRS. The most common symptoms were fever, tachycardia, hypotension, nausea/vomiting, and headache. Thirteen patients were treated with one dose of tocilizumab and five patients received more than one dose. Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS) has also been observed following administration of Tecelra. One patient (2%) had Grade 1 ICANs. Symptoms included mild mental status changes. Other symptoms can include disorientation to time and place, mild drowsiness, mild inattention. Severe symptoms 6 169 may include altered level of consciousness, seizures, cerebral edema, impairment of cognitive skills, progressive aphasia, motor weakness.

Other warnings include prolonged severe cytopenia, including neutropenia and thrombocytopenia, risk of infection/viral reactivation, secondary malignancies, hypersensitivity reactions, and the potential for HIV nucleic acid test false-positive results.

In clinical trials, serious adverse reactions occurred in 52% of patients with synovial sarcoma treated with Tecelra. The most common serious adverse reaction include CRS and pleural effusion. The most common adverse reactions were CRS, nausea, vomiting, fatigue, infections, pyrexia, constipation, dyspnea, abdominal pain, non-cardiac chest pain, decreased appetite, tachycardia, back pain, hypotension, diarrhea, and edema. The most common grade 3 or 4 laboratory abnormalities were decreased lymphocyte count, decreased neutrophil count, decreased white blood cell count, decreased red blood cell count, and decreased platelets.

The safety and efficacy of Tecelra has not been established in pediatric patients. Of the 44 patients with synovial sarcoma in the SPEARHEAD-1 study, 6.8% were 65 years of age and older. Clinical studies did not include sufficient numbers of patients aged 65 years and older to determine if they respond differently from younger patients. A Clinical Review including Clinical Information, Efficacy Evidence, Safety Evidence, Other Considerations and a Financial Review Based on Cost Analysis were presented.

Clinical Discussion: Dr. Bret Yarczower stated that this medication may only be available at Penn in Pennsylvania. Kim Reichard, PharmD, stated that this medication is limited distribution. Ben Andrick, PharmD, confirmed that it is limited distribution and the clinical enterprise are holding off on initial adoption of this therapy until more data becomes available. Dr. Yarczower asked if the health plan is able hold off until we get more data or if we are required to cover since it is now FDA approved and available. Kim Reichard, PharmD, stated that the preference would be to have criteria in place for medical since we may be seeing requests for the drug. Kim Clark, PharmD, stated that they got clarification from the office of CHIP that gene therapies are not eligible for coverage – if the member were to qualify for this they would be directed to Medicaid. Dr. Yarczower asked how the contracts with Penn are structured since percent of charge will lead to increased spend and if we should contact the contracting process. The committee unanimously voted to accept the recommendations as presented (36 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (37 approvals). None were opposed.

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

- Medical record documentation that Tecelra 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 unresectable or metastatic synovial sarcoma **AND**
- Medical record documentation of at least one (1) prior chemotherapy treatment AND
- Medical record documentation that member is HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P, and HLA-A*02:06P allele–positive* **AND**
- Medical record documentation that the member has not had a prior allogeneic hematopoietic stem cell transplant **AND**
- Medical record documentation of tumor expression of melanoma-associated antigen A4 (MAGE-A4)

NOTE: Tecelra is contraindicated for patients who are heterozygous or homozygous for HLA-A*02:05P based on an alloreactivity screen which indicated in vitro alloreactivity against HLA-A*02:05.

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

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

XOLREMDI (mavorixafor)

Review: Xolremdi is a selective CXC chemokine receptor 4 (CXCR4) antagonist indicated for patients 12 years of age and older with warts, hypogammaglobulinemia (deficiency in immunoglobulins), infections and myelokathexis (retention of neutrophils in the bone marrow), or WHIM syndrome, to increase the number of circulating mature neutrophils and lymphocytes. The recommended dosing of Xolremdi is 400mg once daily for patients weighing more than 50kg and 300mg once daily for patients weighing less than or equal to 50kg. Xolremdi is available as 100mg capsules and should be given on an empty stomach after an overnight fast and at least 30 minutes before food. Xolremdi should be stored in its original container and refrigerated at 36°F to 46°F until expiration date. Xolremdi capsules should be swallowed whole and should not be opened, broken or chewed. If a dose of Xolremdi is missed, the next dose should be taken as scheduled.

WHIM syndrome is an ultra-rare primary immunodeficiency predominantly caused by genetic variations to the CXCR4 receptor. This receptor regulates the mobilization of white blood cells from the bone marrow to the peripheral bloodstream. Mutations to CXCR4 causes an increased white blood cell response to CXCR4 ligand, CXCL12. The enhanced response disrupts the signaling pathway and the mobilization of white blood cells from the bone marrow to the peripheral bloodstream is decreased. This results in almost all patients having neutropenia and myelokathexis. Due to immunodeficiencies, patients have increased susceptibility to bacterial and viral infections, skin and genital warts, and an increased risk of cancer caused by human papillomavirus (HPV) infections.

The manufacturer estimates that only one in four patients have all four key features of the disease present which makes diagnosis difficult. Diagnosis for WHIM can be made based on symptoms, patient history, clinical testing, and genetic testing. Some patients with symptoms of WHIM do not have a detectable mutation in the CXCR4 gene, so the disorder may have other genetic causes and demonstration of enhanced white blood cell responsiveness to CXCL12 in patients without a confirmed CXCR4 defect may be observed. A bone marrow biopsy may also be performed, which could reveal myelokathexis, which strongly suggests WHIM syndrome. Most patients develop symptoms in early childhood with some having mild symptoms that usually respond to antibiotic therapy, while others develop potentially life-threatening complications. There are approximately 100 reported cases in medical literature, but the manufacturer estimates that there are at least 1,000 patients with WHIM syndrome in the United States. Due to this ultra-rare type of disease, patients with WHIM syndrome are likely underdiagnosed.

There are no current guidelines for WHIM syndrome and current treatment therapies are directed to target symptoms of WHIM syndrome, as there have not been any FDA-approved medication to treat the underlying cause. Colony stimulating factor injections have been used to treat neutropenia, immunoglobulin injections have been used to treat hypogammaglobulinemia, antivirals and antibiotics have been used to treat infections, and prophylactic use of antibiotics may be considered. HPV vaccines can be administered to help prevent HPV infections, but patients may have a reduced vaccine response. Plerixafor, a CXCR4 antagonist, has been studied in WHIM syndrome, but is not FDA-approved for use and there are no formal recommendations for its use. A bone marrow transplant may cure some symptoms of WHIM syndrome, but risk may outweigh the benefits. Xolremdi is the first and only FDA-approved treatment specifically indicated for the underlying cause of WHIM syndrome. Xolremdi works to block CXCL12 from binding to both wild-type and mutated CXCR4 variants to inhibit the enhanced responsiveness and retention of white blood cells in the bone marrow. This results in increased mobilization of white blood cells from the bone marrow to the peripheral bloodstream.

The efficacy of Xolremdi was evaluated in the randomized, double-blind, multicenter 4WHIM trial (NCT03995108). The 4WHIM trial compared Xolremdi to placebo with 31 participants aged 12 years and older. All patients had a genotype-confirmed variant of CXCR4 consistent with WHIM syndrome and a confirmed absolute neutrophil count (ANC) of less than or equal to 400 cells/μL. Patients diagnosed with an active infection (excluding warts), use of other CXCR4 antagonists, use of plerixafor within 6 months, use of chronic or prophylactic colony stimulating factors or systemic glucocorticoids within 2 weeks, or use of any investigational therapy within less than or equal to 5 half-lives of the drug or 2 weeks (whichever was longer) were excluded from the trial. Patients were allowed to continue, but not initiate, immunoglobulin therapy at the same dose during the trial. The study lasted 52 weeks and 14 patients received Xolremdi, while 17 patients received placebo. Xolremdi was administered orally once daily with patients receiving 400mg if weight was more than 50kg and 200mg if weight was less than or equal to 50kg.

The primary endpoint was the effect of Xolremdi on improvement of ANC. The mean time above threshold in hours for an ANC of 500 cells/μL over a 24-hour period was assessed every 3 months for a total of 4 times throughout the trial. Xolremdi-treated patients had significantly more time above the threshold, with a least squares (LS) mean time above threshold of 15 hours, versus a least squares (LS) mean time above threshold of 2.8 hours for placebo-treated patients.

The secondary endpoint was the effect of Xolremdi on improvement of absolute lymphocyte counts (ALC). The mean time above threshold in hours for an ALC of 1,000 cells/μL over a 24-hour period was assessed every 3 months for a total of 4 times throughout the trial. Xolremdi-treated patients had significantly more time above the threshold, with a least squares (LS) mean time above threshold of 15.8 hours, versus a least squares (LS) mean time above threshold of 4.6 hours for placebo-treated patients.

The efficacy of Xolremdi was further assessed in a composite endpoint consisting of total infection score and total wart change score using a win-ratio method. The win-ratio was calculated by dividing the number of pairs where the Xolremdi-treated patient had a better outcome, or "win", by the number of pairs where the placebo-treated patient had a better outcome.

For every pair of patients, the Xolremdi-treated patient was 2.76 times more likely to have a better outcome compared to placebo-treated patients. Analyses of individual components of the composite endpoint showed an approximate 40% reduction in the total infection score, weighted by infection severity, in Xolremdi-treated patients versus placebo-treated patients. The annualized infection rate was reduced by approximately 60% in Xolremdi-treated patients versus placebo-treated patients. The total wart change score did not have any significant difference between the Xolremdi-treated patients and placebo-treated patients.

The safety of Xolremdi was evaluated in the 4WHIM trial. The most common adverse reactions were thrombocytopenia, pityriasis, rash, rhinitis, epistaxis, vomiting, and dizziness, which was experienced in more than 10% of Xolremdi-treated patients versus placebo-treated patients. Safety and efficacy of Xolremdi have not been established in patients less than 12 years of age. Two patients in the 4WHIM trial were aged 65 and older, but no patients were aged 75 years and older. The trial did not include enough patients aged 65 and older to determine whether they respond differently. Xolremdi is not recommended for use in patients with severe renal impairment, end-stage renal disease, or moderate to severe hepatic impairment. No dosage adjustment is recommended for patients with mild to moderate renal impairment or mild hepatic impairment.

Xolremdi is contraindicated with concomitant use of drugs that are highly dependent on CYP2D6 for clearance. Warnings and precautions include embryo-fetal toxicity and QTc interval prolongation. There is no available data on Xolremdi use in pregnant patients, but Xolremdi is expected to cause fetal harm when administered to pregnant patients due to the mechanism of action. Pregnancy status of female patients should be verified prior to starting the medication. Breastfeeding is not recommended and an effective method of contraception should be advised to females of reproductive potential during treatment with Xolremdi and for three weeks after the final dose. Xolremdi causes concentration-dependent QTc interval prolongation and therefore can cause QT interval prolongation when taken with concomitant medications that increase Xolremdi exposure and/or drug products with known potential to prolong QT. Modifiable risk factors should be corrected, QTc should be assessed at baseline, and QTc should be monitored during treatment. The dose of Xolremdi may need to be reduced or discontinued due to drug-drug interactions. The daily dose of Xolremdi should be decreased by increments of 100mg, if necessary, but not to a dose less than 200mg when used with strong or moderate CYP3A4 inhibitors and P-gp inhibitors. Xolremdi should be avoided with strong CYP3A4 inducers.

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

Clinical Discussion: Dr. Bret Yarczower stated this is a rare disease state and asked if there was a status of these patients before they stopped their treatment and then a comparison to how patients responded to stopping this treatment. Dr. Yarczower stated that there was a high rate of infections and stated there are other treatments for the symptoms of WHIM syndrome and maybe plerixafor is a better option. Kirsten Smith, PharmD, stated that there were no efficacy studies of use of plerixafor in WHIM syndrome patients. The committee unanimously voted to accept the recommendations as presented (35 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (37 approvals). None were opposed.

Outcome: Xolremdi will be a pharmacy benefit and will be added to the Commercial, Exchange, and CHIP formularies at the Specialty tier or Brand Non-Preferred tier for members with a three-tier benefit. The following prior authorization criteria should apply:

- Medical record documentation of a diagnosis of WHIM (warts, hypogammaglobulinemia, infections, and myelokathexis) syndrome **AND**
- Medical record documentation of symptoms and complications associated with WHIM syndrome **AND**
- Medical record documentation that member is 12 years of age or greater **AND**
- Medical Record documentation that Xolremdi is being prescribed by an immunologist or hematologist **AND**
- Medical record documentation of member's weight **AND**

- Medical record documentation of baseline absolute neutrophil count (ANC) and absolute lymphocyte count (ALC)

AUTHORIZATION DURATION: Approval will be given for an initial duration of **6 months** or less if the reviewing provider feels it is medically appropriate. After the initial 6 month approval, subsequent approvals will be for a duration of **12 months** or less if the reviewing provider feels it is medically appropriate, requiring medical record documentation of:

- Medical record documentation or provider attestation of continued disease improvement (such as, but not limited to, a decrease in infections, or sustained improvement in absolute neutrophil count (ANC) and absolute lymphocyte count (ALC))

QUANTITY LIMIT: 4 capsules per day

GPI LEVEL: GPI-10

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

WINREVAIR (sotatercept)

Review: Winrevair is an activin signaling inhibitor indicated for the treatment of adults with pulmonary arterial hypertension (PAH, WHO Group 1) to increase exercise capacity, improve WHO functional class (FC) and reduce the risk of clinical worsening events. Winrevair improves the balance between pro-proliferative and anti-proliferative signaling to modulate vascular proliferation. In rat models, Winrevair reduced inflammation and inhibited proliferation of endothelial and smooth muscle cells in diseased vasculature. Winrevair offers a new mechanism of action compared to other treatment options for PAH.

