P&T Committee Meeting Minutes
Commercial/Exchange/CHIP
May 21, 2024

Present (via Teams):	**Absent:**
Bret Yarczower, MD, MBA – Chair	Alyssa Cilia, RPh
Amir Antonius, Pharm.D.	Michael Evans, RPh
Emily Bednarz, Pharm.D.	Kelly Faust, Pharm.D.
Kristen Bender, Pharm.D.	Nichole Hossler, MD
Jeremy Bennett, MD	Jason Howay, Pharm.D.
Kim Castelnovo, RPh	Tyreese McCrea, Pharm.D.
Kimberly Clark, Pharm.D.	Perry Meadows, MD
Bhargavi Degapudi, MD	Mark Mowery, Pharm.D.
Michael Dubartell, MD	William Seavey, Pharm.D.
Tricia Heitzman, Pharm.D.	Aubrielle Smith-Masri, Pharm.D.
Keith Hunsicker, Pharm.D.	Michael Spishock, RPh
Kelli Hunsicker, Pharm.D.	Brandon Whiteash, Pharm.D.
Derek Hunt, Pharm.D.	Margaret Whiteash, Pharm.D.
Emily Jacobson, Pharm.D.	Benjamin Andrick, Pharm.D. (non-voting participant)
Dennis Janosczyk, Pharm.D.	
Kerry Ann Kilkenny, MD	Alfred Denio, MD (non-voting participant)
Philip Krebs, R.EEG T	Andrei Nemoianu, MD (non-voting participant)
Briana LeBeau, Pharm.D.	
Ted Marines, Pharm.D.	
Lisa Mazonkey, RPh	
Jamie Miller, RPh	
Austin Paisley, Pharm.D.	
Jonas Pearson, RPh	
Lauren Pheasant, Pharm.D.	
Kimberly Reichard, Pharm.D.	
Melissa Sartori, Pharm.D.	
Kristen Scheib, Pharm.D.	
Michael Shepherd, MD	
Leslie Shumlas, Pharm.D.	
Kirsten Smith, Pharm.D.	
Todd Sponenberg, Pharm.D.	
Jill Stone, Pharm.D.	
Luke Sullivan, DO	
Kevin Szczecina, RPh	
Amanda Taylor, MD	
Ariana Wendoloski, Pharm.D.	
Marika Bergenstock, DO (non-voting participant)	
Birju Bhatt, MD (non-voting participant)	
Sherry Beagle, LPN (non-voting participant)	
Abigail Chua, DO (non-voting participant)	
Keri Jon Donaldson, MD (non-voting participant)	
Jeremy Garris, Pharm.D. (non-voting participant)	
Chidubem Ifeji, Pharm.D. (pharmacy resident)	

Call to Order:
Dr. Bret Yarczower called the meeting to order at 1:04 p.m., Tuesday, May 21, 2024.

Review and Approval of Minutes:
Dr. Bret Yarczower asked for a motion or approval to accept the February 2024 e-vote and March 19, 2024 minutes as written. Minutes approved unanimously. None were opposed.

DRUG REVIEWS

CABTREO (clindamycin phosphate, adapalene, and benzoyl peroxide)

Review: Cabtreo is a first and only combination topical gel consisting of 1.2% clindamycin phosphate, 0.15% adapalene, and 3.1% benzoyl peroxide which is FDA approved for the topical treatment of acne vulgaris in adult and pediatric patients 12 years of age and older. Cabtreo should be applied in a thin layer to the affected area once daily, avoiding the eyes, mouth, paranasal creases, mucous membranes, and areas of broken, eczematous, or sunburned skin. This product is not for oral, ophthalmic, or intravaginal use. It is supplied in 20 gram and 50 gram pumps which should be refrigerated prior to dispensing. Once removed from refrigeration, Cabtreo can be stored at room temperature for up to 10 weeks.

The efficacy of Cabtreo was evaluated in two multicenter, randomized, double-blind clinical trials in 363 adult and pediatric subjects 10 years of age and older with facial acne vulgaris. Patients were randomized 2:1 to Cabtreo or vehicle applied topically once daily for 12 weeks. The median age of participants was 18 years of age with 58% of patients being female and 42% male. Enrolled subjects had a score of moderate (3) or severe (4) on the Evaluator's Global Severity Score (EGSS), 30 to 100 inflammatory lesions (papules, pustules, and nodules), 35 to 150 non-inflammatory lesions (open and closed comedones) and two or fewer facial nodules. At baseline, 91% of subjects had EGSS scores that equated to moderate acne. The co-primary efficacy endpoints of success on EGSS, absolute change in non-inflammatory lesion count and absolute change in inflammatory lesions count were assessed at week 12. Success on the EGSS was defined as at least a 2-grade improvement from baseline and an EGSS of clear (0) or almost clear (1).

Cabtreo is contraindicated in patients with a known hypersensitivity to clindamycin, adapalene, benzoyl peroxide, or any other component of Cabtreo, or known hypersensitivity to lincomycin, and patients with a history of regional enteritis, ulcerative colitis or antibiotic associated colitis. Cabtreo may increase sensitivity to UV light, therefore, patients should be instructed to avoid or minimize sun exposure following application. Stinging/burning/pain, erythema, dryness, irritation, exfoliation, and dermatitis have been reported with use of Cabtreo and are most likely to occur during the first four weeks of treatment. Weather extremes, including cold and wind may be irritating to patients using Cabtreo and they should be instructed to use a moisturizer, reduce frequency of application, or discontinue use based on severity of reaction. Avoid concomitant use of other potentially irritating topical products. Use with concomitant topical acne therapy as not been evaluated.

Available data with Cabtreo in pregnant women are insufficient to evaluate a drug associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproductive studies have not been conducted. In animal studies of individual components, clindamycin did not cause malformations or embryofetal toxicity; topical adapalene studies are insufficient to determine risk, however, oral adapalene at doses 64 and 128 times maximum recommended human dose resulted in fetal skeletal and visceral malformations; systemic exposure of topical benzoyl peroxide is unknown and maternal use is not expected to result in fetal exposure as it is rapidly metabolized to benzoic acid (an endogenous substance) which is eliminated in the urine. It is not known if any of the components of Cabtreo are present in breast milk following topical application.

The safety and effectiveness has not been established in pediatric patients younger than 12 years of age, as reflected in the FDA approved indication. Clinical studies did not include any subjects 65 and older to determine whether they responder differently from younger subjects.

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

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

Financial Discussion: Dr. Bret Yarczower asked if there is anything that justifies the cost of Cabtreo? The convenience of not having to use three separate products is the only advantage. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Cabtreo is a pharmacy benefit and will not be added to the Commercial/Exchange/CHIP formularies at this time. It is recommended that Cabtreo be added to the existing policy for Non-Preferred Acne Medications (476.0) and reviewed with the existing criteria, as follows:

- Medical record documentation a diagnosis of acne, acne vulgaris, or adult-onset acne **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives

GPI LEVEL: GPI-14

RPH SIGNOFF REQUIRED: No

FORMULARY ALTERNATIVES: adapalene, benzoyl peroxide, topical clindamycin, clindamycin/benzoyl peroxide, oral doxycycline, topical erythromycin, erythromycin/benzoyl peroxide, isotretinoin, oral minocycline, sulfacetamide/sulfur, topical tretinoin

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

ADZYNMA (ADAMTS13, recombinant-krhn)

Review: Adzynma is a human recombinant "A disintegrin and metalloproteinase with thrombospondin motifs 13" (rADAMTS13) indicated for prophylactic or on demand enzyme replacement therapy (ERT) in adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP). ADAMTS13 regulates the activating of von Willebrand factor (VWF) and reduces the platelet binding properties of VWF and its propensity to form microthrombi. Adzynma is the first approved treatment for cTTP, a disease which results from a deficiency in ADAMTS13 and that can be fatal if left untreated (mortality rate >90%). Prior to the approval of Adzynma, patients could be treated with prophylactic plasma-based therapy to reduce the risk of clotting.

Adzynma is administered via intravenous infusion for prophylactic and on demand treatment. Each vial of Adzynma is labeled with the actual rADAMTS13 activity, measure in International Units (IU) based on potency. The recommended dosage for prophylactic use is 40 IU/kg body weight administered once every other week. Dosing frequency may be adjusted to 40 IU body weight once weekly based on prior prophylactic dosing regimen or clinical response.

Adzynma is supplied as lyophilized powder in single-dose vials containing 500 to 1500 IU per vial and comes with 5 mL of sterile water for injection.

The safety and efficacy of Adzynma was evaluated in a randomized, active controlled, open-label, two-period crossover study followed by a single arm continuation period (Study 1). This study evaluated Adzynma in patients with cTTP for prophylactic and on-demand ERT compared to plasma-based therapies. Forty-six patients were randomized to receive 6 months of treatment with either 40 IU/kg of Adzynma or plasma-based therapies (Period 1), then crossed over to the other treatment for 6 months (period 2). Thirty-five patients enter a 6-month single arm period with Adzynma (Period 3).

The efficacy was demonstrated based on the incidence of protocol defined acute and subacute TTP events and TTP manifestations, as well as the incidence of supplemental disease prompted by subacute TTP events over a 6-month time period. No patient received Adzynma for an acute TTP event throughout the study, including Period 3 (median duration of exposure of 14 months for patients >12, 4 months in patients 6 to <12 months, and 1 month in patients < 6 years of age. One acute TTP event occurred in a patient receiving plasma-based therapies (FFP) prophylactically during Period 1.

No subacute TTP events were reported in patients receiving Adzynma during Periods 1 and 2. In period 3, two patients receiving Adzynma prophylaxis had two subacute events of which one was treated with four supplement doses, 2 of FFP and 2 of Adzynma. Four patients receiving plasma-based therapies had five subacute TTP events in Periods 1 and 2. A total of seven supplemental doses, 2 of FVIII-VWF concentrate, 1 FFB, and 4 of Adzynma were given to three of these patients.

The efficacy of On-demand (OD) enzyme replacement therapy was evaluated based on the proportion of acute TTP events responding to Adzynma in both the prophylactic and the OD cohorts throughout the duration of the study. An acute TTP event responding to Adzynma was defined as a resolved TTP event when platelet count was ≥150,000/μL or platelet count was within 25% of baseline, whichever occurs first, without requiring the use of another ADAMTS13-containing agent.

Five adult patients enrolled in the OD cohort and had a total of 6 acute TTP events. Of these five patients, two patients were randomized to receive on-demand treatment with Adzynma and three patients were randomized to receive plasma-based therapies. All 6 acute TTP events resolved after treatment with either Adzynma or plasma-based therapies.

There are no black box warnings for Adzynma. Warnings include risk allergic type hypersensitivity reactions, including anaphylaxis, and the potential for immunogenicity. Patients may develop neutralizing antibodies to ADAMTS13. Neutralizing antibodies were not reported in cTTP clinical trials. All patients had previously been exposed to ADAMTS13 through plasma-based products. In clinical trials, the most common adverse reactions were headache, dizziness, migraine, abdominal pain, nausea, upper respiratory tract infection, dizziness, and vomiting.