Current treatment guidelines for patients with PAH recommend upfront dual therapy with an endothelin receptor antagonist (ERA) and phosphodiesterase-5 inhibitor (PDE5i) in patients with a low- or intermediate risk status and triple therapy (one drug targeting each vasodilatory pathway) for patients with high mortality risk.

Winrevair is administered once every 3 weeks by subcutaneous injection according to body weight. The recommended starting dose is 0.3 mg/kg. Patients' hemoglobin (Hgb) and platelet count prior to initiation of Winrevair and Winrevair should not be initiated in patients with platelet count is <50,000/mm^3 (<50 x 10^9/L).

The patient's Hgb and platelet count should be checked prior to each dose for the first 5 doses, or if values are unstable, and then periodically thereafter. Treatment should be delayed for at least three weeks the following circumstances:

- Hgb increases >2.0 g/dL from the previous dose and is above ULN.
- Hgb increases >4.0 g/dL from baseline.
- Hgb increases >2.0 g/dL above ULN.
- Platelet count decreases to <50,000/mm^3 (<50 x 10^9/L)

The Hgb and platelet count should be rechecked prior to reinitiating treatment. For treatment delays lasting >9 weeks, restart treatment at 0.3 mg/kg and escalate to 0.7 mg/kg after verifying acceptable Hgb and platelet count.

Winrevair should be used under the guidance of a healthcare professional but can be administered by patients and caregivers when appropriate.
Winrevair is supplied as single-dose vials (45 mg or 60 mg) packaged in kits (Table 8) that contain one or two single-dose vials, one measuring syringe, and one safety needle.

The efficacy of Winrevair was evaluated in 323 adult patients with PAH (WHO Group 1 FC II or III) in STELLAR, a double-blind, placebo-controlled, parallel group trial. Patients were randomized 1:1 to receive Winrevair (n=163) or placebo (n=160) administered subcutaneously every 3 weeks.

Most participants were receiving three (61%) or two (35%) background drugs for PAH, and 40% were receiving prostacyclin infusions. Patients included had a WHO FC II (49%) or III (51%) at baseline.

The primary efficacy endpoint was the change from baseline at Week 24 in 6-minute walk distance (6 MWD). In the Winrevair group, the placebo-adjusted median increase in 6 MWD was 41 meters (95% CI: 28, 54; p<0.001). Treatment with Winrevair led to an improvement from baseline by at least 1 WHO FC at Week 24 in 29% of patients compared to 14% of placebo treated patients (p<0.001). Treatment with Winrevair resulted in 84% reduction in the occurrence of death from any cause or PAH clinical worsening events compared to placebo.

Winrevair includes warnings for increases in hemoglobin and risk of erythrocytosis which may increase the risk of thromboembolic events or hyperviscosity syndrome. In clinical studies, moderate elevations in Hgb (> 2 g/dL above ULN) occurred in 15% of patients taking Winrevair while no elevations ≥ 4 g/dL above ULN were observed. Winrevair also includes warnings for decreased platelet count and risk of severe thrombocytopenia which may increase the risk of bleeding. In clinical studies, severe thrombocytopenia (platelet count <50,000/mm3 [<50 x 109/L]) occurred in 3% of patients taking Winrevair. Other warnings include risk of serious bleeding, embryo-fetal toxicity, and impaired fertility.

The most common adverse reactions in the STELLAR trial included headache, epistaxis, rash, telangiectasia, diarrhea, dizziness, and erythema. Increases in hemoglobin from normal to above normal limits occurred in 87 (53%) of patients and were managed by dose delays, dose reductions, or both. Decreases in platelets from normal to below normal occurred in 40 (25%) of patients and were managed by dose delays, dose reductions, or both.

The incidence of treatment discontinuation due to adverse reaction were 4% in the Winrevair group and 7% in the placebo group. No specific adverse reactions causing treatment discontinuation occurred with a frequency greater than 1% and more often in the Winrevair group.

The safety and efficacy of Winrevair has not been established in patients less than 18 years of age. A total of 81 patients ≥ 65 years of age participated in clinical studies for PAH, of which 52 were treated with Winrevair. No differences in efficacy were observed between older and younger patients. With the exception of bleeding events, there were no differences in safety between older and younger groups. Bleeding events occurred more commonly in the older Winrevair subgroup, but with no imbalance between age subgroups for any specific bleeding events. Clinical studies did not include sufficient numbers of patients aged 75 and older to determine whether they respond differently from younger patients.

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

Clinical Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (36 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (38 approvals). None were opposed.

Outcome: Winrevair is a pharmacy benefit and will not be added to the Commercial, Marketplace, and GHP Kids formularies. The following prior authorization criteria will apply:

- Medical record documentation that Winrevair is prescribed by a cardiologist or pulmonologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of World Health Organization (WHO) Group 1 pulmonary arterial hypertension b
- Medical record documentation of World Health Organization (WHO) functional class II or III symptoms **AND**
- Medical record documentation of a baseline 6-minute walking distance **AND**
- Medical record documentation of therapeutic failure, intolerance to, or contraindication to one (1) formulary endothelin receptor antagonist (ERA) in combination with one (1) formulary phosphodiesterase-5 inhibitor (PDE5i) or one (1) soluble guanylate cyclase (sGC) stimulator

AUTHORIZATION DURATION: Initial authorization will be for 6 months. Subsequent authorizations will be for 6 months and will require:

- Medical record documentation of a 6-minute walking distance improved from baseline

QUANTITY LIMIT:

- **45 mg x 1 (1 mL) Syringe Kit (NDC 0006-5090-01)** – 2 Kits (2 milliliter) per 21 days
- **60 mg x 1 (1.3 mL) Syringe Kit (NDC 0006-5091-01)** – 2 Kits (2.6 milliliter) per 21 days
- **45 mg x 2 (1 mL) Syringes Kit (NDC 0006-5087-01)** – 1 Kits (2 milliliter) per 21 days
- **60 mg x 2 (1.3 mL) Syringes Kit (NDC 0006-5088-01)** – 1 Kits (2.6 milliliter) per 21 days

GPI LEVEL: GPI-12

FORMULARY ALTERNATIVES:

endothelin receptor antagonist (ERA) : ambrisentan*, bosentan*, Opsumit*, Tracleer*
phosphodiesterase-5 inhibitor (PDE5i) :alyq*, sildenafil 20 mg tablet*, sildenafil 10 mg/mL suspension*, tadalafil (pah) 20 mg tab*
soluble guanylate cyclase (sGC) stimulator : Adempas*
Prostaglandin Vasodilators: epoprostenol*, treprostinil*, Tyvaso*, Tyvaso DPI*, Ventavis*

Prostacyclin Receptor Agonist: Uptravi*

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

OPSYNVI (macitentan-tadalafil)

Review: Opsynvi is a combination drug that contains macitentan and tadalafil. It is FDA approved for the indication of chronic treatment of adults with pulmonary arterial hypertension (PAH, WHO Group I and WHO Functional Class (FC) II-III). Individually, macitentan is approved for PAH to reduce the risk of clinical worsening events and hospitalization, and tadalafil for PAH to improve exercise ability. Macitentan is an endothelin receptor antagonist (ERA) for receptors ETa and ETb on vascular endothelium and smooth muscle. When these receptors are stimulated, vasoconstriction, fibrosis, proliferation, hypertrophy, and inflammation occur. Macitentan blocks receptor to avoid stimulation. Tadalafil is a phosphodiesterase-5 enzyme inhibitor (PDE-5 Inhibitor). PDE-5 enzyme is responsible to break down cyclic guanosine monophosphate (cGMP), which results in more vasoconstriction. When PDE-5 is inhibited, more cGMP is kept and results in greater pulmonary vasculature relaxation and vasodilation.

Opsynvi is supplied as an oblong tablet that is either pink or white, depending on strength. Two strengths exist, macitentan 10mg/tadalafil 20mg and macitentan 10mg/tadalafil 40mg. Opsynvi is dosed once daily with or without food. Tablets should be swallowed whole, and should not be cut, crushed, or chewed. If a dose is missed, take the missed tablet as soon as possible and resume next dose at regularly scheduled time. A patient should not take 2 doses at the same time. For those who are treatment naïve to any PAH specific therapy OR transitioning from ERA monotherapy, it is recommended to start dose at Opsynvi 10 mg/20mg daily for one week and titrate to 10 mg/40 mg if tolerated. For those transitioning from PDE-5 inhibitor monotherapy or PDE-5 inhibitor and ERA therapy in combination, it is recommended to start at the Opsynvi 10 mg/40mg dose daily dose.

Pulmonary arterial hypertension (PAH) treatments vary on the subset group being treated. Treated groups are either vasoreactive or nonvasoreactive. Only 10 to 20% who test will demonstrate a vasoreactive response. If the type of PAH is deemed vasoreactive and in the WHO class I to III, they will start with a trial of a calcium channel blocker (CCB) for one to three months. Only about half of the CCB-treated vasoreactive patients respond to that treatment initially, and only about 5% achieve a long-term response on CCBs alone; Long term response defined as an improvement in the WHO functional class that is sustained for at least 1 year. For vasoreactive patients who have failed CCB monotherapy or for nonvasoreactive patients, suitable agents are dictated by WHO functional classification.

WHO functional class I is a monotherapy approach based on high-risk features. Due to most patients being asymptomatic in this class, most are not identified and diagnosed. If diagnosed and deemed treatable, any PAH-indicated agent may be started on monotherapy agent; although more suggest that starting dual-therapy earlier may be better long-term results. For WHO functional class II or III and treatment naïve, dual combination therapy with an ERA and a cGMP targeted therapy like PDE-5 Inhibitor is recommended. Experts prefer ambrisentan and tadalafil combination. If there is a contraindication to either agent, another oral agent in the same class can be substituted; both agents being taken must be of separate classes. Such combinations are less proven and drug interactions can limit the outcome. The preference for the ambrisentan/tadalafil combination stems from results found from the AMBITION trial. Outcomes seen in this trial may not correlate to similar class combinations (ie. Macitentan/tadalafil, bosentan/sildenafil) due to increased metabolism and a resulting lowered plasma concentration of the PDE-5 inhibitor. Following the preferred combination agents, data with the strongest level of support are macitentan/sildenafil (SERAPHIN trial), bosentan/tadalafil (PHIRST trial), bosentan/riociguat (PATENT-1 study), and selexipag plus ERA and/or PDE5I (GRIPHON trial). The current CHEST guidelines do not address the consideration of the Opsynvi combination currently. Finally, WHO functional class IV is usually the dual-combination treatment we see in class II and III, plus a third agent, parenteral prostanoid (IV epoprostenol or SQ treprostinil).

A multi-national, multi-center, double-blind, adaptive, randomized, active-controlled, parallel-group study [“A DUE”] was conducted in 187 patients with PAH, WHO FC II-III to compare the efficacy and safety of Opsynvi to each monotherapy macitentan or tadalafil. Patient with pulmonary vascular resistance (PVR) of at least 240 dyn-s/cm5 were randomized to receive Opsynvi (n=108), 10mg macitentan monotherapy (n=35) or 40mg tadalafil monotherapy (n=44) once daily. The primary endpoint was change from baseline in PVR versus the individual component monotherapies after 16 weeks. Opsynvi demonstrated greater reduction in PVR after 16 weeks, showing statistically significant effect of 29% reduction in PVR as compared to macitentan [0.71 (95% CL 0.61, 0.82, $p < 0.0001$)] and a 28% reduction in PVR as compared to tadalafil [0.72 (95% CL 0.64, 0.80, $p < 0.0001$)].

Contraindications to Opsynvi include pregnancy (macitentan shows teratogenic effects and risk to fetus), hypersensitivity to any component of the drug, concomitant use of organic nitrates within 48 hours of each other (tadalafil potentiates

hypotensive effect of nitrates), and concomitant guanylate cyclase (GC) stimulators (tadalafil potentiates hypotensive effect of nitrates). Warnings and precautions to Opsynvi include:

- Embryo-fetal toxicity - macitentan-containing product REMS program available for females to comply with pregnancy testing and contraception requirements.
- Hepatotoxicity - ERAs cause elevated aminotransferases and liver failure; liver enzymes should be tested on initiation and during treatment. If aminotransferases elevate, if that elevation is accompanied by bilirubin increase >2x ULN, or presence of symptoms of hepatotoxicity or injury (nausea, vomiting, right upper quadrant pain, fatigue, anorexia, jaundice, dark urine, fever, or itching), Opsynvi should be discontinued. Re-initiation may be considered if hepatic enzymes normalize with no clinical hepatotoxic symptoms. Initiation should not be done with elevated aminotransferases (>3 x ULN at baseline). To note, Opsynvi is not advised for use in hepatic cirrhosis due to lack of study in patient population.
- Hypotension – Due to vasodilatory properties of Opsynvi, patients with pre-existing hypotension, autonomic dysfunction, or with left ventricular outflow obstruction may be more sensitive to hypotensive issues.
- Hemoglobin Decrease – ERAs can decrease hemoglobin concentration and hematocrit have occurred early during initiation but often stabilize thereafter. Hemoglobin should be measured on initiation and during treatment. It is not recommended to use in those with severe anemia.
- Worsening Pulmonary Veno-Occlusive Disease (PVOD) – Vasodilators can significantly worsen cardiovascular status with those with PVOD. Development of pulmonary edema while on Opsynvi could be an indication of PVOD. It is not recommended for use in those with PVOD.
- Visual Loss – Post marketing reports have been made for non-arteritic anterior optic neuropathy (NAION) in association with PDE5 Inhibitors. Use is not recommended in those with known hereditary degenerative retinal disorders.
- Fluid Retention – While PAH, CHF and side effects of ERAs are known to have fluid retention symptoms, patients with left ventricular dysfunction may be at particular risk to develop fluid retention after starting an ERA. Discontinuation of Opsynvi may be considered and is dependent on original cause.
- Decreased Sperm Count – ERAs have known spermatogenesis and may affect fertility.
- Prolonged Erection – The PDE5 inhibitor component of Opsynvi is associated with prolonged erections greater than 4 hours and priapism (painful erections greater than 6 hours. Risk increases in those with a predisposition to priapism (i.e. sickle cell anemia, multiple myeloma, leukemia) or in those with a preexisting anatomical deformation of the penis (angulation, cavernosal fibrosis). Patients must seek emergent medical attention for an erection lasting greater than 4 hours.