The safety and efficacy of Adzynma has been established in pediatric patients 2 years of age and older. Based on pharmacokinetic data, no dose adjustments are needed for the pediatric population and pediatric patients will follow the same body-weight based dosing regimen as adult patients. Clinical studies did not include patients 65 years of age and older to determine if they respond differently than younger patients. Based on pharmacokinetic analysis, no dose adjustment is required in elderly 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 asked how we chose a platelet count of 150,000/μl as a requirement for re-authorization? This was included based on the clinical trials. Dr. Yarczower stated that in a typical patient if their platelet count is around 100,000/μl they are not in a danger zone unless having a procedure, etc. Kim R. stated that typically Less than 100,000/μl is considered a sign of a severe cTTP event so in the re-authorization criteria we are looking to see that there was resolution of the event. Dr. Yarzcower asked if we know how many members we have with this disease state? Kim Reichard stated that we do not know specifically, but there are estimated to be approximately 1,000 within the United States. Dr. Yarczower suggested that when looking at therapies such as this it might be worth determining the incidence within the Health Plan in the future. Kim will consider reaching out to hem/onc for this particular product to determine if they can provide any insight. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.
Financial Discussion: Keith Hunsicker asked if this is something that could be eligible for home infusion? Kim Reichard stated that she would look into it and we will consider it for inclusion in the site-of-

case policy for 2025. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Adzynma is a medical benefit that will require a prior authorization. Adzynma will be added to the medical benefit cost share list. When processed at a specialty pharmacy, Adzynma will process at the Specialty tier or Brand NP tier for members with a three-tier benefit. The following prior authorization criteria will apply:

- Medical record documentation that Adzynma is prescribed by a hematologist or oncologist **AND**
- Medical record documentation that member is currently receiving prophylactic therapy **OR** medical record documentation of at least one thrombotic thrombocytopenia purpura (TTP) event **AND**
- Medical record documentation of a diagnosis congenital thrombotic thrombocytopenia purpura (TTP) and both of the following:
    - Documentation of confirmed molecular genetic testing **AND**
    - Documentation of ADATS13 activity less than 10% of normal activity as measured by the fluorescent resonance energy transfer-von Willebrand factor 73 (FRETS-VWF73) assay

GPI LEVEL: GPI-12

AUTHORIZATION DURATION: Initial approval will be for 6 months or less if the reviewing provider feels it is medically necessary. Subsequent approvals will be for an additional 12 months or less if the reviewing provider feels it is medically necessary. Requests for continuation of coverage will be approved for members who meet the following criteria:

- Medical record documentation of a positive clinical response as defined by one of the following:
    - Documentation of a reduction in or improvement in acute and subacute thrombotic thrombocytopenia purpura (TTP) events **OR**
    - Documentation of an improvement in clinical symptoms of congenital thrombotic thrombocytopenia purpura (TTP) **OR**
    - If used for on-demand Adzynma treatment, documentation of improved platelet level to greater than or equal to 150,000/µL or platelet count within 25% of baseline (prior to the acute event)

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.

IXCHIQ (Chikungunya Vaccine, Live)

Review: Ixchiq was approved November 9, 2023, and is the first vaccine approved by the FDA indicated for the prevention of disease caused by the chikungunya virus (CHIKV) in individuals 18 years of age and older who are at increased risk of exposure to CHIKV. This indication is approved under accelerated approval based on anti-CHIKV neutralizing antibody titers. The CDC states that traditional approval would have been challenging and clinical development would likely have been delayed. CHIKV outbreaks are unpredictable and duration can be relatively short. Also, there was no established immunologic correlate of protection. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory studies.

Ixchiq contains live, attenuated CHIKV. The attenuated virus has a deletion in non-structural protein 3, which encodes a component of the viral replicase complex, and replicates less efficiently than the wild-type CHIKV. The vaccine virus is propagated in Vero cells (a continuous line of monkey kidney cells) in

media containing amino acids, vitamins, minerals, and fetal bovine serum. The viral harvests are pooled, clarified, and concentrated. The virus is purified by chromatography and ultracentrifugation, mixed with formulation buffer, and lyophilized.

The Advisory Committee on Immunization Practices (ACIP) recommends the CHIKV vaccine for persons aged ≥ 18 years traveling to a country or territory where there is a CHIKV outbreak. In addition, the CHIKV vaccine may be considered for the following persons traveling to a country or territory without an outbreak but with evidence of CHIKV transmission among humans within the past 5 years: persons aged > 65 years (particularly those with underlying medical conditions, who are likely to have at least moderate exposure to mosquitoes [could include travelers who might have at least 2 weeks total of exposure to mosquitoes in indoor or outdoor settings] or persons staying for a cumulative period of 6 months or more. ACIP also recommends the CHIKV vaccine for laboratory workers with potential for exposure to CHIKV. These recommendations were approved by ACIP February 28, 2024.

Ixchiq was evaluated in a single Phase 3 clinical trial (Study 1, NCT04546724). This study included 3,082 participants. Seroresponse to the vaccine was evaluated among a subset of participants who were randomized 2:1 to receive Ixchiq or placebo. Seroresponse was defined as an anti-CHIKV neutralizing antibody level above a threshold (≥150) as measured by a 50% reduction in a micro plaque reduction neutralizing test (μPRNT50) titer. The seroresponse rate 28 days after Ixchiq injection is presented in Table 1. The seroresponse rate 180 days after Ixchiq was 96.3%, and at one year, 99% of participants retained neutralizing antibody titers above the seroresponse threshold of ≥150. The manufacturer will continue to evaluate antibody persistence for at least 5 years. Results were comparable for patients 18 to 64 years of age and those 65 years of age and older. Ixchiq was granted accelerated approval based on these study results. Confirmatory clinical trials will be required in order to verify the clinical benefit of Ixchiq and obtain fill FDA approval.

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

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

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

Outcome: Ixchiq will be a medical benefit if the member's specific plan allows for coverage of travel vaccines. Ixchiq will be excluded from the Commercial Pharmacy Formulary. Ixchiq will not 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.

ZITUVIO (sitagliptin)

Review: Zituvio is a dipeptidyl peptidase-4 (DPP-4) inhibitor that is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes. Zituvio is not recommended for use in type-1 diabetes mellitus. Due to lack of studying, it is also not recommended for use in those with a history of pancreatitis.

Zituvio is supplied as 25 mg, 50 mg, and 100 mg biconvex, film coated tablets debossed with "12" on one side. Depending on the strength, the color and the number listed on the other side will vary (25 mg tablets are white/off-white with "40", 50 mg tablets are pale yellow with "41", and 100 mg tablets are beige with "42"). Before initiation of Zituvio, renal function should be assessed. The recommended dose is 100 mg tablet by mouth once daily with or without food. Renal function should be assessed periodically to ensure

appropriate dose is taken. If estimated glomerular filtration rate (eGFR) is greater than or equal to 45 mL/min/1.73 m2, no dose adjustment is needed. For moderate renal impairment with an eGFR greater than or equal to 30 mL/min/1.73 m2 to less than 45 mL/min/1.73 m2, dose should be reduced to 50 mg once daily. For severe renal impairment with an eGFR less than 30 mL/min/1.73 m2 or with end-stage renal disease (ESRD) requiring hemodialysis or peritoneal dialysis, dose should be reduced to 25 mg once daily and given without regard to timing of dialysis.

DPP-4 Inhibitors are a second-line treatment option to metformin for type-2 diabetes mellitus. SGLT-2 Inhibitors and GLP-1 Agonists are generally preferred over DPP-4 inhibitors due to their heart and kidney protective properties, low hypoglycemic risk, associated weight loss, and good blood sugar management and A1c reduction. DPP-4 inhibitors are safer than some other glycemic control medications such as sulfonylureas and thiazolidinediones (TZDs) due to lower hypoglycemic risk; they are not as preferred to SGLT-2 inhibitors and GLP-1 agonists due to modest A1c reduction, no cardio/renal- protective properties, and being weight neutral. Depending on patient specific needs, risk, and cost concerns will help dictate which medication to use for management.

Zituvio is contraindicated to those with a hypersensitivity to sitagliptin or its' excipients. Precautions for the use of Zituvio should be taken for those with a history of pancreatitis due to increased risk of developing it. Other precautions to be aware of are for those with existing or development of heart failure or renal failure, hypoglycemia when used with insulin or insulin secretagogues, development of severe arthralgia and joint pain, and formation of a bullous pemphigoid. Other adverse reactions to be aware of include upper respiratory tract infection, nasopharyngitis, headache, nausea, diarrhea, and abdominal discomfort. Special consideration should be given with when using Zituvio in certain populations. Available data for use in pregnant woman is insufficient and only tested in animals. Due to lack of knowledge on relationship to development of birth defects, risks outweigh benefit in most instances and is not supported for blood sugar management. Presence in human milk is also not confirmed, although is present in rat milk. Use is lactating mothers is also not supported currently. Safety and effectiveness is not established for use in pediatric patients, and is not advised for use. Overall safety and effectiveness shown no clinical difference in use of those younger than 65 compared to those older than 65 years. Due to possible effect on kidneys and elderly more prone to kidney related issues, kidney function is recommended to be monitored initially and more frequently thereafter, and dosing may require adjustment depending on results, but otherwise no further consideration needs to be given.

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

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

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

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

- Medical record documentation of a diagnosis of type 2 diabetes mellitus (T2DM) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Tradjenta

GPI LEVEL: GPI-12

QUANTITY LIMIT: 1 tablet per day

RPH SIGNOFF REQUIRED: no

FORMULARY ALTERNATIVES: Tradjenta

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

AGAMREE (vamorolone)

Review: Agamree is a corticosteroid for the treatment of Duchenne muscular dystrophy (DMD), in patients 2 years and older. DMD is a rare, progressive, degenerative neuromuscular disease affecting young males that results in disabling muscle weakness and eventually leads to early death. The current treatments for DMD are corticosteroid therapy (prednisone and deflazacort). Agamree comes in 40mg/mL and is administered as an oral suspension once daily.

The approval of Agamree was based on data from a phase 2b, randomized, double blind, placebo controlled, VISION DMD trial, supplemented by safety data from three open label studies.121 patients were randomized to receive Agamree 6 mg/kg/day (n=30), Agamree 2 mg/kg/day (n=30), prednisone 0.75 mg/kg/day (n=31), and placebo (n=30). After 24 weeks patients who received prednisone and placebo received either Agamree 6mg/kg/day (n=29) or Agamree 2 mg/kg/day (n=29) for an additional 20 weeks. Patients who were included where those who had a DMD gene loss of function variation or lack of muscle dystrophin, ≥ 4 years and < 7 years of age at enrollment, and 13.0kg and 39.9kg at screening, able to walk independently without assistive devise, able to complete the time to stand (TTSTAND) without assistance in <10 seconds, and able to swallow tablets successfully Those who were excluded were anyone who had a current of history of major renal or hepatic impairment, diabetes of immunosuppression, evidence of symptomatic CM (asymptomatic cardiac abnormality not exclusionary), and anyone taking/has taken 3 months prior to first dose of study medication any drug indicated for DMD. The mean age was 5.4 years old who were all boys, 83% were Caucasian. The primary endpoint of the study is the change from baseline (CFB) to week 24 in TTSTAND velocity(rises/sec) for Agamree 6mg/kg/day vs. placebo. The primary endpoint was met, TTSTAND velocity at 6 mg/kg/day versus placebo at 24 weeks of treatment, with a difference from placebo 95% CI 0.060(0.023,0.098, P = 0.002). The safety endpoint was assessed looking at growth, bone biomarkers, and corticotropin. It was seen that height declined in prednisone treated but not Agamree treated patients' baseline [standard deviation (SD)]: prednisone, −1.88 [8.81] percentile; Agamree 6 mg/kg/day, +3.86 [6.16] percentile; P = 0.02). Biomarkers of bone formation and bone turnover showed a statistically significant decline in the prednisone group and not in the Agamree group. All three treatment groups had increased adrenal Insufficiency at baseline. Agamree 2 mg/kg per day, group showed less adrenal suppression than prednisone (mean [SD] change from baseline, −99 [84] nmol/L vs −143 [80] nmol/L; P < .001; whereas Agamree, 6 mg/kg per day, showed greater adrenal suppression than prednisone (mean [SD] change from baseline, −195 [84] nmol/L vs −143 [80] nmol/L; P = .03). In terms of adverse events there were more adverse events in the prednisone group in comparison to the Agamree groups.

Looking at the safety profile of Agamree, there are no major contraindications to Agamree besides any hypersensitivity reactions to components of Agamree. Common side effects include cushingoid features, weight gain, and vitamin d deficiency. Pertinent warnings and precautions include that Agamree can cause adrenal insufficiency, increased risk of infections, and to avoid live vaccines during the treatment of Agamree.

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

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

Financial Discussion: No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.
Outcome: Agamree will be a pharmacy benefit. Agamree will not be added to the commercial, exchange and CHIP formularies at this time and will require prior authorization. The following prior authorization criteria will apply:

- Medical record documentation that Agamree is prescribed by a neurologist or pediatric neurologist **AND**
- Medical record documentation of interdisciplinary team involvement including, but not limited to, neurology, pulmonology, and cardiology **AND**
- Medical record documentation of a diagnosis of Duchenne muscular dystrophy (DMD), confirmed by genetic testing **AND**
- Medical record documentation of age greater than or equal to 2 years **AND**
- Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to prednisone **AND** deflazacort

QUANTITY LIMIT: 300 mg/day

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.

FABHALTA (iptacopan)

Review: Fabhalta is a complement factor B inhibitor indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH). It binds Factor B of the alternative complement pathway and regulates the cleavage of C3, controlling C3b-mediated extravascular hemolysis and terminal compliment-mediated intravascular hemolysis. Fabhalta is the first approved oral complement inhibitor indicated for PNH.

The recommended dosage of Fabhalta is 200 mg orally twice daily without regard to food. Patients switching from Soliris should initiate Fabhalta no later than 1 week after the last dose of Soliris. Patients switching from Ultomiris should initiate Fabhalta no later than 6 weeks after the last dose of Ultomiris. Fabhalta is supplied as 200 mg capsules. Prior to initiating Fabhalta, patients should be vaccinated against encapsulated bacteria, including Streptococcus pneumoniae and Neisseria meningitidis (serogroups A, C, W, Y and B), according to current ACIP recommendations.

The safety and efficacy of Fabhalta was evaluated in the APPLY-PNH, an open-label, 24-week, active comparator-controlled trial in 97 anti-C5 treatment-experienced adult patients with PNH. The study included patients with PNH and residual anemia (hemoglobin < 10 g/dL) despite previous treatment with a stable regimen of anti-C5 treatment (Soliris or Ultomiris) for at least 6 months prior to randomization. Patients were randomized in 8:5 ratio to switch to Fabhalta 200 mg twice daily or continue anti-C5 treatment throughout the duration of the 24-week randomized controlled period. Following completion of the 24-week randomized controlled period, all patients were eligible to enroll in a 24-week treatment extension period and receive Fabhalta monotherapy. Subsequently, patients were eligible to enter a long-term extension study.

Efficacy was based on superiority of switching to Fabhalta compared to continuing on anti-C5 therapy in achieving hematological response after 24 weeks of treatment, without need for transfusion, by assessing proportion of patients demonstrating a sustained increase (≥ 2 g/dL) in Hgb levels from baseline and sustained Hgb levels ≥ 12 g/dL. Additional endpoints included transfusion avoidance, change from baseline in hemoglobin levels, and change from baseline in absolute reticulocyte counts.

The APPOINT-PNH study, was a single-arm study evaluating the efficacy in 40 complement inhibitor naïve adult patients with PNH. Patients included in the trial had hemoglobin < 10 g/dL and LDH > 1.5 times the upper limit of normal (ULN). The trial excluded patients with evidence of bone marrow failure, active systemic infections, history of recurrent invasive infections caused by encapsulated organisms, and

major concurrent comorbidities. All patients received Fabhalta 200 mg orally twice daily during the 24-week open-label core treatment period. Subsequently, patients were eligible to enroll in a 24-week treatment extension period and continue to receive Fabhalta, followed by a long-term extension study.

In total, 77.5% of patients achieved a sustained increase (between Day 126 and Day 168) in hemoglobin levels from baseline of ≥ 2 g/dL in the absence of RBC transfusions. In a sensitivity analysis, 87.5% of patients achieved a sustained increase (between Day 126 and Day 168) in hemoglobin levels from baseline of ≥ 2 g/dL in the absence of RBC transfusions.
Fabhalta has a black box warning for serious infections caused by encapsulated bacteria. Life threatening and fatal infections with encapsulated bacteria has occurred with both vaccinated and unvaccinated patients treated with complement inhibitors. Fabhalta should not be initiated in patients with unresolved serious infections caused by encapsulated bacteria. Patients established on Fabhalta who require treatment for serious infections should consider interruption of Fabhalta. Fabhalta is available through a REMS program due to the risk of serious infection.

Other warnings for Fabhalta include hyperlipidemia, including increases in total cholesterol, LDL-cholesterol, and serum triglycerides. Patients discontinuing Fabhalta will need to continue to be closely monitored for at least 2 weeks after the last dose for signs and symptoms of hemolysis, including elevated lactate dehydrogenase (LDH) levels along with sudden decrease in hemoglobin or PNG clone size, fatigue, hemoglobinuria, abdominal pain, dyspnea, major adverse vascular events (i.e. thrombosis, stroke, MI), dysphagia, or erectile dysfunction.

In APPLY-PNH, serious adverse reactions were reported in 2 (3%) of patients and included pyelonephritis, urinary tract infection, and COVID-19. IN APPOINT-PNH, serious adverse reactions were reported in 2 (5%) of patients and included COVID-19 and bacterial pneumonia. The most common adverse reactions reported with Fabhalta treatment were headache, nasopharyngitis, diarrhea, abdominal pain, bacterial infection, viral infection, nausea, and rash.

Drug interactions of Fabhalta include CYP2C8 inducers (decrease Fabhalta exposure, decreased efficacy) and CYP2C8 inhibitors (increase Fabhalta exposure, increased risk of adverse reactions). Coadministration with a strong CYP2C8 inhibitor is not recommended.

The safety and efficacy of Fabhalta has not been established in pediatric patients. During the 24-week treatment period in APPLY-PNH and APPOINT-PNH, 21 (20.6%) of patients were 65 years and older and 7 (6.9%) were 75 years and older. Clinical studies did not include sufficient numbers of patients aged 65 years and older to determine if they respond differently from younger subjects. The use of Fabhalta is not recommended in patients with severe renal impairment with or without hemodialysis. No dose adjustment is required in patients with mild or moderate renal impairment. The use of Fabhalta is not recommended in patients with severe hepatic impairment. No dose adjustment is required for patients with mild or moderate hepatic impairment.

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

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

Financial Discussion: Dr. Yarczower suggested that we look into prevalence within the GHP population to assist with projections. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Outcome: Fabhalta is a pharmacy benefit that will be added to the Specialty tier or the Brand Non-preferred tier for members with a three-tier benefit of the Commercial, Marketplace, and CHIP formularies. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) **AND**

- Medical record documentation of flow cytometry confirming diagnosis **AND**
- Medical record documentation that Fabhalta is prescribed by a hematologist **AND**
- Medical record documentation that member has received vaccinations against encapsulated bacteria, including Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae type B **AND**
- Medical record documentation of one of the following:
    - member is transfusion-dependent (i.e., has at least 1 transfusion in the 24 months prior to initiation of iptacopan due to documented hemoglobin less than 7 g/dL in persons without anemic symptoms or less than 9 g/dL in persons with symptoms from anemia) prior to initiation of iptacopan treatment; **OR**
    - there is a significant adverse impact on the insured individual's health such as end organ damage or thrombosis without other cause

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

- Medical record documentation of:
    - Hemolysis control measured by lactic acid dehydrogenase (LDH) level less than 1.5 times the upper limit of normal (ULN) **AND**
    - Reduced need or elimination of transfusion requirements **OR**
    - Stabilization of hemoglobin levels

QUANTITY LIMIT: 2 capsules per day, 30 day supply per fill

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.

COXANTO (oxaprozin)

Review: Coxanto is a non-steroidal anti-inflammatory drug indicated for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, or juvenile rheumatoid arthritis (6 to 16 years old). Oral non-steroidal anti-inflammatory drugs (NSAIDs) are a mainstay of treatment for arthritis and are included in the management of symptom relief.

Coxanto was approved from clinical studies using other formulations of oxaprozin. For osteoarthritis, oxaprozin was evaluated for the management of signs and symptoms in active-controlled trials against aspirin (N=464), piroxicam (N=102) and other NSAIDs. Oxaprozin was given in doses of 600 to 1,200 mg in either divided or single doses. It was shown oxaprozin was comparable in efficacy to 2,600 mg to 3,200 mg per day of aspirin or 20 mg per day of piroxicam. For rheumatoid arthritis, oxaprozin was evaluated for the management of signs and symptoms in placebo and active-controlled clinical trials. It was shown that the efficacy of oxaprozin 600 to 1,800 mg per day in single or divided doses was comparable to 2,600 to 3,900 mg per day of aspirin with a trend of less gastrointestinal side effects. Regarding juvenile rheumatoid arthritis, a 3-month open-label study was conducted with oxaprozin (N=59) and ended with 52 patients completing the 3-month therapy with a mean dose of 20mg/kg/day. As noted in the studies, it took several days of oxaprozin therapy to reach its full effect.

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

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

Financial Discussion: Dr. Bhatt asked if this can be used in ankylosing spondylitis? Jill Stone responded that it's not FDA approved but it can likely be used in any disease state typically treated with an NSAID. Given the significant cost versus alternatives it does not provide significant advantages to alternatives. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

- Medical record documentation of a diagnosis of osteoarthritis, rheumatoid arthritis, OR juvenile rheumatoid arthritis **AND**
- Medical record documentation of age ≥ 6 years **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three (3) formulary alternatives, one of which must be oxaprozin 600mg tablet

QUANTITY LIMIT: 4 capsules per day

GPI LEVEL: GPI-12

RPH SIGNOFF REQUIRED: no

FORMULARY ALTERNATIVES: celecoxib, choline magnesium salicylate, diclofenac, diclofenac extended release, diflunisal, etodolac, etodolac extended release, fenoprofen, flurbiprofen, ibuprofen, indomethacin, indomethacin sustained-release, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, naproxen ec, oxaprozin, piroxicam, salsalate, sulindac, tolmetin

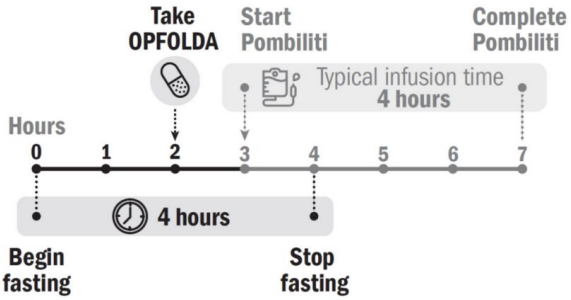
Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

POMBILITI (cipaglucosidase alfa-atga) & OPFOLDA (miglustat)

Review: Pombiliti and Opfolda are indicated in combination for the treatment of adults with late-onset Pompe disease (lysomal acid alpha-glucosidase [GAA] deficiency) weighing at least 40 kg and who are not improving on their current enzyme replacement therapy (ERT). Pombiliti provides an exogenous source of GAA. It binds M6P receptors on the cell surface, is internalized where it undergoes proteolytic cleavage, and then exerts enzymatic activity in cleaving glycogen. Opfolda is a stabilizer that reduces inactivation of Pombiliti in the blood after infusion.

Pombiliti and Opfolda are initiated 2 weeks after the last ERT dose. Opfolda is administered orally 1 hour prior to the intravenous administration of Pombiliti (Figure 2). The recommended dosage of Opfolda is based on body weight: for patients ≥ 50 kg, the dosage is 260 mg orally every other week, for patients ≥ 40 kg to < 50 kg, the recommended dosage is 195 mg orally every other week. Opfolda is administered whole with only unsweetened beverages and no other beverages or food should be consumed for at least two hours prior and two hours after administration of Opfolda. The recommended dosage of Pombiliti is 20 mg/kg (of actual body weight) administered every other week as an intravenous infusion over approximately 4 hours.

Figure 2. Pombiliti/Opfolda Dosing Timeline



If Pombiliti cannot be started within 3 hours of the oral administration of Opfolda, administration of both meds should be rescheduled for at least 24 hours after Opfolda was last taken. Prior to the Pombiliti administration, pretreatment should be considered with antihistamines, antipyretics, and/or corticosteroids and should be used if pretreatment was used with previous enzyme replacement therapy.

A dosage reduction for Opfolda is recommended in patients with moderate or severe renal impairment (Table 5). No dosage adjustments are recommended for patients with mild renal impairment.