Adverse reactions to Opsynvi include edema, anemia, headache, abdominal pain, hypotension, myalgia, nasopharyngitis, nausea, increased uterine bleeding, back pain, flushing, vomiting, palpitations, and epistaxis.

Use of Opsynvi in pregnant women is contraindicated. Use in lactating patients is not recommended; presence of tadalafil has been found in lactating rats in animal studies. The safety and efficacy of Opsynvi in pediatric population younger than 18 years is not established and not recommended. No overall differences in safety and effectiveness were observed between those 65 and older and younger subjects. Opsynvi use should be avoided in those with severe renal impairment (CrCl 15-29 mL/min) or those on dialysis due to increased tadalafil exposure. Opsynvi use should be avoided in those with severe hepatic impairment (Model for End Stage Liver Disease score >/= 19), or those with elevated hepatic aminotransferases (3 x UNL).

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

Clinical Discussion: Dr. Bret Yarczower asked if we could send the chart on the cost to his clinical colleagues who treat PAH. Emily Bednarz, PharmD, stated she can send the chart to Dr. Yarczower. The committee unanimously voted to accept the recommendations as presented (36 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (35 approvals). None were opposed.

Outcome: Opsynvi is a pharmacy benefit. It is recommended to be non-formulary. Opsynvi will require a prior authorization with the following criteria:

- Medical record documentation that Opsynvi is prescribed by a cardiologist or pulmonologist **AND**
- Medical record documentation of World Health Organization (WHO) functional class II, III, or IV pulmonary arterial hypertension **AND**
- Medical record documentation of a negative pregnancy test in females of childbearing potential b
- Medical record documentation that Opsynvi will not be used concomitantly with organic nitrate therapy and guanylate cyclase (GC) stimulators **AND**

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to 3 formulary alternatives

QUANTITY LIMIT: 30 tablets per 30 days

FORMULATY ALTERNATIVES: Ambrisentan tablet, Bosentan tablet, Opsumit tablet, Tracleer 32mg tablet, Sildenafil tablet, Sildenafil Suspension, Alyq tablet, Tadalafil tablet

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

ALYGLO (immune globulin (human)-stwk)

Review: Alyglo is indicated for the treatment of primary humoral immunodeficiency (PI) in adults (age 17 and older.) This includes, but is not limited to, the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiency (SCID).

Alyglo (immune globulin intravenous, human-stwk) is a 10% immune globulin liquid for intravenous injection indicated for the treatment of primary humoral immunodeficiency (PI.) Alyglo supplies a broad spectrum of neutralizing IgG antibodies to bacterial and viral pathogens, and their toxins. The mechanism of action has not been fully elucidated in PI.

Alyglo contains mainly IgG with a broad spectrum of antibodies against various infectious agents reflecting the IgG activity found in the donor population. Alyglo which is prepared from pooled material, has an IgG subclass distribution similar to that of native human plasma. An adequate dose of IVIG can restore abnormally low IgG level to the normal range. Standard pharmacodynamics studies were not performed.

GC Biopharma reports that Alyglo is manufactured using a novel Cation Exchange Chromatography (CEX) process to remove coagulation factor XIa (FXIa) to undetectable levels. FXIa is potentially a cause of small numbers of thromboembolic events in patients receiving immunoglobulin infusions. However, Alyglo prescribing information retains the class warning that thrombosis may occur with immune globulin intravenous (IGIV) products, including Alyglo.

Intravenous formulations of immune globulin include Asceniv, Gamunex-C, Gammagard, Octagam, Privigen, Flebogamma DIF, Gammaplex, Gammaked, Panzyga, Bivigam, and now Alyglo. Yimmugo was FDA approved in June 2024, release date currently unknown. Subcutaneous formulations of immune globulin include Hizentra, Hyqvia, Cuvitru, Cutaquig, Gamunex-C, Gammagard, Gammaked and Xembify. Yimmugo received FDA approval on June 13, 2024.

Clinical studies involving Alyglo showed similar efficacy results to other immune globulin products in regard to the primary endpoint of acute bacterial infections. No clinical differentiation has been shown between Alyglo and the products already on the market.

Alyglo (immune globulin intravenous, human-stwk) is supplied in single-dose, tamper-evident vial containing the labeled amount of functionally active IgG. The components used in the packaging for Alyglo are not made with natural rubber latex.

A prospective, open-label, single-arm, multi-center study was conducted in North America (the United States and Canada) [NCT02783482] to determine efficacy, safety and pharmacokinetics of Alyglo (immune globulin intravenous, human-stwk) in adults and pediatric subjects with PI. Prior to enrollment, all subjects were receiving stable doses between 300 and 900 mg/kg of IGIV replacement therapy. Subjects received Alyglo infusion administered every 21 or 28 days, the dose and schedule per their prior therapy, for 12 months. Thirty-three adults aged 17 to 70 years were enrolled and received doses ranging from 319 to 817 mg/kg. Eighteen (54.5%) subjects were female, and 15 (45.5%) subjects were male; 32 (97.0%) were White and 1 (3.0%) was other. The primary efficacy analysis was annualized rate of acute serious bacterial infections (SBIs), defined as bacterial pneumonia, bacteremia/sepsis, bacterial meningitis, visceral abscess, and osteomyelitis/septic arthritis per subject per year. Secondary analyses were annual rate or days of other infections, antibiotic use, days out of work/school/day care or unable to perform normal activities due to infection, and days of hospitalization due to infection. During the 12-month study period, the acute SBI rate was 0.03 with an upper one-sided 99% confidence limit: 0.31, which met the predefined success rate of less than one acute SBI per subject per year. One adult subject experienced an acute SBI, bacterial pneumonia.

Alyglo is contraindicated in patients who have a history of anaphylactic or severe systemic reaction to the administration of human immune globulin and in IgA-deficient patients with antibodies to IgA and a history of hypersensitivity due to trace amounts of IgA contained in the finished product. Alyglo has warnings and precautions for:

- Hypersensitivity: Alyglo contains trace amounts of IgA (≤ 100 mcg/mL). Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions. Alyglo is contraindicated in IgA-deficient patients with antibodies against IgA or a history of hypersensitivity reaction.
- Thrombotic Events
- Renal Failure
- Hyperproteinemia, Increase Serum Viscosity, and Hyponatremia
- Aseptic Meningitis Syndrome
- Hemolysis
- Transfusion-Related Acute Lung Injury (TRALI)
- Transmissible Infectious Agents

The most common adverse reactions, observed in ≥ 5% of study subjects, were headache, nausea/vomiting, fatigue, nasal/sinus congestion, rash, arthralgia, diarrhea, muscle pain/aches, infusion site pain/swelling, abdominal pain/discomfort, cough, and dizziness.

Twenty-eight subjects (85%) experienced a total of 145 temporally associated adverse reactions (adverse events that occurred during or within 72 hours after the end of an infusion) during the study. The temporally associated ARs were headache (13 subjects, 39%), nausea/vomiting (11 subjects, 33%), fatigue (6 subjects, 18%), nasal/sinus congestion (5 subjects, 15%), rash (4 subjects, 12%), arthralgia, diarrhea (3 subjects, 9% each), muscle pain/aches, Infusion site pain/swelling, abdominal pain/discomfort, cough, dizziness (2 subjects, 6% each). There were no deaths and no adverse reactions leading to withdrawal from the study.

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 (32 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (35 approvals). None were opposed.

Outcome: Alyglo is a medical benefit. Alyglo will be added to the medical benefit cost share list when processed on the medical benefit. If processed at a specialty pharmacy, Alyglo will process at the Specialty tier or the Brand Non-preferred tier for members with a three-tier benefit. Alyglo will be added to the Medical Benefit Policy 4.0. For commercial members Alyglo will also apply to Site of Care policy, MBP 181.0.

MBP 4.0 Intravenous Immune Globulin

DESCRIPTION:
Immune Serum Globulins are used to provide passive immunity or to alter the immune response by increasing the recipients' antibody titer and antigen-antibody reaction potential. IgG antibodies help to prevent or modify certain infectious diseases in susceptible individuals. Five major classes of immunoglobulin proteins exist in human serum and other body fluids (IgA, IgD, IgE, IgG, and IgM). Immune globulin is an antibody-containing solution obtained from the pooled plasma of pre-screened, presumably healthy blood donors. Throughout the policy, the term "intravenous immune globulin" and "IVIG" is intended to refer to all immune globulin injections, including intravenous, intramuscular and subcutaneous administrations.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

This policy refers to the following intravenous immune globulin drug products:

Alyglo
Asceniv
Bivigam
Carimune NF
Cutaquig
Cuvitru
Flebogamma
Flebogamma DIF
Gammagard Liquid
Gammagard S/D
Gammaked

Gammaplex
Gamunex
Gamunex-C
Hizentra
Hyqvia
Octagam
Panzyga
Privigen
Xembify

IVIG is considered to be medically necessary for the Commercial, Exchange, CHIP and Medicaid lines of business for the following, however not limited to, indications when specified criteria are met (Note: The Medicare line of business is reviewed according to Centers for Medicare and Medicaid Services [CMS] Local Coverage Determination [LCD]):

- **Primary Humoral Immunodeficiencies, including combined immunodeficiencies**
  Congenital Agammaglobulinemia (X-linked agammaglobulinemia, Bruton's disease)
  Autosomal recessive agammaglobulinemia
  Common Variable Immunodeficiency (CVID)
  Wiskott-Aldrich Syndrome
  X-linked or autosomal recessive immunodeficiency with hyperimmunoglobulin M
  Severe Combined Immunodeficiency (SCID)
  Ataxia-telangectasia
  DiGeorge syndrome
  Nijmegen breakage syndrome
  Gruscelli syndrome
  NEMO deficiency
  WHIM (warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis) syndrome
  X-linked lymphoproliferative disease (in patients with hypogammaglobulinemia or dysgammaglobulinemia and infections)
  Hypogammaglobulinemia provided the appropriate work up is performed to determine extent (ex. flow cytometry and anamnestic response to recall antigens)

  Patients with primary immunodeficiencies must meet the following criteria:
  1. Medical record documentation/laboratory results of immunoglobulin deficiency; **AND**
  2. Medical record documentation of an inability to amount an adequate immunologic response to inciting antigens; **AND**
  3. Medical record documentation of persistent and severe infections

- **Idiopathic Thrombocytopenia Purpura (ITP)**
  1. Acute ITP when one of the following are present:
     - Active bleeding and a platelet count of less than 30,000/mm^3 **or** documented history of significant bleeding and a platelet count of less than 30,000/mm^3; **AND**
     - Medical record documentation of use in conjunction with a corticosteroid or a contraindication to or failure on corticosteroid therapy

     OR

     - As a preoperative treatment prior to major invasive surgical procedures; **AND**
     - IVIG be used with corticosteroids when a more rapid increase in platelet count is required

     OR

     - A platelet count of less than 20,000/mm^3; **AND**
     - Medical record documentation of use in conjunction with a corticosteroid or a contraindication to or failure on corticosteroid therapy

  2. Chronic ITP when one of the following criteria are met:
     - Duration of Immune Thrombocytopenia (ITP) greater than 12 months; **AND**
     - No concurrent illness or disease explaining thrombocytopenia; **AND**

- Medical documentation of prior treatment with corticosteroids (ex, prednisone 2 mg/kg/day for ≤ 6 weeks (for adults) or 4 mg/kg/day for ≤ 7 days (for children)); AND a splenectomy, if over 12 months have elapsed from date of initial diagnosis;
  OR
- Active bleeding and a platelet count of less than 30,000/mm^3 **or** documented history of significant bleeding and a platelet count of less than 30,000/mm^3;
  OR
- A platelet count of less than 20,000/mm^3;
  OR
- As a preoperative treatment prior to major invasive surgical procedures

3. ITP in pregnancy with medical documentation of the following:
   - One of the following:
     - Active bleeding and a platelet count of less than 30,000/mm^3; or documented history of significant bleeding and a platelet count of less than 30,000/mm^3; **OR**
     - A platelet count of less than 20,000/mm^3; **OR**
     - Intent to increase platelet counts to a level considered safe for procedures;

     AND
   - A contraindication to, intolerance to or therapeutic failure on corticosteroid therapy OR a more rapid increase in platelets is necessary, as determined by the prescriber*

   *Note: initial response to corticosteroids usually occurs within 4-14 days and reaches a peak response within 1-4 weeks. Initial response to IVIG usually occurs within 1-3 days and reaches a peak response within 2-7 days.

4. Secondary ITP
   a. *H-pylori*-associated
      i. Eradication of H-pylori in patients testing positive

- **Acquired Hypogammaglobulinemia Secondary to Chronic B-cell Lymphocytic Leukemia or Multiple Myeloma**
  The following criteria must be met:
  1. IgG less than 500 mg/dl; **AND**
  2. a documented history of repeated bacterial infection two times in one year or a severe bacterial infection within the last 6 months

- **Post-transfusion purpura**
  The following criteria must be met:
  1. Medical record documentation of an onset of severe thrombocytopenia (platelet count less than 30,000/mm3) occurring 2-14 days post blood product transfusion.

- **Kawasaki Disease**
  The following criteria must be met:
  1. Documentation of a diagnosis of Kawasaki disease;

  AND
  2. Treatment with IVIG is begun within 10 days of the onset of fever; **OR**
  3. Patient has a delayed diagnosis (i.e., later than day 10 of fever) with ongoing systemic inflammation as manifested by elevation of ESR or CRP (CRP>3.0mg/dL) together with either persistent fever without other explanation or coronary artery aneurysms.

- **Pediatric HIV infection – Bacterial infection prevention**
  The following criteria must be met:
  1. Indicated in HIV positive children with humoral immunodeficiency; **AND**
  2. Entry CD4+ lymphocyte count of 200/mm^3 or greater; **AND**
  3. Hypogammaglobulinemia AND one or more of the following:
  4. Recurrent serious bacterial infections; **OR**
  5. Failure to form antibodies to common antigens; **OR**
  6. There is a high risk for measles; **OR**
  7. There is a documented bronchiectasis that has not adequately responded to antimicrobial and pulmonary therapy.

- **Bone Marrow Transplantation (for lines of business not covered by the transplant vendor only)**
  The following criteria must be met:
  1. The transplant recipient is within the first 100 days after transplant from a matched unrelated donor; **OR**

2. Documentation of treatment of Graft vs. Host Disease in a transplant recipient receiving allogenic matched bone marrow transplant with chronic repeated infections or hypogammaglobulinemia (IgG levels less than 400 mg/dL); **OR**
3. Documentation of autologous transplant with hypogammaglobulinemia (IgG level less than 400 mg/dL) or repeated infections.

- **Myasthenia Gravis (Acute use)**
  The following criteria must be met:
  1. Must be prescribed by a neurologist; **AND**

  Medical documentation of one of the following indications:
  2. Diagnosis of acute myasthenic crisis with decompensation; **OR**
  3. Use during postoperative period following a thymectomy for acute exacerbations; **OR**
  4. Use prior to planned thymectomy; **OR**
  5. For short term bridge therapy (one-course of treatment) in patients with acute worsening symptoms with plans to start other immunosuppressive treatments or corticosteroids.

IVIG for any of the above acute indications will be approved for one course of treatment. One course of treatment will be limited to 5 days of IVIG therapy.

- **Refractory Chronic Debilitating Myasthenia Gravis**
  1. Medical record documentation of refractory Chronic Debilitating Myasthenia Gravis; **AND**
  2. Prescribed by or in consultation with a neuromuscular specialist; **AND**
  3. Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one corticosteroid; **AND**
  4. Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one cholinesterase inhibitor; **AND**
  5. Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one non-steroidal immunosuppressive therapy

- **Dermatomyositis and Polymyositis**
  All of the following criteria must be met:
  1. Diagnosis of dermatomyositis or polymyositis confirmed by biopsy; **AND**
  2. Documented evidence of active disease; **AND**
  3. Must be prescribed by a neurologist; **AND**
  4. Documented evidence that the condition is refractory to both of the following therapies
     A) First line therapy: corticosteroids (at least 4 months of therapy)
     B) Second line therapy: at least two immunosuppressants (e.g. cyclosporine, azathioprine, methotrexate, cyclophosphamide)

- **Guillain-Barre Syndrome/Ascending Paralysis**
  The following criteria must be met:
  1. A diagnosis of either acute or chronic Guillain-Barre syndrome; **AND**
  2. Must be prescribed by a neurologist; **AND**
  3. IVIG will be initiated within 2 weeks but no longer than 4 weeks of neuropathic symptom onset if acute onset; **AND**
  4. No plan for combining IVIG with plasma exchange or sequential plasma exchange and IVIG.

- **Chronic Inflammatory Demyelinating Polyneuropathy**
  All of the following criteria must be met:
  1. Must be prescribed by a neurologist; **AND**
  2. Documented evidence of focal or symmetric neurologic deficits that are slowly progressive or relapsing over 2 months or longer; **AND**
  3. Physician provided documentation of EMG abnormalities consistent with the diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy with the presence of at least ONE of the following:
     a. Motor distal latency prolongation $\geq$ 50% above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome), **OR**
     b. Reduction of motor conduction velocity $\geq$ 30% below LLN in two nerves, **OR**
     c. Prolongation of F-wave latency $\geq$ 30% above ULN in two nerves ($\geq$ 50% if amplitude of distal negative peak CMAP <80% of LLN values), **OR**

d. Absence of F-waves in two nerves if these nerves have distal negative peak CMAP amplitudes ≥ 20% of LLN + ≥ 1 other demyelinating parameter in ≥ 1 other nerve, **OR**
e. Partial motor conduction block: ≥ 50% amplitude reduction of the proximal negative peak CMAP relative to distal, if distal negative peak CMAP ≥ 20% of LLN, in two nerves, or in one nerve + ≥1 other demyelinating parameter in ≥ 1 other nerve, **OR**
f. Abnormal temporal dispersion (>30% duration increase between the proximal and distal negative peak CMAP) in ≥ 2 nerves, **OR**
g. Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) increase in ≥ 1 nerve (median ≥ 6.6 ms, ulnar ≥ 6.7 ms, peroneal ≥ 7.6 ms, tibial ≥ 8.8 ms) + ≥ 1 other demyelinating parameter in ≥ 1 other nerve

Improvement should be apparent after 3 months of treatment; otherwise, requests for further treatment will require Medical Director review.

- **Fetal or Neonatal Alloimmune Thrombocytopenia (FNAIT)**
  The following criteria must be met:
  1. History of previous fetus or newborn with serologically confirmed Fetal or Neonatal Alloimmune Thrombocytopenia (FNAIT) with thrombocytopenia; **OR**
  2. History of previous fetus or newborn with serologically confirmed Fetal or Neonatal Alloimmune Thrombocytopenia (FNAIT) with intracranial hemorrhage; **OR**
  3. History of previous fetus or newborn with thrombocytopenia or intracranial hemorrhage of unknown etiology **AND** documentation a complete diagnostic workup was performed*

*Note, a complete diagnostic workup, per ACOG guidelines may include:
- Maternal anti-HPA antibody screening and cross matching with paternal platelets at 12, 24 and 32 weeks OR
- Paternal incompatibility for human platelet antigen OR
- A single antibody screening study including the crossmatching of paternal and maternal platelets at 30 weeks gestation

- **Multifocal Motor Neuropathy**
  The following criteria must be met:
  1. Must be prescribed by a neurologist; **AND**
  2. Medical documentation of progressive symptoms for a minimum of 1 month; **AND**
  3. Asymmetric limb weakness in at least two nerves; **AND**
  4. No objective sensory abnormalities except for minor vibration sense abnormalities in the lower limb; **AND**
  5. Documentation of a diagnosis of multifocal motor neuropathy with conduction block as shown on electrophysiologic study as evidenced by:
     - Definite Conduction block on a single nerve
       OR
     - Probable Conduction block in at least two nerves
       OR
     - Probable Conduction block in at least one nerve AND at least two (2) of the following:
       i. Elevated IgM anti-ganglioside GM1 antibodies
       ii. Increased CSF protein
       iii. increased T2-signal intensity on MRI of brachial plexus with diffuse nerve swelling
       iv. Objective clinical improvement following IVIG treatment

- **CMV Interstitial Pneumonia in Allogenic Bone Marrow Transplant or HSCT patients** (IIb/A)
  The following criteria must be met:
  1. Medical record documentation of CMV pneumonia
  2. Medical record documentation that IVIG is being used in combination with or patient has a contraindication to ganciclovir

- **Toxic shock syndrome** (III/C)
  The following criteria must be met:
  1. Medical record documentation of severe disease and failure on, intolerance to, or contraindication to conventional therapy, which may include, but is not limited to surgical debridement, fluid replacement, vasopressors or antibiotic therapy; **AND**
  2. Caused by staphylococcal organisms

  OR

1. Medical record documentation of Streptococcal Toxic Shock Syndrome (TSS)

- **Graves' Ophthalmopathy** (Ib/A)
  The following criteria must be met:
  1. Medical record documentation of failure on, contraindication to, or intolerance to conventional treatment (corticosteroids)
  2. Prescription must be written by an ophthalmologist

- **Autoimmune Mucocutaneous Blistering Diseases (pemphigus, pemphigoid, pemphigus vulgaris, pemphigus foliaceus, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis** (III/C)
  The following criteria must be met:
  1. Diagnosis must be substantiated by biopsy; **AND**
  2. Failure or contraindication to two or more conventional therapies (corticosteroids, azathioprine, cyclophosphamide, etc.);
     OR
  3. Have rapidly progressive disease in which a clinical response could not be quickly achieved utilizing conventional therapy. IVIG would be given in conjunction with conventional therapy and only until such time as conventional therapy could take effect

Note: IVIG for the treatment of autoimmune mucocutaneous blistering disease must be used only for short-term therapy and not as maintenance therapy.

- **Solid Organ Transplant**
  The following criteria must be met:
  Prevention of acute humoral rejection
    - Medical record documentation that patient is at high risk for antibody-mediated rejection, including highly sensitized patients or receiving ABO incompatible organ

  OR
  Treatment of acute humoral rejection
    - Medical record documentation of antibody-mediated rejection

- **Rasmussen's Encephalitis** (IIb/B)
  The following criteria must be met:
  1. Medical record documentation that short-term amelioration of encephalitis is needed prior to definitive surgical therapy
  2. Medical record documentation of intractable focal motor seizures and progressive neurologic deterioration

- **Stiff-Person Syndrome** (Ib/A)
  The following criteria must be met:
  1. Prescription written by a neurologist
  2. Medical record documentation of failure on, intolerance to, or contraindication to all standard therapies (muscle relaxants, benzodiazepines, and gabapentin-related medications)

- **Eaton-Lambert myasthenic syndrome** (Ib/A)
  All of the following criteria must be met:
  1. Prescription written by a neurologist
  2. Medical record documentation of failure on, contraindication to, or intolerance to other treatments including corticosteroids or other immunosuppressants, cholinesterase inhibitors, and 3,4-diaminopyridine.

- **Multiple Sclerosis (relapsing/remitting type)**
  All of the following criteria must be met:
  1. Must be prescribed by a neurologist; **AND**
  2. Medical record documentation of RRMS; **AND**
  3. Medical record documentation of current MS exacerbation; **AND**
  4. Medical record documentation of therapeutic failure on, contraindication to, or intolerance to an appropriate trial of high dose corticosteroids

Improvement should be apparent after 2 courses of monthly treatment, otherwise, requests for further treatment will require Medical Director review of supporting documentation of expected outcome.

Note: IVIG is considered investigational for primary or progressive multiple sclerosis and will not be covered.

- **Warm Antibody Autoimmune hemolytic anemia** (III/D)
  The following criteria must be met:
  1. Refractory to or contraindicated to corticosteroids and immunosuppressive agents
  2. Refractory to splenectomy

- **Parvovirus B19 Infection**
  All of the following criteria must be met
  1. Prescribed by or in consultation with an infectious disease specialist, immunologist, hematologist, or transplant specialist
  2. Medical record documentation of chronic immunodeficient condition (HIV, solid organ transplant, etc.)
  3. Medical record documentation of chronic parvovirus B19 infection
  4. Medical record documentation of severe anemia as defined by hemoglobin < 8 g/dL

- **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 two 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 three 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).

AUTHORIZATION DURATION: Each treatment period will be defined as 6 months or less, unless otherwise stated (e.g. Chronic Inflammatory Demyelinating Polyneuropathy, Multiple Sclerosis, and Multifocal Motor Neuropathy). Re-review will occur every 6 months or less, dependent on the indication. Documentation of clinical response to therapy is required after initiation of therapy. If initial benefit is seen and continued therapy is deemed necessary, documentation of objective monitoring must be seen. Clinical improvement is superior to laboratory monitoring. IVIG will no longer be covered if there is a medical record documentation of disease progression.

LIMITATIONS: When approved, IVIG will be administered in a setting determined by the Plan, in consultation with the requesting physician to be the most clinically appropriate and/or medically necessary.