Table 5. Recommended dosage of Opfolda with Renal Impairment

Patient Weight	Moderate Renal Impairment* (CLcr 30-59 mL/minute)	Severe Renal Impairment* (CLcr 15-29 mL/minute)
≥50 kg	195 mg	195 mg
≥40 kg to <50 kg	130 mg	130 mg

* Renal function classified by CLcr (creatinine clearance) based on the Cockcroft-Gault equation.

Opfolda is supplied as 65 mg capsules. Pombiliti is supplied as single dose vials containing 105 mg as lyophilized powder for reconstitution.

The efficacy and safety of Pombiliti and Opfolda were evaluated in a randomized, double-blind, active-controlled clinical trial in 123 adult patients diagnosed with late-onset Pompe disease (LOPD). Patients were randomized 2:1 to receive the recommended dosage of Opfolda + Pombiliti or non-U.S. approved alglucosidase alfa product with placebo every other week for 52 weeks. The efficacy population included 123 patients of whom 95 (77%) had received prior treatment with alglucosidase alfa (ERT-experienced) and 28 (23%) were ERT-naïve. Key efficacy endpoints included assessment of sitting FVC (% predicted) and 6MWD. Efficacy results are shown in Table 6.

Table 6. Efficacy Results of PROPEL Study by ERT Status at Week 52

Table 4. PROPEL Study: Efficacy Results by ERT Status at 52 Weeks				
Efficacy Endpoint	**ERT-Experienced**		**ERT-Naïve[a]**	
6MWD	**Opfolda + Pombiliti**	**Alglucosidase Alfa[b] + Placebo**	**Opfolda + Pombiliti**	**Alglucosidase Alfa[b] + Placebo**
Baseline, Mean (SD)	347 (110)	335 (114)	394 (112)	421 (136)
CFB at Week 52, Mean (SD)	16 (39)	1 (40)	33 (49)	38 (29)
Change to Week 52 Difference of Means (SE) (95% CI)	17[c] (8) (0.2, 33)		−5 (20) (−45, 36)	
Sitting FVC (% Predicted)	**Opfolda + Pombiliti**	**Alglucosidase Alfa[b] + Placebo**	**Opfolda + Pombiliti**	**Alglucosidase Alfa[b] + Placebo**
Baseline, Mean (SD)	67.9 (19.1)	67.5 (21.0)	80.2 (18.7)	79.6 (21.0)
CFB at Week 52, Mean (SD)	0.1 (5.9)	−3.5 (4.7)	−4.7 (6.2)	−2.4 (6.3)
Change to Week 52 Difference of Means (SE) (95% CI)	3.5 (1.3) (1.0, 6.0)		−1.9 (2.7) (−7.3, 3.6)	

Abbreviations: 6MWD, 6-minute walking distance; CFB, change from baseline; CI, confidence interval; ERT, enzyme replacement therapy; FVC, forced vital capacity; SD, standard deviation; SE, standard error. aOpfolda in combination with Pombiliti is not approved for use in ERT-naïve patients with LOPD. The ERT-naïve patient subgroup enrolled too few patients to conclusively interpret the data. bAn FDA-approved alglucosidase alfa product was not used in this clinical trial. Conclusions cannot be drawn from this clinical trial regarding comparative effectiveness between an FDA-approved alglucosidase alfa product and Opfolda in combination with Pombiliti for the treatment of adult patients with LOPD weighing ≥40 kg and who are not improving on their current ERT. c For the ERT-experienced group, the treatment difference of the mean was estimated by nonparametric analysis of covariance which included treatment, gender, baseline 6MWD, age, weight, and height in the model. Nominal P = 0.047. Missing data at Week 52 was imputed using last observed values.

ERT-experienced patients treated with Pombiliti+Opfolda had a numerically favorable change in sitting FVC and 6MWD from baseline at Week 52.

Warnings for Opfolda includes embryo-fetal toxicity and risks associated with Pomboliti. Based on animal reproduction studies, Opfolda in combination with Pombiliti may cause embry-fetal harm and is contraindicated during pregnancy. Since Opfolda must be administered in combination with Pombiliti, other warnings are based on additional risks associated with Pombiliti.
In addition to embryo-fetal toxicity, warnings for Pombiliti include hypersensitivity reactions, infusion-associated reactions, risk of acute cardiorespiratory failure in susceptible patients. Life-threatening hypersensitivity reactions, including anaphylaxis, have been reported in Pombiliti-treated patients. In clinical trials, 27% of patients experienced hypersensitivity reactions, including 4 (3%) patients who reported severe hypersensitivity reactions and 4 (3%) patients who experienced anaphylaxis. Infusion-related reactions were reported to occur at any time during and/or within a few hours after the Pombiliti infusion. IARs were reported in 48 (32%) Pombiliti-treated patients in clinical trials. Four (3%) Pombiliti-treated patients reported 11 severe IARs, including pharyngeal edema, anaphylactic reaction, urticaria, pruritis, chills, dyspnea, and flushing. The majority of IARs were mild to moderate in severity. Premedication can be given prior to Pombiliti administration to reduce the risk of IARs, but IARs can still occur.

Patients susceptible to fluid volume overload or those with acute underlying respiratory illness or compromised cardiac or respiratory function for whom fluid restriction is indicated may be at risk of exacerbation of cardiac or respiratory status during infusion.

In the pooled safety data from clinical trials, the most common adverse reactions included headache, diarrhea, fatigue, nausea, abdominal pain, and pyrexia. In the PROPEL Study, the most common adverse reactions were headache and diarrhea. Additional adverse reactions reported in at least 2% of patients include myalgia, arthralgia, increased blood pressure, pain, tremor, dyspepsia, asthenia, constipation, infusion site swelling, flank pain, malaise, paresthesia, and decreased platelet count.

The safety and efficacy of Pombiliti and Opfolda have not been established in pediatric patients. Of the total number of patients with LOPD treated with combination Opfolda + Pombiliti, 17(11%) were 65 to 74 years old and none were 75 years and older. Clinical trials did not include sufficient numbers of patients 65 years of age and older to determine if they respond different from younger adult patients.

Plasma concentrations of Opfolda increased in patients with renal impairment. No adjustment is needed for patients with mild impairment. Patients with moderate to severe impairment should adjust the dosage as noted above (see Table 5).

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. Yarczower suggested reaching out to Dr. Priya Kishnani at Duke for additional clinical input. She has previously provided feedback on Lumizyme and Nexviazyme. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

Financial Discussion: Keith Hunsicker proposed adding Pombiliti to the site-of-care policy at the next available opportunity given the other enzyme replacement therapies are included in the program. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

Pombiliti is a medical benefit that will require a prior authorization. Pombiliti will be added to the medical benefit cost share list. Pombiliti will also be reviewed with the MBP 181.0 Site of Care Policy. The following prior authorization criteria will apply:

- Medical record documentation of a diagnosis of late-onset Pompe disease supported by:
    - Acid alpha-glucosidase (GAA) assay performed on dried blood spots, skin fibroblasts or muscle biopsy **AND**
    - Genetic testing showing a mutation in the GAA gene

AND

- Medical record documentation of a consultation with a metabolic specialist and/or biochemical geneticist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of baseline percent-predicted forced vital capacity (% FVC) and 6-minute walk test (6MWT) **AND**
- Medical record documentation of member weight ≥ 40 kg **AND**
- Medical record documentation that Opfolda and Pombiliti will be used in combination **AND**
- Medical record documentation that member is currently receiving enzyme replacement therapy (e.g. Lumizyme, Nexviazyme) and is not experiencing improvement **AND**
- Medical record documentation that Polmbiliti and Opfolda will not be used concurrently with other enzyme replacement therapy (e.g. Lumizyme, Nexviazyme)

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

- Medical record documentation of improvement or stabilization in percent-predicted forced vital capacity (% FVC) and/or 6-minute walk test (6MWT) **AND**
- Medical record documentation of member weight ≥ 40 kg **AND**
- Medical record documentation that Opfolda and Pombiliti will be used in combination **AND**
- Medical record documentation that Polmbiliti and Opfolda will not be used concurrently with other enzyme replacement therapy (e.g. Lumizyme, Nexviazyme)

QUANTITY LIMIT: Opfolda: 8 capsules per 28 days

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.

PENBRAYA (Meningococcal Serotypes A,B,C,W and Y Vaccine)

Review: In the United States, there are 3 different types of meningococcal vaccines available. Those vaccines include Meningococcal Conjugate which protects against the MenACWY serotypes(Menveo and Menquadfi), Meningococcal B vaccine which offers protection against serotype B(Bexsero or Trumenba) and Penbraya (Meningococcal Serotype A,B,C,W,Y) which is the first pentavalent vaccine that offers protections against 5 different meningococcal serotypes in a single vaccine. Penbraya was FDA approved in 2023 and is indicated for active immunization to prevent invasive disease caused by Neisseria meningitidis serogroups A, B, C, W, Y and is approved for use in individuals 10 through 25 years of age who would generally be indicated to receive 2 different Meningococcal vaccines Men B (Trumenba and Bexsero) and MenACWY(Menveo and Menquadfi) at the same clinic visit. According to the ACIP (Advisory Committee on Immunization Practices) recommendations, MenACWY serotype vaccines are indicated as part of the routine childhood vaccination schedule and should be administered as a first dose between the ages of 11-12 years of age. A booster or second dose of MenACWY is indicated at age 16 years of age with a catch-up schedule established for those individuals that had a delay in vaccination. MenB serotype vaccines (Bexsero and Trumenba) are not routinely administered as part of the childhood vaccination schedule but are reserved for those that have risk factors that would cause an increased risk of infections. Special circumstances for MenB administration include anatomic or functional asplenia (including sickle cell disease), persistent complement component deficiency and complement inhibitor (e.g., eculizumab, ravulizumab) use. Other high-risk individuals potentially recommended to receive MenB vaccine include college students, particularly first-year students living in on-campus housing and children, adolescents and young adults residing in institutional settings, glucocorticoid excess, diabetes mellitus, alcoholism, hypogammaglobulinemia, and HIV infection. Meningitis is an infection that causes inflammation of the fluid and membranes surrounding the brain and spinal cord. Neisseria meningitidis is the leading cause of bacterial meningitis in children and young adults in the United States, with an overall mortality rate of 13 percent, and it is the second most common cause of community-acquired adult bacterial meningitis [1]. The typical presentation of disease is a sudden onset of fever, headache, nausea, vomiting and decreased ability to concentrate. The classic triad of symptoms are fever, neck stiffness and altered mental status. The disease can also present with severe myalgias. Transmission of meningitis occurs via three major routes which includes colonization of the nasopharynx, with subsequent bloodstream invasion followed by central nervous system (CNS) invasion. Invasion of the CNS following bacteremia due to a localized source and direct entry of organisms into the CNS from a contiguous infection (e.g., sinuses, mastoid), trauma, or a cerebrospinal fluid (CSF) leak. To prevent infection with A,B,C,W,Y serotypes, the ACIP guidelines recommend Penbraya be administered to children aged 10 years or older as an alternative to separate administration of MenACWY and MenB when both vaccines would be given on the same clinic day. For age-eligible children not at increased risk, if Penbraya is used for dose 1 MenB, MenB-FHbp (Trumenba) should be administered 6 months later for dose 2 of MenB since MenB vaccines(Trumenba and Bexsero) are not interchangeable. For age-eligible children at increased risk of meningococcal disease, Penbraya may be used for an additional MenACWY and MenB dose (including booster doses) if both would be given on the same clinic day and at least 6 months have elapsed since most recent Penbraya dose. Penbraya is supplied as a vial of lipolyzed MenACWY vaccine powder to be reconstituted with a prefilled solution of MenB vaccine. The components are then to be drawn up in a syringe with a final volume of 0.5 ml to be administered intramuscularly according to the ACIP guidelines and clinical decision making for those that may be at risk of disease. Penbraya works by complement-mediated antibody-dependent killing of N. meningitidis. Vaccination induces the production of bactericidal antibodies specific to the capsular polysaccharides of N. meningitidis serogroups A, C, W,