Initial Dosing: Dosing should be calculated using adjusted body weight (ABW) if one or more of the following criteria are met:
- Patient's body mass index (BMI) is 30 kg/m^2 or more
- Patient's actual body weight is 20% higher than his or her ideal body weight (IBW)

Dosing formulas:
- BMI = weight in kg / height in meters^2
- IBW (kg) for males = 50 + [2.3 (height in inches – 60)]

- IBW (kg) for females = 45.5 + [2.3 * (height in inches – 60)]
- ABW = IBW + 0.5 (actual body weight – IBW)

Geisinger Health Plan considers some conditions other than those listed under Indications to be **Experimental, Investigational or Unproven** and **NOT Medically Necessary**. These conditions include:

- Alzheimer's disease
- amyotrophic lateral sclerosis
- atopic dermatitis
- autism
- chronic fatigue syndrome
- chronic mucocutaneous candidiasis (CMCC)
- complex regional pain syndrome (CRPS)
- epilepsy
- inclusion body myositis
- Lyme disease
- neuromyelitis optica (NMO) (Devic's Disease)
- optic neuritis
- paraproteinemic demyelinating neuropathy (PDN)
- post-polio syndrome
- recurrent spontaneous miscarriage
- rheumatic fever
- secondary progressive multiple sclerosis (SPMS)

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

VOYDEYA (danicopan)

Review: Voydeya is a complement factor D inhibitor indicated as add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH). Voydeya has not been shown to be effective as monotherapy and should only be prescribed as add-on to ravulizumab or eculizumab. Voydeya is the second oral treatment option for patients with PNH. Voydeya reversibly binds complement Factor D and selectively inhibits the alternative complement pathway. In PNH, it acts proximally in the alternative pathway of the complement cascade to control preferentially C3 fragment-mediated EVH when co-administered with ravulizumab or eculizumab to maintain control over MAC-mediated IVH.

At least 2 weeks prior to initiation of Voydeya, patients should be vaccinated against encapsulated bacteria, including Neisseria meningitidis (serogroups A, C, W, Y, and B) and Streptococcus pneumoniae according to current ACIP recommendations. The recommended starting dose of Voydeya is 150 mg orally three times daily. Voydeya can be taken with or without food. The dose can be increased to 200 mg three times daily if the patient's hemoglobin has not increased by greater than 2 g/dL after 4 weeks of therapy, if the patient required transfusion during the previous 4 weeks, or to achieve an appropriate Hgb response based on clinical judgement. Voydeya comes in 50 mg and 100 mg tablets and is supplied as bottles of 100 mg tablets and as a 150 mg therapy pack which contains 90 each of 50 mg and 100 mg tablets.

The efficacy of Voydeya was evaluated in a randomized, double-blind, placebo-controlled study in adults with PNH and clinically significant EVH, defined as anemia (hemoglobin [Hgb] ≤ 9.5 g/dL) with absolute reticulocyte count ≥ 120 x 109/L with or without transfusion support. The study enrolled patients with PNH who had been treated with a stable dose of ravulizumab or eculizumab for at least the previous 6 months.

Patients were randomized 2:1 to receive Voydeya or placebo for 12 weeks in addition to background ravulizumab or eculizumab treatment. After week 12, all patients received Voydeya in combination with background ravulizumab or eculizumab treatment up to week 24, after which they could enter a long-term extension period and continue to receive Voydeya with background ravulizumab or eculizumab.

Efficacy was based on the change in Hgb level from baseline to Week 12. Other efficacy measures included proportion of patients with Hgb increase of 2 g/dL at week 12 in the absence of transfusions, the proportion of patients with transfusion avoidance through Week 12, the change from baseline in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue scores at Week 12, and change from baseline in absolute reticulocyte count at Week 12. Transfusion avoidance was considered achieved by patients who did not receive a transfusion and did not meet the protocol specified guidelines for transfusion from baseline through Week 12. Baseline characteristics were generally balanced between treatment groups.

Voydeya efficacy was established on the basis of superiority compared to placebo in all efficacy measures with statistically significant results.

Voydeya has a black box warning for the risk of serious infections caused by encapsulated bacteria, including Neisseria meningitidis, Streptococcus pneumoniae, or Haemophilus influenzae type B. Voydeya is contraindicated for initiation in patients with unresolved serious infection caused by encapsulated bacteria. Patients receiving Voydeya are at increased risk of these infections and should be vaccinated against them prior to initiation and monitored throughout treatment for signs and symptoms of serious infections. Based on the risk of these infections, Voydeya is available through a restricted Voydeya REMS program.

Other warnings include risk of hepatic enzyme elevations, PNH manifestations after Voydeya discontinuation, increases in total cholesterol and LDL-cholesterol. During clinical trials, the safety of Voydeya was evaluated in 86 adults with PNH. Serious adverse reactions were reported in 5% of patients who received Voydeya and included pancreatitis, cholecystitis, and increased blood bilirubin. No specific serious adverse reaction was reported in more than 1 patient treated with Voydeya. Permanent discontinuation occurred in 5% of patients and dosage reduction occurred in 1 patients treated with Voydeya. The most common adverse reaction reported in patients was headache. Other adverse reactions that occurred in more than 5% of patients treated with Voydeya included vomiting, pyrexia, increased alanine aminotransferase, hypertension, and pain in extremity. Clinically relevant adverse reactions occurring in less than 5% of patients include increased serum triglycerides.

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 (34 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (36 approvals). None were opposed.

Outcome: Voydeya is a pharmacy benefit and will not be added to the Commercial, Marketplace, and GHP Kids pharmacy formularies. The following prior authorization criteria will apply.
Medical record documentation of age greater than or equal to 18 years **AND**

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) **AND**
- Medical record documentation that Voydeya is prescribed by a hematologist **AND**
- Medical record documentation that member has received vaccinations against encapsulated bacteria, including Streptococcus pneumoniae and Neisseria meningitidis **AND**
- Medical record documentation that member continues to experience clinically significant extravascular hemolysis (EVH)* despite at least 6 months of treatment with eculizumab or ravulizumab **AND**
- Medical record documentation that member will continue eculizumab or ravulizumab treatment in combination with Voydeya

***NOTE:** In clinical trials, clinically significant EVH was defined as anemia (hemoglobin [Hgb] ≤ 9.5 g/dL) with absolute reticulocyte count ≥ 120 x 10^9/L with or without transfusion support.

QUANTITY LIMIT:

- **Voydeya 100 mg Tablets:** 6 tablets per day
- **Voydeya 150 mg Therapy Pack:** 6 tablets per day

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

- Medical record documentation that member continues to receive Voydeya in combination with ravulizumab or eculizumab **AND**
- Medical record documentation of improvement of symptoms of extravascular hemolysis (EVH)*, including but not limited to increased hemoglobin levels, reduction in transfusions, improvement in hemolysis, decreases in LDH, and increased reticulocyte count

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: Yes

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

SIMLANDI (adalimumab-ryvk)

Review: Simlandi is an interchangeable Humira biosimilar indicated for adult rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA) in patients 2 years of age and older, adult psoriatic arthritis (PsA), adult ankylosing spondylitis (AS), Crohn's disease (CD) in patients 6 years and older, adult ulcerative colitis (UC), adult plaque psoriasis (Ps), adult hidradenitis suppurativa (HS), and adult uveitis (UV).

Simlandi, similar to the other Humira biosimilars, shares all the same indications as Humira, with the exception of pediatric UC, adolescent HS, pediatric UV (see chart below). These indications are missing from all biosimilar products due to the Orphan Drug Exclusivity patents that have not expired. Pediatric UV is protected until September 28, 2025, adolescent HS until October 16, 2025 and pediatric UC until February 24 2028.

Simlandi is the first high-concentration, citrate free, interchangeable biosimilar to Humira. Hadlima, Hyrimoz/adalimumab adaz [unbranded Hyrimoz], Yuflyma, Amjevita, Cyltezo, are available in high concentrations. Yusimry has a high concentration formulation in development. Abrilada and Cyltezo (not high concentration) also have interchangeable status. All biosimilars are available as citrate free.

The delay in approval is due to a series of complete response letters issues to Alvotech by the FDA over manufacturing concerns at Alvotech's manufacturing plant in Reykjavik, Iceland. A follow-up inspection was completed by the FDA in January 2024 and Alvotech reported one observation that needed to be addressed.

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 (32 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (35 approvals). None were opposed.

Outcome: Simlandi will be a pharmacy benefit. It is recommended to not add Simlandi to formulary. Simlandi will require a prior authorization and will be added to the non-preferred adalimumab biosimilars and Humira policy 788.1 with the following highlighted changes:

For adult rheumatoid arthritis, polyarticular juvenile idiopathic arthritis or juvenile rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, plaque psoriasis, adult ulcerative colitis, adult hidradenitis suppurativa, adult non-infectious intermediate, posterior, and panuveitis
An exception for coverage of Abrilada, Cyltezo, Adalimumab-adbm (unbranded Cyltezo), Hulio, Humira, Hyrimoz, Adalimumab-adaz (unbranded Hyrimoz), Idacio, Yuflyma, or Simlandi may be made for members who meet the following criteria:

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Adalimumab-fkjp **AND** Hadlima **AND** Yusimry

NOTE: HUMIRA MAINTAINS BRAND EXCLUSIVITY FOR PEDIATRIC UVEITIS, PEDIATRIC ULCERATIVE COLITIS, AND ADOLESCENT HIDRADENITIS SUPPURATIVA

AUTHORIZATION DURATION: Approval will be given for a duration of twelve (12) months. For continuation of coverage, medical record documentation of clinical improvement or lack of progression in signs and symptoms of treated condition on adalimumab therapy is required.

MEDISPAN AUTHORIZATION LEVEL: NDC-9

QUANTITY LIMITS: See adalimumab quantity limit reference document.
Humira for Pediatric Ulcerative Colitis
An exception for coverage of BIWEEKLY (every other week) administration of Humira may be made for members who meet all the following criteria:

- Medical record documentation of a diagnosis of moderate to severe ulcerative colitis AND
- Medical record documentation that adalimumab is prescribed by a gastroenterologist AND

- Medical record documentation of age greater than or equal to 5 years and less than 18 years AND
- Medical record documentation of therapeutic failure on, intolerance to, at least one conventional therapy: corticosteroids, aminosalicylates, or immunomodulators (azathioprine or 6-mercaptopurine (6-MP)) AND
- Medical record documentation that Humira is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent

An exception for coverage of WEEKLY administration of Humira may be made for members who meet all the following criteria:

- Medical record documentation of a diagnosis of moderate to severe ulcerative colitis AND
- Medical record documentation that adalimumab is prescribed by a gastroenterologist AND
- Medical record documentation of age greater than or equal to 5 years and less than 18 years AND
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least one conventional therapy: corticosteroids, aminosalicylates, or immunomodulators (e.g., 6-mercaptopurine or azathioprine) AND
- Medical record documentation that Humira is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent AND
- Medical record documentation that the member is less than 18 years of age and receiving an appropriate dose based on body weight

NOTE:

- For patients with an adequate drug trough, American Gastroenterological Association (AGA) does not recommend antibody levels to guide therapy. Patients should be switched to another agent.
- For patients with an inadequate drug trough & undetectable antibodies, a dose increase may be warranted.
- For patients with an inadequate drug trough & detectable antibodies, a switch to another agent is recommended. However, patients with low antibody levels may be considered for a dose increase, in hopes of overcoming antibody level and achieving response.

MEDISPAN AUTHORIZATION LEVEL: NDC-9
QUANTITY LIMIT: See adalimumab quantity limit reference document.

Humira for Pediatric Hidradenitis Suppurativa (HS)
An exception for coverage of Humira may be made for members who meet all the following criteria:

- Medical record documentation that Humira is prescribed by a dermatologist AND
- Medical record documentation of age greater than or equal to 12 years and less than 18 years AND
- Medical record documentation of a diagnosis of moderate to severe hidradenitis suppurativa (HS), defined as Stage II or III on the Hurley staging system* AND
- Medical record documentation of at least 3 abscesses or inflammatory nodules AND
- Medical record documentation of concomitant use of oral or systemic antibiotics AND
- Medical record documentation that the member has received counseling on weight management (if overweight) and smoking cessation (if the member is an active smoker) AND
- For members 12 to 18 years of age weighing 30 to less than 60 kg: medical record documentation of Humira being dosed at a maximum dose of 40 mg every other week AND
- Medical record documentation that Humira is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent

*Hurley staging system:

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

AUTHORIZATION DURATION: Approval will be given for a duration of twelve (12) months. For continuation of coverage, medical record documentation of clinical improvement or lack of progression in signs and symptoms of hidradenitis suppurativa on Humira therapy is required.

MEDISPAN AUTHORIZATION LEVEL: NDC-9

QUANTITY LIMIT: See adalimumab quantity limit reference document.

Humira for the treatment of Non-Infectious Intermediate, Posterior and Panuveitis
An exception for coverage of Humira may be made for members who meet all the following criteria:

- Medical record documentation that Humira is prescribed by an ophthalmologist or rheumatologist AND

- Medical record documentation of age greater than or equal to 2 years and less than or equal to 18 years AND
- Medical record documentation of a diagnosis of non-infectious intermediate, posterior or panuveitis AND
- Medical record documentation that Humira is being given in combination with methotrexate OR medical record documentation of contraindication to methotrexate AND
- Medical record documentation that member is receiving appropriate dose of Humira based on weight and age AND
- Medical record documentation that Humira is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent

AUTHORIZATION DURATION: Approval will be given for a duration of twelve (12) months. For continuation of coverage, medical record documentation of clinical improvement or lack of progression in signs and symptoms of uveitis on Humira therapy is required.

MEDISPAN AUTHORIZATION LEVEL: NDC-9

QUANTITY LIMIT: See adalimumab quantity limit reference document.

Updated Quantity Limit: It is recommended to add Simlandi to row 3 in the quantity limit reference document.

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

VARIZIG (varicella zoster immune globulin (human))

Review: Varizig was approved in December 2012 and is a varicella zoster immune globulin (human) indicated for post-exposure prophylaxis of varicella in high-risk individuals. High-risk groups include:

- Immunocompromised children and adults
- Newborns of mothers with varicella shortly before or after delivery
- Premature infants
- Neonates and infants less than one year of age
- Adults without evidence of immunity
- Pregnant women

Varizig is intended to reduce the severity of varicella. Administer Varizig as soon as possible following varicella zoster virus (VZV) exposure, ideally within 96 hours for greatest effectiveness. There is no convincing evidence that Varizig reduces the incidence of chickenpox infection after exposure to VZV. There is no convincing evidence that established infections with VZV can be modified by Varizig administration. There is no indication for the prophylactic use of Varizig in immunodeficient children or adults when there is a history of varicella, unless the patient is undergoing bone marrow transplantation.

Varizig is a solvent/detergent-treated sterile liquid preparation of purified human immune globulin G (IgG) containing antibodies to varicella zoster virus (anti-VZV). VZV is the causative agent of chickenpox. Varizig is prepared from plasma donated by healthy, screened donors with high titers of antibodies to VZV, which is purified by an anion-exchange column chromatography manufacturing method. This donor selection process includes donors with high anti-VZV titers due to recent natural infection by VZV, or due to recent zoster infections (shingles).

The CDC recommends administration of Varizig as soon as possible after exposure to varicella zoster virus and within 10 days. The decision to administer Varizig depends on three factors: 1) whether the patient lacks evidence of immunity to varicella, 2) whether the exposure of likely to result in infection, 3) whether the patient is at greater risk for varicella complications than the general population. For high-risk patients who have additional exposures to varicella zoster ≥ 3 weeks after initial Varizig administration, another dose of Varizig should be considered. Patients without evidence of immunity to varicella who are at high risk for severe varicella and complications, who have been exposed to varicella or herpes zoster, and for whom the varicella vaccine is contraindicated, should receive Varizig. Patient groups recommended by the CDC to receive Varizig include the following:

- Immunocompromised patients without evidence of immunity
- Newborn infants whose mothers have signs and symptoms of varicella around the time of delivery (i.e., 5 days before to 2 days after)
- Hospitalized premature infants born at ≥ 28 weeks of gestation whose mothers do not have evidence of immunity to varicella
- Hospitalized premature infants born at < 28 weeks of gestation or who weigh ≤ 1,000 grams at birth, regardless of their mothers' evidence of immunity to varicella

- Pregnant women without evidence of immunity

Dosing of Varizig is based on body weight. Administer a single dose of Varizig intramuscularly. The intramuscular dose should be divided and administered in two sites, dependent on the patient size. Do not exceed 3 ml per injection site. Varizig is supplied as a sterile solution for intramuscular injection and is available in a single-use vial of 125 international units in 1.2 ml.

Study 1 was a randomized, open-label, multicenter, active controlled trial conducted in 60 pregnant women without immunity to VZV as confirmed by a latex agglutination test. Patients were stratified based on time from first exposure to varicella as follows: one to four days post-exposure and five to 14 days post-exposure. The women were randomized into one of three study arms: a single IV dose of 125 IU/10 kg body weight to a maximum dose of 625 IU of Varizig, a single IM dose of 125 IU/10 kg body weight to a maximum dose of 625 IU of Varizig, or a single IM dose of 125 IU/10 kg body weight to a maximum dose of 625 IU of VZIG (licensed comparator product). Patients were followed for 42 days. Incidence of clinical varicella was similar across all treatment groups with an overall incidence of 33%. However, in a subset of 28 patients with more than 24 hours exposure to varicella, the incidence of clinical varicella in the combined treatment groups was 64%.

Study 2 was an open-label, Expanded Access Protocol (EAP) conducted in the United States designed to provide Varizig to high-risk individuals who were exposed to VZV. Although the study was not designed to evaluate efficacy, the objective of the study was to further access and confirm the safety and efficacy of IM injection of Varizig in the prevention and reduction of severity of complications from varicella infections in the indicated high-risk populations. Initially, enrollment was limited to allow treatment with Varizig only within 96 hours of exposure, but the protocol was amended to expand the treatment window to 10 days post-exposure.
The incidence of clinical varicella (chickenpox lesions) was compared to predefined historical reference rates. The incidence of severe varicella complications, including pneumonia, encephalitis, severe varicella with pox counts greater than 100 pox, mortality and all complications was also evaluated. The overall incidence of clinical varicella was evaluated in an interim analysis, where 10% (31/311) of high-risk individuals exposed to VZV and treated with Varizig for all combined populations, for whom complete or partial efficacy data was available. Clinical varicella was more common after prolonged VZV exposure. The final report confirmed the efficacy results in the interim analysis. In addition, a comparison of the incidence of varicella based on treatment window revealed that treatment between 5 and 10 days post-exposure was no different from treatment within 96 hours.

Contraindications include history of anaphylactic or severe systemic reactions to human immune globulins and IgA-deficient patients with antibodies against IgA and a history of hypersensitivity. Warnings and precautions include the following: Thrombotic Events - Thrombotic events may occur during or following treatment with immune globulin products; Coagulation Disorders - In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, only administer if expected benefits outweigh the potential risks; Hypersensitivity - Severe hypersensitivity reactions may occur following Varizig administration. Administer in a setting equipped to treat a hypersensitivity reaction; and Transmissible Infectious Agents - Because Varizig is made from human plasma, it may carry a risk of transmitting infectious agents. The plasma donors are screened for the presence of certain infectious agents and the manufacturing process includes measures to inactivate and remove certain viruses. The most common adverse reactions overserved in clinical trials for all subjects and patients are the following: injection site pain (3%), headache (2%), rash (1%), fatigue (1%) , chills (1%), and nausea (1%).

Clinical studies did not include sufficient numbers of geriatric patients to determine whether they respond differently than younger patients to Varizig. 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 (34 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (35 approvals). None were opposed.

Outcome: Varizig will be a medical benefit and should be added to the medical benefit cost share list. No prior authorization criteria 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

ACTEMRA BIOSIMILAR CLASS REVIEW

Review:

Actemra Biosimilars		
Brand Name/Biosimilar	**Manufacturer**	**Formulation**
Actemra	Genentech, Inc.	**Intravenous Infusion** Injection: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL) in single-dose vials for further dilution **Subcutaneous Injection** Injection: 162 mg/0.9 mL in a single-dose prefilled syringe or single-dose prefilled ACTPen® autoinjector
Tofidence	Biogen MA, Inc.	**Intravenous Infusion** Injection: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL) in single-dose vials for further dilution
Tyenne	Fresenius Kabi USA, LLC	**Intravenous Infusion** Injection: 80 mg/4 mL (20 mg/mL), 200 mg/10 mL (20 mg/mL), 400 mg/20 mL (20 mg/mL) in single-dose vials for further dilution **Subcutaneous Injection** Injection: 162 mg/0.9 mL in a single-dose prefilled syringe or single-dose prefilled autoinjector

Tofidence: Pharmacokinetic similarity was demonstrated between Tofidence and US-Actemra and supported a demonstration of no clinically meaningful difference between Tyenne and US-Actemra for the IV route of administration. Additionally, a scientific bridge was established between Tofidence, US-Actemra, and EU-RoActemra to support the relevance of comparative data generated using EU-RoActemra in the biosimilarity assessment.

Tofidence was compared to EU-RoActemra in Study BAT-1806-002-CR, a double, randomized, parallel group, active-controlled study in patients with RA and inadequate response to methotrexate. The primary endpoint was the percentage of subjects achieving an American College of Rheumatology 20% (ACR20) response at Week 24. Secondary endpoints included change from baseline in Disease Activity Score on 28 Joints (DAS28), percentage of patients achieving ACR20, ACR50, and ACR70 response, and change from baseline in ACR and DAS28 individual components.

At Week 24, the adjusted ACR20 response rates were 68% and 70% in the EU-RoActemra and Tofidence groups, respectively. The 90% CI was within the prespecified similarity margins. The supportive and sensitivity analysis of the primary and secondary endpoints at Week 24 support the conclusion of similar efficacy and a demonstration of no clinically meaningful differences between Tofidence, EU-RoActemra, and US-Actemra.

Similar incidence of anti-drug antibody (ADA) and neutralizing antibody (NAb) formation was demonstrated in Study BAT-1806-002-CR between Tofidence and EU-RoActemra in subjects with RA as well as between Tofidence, EU-RoActemra, and US-Actemra in healthy subjects. This suggests a demonstration of no clinically meaningful differences in collective immunogenicity results.

No new safety signals were identified in the Tofidence treatment arm compared to the known adverse event profile of US-Actemra. Overall treatment emergent adverse events were similar between treatment arms in all studies. There were no major differences in SAE, TEAEs, AEs leading to discontinuation, and adverse events of special interest (AESI) based on the known safety profile of US-Actemra between the treatment groups.

Tofidence is indicated for intravenous use in pediatric patients 2 years of age and older with PJIA and SJIA. The safety and efficacy of Tofidence in pediatric patients with conditions other than PJIA and SJIA has not been established. The safety and efficacy of use of Tofidence in pediatric patients less than 2 years of age has not been established.

The safety and efficacy of Tofidence in geriatric patients is based on clinical studies of Actemra which showed that the frequency of serious infection in tocilizumab treated patients was higher in patients 65 years of age and older compared to those under the age of 65. As there is a higher incidence of infections in the elderly population in general, caution should be used when treated elderly patients with Tofidence.

Tyenne: Pharmacokinetic similarity was demonstrated between Tyenne and US-Actemra and supported a demonstration of no clinically meaningful difference between Tyenne and US-Actemra for both the IV and SC routes of administration.

Additionally, a scientific bridge was established between Tyenne, US-Actemra, and EU-RoActemra to support the relevance of comparative data generated using EU-RoActemra in the biosimilarity assessment.

Tyenne was compared to EU-RoActemra in Study FKS456-001, a randomized, double-blind, active comparator, 2-arm parallel group study evaluating the efficacy, safety, and immunogenicity of SC administration in patients with moderately to severely active RA. The primary endpoint was mean change from baseline in Disease Activity Score-28 Erythrocyte Sedimentation Rate (DAS28-ESR) at Week 24. The key secondary endpoint was based on 20% improvement in American College of Rheumatology (ACR) Core Set Measurements (ACR20) response rate at Week 24.

At Week 24, the estimated mean change from baseline in DAS28-ESR was -3.53 in the Tyenne treatment arm compared to -3.54 in the EU-RoActemra arm. Analysis of the key secondary endpoint showed similarity between the treatment arms. Results of the primary and secondary endpoints support the finding of no meaningful differences in efficacy between Tyenne and EU-RoActemra.

Similar incidence of anti-drug antibody (ADA) and neutralizing antibody (NAb) formation was demonstrated in Study FKS456-001 between Tyenne and EU-RoActemra in subjects with RA as well as between Tyenne and US-Actemra in healthy subjects. This suggests a demonstration of no clinically meaningful differences in collective immunogenicity results.

The safety risks identified in Study FKS456-001 were consistent with the known adverse event profile of US-Actemra. Treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), deaths, adverse events leading to IMP discontinuation, and development of anti-drug antibodies (ADA) were generally similar between the treatment groups in the comparative clinical study FKS456-001.

Tyenne is indicated for both intravenous and subcutaneous use in pediatric patients 2 years of age and older with PJIA and SJIA. The safety and efficacy of pediatric patients with conditions other than PJIA or SJIA have not been established. The safety and efficacy of Tyenne use in pediatric patients less than 2 years of age has not been established.

The safety and efficacy of Tyenne in geriatric patients is based on clinical studies of Actemra which showed that the frequency of serious infection in tocilizumab treated patients was higher in patients 65 years of age and older compared to those under the age of 65. As there is a higher incidence of infections in the elderly population in general, caution should be used when treated elderly patients with Tyenne.

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

Clinical Discussion: Austin Paisley, PharmD, asked if we can add criteria to require failure of biosimilars in the reauth criteria for Commercial medical benefit. Kimberly Reichard, PharmD, stated that we can add. The committee unanimously voted to accept the recommendations as presented (34 approvals). None were opposed.

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented (32 approvals). None were opposed.

Outcome: Tofidence IV Solution is a medical benefit for Commercial, Marketplace, and GHP Kids and will require a prior authorization. Tolifdence IV will be added to the medical benefit cost share list. When processed at a specialty pharmacy, Tolfidence IV will process on the Specialty tier or Brand NP for members with a three-tier benefit. Tofidence IV Solution will be added to the Medical Benefit 76.0 Actemra Policy as outlined below.

Tyenne IV Solution is a medical benefit for Commercial, Marketplace, and GHP Kids and will require a prior authorization. Tyenne IV Solution will be added to the medical benefit cost share list. When processed at a specialty pharmacy, Tyenne IV Solution will process on the Specialty tier or Brand NP for members with a three-tier benefit. Tyenne IV Solution will be added to the Medical Benefit 76.0 Actemra Policy as outlined below.

Tyenne Auto-injector and Prefilled Syringe (self-administered) is a pharmacy benefit and will be added to the Specialty tier or Brand NP tier for members with a three-tier benefit on the Commercial, Marketplace, and GHP Kids formulary. Tyenne Auto-injector and Prefilled Syringe will be added to Commercial Policy 321.0 Actemra Self-Injectable Policy as outlined below.

Commercial Policy 321.0 Actemra Self Injectable

An exception for coverage of Actemra Self Injectable or Tyenne Self-Injectable may be made for members who meet the following criteria:

Rheumatoid Arthritis

- Medical record documentation that Actemra Self Injectable or Tyenne Self Inejctable 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 formulary biologics for the treatment of rheumatoid arthritis **AND**
- Medical record documentation that Actemra or Tyenne is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- For tocilizumab reference product requests (i.e. Actemra), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-aazg (Tyenne).