and Y and to fHbp subfamily A and B variants of N. meningitidis group B. The effectiveness of Penbraya was determined in Study 1 {NCT04440163},a non-inferiority study, which was a phase 3, randomized, active controlled, observer-blinded, multicenter study conducted across 78 study locations in the United States and Europe. Inclusion criteria included patients aged 10-26 years old, negative pregnancy test, serotype ACWY naïve and exposed with patients not having been vaccinated no sooner than 4 years prior. All participants were excluded if they had a prior vaccine with serotype MenB. Participants were randomized to receive either a dose of Penbraya at 0 and 6 months or a dose of Trumenba (MenB) at 0 and 6 months plus MenACWY-CRM(Menveo) at 0 months. Efficacy was determined per meningitis serotype(ACWY and B) and previous meningitis vaccination naïve vs non-naïve vaccine by measuring antibodies with assays that used human complement to assess serum bactericidal activity (hSBA). Primary endpoints included a 4-fold or greater increase in titer for each strain, and the proportion of subjects with a titer greater than or equal to the lower limit of quantitation (LLOQ) which was 1:4. Seroresponse rates to serogroups A, C, W, and Y following 2 doses of Penbraya were determined to be non-inferior to seroresponse rates following a single dose of MenACWY-CRM(Menveo). Seroresponse rates to serogroup B primary strains among participants who received 2 doses of Penbraya were demonstrated to be non-inferior to seroresponse rates following 2 doses of Trumenba. However, according to the ACIP guidelines, 2 doses of Penbraya administered 6 months apart are recommended as an alternative for high-risk patients instead of administering MenACWY and Trumenba at dose 1 followed by a 2nd dose of Trumenba 6 months later. For patients, not at high risk but still indicated to receive both MenACWY and MenB vaccines, Penbraya can be administered followed by a dose of Trumenba 6 months later, the outcome for this scenario was not compared in this study.
Adverse reactions after Dose 1 and Dose 2, respectively, were pain at the injection site (89% and 84%), fatigue (52% and 48%), headache (47% and 40%), muscle pain (26% and 23%), injection site redness (26% and 23%), injection site swelling (25% and 24%), joint pain (20% and 18%), and chills (20% and 16%).

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

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

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

Outcome: Penbraya will be both a medical and pharmacy benefit for members 10 years and older. It will be added to the vaccine tier and will be covered as a preventative vaccine for $0 copay.
Additional evidence of the criteria used to make this decision can be found in the drug review presented to the committee.

JYLAMVO (methotrexate oral solution)

Review: Jylamvo is a new formulation of methotrexate indicated for the treatment of adults with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen, mycosis fungoides (cutaneous T-cell lymphoma) as a single agent or part of combination chemotherapy maintenance regimen, relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination regimen, rheumatoid arthritis, and severe psoriasis.

The efficacy and safety of Jylamvo is based on previous findings of safety and efficacy of methotrexate oral tablets. No new clinical trials were conducted to evaluate the safety and efficacy of Jylamvo. The approval of Jylamvo was supported by one comparative bioavailability study comparing Jylamvo oral solution to methotrexate sodium tablets and assessment of food-effect evaluating methotrexate oral solution in the fasted and fed states. No new safety signals have been identified.

Methotrexate has been available since 1953 in several different formulations including tablets, intramuscular injection, intravenous injection, subcutaneous injection, intra-arterial injections, and intra-thecal injections. Xatmep is another methotrexate oral solution formulation approved in 2017 indicated for the treatment of pediatric patients with ALL as a component of chemotherapy and active polyarticular juvenile idiopathic arthritis (pJIA) who are intolerant of or had an inadequate response to first-line therapy. Xatmep currently has exclusivity for use in children with ALL and pJIA.

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

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

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

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

Neoplastic Diseases

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of one of the following:
    - Acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen **OR**
    - Relapsed or refractory non-Hodgkin lymphoma as part of a metronomic combination chemotherapy regimen **OR**
    - Mycosis fungoides (cutaneous T-cell lymphoma) as a single agent or part of combination chemotherapy regimen **AND**
- Medical record documentation that member is unable to swallow tablets **OR** medical record documentation of therapeutic failure on, intolerance to, or contraindication to methotrexate tablets

Rheumatoid Arthritis

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of rheumatoid arthritis **AND**
- Medical record documentation that member is unable to swallow tablets **OR** medical record documentation of therapeutic failure on, intolerance to, or contraindication to methotrexate tablets

Psoriasis

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of severe psoriasis characterized by greater than or equal to 5% of body surface area involved or disease involving crucial body areas such as the hands, feet, face, or genitals **AND**
- Medical record documentation that member is unable to swallow tablets **OR** medical record documentation of therapeutic failure on, intolerance to, or contraindication to methotrexate tablets

QUANTITY LIMIT: 30 single-dose container (6mL) per 30 days

GPI LEVEL: GPI-12

FORMULARY ALTERNATIVES:

ALL: methotrexate tablets
RA: methotrexate tablets, celecoxib, choline magnesium salicylate, diclofenac, diclofenac extended release, diflunisal, etodolac, etodolac extended release, fenoprofen, flurbiprofen, ibuprofen, indomethacin, indomethacin sustained release, ketoprofen, ketorolac, meclofenamate, meloxicam, nabumetone, naproxen, naproxen sodium, naproxen EC, oxaprozin, piroxicam,

salsalate, sulindac, tolmetin
Psoriasis: methotrexate tablets
Low-potency topical corticosteroids: alclometasone dipropionate 0.5% cream and ointment (Aclovate); desonide 0.05% cream, ointment and lotion (Desowen); fluocinolone acetonide 0.01% cream, solution, body and scalp oil (Synalar/Derma-Smoothe); hydrocortisone 1% and 2.5% cream, ointment, and lotion (Hytone)
Medium-potency topical corticosteroids: betamethasone valerate 0.1% cream and lotion (Valisone); fluocinolone acetonide 0.025% cream and ointment (Synalar); flurandrenolide 0.05% cream, ointment, and lotion (Cordran); fluticasone propionate 0.05% cream and lotion (Cutivate); hydrocortisone butyrate 0.1% cream, ointment and solution (Locoid); hydrocortisone valerate 0.2% cream and ointment (Westcort); mometasone 0.1% cream (Elocon); prednicarbate 0.1% cream and ointment (DermAtop); triamcinolone acetonide 0.025% cream, ointment and lotion (Kenalog); triamcinolone 0.1% cream, ointment and lotion (Kenalog); triamcinolone acetonide 0.147 mg/g aerosol (Kenalog Spray)
High-potency topical corticosteroids: amcinonide 0.1% cream, ointment and lotion (Cyclocort); augmented betamethasone dipropionate 0.05% cream (Diprolene AF); betamethasone dipropionate 0.05% cream, ointment and lotion (Diprolene); betamethasone valerate 0.1% ointment (Valisone); betamethasone valerate 0.12% foam (Luxiq); desoximetasone 0.25% cream, ointment and 0.05% cream, gel, ointment (Topicort/Topicort LP);); diflorasone 0.05% cream (Florone/Psorcon); fluocinonide 0.05% cream, ointment, gel and solution (Lidex); fluticasone 0.005% ointment (Cutivate); mometasone 0.1% ointment (Elocon); triamcinolone 0.5% cream and ointment (Kenalog)
Very high-potency topical corticosteroids: augmented betamethasone dipropionate 0.05% ointment, gel and lotion (Diprolene); clobetasol 0.05% cream, ointment, scalp lotion, shampoo, foam (Temovate/Clobex/Olux); diflorasone diacetate 0.05% ointment (ApexiCon/Psorcon E); fluocinonide 0.1% cream (Vanos); halobetasol 0.05% cream and ointment (Ultravate)

RPH SIGNOFF REQUIRED: no

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

VEVYE (cyclosporine ophthalmic solution)

Review: Vevye is a calcineurin inhibitor indicated for the treatment of the signs and symptoms of dry eye disease. Vevye is a selective immunomodulator, but the exact mechanism of action is unknown. The preservative free solution delivers 0.01mg of cyclosporine per one drop (0.01mL) and is supplied in a multi-dose 2mL bottle. Patients should instill one drop of Vevye twice a day in each eye approximately 12 hours apart.

The safety and efficacy of Vevye was evaluated using two multicenter, randomized clinical studies (CYS-002:NCT02617667 and CYS-004:NCT04523129) in a total of 1,369 patients with dry eye disease, of which 738 patients received Vevye treatment. After 29 days of treatment, 10% of Vevye-treated patients had an increase of 10mm or more from baseline in Schirmer wetting versus 6% of vehicle-treated patients. There were no clinical trials performed directly comparing Vevye to other formulations of cyclosporine or dry eye disease treatments.

There are no contraindications to Vevye. Like other ophthalmic solutions, patients should not touch the bottle tip to the eye or other surfaces to avoid potential for eye injury and/or contamination. Vevye should not be administered while wearing contact lenses. Once administered, contact lenses should be reinserted 15 minutes later. The most common adverse reactions in patients in clinical trials receiving at least 1 dose of Vevye were instillation site reactions (8%) and temporary decreases in visual acuity (3%). The safety and efficacy of Vevye in pediatric patients have not been established. No overall differences in safety and efficacy of Vevye has been observed between patients 65 years of age and older and younger adult patients.

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

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

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

Outcome: Vevye is a pharmacy benefit and will not be added to Commercial, Marketplace, and CHIP formularies. It will be added to the Commercial Policy 596.0 Cequa, which has the following prior authorization criteria:

- Medical record documentation of a diagnosis of keratoconjunctivitis sicca (dry eye) **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Xiidra (lifitegrast) **AND** cyclosporine (generic Restasis)

GPI LEVEL: GPI-12

QUANTITY LIMIT: Update policy to reflect Cequa quantity limits only:

- For Cequa: 2 vials per day

RPH SIGNOFF REQUIRED: no

FORMULARY ALTERNATIVES: cyclosporine 0.05% emulsion (generic Restasis), Xiidra

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

BIMZELX (bimekizumab-bkzx)

Review: Bimzelx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. Bimzelx is a humanized immunoglobulin IgG1/κ that selectively binds to human interleukin 17A (IL-17A), interleukin 17F (IL-17F), and interleukin 17 AF cytokines, and inhibits the interaction with the IL-17 receptor complex. IL-17A and IL-17F are naturally occurring cytokines that are involved in normal inflammatory and immune responses. Bimzelx inhibits the release of proinflammatory cytokines and chemokines.
The recommended dosage of Bimzelx is 320 mg (given as 2 subcutaneous injections of 160 mg each) at Weeks 0, 4, 8, 12 , and 16, then every 8 weeks thereafter. For patients ≥ 120 kg, consider a dosage of 320 mg every 4 weeks after week 16. Prior to initiating Bimzelx, patients should be evaluated for tuberculosis infection, liver enzyme, alkaline phosphatase, and bilirubin levels, and complete all age-appropriate vaccinations according to guidelines. Bimzelx is supplied as a single-dose prefilled syringe or a single-dose prefilled autoinjector containing 160 mg/mL.

The efficacy and safety of Bimzelx was evaluated in BE VIVID, BE READY, and BE SURE, three randomized, double-blind trial in 1480 patients 18 years and older with moderate to severe plaque psoriasis who had a body surface area (BSA) involvement of at least 10%, an Investigator's Global Assessment (IGA) score of ≥ 3 in the overall assessment of psoriasis on a severity scale of 0 to 4, and a Psoriasis Area Severity Index (PASI) score ≥ 12.

In BE VIVID, 567 patients were randomized to receive Bimzelx 320 mg subcutaneously every 4 weeks, ustekinumab, or placebo through Week 52. At week 16, subjects originally randomized to placebo received Bimzelx 320 mg every 4 weeks through Week 52.

In BE READY, 435 patients were randomized to either Bimzelx 320 mg subcutaneously every 4 weeks or placebo. At Week 16, patients who achieved a PASI 90 response continued into a 40-week randomized withdrawal period. Patients originally randomized to Bimzelx 320 mg every 4 weeks were re-randomized to Bimzelx 320 every 4 weeks or Bimzelx 320 mg every 8 weeks or placebo. Patients originally randomized to placebo continued to receive placebo if they were PASI 90 responders. Subjects who did not achieve a PASI 90 response at week 16 entered an open-label escape arm and received Bimzelx 320 mg every 4 weeks for 12 weeks. Subjects who relapsed, defined as less than PASI-75 response compared to baseline, during the randomized withdrawal period also entered the 12-week escape arm.
In BE SURE, 478 patients were randomized to receive either Bimzelx 320 mg every 4 weeks through week 56, Bimzelx 320 mg every 4 weeks through week 16 followed by Bimzelx every 8 weeks through week 56, or adalimumab (80 mg as an initial dose followed by 40 mg every other week starting 1 week after initial dose through Week 24) followed by Bimzelx 320 mg every 4 weeks through Week 56.
At baseline, subjects had a median baseline PASI score of 18, median baseline for BSA of 20%, and baseline IGA score of 4 ("severe") in 33% of subjects. A total of 93% subjects had psoriasis of the scalp (Scalp IGA score of ≥1) and a total of 26% of subjects had a history of psoriatic arthritis. Additionally, 38% had received prior biologic therapy.

Coprimary endpoints in BE VIVID and BE READY compared Bimzelx to placebo at Week 16 for the proportion of patients who achieved and IGA score of 0 or 1 with at least a 2-grade improvement from baseline and proportion of patients who achieved at least a 90% reduction from baseline PASI (PASI 90). Secondary endpoints included the proportion of patients who achieved PASI 100, IGA 0, and SCALP IGA response at Week 16, and PASI 75 at week 4. Additional endpoints included assessment of psoriasis symptoms (itching, pain, and scaling) measured by Patients Symptom Diary (PSD) at Week 16. Table 5 shows the proportion of patients who achieved IGA 0 or 1, PASI 90, IGA O, and PASI 100 responses.

Table 5. Efficacy Results at Week 16 In Bimzelx or Placebo-Treated Adults with Plaque Psoriasis in BE VIVID and BE READY

	Trial-Ps-1		**Trial-Ps-2**	
	BIMZELX 320 mg every 4 weeks (N=321) n (%)	**Placebo (N=83) n (%)**	**BIMZELX 320 mg every 4 weeks (N=349) n (%)**	**Placebo (N=86) n (%)**
IGA 0 or 1 ("clear" or "almost clear") [a]	270 (84%)	4 (5%)	323 (93%)	1 (1%)
Difference (95% CI)	79% (73%, 85%)		91% (88%, 95%)	
PASI 90[a]	273 (85%)	4 (5%)	317 (91%)	1 (1%)
Difference (95% CI)	80% (74%, 86%)		90% (86%, 93%)	
IGA 0 ("clear")	188 (59%)	0 (0%)	243 (70%)	1 (1%)
Difference (95% CI)	59% (53%, 64%)		69% (64%, 74%)	
PASI 100	188 (59%)	0 (0%)	238 (68%)	1 (1%)
Difference (95% CI)	59% (53%, 64%)		67% (62%, 73%)	

[a] Co-primary endpoints

Responses were consistent across all subgroups including age, gender, race, baseline IGA score, and previous treatment with systemic or biologic agents at week 16.

A greater proportion of subjects randomized to Bimzelx achieved PASI 75 at Week 4 in both trials compared to placebo. In BE VIVID, 77% of patients achieved PASI 75 compared to 2% with placebo. In BE READY, 76% of patients treated with Bimzelx achieved PASI 75 compared to 1% treated with placebo. Among patients with Scalp IGA score of at least 2 at baseline, a greater proportion of patients randomized to Bimzelx achieved Scalp IGA response at week 16 compared to placebo. In BE VIVID, 845 of patients achieved Scalp IGA response compared to 15% of placebo treated patients. In BE READY,

92% of subjects treated with Bimzelx achieved Scalp IGA response compared to 7% of placebo treated patients.

In BE READY, subjects randomized to Bimzelx every 4 weeks at Week 0 and who were PASI 90 responders at Week 16, were re-randomized to continue treatment with Bimzelx every 4 weeks, switched to Bimzelx every 8 weeks, or be withdrawn from therapy. For IGA 0 or 1 responders at Week 16 who were re-randomized to treatment withdrawal, the median time to loss of IGA 0 or 1 response was approximately 24 weeks. Among the subjects with IGA score of 2 at retreatment, 58% achieved IGA score of 0 within 12 weeks of restarting treatment with Bimzelx 320 mg every 4 weeks. Among these subjects with IGA score ≥ 3 at retreatment, 87% regained IGA or 1 with at least 2-grade improvement from retreatment within 12 weeks of restarting treatment with Bimzelx. For PASI 90 responders at Week 16 who were re-randomized to treatment withdrawal (i.e., placebo), the median time to loss of PASI 90 response was approximately 24 weeks.

Patient Reported Outcomes Greater improvements in itch, pain, and scaling at Week 16 with BIMZELX compared to placebo were observed in both trials as measured by the Patient Symptom Diary (PSD).

Warnings include suicidal ideations, increased risk of infection, tuberculosis infection, liver biochemical abnormalities, inflammatory bowel disease, and risk when administering vaccines. During the 16-week, placebo-controlled period of BE VIVID and BE READY, higher rates of suicidal ideation were reported in Bimzelx treated patients compared to placebo-treated patients. Prescribers should weigh the potential risks and benefits before using Bimzelx in patients with a history of severe depression or suicidal ideation or behavior. During clinical trials, infections occurred in 36% of patients treated with Bimzelx compared to 23% in the placebo group through 16 weeks of treatment. Upper respiratory tract infections, Candida infections, tinea infections, gastroenteritis, and Herpes Simplex infections occurred more frequently in the Bimzelx group compared to placebo. Serious infections occurred in 0.3% of Bimzelx treated patients and 0% treated with placebo.

The most common adverse reactions occurring in at least 1% of patients treated with Bimzelx included upper respiratory infection (URI), oral candidiasis, headache, injection site reactions, tinea infections, gastroenteritis, herpes simplex infections, acne, folliculitis, other candida infections, and fatigue.

The safety and efficacy of Bimzelx has not been established in pediatric patients. Of the 1789 patients exposed to Bimzelx, a total of 153 subjects were 65 years of age or older and 18 subjects were 75 years and older. Although no differences in safety or efficacy were observed between older and younger patients, trials did not include sufficient numbers to determine whether geriatric patients respond differently from younger adult 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. Yarczower asked if it has been evaluated in psoriatic arthritis? Kim Reichard and Dr. Bhatt commented that there are still some clinical trials in progress but it has not yet been approved in PsA. No additional comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

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

- Medical record documentation that Bimzelx is prescribed by a dermatologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of moderate to severe plaque psoriasis characterized by greater than 5% of body surface area involved or disease involving crucial body areas such as the hands, feet, face, or genitals **AND**

- Medical record documentation of an intolerance to, contraindication to or therapeutic failure on four (4) preferred formulary biologics for the treatment of psoriasis **AND**
- Medical record documentation that Bimzelx is not being used concurrently with a tumor necrosis factor (TNF) blocker or other biologic agent **AND**
- If the requested maintenance dosage is 320 mg every 4 weeks, medical record documentation that the prescribed dosing is appropriate for patient's weight

  NOTE: In patients weighing ≥ 120 kg, a dosage of 320 mg every 4 weeks after Week 16 can be considered.

  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 plaque psoriasis on Bimzelx therapy is required.

  RE-AUTHORIZATION CRITERIA:
  - Medical record documentation of continued disease improvement or lack of disease progression** **AND**
  - Medical record documentation of one of the following:
    - Repeated administrations are not being given more frequently than once every 12 weeks **OR**
    - Peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing more frequently than every 12 weeks.

  QUANTITY LIMIT: QLs must be entered within the authorization.
  - 320 mg at Weeks 0, 4, 8, 12, and 16, then 320 mg every 8 weeks.
    1. In NCRx: Add Treat as "Include" Process Modifier, Ignore Misc Handler, 5 in Max Scripts, Max Script Quantity 2, and Max Script Days 28 with a duration of sixteen weeks.
    2. In PA Hub: Add Treat as "Include Process Modifier" with a start date 1 day after the loading dose ends for the remainder of the authorization.
       - **QL for letter:** Loading dosage: 2 milliliters per 28 days, Maintenance dose: 2 milliliters per 56 days
  - 320 mg every 4 weeks
    1. In PA Hub: Add Treat as "Include" Process Modifier, Ignore Misc Handler, Max Script Quantity 2, and Max Script Days 28
       - **QL for letter:** 2 milliliters every 28 days

  GPI LEVEL: GPI-12

  RPH SIGNOFF REQUIRED: Yes

  FORMULARY ALTERNATIVES: adalimumab-fkjp*, Enbrel*, Hadlima*, Humira*, Otezla*, Skyrizi*, Tremfya*, Cosentyx*, Cimzia*, Ilumya*, Siliq*, Yusimry* (*prior authorization required)

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

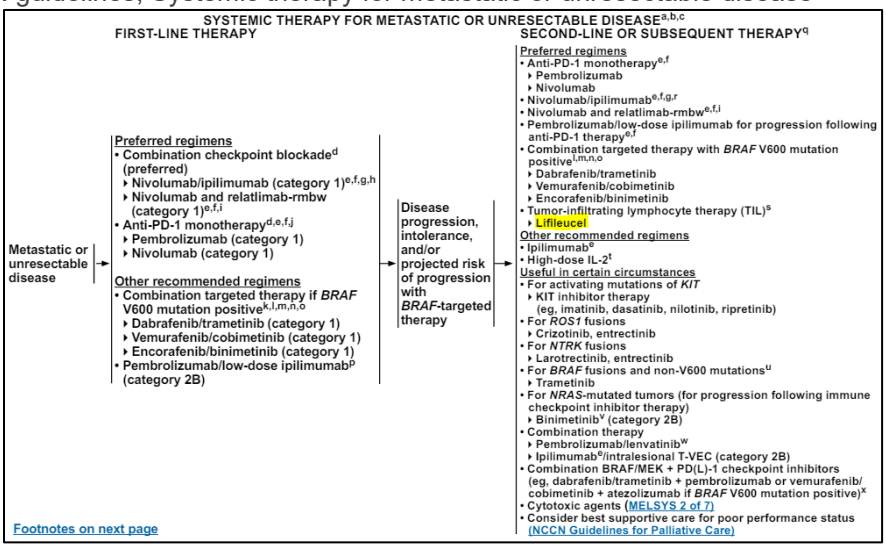
AMTAGVI (lifileucel)

Review: Amtagvi is a tumor-derived autologous T cell immunotherapy indicated for the treatment of adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor. The indication was approved under accelerated approval based on objective response rate (ORR). Continued approval for

the indication will be based on verification and description of clinical benefit in a confirmatory trial. The specific mechanism of action of Amtagvi is unknown.

Amtagvi is the first autologous T cell immunotherapy approved for melanoma. Per NCCN guidelines, preferred first line therapy for metastatic or unresectable disease includes combination checkpoint blockade or anti-PD-1 monotherapy. Other recommended first line therapies are combination BRAF therapies if positive for the BRAF V600 mutation. Amtagvi is listed as a preferred second-line or subsequent therapy, with other subsequent therapies including Anti-PD-1 monotherapy or combination BRAF therapies, assuming not previously used. Before approval of Amtagvi, there was no approved therapies to be given in metastatic disease after failure on a PD-L1 and a BRAF/MEK inhibitor.

Figure 1. NCCN guidelines, Systemic therapy for metastatic or unresectable disease



A future trial is evaluating Amtagvi in combination with Keytruda compared to Keytruda alone for untreated unresectable or metastatic disease (NCT05727904, TILVANCE-301). The estimated primary completion date is March 1, 2028, and full completion on March 1, 2030. RP1, a potential competitor to Amtagvi, is being studied in the Phase 2 trial IGNYTE (NCT03767348) which has expected results March 2024 and submission for Biologics License Application (BLA) in the second half of 2024. RP1 is given intratumorally and given in combination with Opdivo for patients who have progression on at least 8 weeks of anti-PD-1.