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: 3.6 mL per 28 days

RE-AUTHORIZATION CRITERIA: Actemra self-injectable and Tyenne self-injectable will be configured as a prior authorization for new starts only. Actemra self-injectable and Tyenne self-injectable 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

Active polyarticular juvenile idiopathic arthritis (PJIA)
- Medical record documentation that Actemra Self Injectable or Tyenne Self Inejctable is prescribed by a rheumatologist **AND**
- Medical record documentation of a diagnosis of active polyarticular juvenile idiopathic arthritis or juvenile rheumatoid arthritis **AND**
- Medical record documentation of age greater than or equal to 2 years **AND**
- Medical record documentation of an intolerance to, contraindication to, or therapeutic failure on a minimum 3 month trial of two (2) preferred formulary biologics for the treatment of juvenile idiopathic arthritis or juvenile rheumatoid arthritis **AND**
- Medical record documentation that Actemra or Tyenne is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent AND
- For tocilizumab reference product requests (i.e. Actemra), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-aazg (Tyenne).

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: 3.6 mL per 28 days

RE-AUTHORIZATION CRITERIA: Actemra self-injectable and Tyenne self-injectable will be configured as a prior authorization for new starts only. Actemra self-injectable and Tyenne self-injectable 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

Active systemic juvenile idiopathic arthritis (SJIA)
- Medical record documentation that Actemra Self Injectable or Tyenne Self Inectable is prescribed by a rheumatologist **AND**
- Medical record documentation of a diagnosis of active systemic juvenile idiopathic arthritis **AND**
- Medical record documentation of age greater than or equal to 2 years **AND**
- Medical record documentation that Actemra or Tyenne is not being used concurrently with a tumor necrosis factor (TNF) or other biologic agent AND
- For tocilizumab reference product requests (i.e. Actemra), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-aazg (Tyenne).

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: 3.6 mL per 28 days

RE-AUTHORIZATION CRITERIA: Actemra self-injectable and Tyenne self-injectable will be configured as a prior authorization for new starts only. Actemra self-injectable and Tyenne self-injectable 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

Giant Cell Arteritis

- Medical record documentation that Actemra Self Injectable or Tyenne Self Inectable is prescribed by a rheumatologist **AND**
- Medical record documentation of a diagnosis of giant cell arteritis **AND**
- Medical record documentation that Actemra is being prescribed in combination with oral glucocorticoids **AND**
- Medical record documentation that Actemra or Tyenne is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent AND
- For tocilizumab reference product requests (i.e. Actemra), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-aazg (Tyenne).

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: 3.6 mL per 28 days

RE-AUTHORIZATION CRITERIA: Actemra self-injectable and Tyenne self-injectable will be configured as a prior authorization for new starts only. Actemra self-injectable and Tyenne self-injectable 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

NOTE: Although traditionally the erythrocyte sedimentation rate and/or C-reactive protein are high in giant cell arteritis, the range of values for both test is broad and non-specific.

Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) (ACTEMRA ONLY)

- Medical record documentation that Actemra Self Injectable is prescribed by or in consultation with a pulmonologist and/or rheumatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of systemic sclerosis according to American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) **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 of systemic sclerosis related to interstitial lung disease confirmed by all of the following: o greater than or equal to 10% fibrosis on a chest high resolution computer tomography **AND**
    - forced viral capacity (FVC) greater than or equal to 40% of predicted normal **AND**
    - DLCO (diffusion capacity of the lung for carbon monoxide) 30-89% of predicted normal

COVID-19 (ACTEMRA ONLY)

If Actemra is being prescribed for COVID-19, see the FDA website for Emergency Use Authorizations at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs for current FDA authorized use. At this time, Actemra is authorized for inpatient use only for COVID-19 and would not be covered for outpatient use.

Medical Benefit Policy 76.0 Actemra IV

Indications which Do Not Require Prior Authorization for use (Actemra IV Only):

Claims submitted with the following diagnosis for use do not require prior authorization for use:

- Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS)

Actemra IV (tocilizumab), Tofidence IV (tocilizumab-bavi), or Tyenne IV (tocilizumab-aazg) will be considered medically necessary for commercial, exchange, and CHIP lines of business when all of the following criteria are met:
1. Adults with moderate to severe rheumatoid arthritis
   - Medical record documentation that member is 18 years of age or greater **AND**
   - Prescription written by a rheumatologist **AND**
   - Physician provided 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 that Actemra or tocilizumab biosimilars are not being used concurrently with a TNF blocker or other biologic agent **AND**
   - Medical record documentation of a therapeutic failure on, contraindication to or intolerance to 12 weeks of Humira*, Rinvoq*, OR Xeljanz* **AND**
   - For tocilizumab reference product requests (i.e. Actemra IV), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-bavi (Tolfidence) and tocilizumab-aazg (Tyenne).

*Requires prior authorization

2. Active systemic juvenile idiopathic arthritis (SJIA)
   - Prescription written by a rheumatologist **AND**
   - Patient is 2 years of age or older **AND**
   - Medical record documentation of a diagnosis of systemic juvenile idiopathic arthritis **AND**
   - Medical record documentation that Actemra or tocilizumab biosimilars are not being used concurrently with a TNF blocker or other biologic agent **AND**
   - For tocilizumab reference product requests (i.e. Actemra IV), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-bavi (Tolfidence) and tocilizumab-aazg (Tyenne).

3. Active polyarticular juvenile idiopathic arthritis (PJIA)
   - Medical record documentation that member is 2 years of age or greater **AND**
   - Prescription is written by a rheumatologist **AND**
   - Medical record documentation of a diagnosis active polyarticular juvenile idiopathic arthritis or juvenile rheumatoid arthritis **AND**
   - Medical record documentation that Actemra or tocilizumab biosimilars are not being used concurrently with a TNF blocker or other biologic agent **AND**
   - Physician provided documentation of a therapeutic failure on, contraindication to or intolerance to a minimum 4 month trial of Humira* **AND**
   - For tocilizumab reference product requests (i.e. Actemra IV), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-bavi (Tolfidence) and tocilizumab-aazg (Tyenne).

*Requires prior authorization

4. Giant Cell Arteritis
   - Medical record documentation of a diagnosis of Giant Cell Arteritis AND
   - Prescription written by a rheumatologist AND
   - Patient is 18 years of age or older AND
   - Medical record documentation that Actemra or tocilizumab biosimilars are not being used concurrently with a TNF blocker or other biologic agent **AND**
   - For tocilizumab reference product requests (i.e. Actemra IV), medical record documentation of a therapeutic failure on, intolerance to, or contraindication to tocilizumab-bavi (Tolfidence) and tocilizumab-aazg (Tyenne).

Note to Reviewer: If Actemra IV or Tofidence IV is being prescribed for COVID-19, see the FDA website for Emergency Use Authorizations at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#coviddrugs for current FDA authorized use. At this time, Actemra is authorized for inpatient use only for COVID-19 and would not be covered for outpatient use.

AUTHORIZATION DURATION: Approval will be given for an initial duration of six (6) months. For continuation of coverage, medical record documentation of clinical improvement or a lack of progression in the signs and symptoms of the targeted disease state at six (6) months of Actemra, Tofidence, or Tyenne therapy is required.

After the initial six (6) month approval, subsequent approvals for coverage will be for a duration of one (1) year. Reevaluation of coverage will be every one (1) year requiring medical record documentation of continued or sustained improvement in the signs and symptoms of the targeted disease while on Actemra, Tofidence, or Tyenne therapy.

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

UPDATES

DEXMETHYLPHENIDATE ER UPDATE

Background: An update to policy 94.0 (Stimulants for ADHD) was presented to committee in the August 2024 electronic vote, as a part of the Relexxi Line Extension review. The recommended update, which was approved by the committee's vote, was to change the prior authorization criteria to include dexmethylphenidate ER as a preferred formulary alternative. Policy criteria was recommended to be updated as follows:

- Medical record documentation of a contraindication to, intolerance to, or therapeutic failure on two generic formulary alternatives (methylphenidate CD, amphetamine/dextroamphetamine SR combination, dexmethylphenidate ER), one of which must contain the same active ingredient as the product requested, if available

Dexmethylphenidate ER currently requires a prior authorization for the commercial/exchange/CHIP lines of business. Noted below are the costs of dexmethylphenidate compared to the current preferred formulary alternatives that do not require prior authorization.

Drug	Dosing	AWP/MAC per unit ($)	AWP/MAC per 28-day supply #	Formulary Status Commercial/ Exchange	Formulary Status Medicare
Dexmethylphenidate ER Capsules 24h: 5, 10, 15, 20, 25, 30, 35, 40 mg	**Once daily dosing; Pediatric starting dose: 5 mg/day; Adult starting dose: 10 mg/day**	**$1.47 - $3.55 [MAC]**	**$41.16 - $99.40**	**Tier 1/Tier 3 (PA)**	**Tier 4**
Methylphenidate ER (CD) Capsules: 10, 20, 30, 40, 50, 60 mg	Once daily dosing; Adult/Pediatric Max Dose: 60 mg/day	$1.67 - $3.88 [MAC]	$46.76 - $108.64	Tier 1/Tier 3	Tier 4
Amphetamine-Dextroamphetamine SR Capsules 24h: 5, 10, 15, 20, 25, 30 mg	Pediatric starting dose: 10 mg/day; Max dose: 30 mg/day Adult starting dose: 20 mg/day	$1.00 - $1.51 [MAC]	$28.00 - $42.28	Tier 1/Tier 3	Tier 4

Recommendation: Based on the cost data presented above, it is recommended to remove the prior authorization from dexmethylphenidate ER capsules for commercial/exchange/CHIP lines of business.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented (33 approvals). None were opposed.

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

PALONOSETRON & FOSAPREPITANT UPDATE

Background: During the OncoHealth implementation process, it was identified that the prices of palonosetron and fosaprepitant have significantly decreased over the past few years and that the prior authorization and associated step therapy may no longer be benefitting Geisinger to the extent that it previously was. Cost and prior authorization analyses were done and is presented in the table below.

Drug	Dose	HCPCS Code	$ Per Dose	PA Volume (Last 12 months)	Approval % (Last 12 Months)

ondansetron	8 mg or 0.15 mg/kg	J2405	$0.74	No PA needed	n/a
granisetron	10 mcg/kg	J1626	$2.09	No PA needed	n/a
palonosetron	0.25 mg	J2469	$9.77	492 cases	97% (475 cases)
fosaprepitant	150 mg	J1453	$24.90	362 cases	99% (359 cases)

Comparing the anticipated cost per prior authorization case, cost per dose of palonosetron and fosaprepitant, and current GHP approval percentage of requested prior authorizations, it appears that there is minimal benefit of requiring prior authorization for these two medications.

Recommendation: It is recommended that the requirement for prior authorization for palonosetron and fosaprepitant be removed for the Commercial/Exchange/CHIP lines of business. Policy MB 24.0 for palonosetron and policy MB 104.0 for fosaprepitant will be retired.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented (36 approvals). None were opposed.

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

SYFOZRE & IZERVAY UPDATE

Background: As part of Eye Disorder CarePath discussions, updates to the Syfovre and Izervay policy were recommended. Among the topics discussed were to delete the criteria point regarding CNV, change the authorization duration to allow for closer monitoring, and add criteria points regarding best corrected visual acuity and safety.

Recommendation: It is recommended to update the prior authorization criteria and update the authorization duration.