Melanoma is the fifth most common cancer, with advanced melanoma (unresectable) affecting 15,000 patients per year, with a 5 year survival of 74% for regional disease, and 35% for metastatic melanoma. About 6,300 patients receive second line treatment for melanoma, while 4,800 patients go on to receive third line therapy. Common sites of metastases include skin, subcutaneous tissue, lungs, liver, bones, and brain, however most melanomas are detected at an early stage. About half of melanomas have the BRAF mutation, for which both BRAF and MEK inhibitors can be used to treat. IPD estimates a total of 7,500 Amtagvi-eligible patients annually.

Amtagvi is for autologous use and intravenous use only. The manufacturing process involves removing a sample of the tumor so that the tumor-infiltrating lymphocytes (TILs) can be amplified in a culture with interleukin-2 (IL-2). It typically takes about 34 days once the manufacturing center receives the sample to have the Amtagvi shipped back to the administering provider, with variations in time possible. Amtagvi is to be administered in an inpatient hospital setting, under the supervision of a physician experienced in the use of anticancer agents. An intensive care unit and specialists skilled in cardiopulmonary or intensive care medicine must be available. Only authorized treatment centers (ATCs) will be permitted to administer the medication, with a target to have 50 ATCs by the end of May 2024.

Once the Amtagvi arrives at the administering facility, it is given as a single dose of 7.5 to 72 x 109 viable tumor derived T cells. Pretreatment lymphodepleting chemotherapy is given, containing cyclophosphamide IV 60 mg/kg with mesna daily for 2 days, followed by fludarabine IV 25mg/m2 daily for 5 days. Amtagvi should then be infused as soon as possible after 24 hours have elapsed following the last dose of fludarabine, and no later than 4 days. Proleukin (aldesleukin) should then be administered 3 to 24 hours after Amtagvi infusion, every 8 to 12 hours for a maximum of up to 6 doses. It is estimated at least 3 days of hospitalization will be required for Amtagvi and Proleukin administration.

Amtagvi is supplied in 1 to 4 infusion bags (NDC 73776-001-11), each bag containing about 100 to 125 mL of frozen suspension of tumor-derived T cells, contained with a protective metal cassette (NDC 73776-001-12). Amtagvi is stored in the vapor phase of liquid nitrogen and supplied in a liquid nitrogen cryoshipper. This is shipped directly to the treatment centers, which should have onsite storage. The bags are thawed and infused individually, at 1 mL per minute for the initial 5 minutes and then 5 to 10 mL per minute thereafter.

The efficacy of Amtagvi was evaluated in a Phase 2, global, multicenter, multicohort, open-label, single arm study (C-144-01, NCT 025360579) in 111 enrolled patients with unresectable or metastatic melanoma. Patients were treated previously with at least one systemic therapy, including a PD-L1, and if BRAF V600 mutation-positive, a BRAF inhibitor or BRAF/MEK inhibitor. Patients also had to have at least 1 resectable lesion (or aggregate of lesions resected) of greater than or equal to 1.5 cm in diameter post resection to generate Tumor-Infiltrating Lymphocytes (TIL). Exclusion criteria was uncontrolled brain metastases, organ allograft or prior cell transfer, melanoma of uveal or ocular origin, systemic steroid therapy for any reason, hemorrhage of Grade 2 or higher 14 days prior to enrollment, LVEF less than 45%, NYHA functional classification greater than Class 1, and FEV1 less than or equal to 60%.
111 patients underwent tumor resection. Of the 111 patients, 22 (20%) did not receive Amtagvi. Reasons patients did not receive Amtagvi included: inability to manufacture Amtagvi (n=6), disease related death (n=3), exclusion criteria (n=5), disease progression (n=3), and consent withdrawn/starting new anti-cancer therapy (n=3). Of these 89 patients, 7 patients did not receive Amtagvi due to product not meeting specifications and product compatibility.

Of the 82 patients included in the efficacy analysis, 9 received Amtagvi at a dose less than the recommended dose of 7.5 x 109 viable cells, and did not achieve an objective response.
All 73 patients (100%) received a PD-L1 inhibitor previously, 63 (86%) received a CTLA-4 inhibitor previously, 42 (58%) received a PD-L1/CTLA-4 previously, and 20 (27%) received a BRAF inhibitor or BRAF/MEK inhibitor previously. Median age was 58 years (25 years min, 74 years max), median of 3 prior lines of therapy, 27% had BRAF V600 mutations, 23% had PD-L1 TPS greater than or equal to 5%, and 63% had brain and/or liver metastases.

A lymphodepleting regimen consisting of cyclophosphamide and mesna daily for 2 days followed by fludarabine 25 mg/m2 daily for 5 days was given. Amtagvi was given following this regimen, with a median dose of 21.1 x 109 viable cells. Aldesleukin at 600,000 IU/kg every 8 to 12 hours 3 to 24 hours after infusion was given for up to 6 doses in order to support cell expansion in vivo. The median time from sample taken to the end of the manufacturing process was 23 days and to infusion was 34 days.
The primary efficacy endpoints were objective response rate (ORR) and duration of response (DoR) in Cohort 4. Results are summarized in Table 1. Median time to initial response was 1.5 months (range: 1.3 to 4.2 months). Median duration of response was not achieved at 18.6 months follow-up.
In a pooled efficacy analysis, including Cohort 2 and 4, 189 patients underwent tumor resection, with 156 then receiving Amtagvi. Of the 156 patients, 2 patients' product did not meet the specifications and one received a dose below the protocol-specified range due to anaphylactic reaction. Of the 153 patients included in the efficacy set, the median administered dose was 21.1 x 109 viable cells and the median number of IL-2 doses was 6. The median DOR was not reached at 21.5 months follow-up. The ORR was 31.4% (95% CI: 24.1%, 39.4%) with a CR of 5.2% (n=8) and PR of 26.1% (n=40). Durable responses were maintained in 63%, 56% and 54% at 6, 9, and 12 months respectively, following initial response.

Table 1. Efficacy Results Among Patients Who Received AMTAGVI Dose Range of 7.5 x 109 to 72 x 109 Viable Cells

Endpoint[a]	**Efficacy Set (N=73)**
Objective Response Rate	
ORR, % (95% CI)	31.5 (21.1, 43.4)
Complete response rate, n (%)	3 (4.1)
Partial response rate, n (%)	20 (27.4)
Duration of Response[b, c]	
Median DoR in months (95% CI)[d]	NR (4.1, NR)
Range[e]	(1.4+, 26.3+)
Patients with DoR ≥ 6 months[f], n (%)	13 (56.5)
Patients with DoR ≥ 9 months[f], n (%)	11 (47.8)
Patients with DoR ≥ 12 months[f], n (%)	10 (43.5)

CI, confidence interval; DoR, duration of response; NR, not reached; ORR, objective response rate.
[a] Per RECIST v1.1 assessed by Independent Review Committee (IRC).
[b] Number of responders was N=23.
[c] Kaplan-Meier estimate of median potential follow-up for DoR was 18.6 months.
[d] Kaplan-Meier estimate in months among all responders. DoR measured from the date of confirmed initial objective response to the date of progression or death from any cause.
[e] + sign indicates a censored value
[f] Observed proportion of patients with duration of response beyond landmark time

Amtagvi has a black box warning for treatment-related mortality, prolonged severe cytopenia, severe infection, and cardiopulmonary and renal impairment. The prescribing information recommends Amtagvi to be administered in the inpatient hospital setting with an intensive care facility to be available and specialists skilled in cardiopulmonary or intensive care medicine to be available. The prescribing information also recommends filgrastim or a biosimilar be administered Day 1 after Amtagvi and continued daily until absolute neutrophil count (ANC) is greater than 1000/m3 for 3 consecutive days, or per institutional standards. The treatment-related mortality rate in clinical trial was reported as 7.5% (12/160), which included death during the lymphodepleting period (n=2), within 30 days following Amtagvi administration (n=6), and 38 to 150 days following Amtagvi administration (n=4). Adverse reactions associated with the deaths included severe infections, internal organ hemorrhage, acute renal failure, cardiac arrythmia, extensive ascites, liver injury, and bone marrow failure. No drug interactions are listed in the prescribing information.

There are no contraindications listed for Amtagvi. Warnings and precautions include treatment-related mortality, prolonged severe cytopenia, internal organ hemorrhage, severe infection, cardiac disorder, respiratory failure, acute renal failure, and hypersensitivity reactions. Adverse reactions that occurred in at least 5% of patients and were Grade 3 or higher included: febrile neutropenia (47%), tachycardia (8%), chills (5%), pyrexia (10%), fatigue (5%), edema (5%), infection with pathogen unspecified (11%), encephalopathy (6%), acute kidney injury (7%), hypoxia (12%), dyspnea (8%), rash (10%), hypotension (11%), and hypertension (7%).

Amtagvi has not been studied in pediatric patients so efficacy and safety cannot be established. 24% of patients were 65 years or older and no differences in safety or efficacy were observed between elderly patients and 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. None were opposed.

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

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

- Medical record documentation that Amtagvi is prescribed by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years old **AND**
- Medical record documentation of a diagnosis of unresectable or metastatic melanoma **AND**
- Medical record documentation of previous treatment with an anti-programmed cell death protein 1/programmed cell death ligand 1 (PD-1/PD-L1) inhibitor **AND**
- If BRAF V600 mutation positive: Medical record documentation of previous treatment with a BRAF inhibitor with or without a MEK inhibitor **AND**
- Medical record documentation that the member has not received prior treatment with tumor-derived T cell therapy or other genetically modified T cell therapy

AUTHORIZATION DURATION: Amtagvi will be approved for a one-time authorization for one administration of Amtagvi.

RPH SIGNOFF REQUIRED: Yes

FORMULARY ALTERNATIVES: none

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

WAINUA (eplontersen)

Review: Wainua is a transthyretin (TTR)–directed antisense oligonucleotide (ASO) indicated for the treatment of polyneuropathy caused by hereditary transthyretin-mediated amyloidosis(hATTR) in adults. Hereditary ATTR (hATTR) amyloidosis is an inherited condition caused by the misfolding of the TTR protein. TTR is a protein made primarily in the liver that carries vitamin A and thyroid hormones throughout the body. In people with hATTR, unstable TTR protein breaks apart, misfolds, and forms amyloid fibrils that can build up and cause damage throughout the body. Clinical presentation of hATTR can involve a neuropathic phenotype, where patients experience polyneuropathy (hATTR-PN); a cardiac phenotype, where patients experience cardiomyopathy (hATTR-CM); or a mixed phenotype, where patients experience both cardiomyopathy and polyneuropathy. In hATTR-PN, amyloid fibrils deposit in the nervous system, causing pain, muscle weakness, and autonomic dysfunction. The disease is progressive, and historically, the average survival of a patient with untreated hATTR-PN ranged from 5 to 15 years. Wainua is a disease-modifying treatment that causes degradation of mutant and wild-type TTR mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.

Wainua is an autoinjector recommended to be self-administered injection. It is dosed at 45mg/0.8mL subcutaneously monthly into the abdomen or upper thigh region. Currently on the market, there is one other self-administered therapy, Tegsedi (inotersen) and two provider-administered therapies, Onpattro (patisiran) and Amvuttra (vutrisiran). Prior to 2018, treatment of hATTR-PN primarily consisted of symptomatic management and liver transplantations. Wainua is differentiated in its ability to be self-administered without frequent laboratory monitoring, as required with Tegsedi, which requires a REMS program and close monitoring due to the risk of glomerulonephritis and thrombocytopenia. The drugs have not been studied head-to-head at this time to compare efficacy, but the treatments are similarly effective. Treatment selection in the hATTR-PN category is driven by patient preferences, prescriber familiarity, and access to provider-administered therapies.