MBP 278.0 Syfovre (pegcetacoplan)
Syfovre (pegcetacoplan) will be considered medically necessary for the Commercial, Exchange, CHIP, and Medicare lines of business when ALL of the following criteria are met:

- Medical record documentation of the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) **AND**
- Medical record documentation of a confirmed diagnosis of geographic atrophy (GA) using imagining modalities, including but not limited to fundus autofluorescence (FAF), fundus photography, or optical coherence tomography (OCT) **AND**
- Medical record documentation of a current (within 3 months) best corrected visual acuity (BCVA) of 20/320 or better (for example 20/200, 20/80, 20/70, etc) in the eye(s) to be treated with Syfovre **AND**
- Medical record documentation that Syfovre will not be administered concurrently with other complement inhibitors for the treatment of geographic atrophy secondary to AMD (i.e. Izervay)
- ~~For new starts only: Medical record documentation of the absence of active, or history of, choroidal neovascularization* (CNV) in the eye(s) to be treated with Syfovre.~~

~~*Note: Age-related macular degeneration (AMD) with CNV is often referred to as exudative AMD (eAMD), neovascular AMD (nAMD), or wet AMD (wAMD).~~

AUTHORIZATION DURATION: ~~Approvals will be given for a lifetime duration.~~ Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for 12 months or less if the reviewing provider feels it is medically appropriate and will require the following criteria:

- Medical record documentation of a current (within 3 months) best corrected visual acuity (BCVA) of better than 20/320 (for example 20/200, 20/80, 20/70, etc.) in the eye(s) being treated with Syfovre **AND**
- Medical record documentation of the absence, or resolution, of Retinal Vasculitis, Retinal Vascular Occlusion, and/or active Intraocular Inflammation (including but not limited to: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare) **AND**
- Medical record documentation that Syfovre will not be administered concurrently with other complement inhibitors for the treatment of geographic atrophy secondary to AMD (i.e. Izervay)

AND

- One of the following:
  - Medical record documentation of the absence of active choroidal neovascularization (CNV), or neovascular (wet) Age Related Macular Degeneration (nAMD) in the Syfovre-treated eye(s) **OR**
  - Medical record documentation that the member's active CNV, or nAMD is NOT worsening **OR**
  - Medical record documentation of rationale for continued use in the setting of worsening CNV, or nAMD (eg. The benefits of Syfovre outweigh the risks of Syfovre administration)

QUANTITY LIMIT: 0.2mL (30mg) per 25 days (15mg per eye per 25 days)

MBP 316.0 Izervay (avacincaptad pegol)

Izervay (avacincaptad pegol) will be considered medically necessary for the Commercial, Exchange, CHIP, and Medicare lines of business when ALL of the following criteria are met:

- Medical record documentation of the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD) **AND**
- Medical record documentation of a confirmed diagnosis of GA using imagining modalities, including but not limited to fundus autofluorescence (FAF), fundus photography, or optical coherence tomography (OCT) **AND**
- Medical record documentation of a current (within 3 months) best corrected visual acuity (BCVA) of 20/320 or better (for example 20/200, 20/80, 20/70, etc) in the eye(s) to be treated with Izervay **AND**
- ~~For new starts only: Medical record documentation of the absence of active, or history of, choroidal neovascularization* (CNV) in the eye(s) to be treated with Izervay **AND**~~
- Medical record documentation that Izervay will not be administered concurrently with other complement inhibitors for the treatment of geographic atrophy secondary to age-related macular degeneration (AMD) (i.e. Syfovre)

AUTHORIZATION DURATION: ~~12 months~~ Initial approval will be for 12 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for 12 months or less if the reviewing provider feels it is medically appropriate and will require the following criteria:

- Medical record documentation of a current (within 3 months) best corrected visual acuity (BCVA) of better than 20/320 (for example 20/200, 20/80, 20/70, etc.) in the eye(s) being treated with Izervay **AND**
- Medical record documentation that Izervay will not be administered concurrently with other complement inhibitors for the treatment of geographic atrophy secondary to AMD (i.e. Syfovre)

AND

- One of the following:
  - Medical record documentation of the absence of active choroidal neovascularization (CNV), or neovascular (wet) Age Related Macular Degeneration (nAMD) in the Izervay-treated eye(s) **OR**
  - Medical record documentation that the member's active CNV, or nAMD is NOT worsening **OR**
  - Medical record documentation of rationale for continued use in the setting of worsening CNV, or nAMD (eg. The benefits of Izervay outweigh the risks of Izervay administration)

QUANTITY LIMIT: 0.2 mL (4 mg) per 28 days (2 mg per eye per 28 days)

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented (37 approvals). 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 UPDATE

Background: Currently the below medications are medical benefits that require prior authorization for the commercial line of business and are not on the Site of Care Program. After review of the respective FDA-approved labels, it has been determined that the below medications are acceptable candidates for the Site of Care program.

Recommendation: It is recommended the following changes (highlighted in green) be made to MBP 181.0 so that this policy may reflect the addition of the below medications to the Site of Care Program. The addition of secukinumab and tezepelumab to the self-injected drug list is recommended.

MBP 181.0 Site of Care

I. Policy:
Site of Care Review Guidelines for Infusion Drugs and Specialty Medications

II. Purpose/Objective:
To provide a policy of coverage regarding the use of hospital-based outpatient facilities as a site of care for drugs that require administration via intravenous infusion or injection. This policy applies to these medications:

1. Abatacept (Orencia IV)
2. ADAMTS13 [Recombinant] (Adzynma)
3. Agalsidase Beta (Fabrazyme)
4. Alglucosidase Alfa (Lumizyme)
5. Alpha1-Proteinase Inhibitor [Human] products
6. Anifrolumab-fnia (Saphnelo)
7. Avalglucosidase alfa-ngpt (Nexviazyme)
8. Belimumab (Benlysta IV)
9. Benralizumab (Fasenra)
10. Beremagene Geperpavec (Vyjuvek)
11. Burosumab (Crysvita)
12. C1 esterase Inhibitor [Human] (Cinryze)
13. Canakinumab (Ilaris)
14. Casimersen (Amondys 45)
15. Certolizumab (Cimzia)
16. Cipaglucosidase alfa (Pombiliti)
17. Crizanlizumab (Adakveo)
18. Denosumab (Prolia, Xgeva)
19. Eculizumab (Soliris)
20. Edaravone (Radicava)
21. Elapegademase-lvlr (Revcovi)
22. Elosulfase alfa (Vimizim)
23. Eptinezumab (Vyepti)
24. Efgartigimod Alfa (Vyvgart & Vyvgart Hytrulo)
25. Eteplirsen (Exondys 51)
26. Evinacumab (Evkeeza)
27. Galsulfase (Naglazyme)
28. Givosiran (Givlaari)
29. Golodirsen (Vyondys 53)
30. Golimumab (Simponi Aria)
31. Idursulfase (Elaprase)
32. Immune Globulin (IVIG)
33. Imiglucerase (Cerezyme)
34. Inclisiran (Leqvio)
35. Inebilizumab (Uplizna)
36. Infliximab & infliximab biosimilar products
37. Laronidase (Aldurazyme)
38. Lenacapavir (Sunlenca)
39. Lumasiran (Oxlumo)
40. Mepolizumab (Nucala)
41. Natalizumab (Tysabri)
42. Ocrelizumab (Ocrevus)
43. Olipudase alfa-rpcp (Xenpozyme)
44. Omalizumab (Xolair)
45. Patisiran (Onpattro)
46. Pegunigalsidase Alfa (Elfabrio)
47. Pozelimab (Veopoz)
48. Ravulizumab (Ultomiris)
49. Romosozumab (Evenity)
50. Rozanolixizumab (Rystiggo)
51. Sebelipase alfa (Kanuma)
52. Secukinumab (Cosentyx IV)
53. Sutimlimab (Enjaymo)
54. Taliglucerase alfa (Elelyso)
55. Teprotumumab (Tepezza)
56. Testosterone udecanoate (Aveed)
57. Tezepelumab (Tezspire)
58. Tildrakizumab (Ilumya)
59. Tocilizumab (Actemra IV)
60. Ublituximab-xiiy (Briumvi)
61. Ustekinumab (Stelara)
62. Vedolizumab (Entyvio)
63. Velaglucerase alfa (Vpriv)
64. Velmanase alfa (Lamzede)
65. Vestronidase alfa-vjbk (Mepsevii)
66. Viltolarsen (Viltepso)
67. Vutrisiran (Amvuttra)

III. Responsibility:

A. Medical Directors
B. Medical Management
C. Pharmacy Department

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than
3. the department requiring/authoring the policy.
4. Devised – the date the policy was implemented.
5. Revised – the date of every revision to the policy, including typographical and grammatical changes.
6. Reviewed – the date documenting the annual review if the policy has no revisions necessary.
7. Site of Care – choice of physical location for administration of intravenous infusions or injections. Site of care locations include hospital inpatient, hospital based outpatient facilities, physician's office, ambulatory infusion centers, or home infusion services.
8. Alternative less intensive site of care facilities include non-hospital affiliated outpatient infusion centers such as ambulatory infusion centers or physician's offices and home infusion
9. Hospital based outpatient facilities include ER services, intravenous drug infusions or injections, observation services, outpatient surgery, lab tests, or x-rays, or any other hospital services where the patient is not admitted as an inpatient.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;

b. provided for the diagnosis and the direct care and treatment of the Member's condition, illness disease or injury;

c. in accordance with current standards good medical treatment practiced by the general medical community;

d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and

e. the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient

DESCRIPTION:

Specific intravenous and injectable drugs must meet applicable medical necessity criteria for coverage. If these criteria are met, this coverage policy will be used to determine the medical necessity of administration in the hospital based outpatient setting. If medical necessity criteria for administration in the hospital based outpatient setting are not met, an alternative less intensive site of care facility should be utilized.

CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee

Administration in the hospital-based outpatient setting will be considered medically necessary and LIMITED to a duration of 60 days (for Xolair (omalizumab), a duration of up to 90 days if the reviewing provider determines it is medically appropriate) when one of the following criteria are met:

1. This is the initial medication infusion **OR**

- Member is reinitiating treatment after not receiving any treatments for at least 6 months.

AUTHORIZATION DURATION: Initial approval will be for a duration of 60 days (for Xolair, up to 90 days). Administration in the hospital-based outpatient setting for longer than the initially approved amount will be required to meet the authorization criteria in the section below.

Administration in the hospital-based outpatient setting will be considered medically necessary for a duration of greater than 60 days when one of the following criteria are met:

- The medication has a site of care restriction for administration per the FDA approved label **OR**
- Documented previous history of severe or potentially life-threatening adverse event during or following administration and the adverse event cannot be managed using pre-medication(s) or adjusting the rate of infusion **OR**
- All of the following:
    - All alternate non-hospital outpatient settings are not within a reasonable distance from the member's home (within 50 miles) **AND**
    - Home healthcare or infusion provider has determined that the patient, home caregiver, or home environment is not appropriate for home infusion or home infusion services are not available due to limited network access **AND**
    - For request of a provider administered drug, for which a self-administered formulation is available, including but not limited to abatacept, belimumab, benralizumab, certolizumab, golimumab, mepolizumab, omalizumab, secukinumab, tezepelumab, tocilizumab, and ustekinumab: medical record documentation of a therapeutic failure of or intolerance to a 3 month trial of the self-administered formulation of the respective product.

  OR
- For IVIG any of the above criteria **OR**
    - Change of immune globulin products (one infusion will be permitted in the hospital outpatient setting) **OR**
    - Laboratory confirmed immunoglobulin A (IgA) deficiency with anti-IgA antibodies

  OR
- For Xgeva (denosumab) any of the above criteria **OR**
    - Patient is receiving Xgeva concomitantly with intravenous chemotherapy as part of the same encounter

AUTHORIZATION DURATION: Initial approval will be for the same length of time as the authorization of the specific drug being administered. Subsequent approvals will be required if the specific drug requires subsequent authorizations.

NOTE: To prevent a delay in care and allow adequate transition time for members to an alternate infusion site, members already established on therapy who do not meet any of the above criteria will be given a 60-day transition auth to allow them to continue receiving therapy at their current hospital based outpatient facility while they transition to a different infusion site.

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented (34 approvals). None were opposed.

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

MEDICAL BENEFIT POLICY UPDATES

Recommendation: It is recommended that the Xofigo and Medical Drug Optimization Program policies are updated as follows:

MBP 110.0 Xofigo (radium Ra 223 dichloride)

- Must be prescribed by hematologist/oncologist or radiation oncologist **AND**
- Medical record documentation of castration-resistant prostate cancer with symptomatic bone metastases and no known visceral metastatic disease

AUTHORIZATION LIMIT: 6 injections total (given at 4 week intervals)

MBP 300.0 Medical Benefit Drug Optimization Program (Commercial, Exchange)

The following (highlighted) products are recommended to be added to the Medical Benefit Drug Optimization Program effective on 3/1/25. No other changes are recommended to the program at this time.

I. Policy:
Medical Benefit Drug Optimization Program

II. Purpose/Objective:
To provide a policy of coverage regarding certain complex, rare disease, and specialty drugs, which are required to be obtained from and billed by a Specialty Pharmacy and are not eligible for direct reimbursement to a provider or facility. This policy applies to these medications:

1. AbobotulinumtoxinA (Dysport)
2. Atezolizumab (Tecentriq)
3. Avelumab (Bavencio)
4. Cemiplimab (Libtayo)
5. Daratumumab (Darzalex)
6. Daratumumab and Hyaluronidase (Darzalex Faspro)
7. DaxibotulinumtoxinA (Daxxify)
8. Dostarlimab (Jemperli)
9. Durvalumab (Imfinzi)
10. Enfortumab Vedotin (Padcev)
11. Eribulin (Halaven)
12. Fam-trastuzumab deruxtecan (Enhertu)
13. IncobotulinumtoxinA (Xeomin)
14. Ipilimumab (Yervoy)
15. Mogamulizumab (Poteligeo)
16. Nivolumab (Opdivo)
17. Obinutuzumab (Gazyva)
18. Octreotide depot (Sandostatin LAR)
19. OnabotulinumtoxinA (Botox)
20. Panitumumab (Vectibix)
21. Pembrolizumab (Keytruda)
22. Polatuzumab vedotin (Polivy)
23. Ramucirumab (Cyramza)
24. Relatlimab and nivolumab (Opdualag)
25. Retifanlimab (Zynyz)
26. RimabotulinumtoxinB (Myobloc)
27. Rituximab (Rituxan)
28. Rituximab and Hyaluronidase (Rituxan Hycela)
29. Tislelizumab (Tevimbra)
30. Toripalimab (Loqtorzi)
31. Trastuzumab (Herceptin)
32. Tremelimumab (Imjudo)

Discussion: No comments or questions.

Outcome: The committee unanimously voted to accept the recommendations as presented (38 approvals). None were opposed.

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

QUARTERLY CASE AUDIT

Background: The Quarterly Case Audit for 2nd quarter 2024 was held on August 29, 2024.

Recommendation: It was discussed that a policy should be created in the future for the Commercial LOB for levocetirizine (prescription only formulation) to ensure consistency amongst reviewers. We will continue to look for opportunities to create more drug specific policies at future quarterly case audit meetings.

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

Meeting adjourned at 3:09 pm.

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

Meeting will be held virtually via phone/Microsoft Teams.