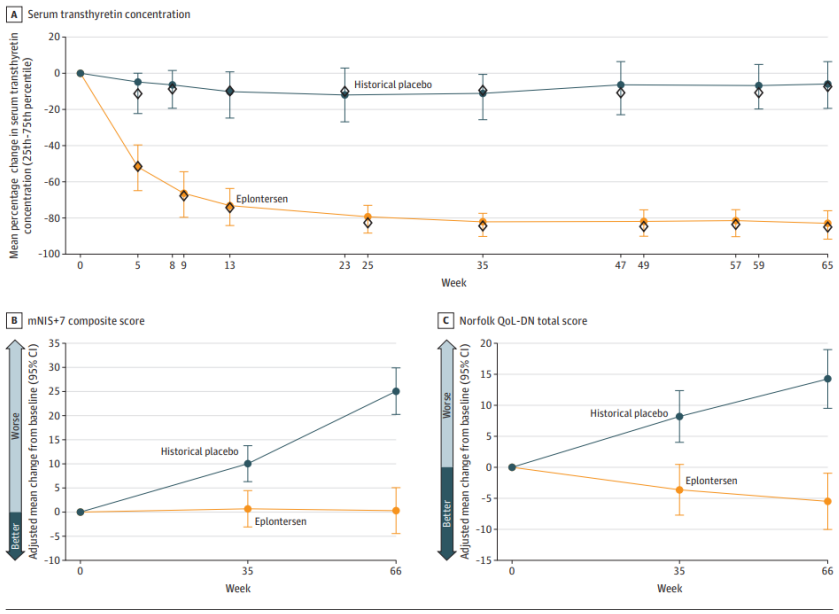
The safety and efficacy of Wainua was studied in the NEURO-TTRansform trial, which was a phase 3,

randomized, open-label, multicenter trial in patients with hATTR-PN. This trial included patients diagnosed with hATTR-PN with genetic mutation in TTR gene and a neuropathy impairment scale score ≥ 10 and ≤ 130 or Stage 1 or 2 FAP or Coutinho stage. The key exclusions from the trial were patients with Karnofsky performance scale status ≤50, prior liver transplant or anticipated liver transplant within 1 year of screening, other causes of sensorimotor or autonomic neuropathy (e.g. autoimmune disease), including uncontrolled diabetes, NYHA functional classification ≥3, current treatment with any approved drug for hATTR, previous treatment with Tegsedi or Onpattro, or other ASO or RNA therapy. Patients were randomized to receive: 45 mg SQ of Wainua once every 4 weeks (n = 144) vs. 300 mg of inotersen once per week (n = 24). The placebo group (n=60) was an external group from the NEURO-TTR trial. The primary efficacy end points at weeks 65 and 66 were changes from baseline in serum transthyretin concentration, modified Neuropathy Impairment Score +7 (mNIS+7) (higher scores indicate poorer function), and Norfolk Quality of Life Questionnaire–Diabetic Neuropathy (Norfolk QoL-DN) (higher scores indicate poorer quality of life). The results showed Wainua significantly lowered serum transthyretin (TTR) concentration, lessened neuropathic impairment, and improved quality of life compared with placebo.

Table 2. Efficacy Results for Wainua Compared to External Placebo Control at Week 35

		Change from Baseline to	Treatment Difference,
End			
mNI			
Norf			

Figure 2. Change From Baseline in Primary End Points (Serum Transthyretin Concentration, mNIS+7 Composite Score, Norfolk QoL-DN Total Score)



There are no contraindications with Wainua. There is a warning for reduced serum vitamin A levels and a recommendation for patients taking the medication to receive supplementation at the recommended daily allowance of vitamin A. If ocular symptoms of vitamin A deficiency occur (i.e., night blindness, dry eye), then a referral to ophthalmology would be recommended. In the trial, 15% of patients experienced reduced serum vitamin A levels. Other adverse reactions reported in the trial were: vomiting (9%), proteinuria (8%), injection site reactions (7%), blurred vision (6%), and cataract (6%).

Wainua was not studied in patients with severe or end stage renal disease or those with moderate or severe hepatic impairment. There is also no available data on Wainua use in pregnancy to inform drug-associated risk of adverse developmental outcomes. Also, no information regarding presence of Wainua in human milk, the effects on breast-fed infants or effect on milk production. The safety and efficacy in pediatric patients have not been established. Dose adjustments in patients ≥65 years old are not required.

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

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

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

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

- Medical record documentation that Wainua is prescribed by or in consultation with a neurologist, board-certified geneticist, or specialist with experience in the treatment of hereditary transthyretin-mediated amyloidosis (hATTR) **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of biopsy of tissue or organ to confirm amyloid presence **OR**
    - Medical record documentation of a clinical manifestation typical of hATTR (i.e., neuropathy or congestive heart failure) without a better alternative explanation **AND**
- Medical record documentation that Wainua will be used to treat polyneuropathy **AND**
- Medical record documentation of one of the following:
    - Medical record documentation of familial amyloid polyneuropathy (FAP) stage 1-2 **OR**
    - Medical record documentation of polyneuropathy disability score (PND) indicating the patient is not wheelchair bound or bedridden **AND**
- Medical record documentation that Wainua will not be used in combination with other RNA interference treatments **AND**
- Medical record documentation that member has been evaluated and treated by a contracted Center of Excellence in amyloidosis management **AND**
- Medical record documentation of an intolerance to, contraindication to, or therapeutic failure of two (2) preferred formulary treatments for hATTR

NOTE:

FAP Stage:
1 - unimpaired ambulation
2 - assistance with ambulation
3 - wheelchair-bound or bedridden

Polyneuropathy Disability Score:
I - preserved walking, sensory disturbances
II - impaired walking without need for stick/crutches
IIIa - walking with 1 stick/crutch
IIIb - walking with 2 sticks/crutches
IV-wheelchair-bound or bedridden

AUTHORIZATION DURATION: 12 months

RE-AUTHORIZATION CRITERIA: The medication will no longer be covered if the member progresses to FAP stage 3 and/or polyneuropathy disability score indicating the patient is wheelchair-bound or bedridden.

QUANTITY LIMIT: 0.8 mL per 30 days

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.

CASGEVY (exagamglogene autotemcel)

Review: Casgevy is an autologous genome edited hematopoietic stem cell-based gene therapy indicated for the treatment of sickle-cell disease (SCD) in patients 12 years and older with recurrent vaso-occlusive crises (VOCs) and transfusion-dependent β-thalassemia (TDT). Casgevy is prepared from the patients own stem cells obtained via apheresis process then enriched for CD34+ cells. After Casgevy infusion, the edited CD34+ cells engraft in the bone marrow and differentiate to erythroid lineage cells with reduced BCL11A expression. Reduced BCL11A expression results in γ-globin expression and HbF protein production in erythroid cells. In patients with severe sickle cell disease HbF expression reduced intracellular hemoglobin S (HbS) concentration, preventing red blood cells from sickling and addressing the underlying cause of disease and eliminates VOCs. In patients with transfusion-dependent β-thalassemia, γ-globin production improves the α-globin to non-α-globin imbalance thereby reducing ineffective erythropoiesis and hemolysis and increasing total hemoglobin levels, addressing the underlying cause of disease, and eliminating the dependence on regular red blood cell (RBC) transfusions.
Patients undergo CD34+ HSC mobilization followed by apheresis to isolate CD34+ cells. A total collection target of 20 x 106 CD34+ cells is recommended for product manufacture. If patients require more than one mobilization/apheresis cycle to collect the required amount of CD34+ cells, the cycles must be separated by a minimum of 14 days. Plerixafor and Granulocyte-Colony Stimulating Factor (G-CSF) were used for mobilization in TDT and single agent plerixafor was used for mobilization in SCD. In patients with SCD, it is recommended that patients be transfused at least 8 weeks prior to the initiation of myeloablative conditioning, with a goal of maintaining hemoglobin S (HbS) levels of < 30% of total Hb and total Hb concentration ≤ 11 g/dL. In patients with TDT, it is recommended that patients be transfused to maintain hemoglobin ≥ 11 g/dL for 60 days prior to myeloablative conditioning. Myeloablative conditioning should not be started until the complete dose of Casgevy has been received. The full myeloablative conditioning should be administered prior to treatment with Casgevy. Casgevy must be administered between 48 hours and 7 days after the last dose of myeloablative conditioning. Patients should be premedicated with an antipyretic and an antihistamine prior to administering Casgevy. Casgevy is for autologous use only. All vials of the Casgevy dose must be administered, one vial at a time. Casgevy is administered through central venous catheter as an intravenous bolus (IV push). Casgevy is supplied as a single dose for infusion containing the suspension of CD34+ cells in one or more vials of frozen suspension of genome edited autologous CD34+ cells in cryopreservative medium. Each vial contains 4 to 13 x 106 CD34+ cells/mL suspended in 1.5 to 20 mL cryopreservative medium. The minimum recommended dosage of Casgevy is 3 x 106 CD34+ cells/kg.

SICKLE CELL DISEASE
The efficacy and safety of Casgevy was evaluated in CLIMB SCD-121, an ongoing single-arm trial in adult and adolescent patients with sickle cell disease. Patients were eligible for inclusion if they had a history of at least 2 protocol-defined severe vaso-occlusive crisis (VOC) events during each of the 2 years prior, defined as the occurrence of at least one of the following:

- Acute pain requiring a visit to a medical facility and administration of pain medications (Opioids or IV NSAIDS) or RBC transfusions
- Acute chest syndrome
- Priapism lasting > 2 hours and requiring a visit to a medical facility
- Splenic sequestrion

The trial excluded patients with advanced liver disease, history of untreated Moyamoya disease, or presence of Moyamoya disease that puts the patient at risk of bleeding. Patients with a 10/10 human leukocyte antigen matched related hematopoietic stem cell donor were also excluded.

Eligible patients underwent mobilization and apheresis to collect CD34+ stem cells for Casgevy manufacture, followed by myeloablative conditioning and infusion of Casgevy. Patients were then followed for 24 months after infusion. Patients who complete or discontinued CLIMB SCD-121 were

encouraged to enroll in an ongoing long-term follow-up trial for additional follow-up for a total of 15 years after Casgevy infusion (Trial 3 - NCT04208529).

At the time of interim analysis, 63 patients enrolled in the trial, of which 58 patients started mobilization. A total of 44 patients received Casgevy infusion and formed the full analysis set (FAS). Thirty-one patients of the FAS had adequate follow-up to evaluate efficacy and were eligible for primary efficacy analysis (i.e. the primary efficacy set [PES]). At interim analysis, the median duration of follow-up was 26.0 months from the time of Casgevy infusion. There were no cases of graft failure or graft rejection.

The primary efficacy outcome was proportion of responders, defined as patients who did not experience any protocol-defined severe VOCs for at least 12 consecutive months within the first 24 months after Casgevy infusion (VF12). The proportion of patients who did not require hospitalization due to severe VOCs for at least 12 consecutive months within the 24-month evaluation period was also assessed (HF12).

Results showed a VF12 response rate was 29/31 (93.5%). The 29 VF12 responders did not experience protocol-defined severe VOCs during the evaluation period with a median duration of 22.2 months at the time of interim analysis. One VF12 responder, after achieving a VF12 response, experience an acute pain episode meeting the definition of severe VOC at month 22.8. The patient was reported to have a parvovirus B19 infection at the time. Of the 31 patients evaluable for VF12 response, one patient was not evaluable for HF12 response. The remaining 30 patients achieved the HF12 endpoint.

TRANSFUSION DEPENDENT β-THALASSEMIA

The safety and efficacy of Casgevy was evaluated in CLIMB THAL-111, an ongoing, open-label, single-arm trial in adult and adolescent patients with transfusion-dependent β-thalassemia. Patients were included in the trial if they had a history of requiring at least 100 mL/kg/year or 10 units/year of RBC transfusions in the 2 years prior to enrollment. Patients were excluded if they had severely elevated iron in the heart, or advanced liver disease, or direct bilirubin value. Patients were also excluded if they had an available 10/10 human leukocyte antigen matched related hematopoietic stem cell donor. Eligible patients underwent mobilization and apheresis to collect CD34+ stem cells for Casgevy manufacture, followed by myeloablative conditioning and infusion of Casgevy. Patients who completed or discontinued from CLIMB THAL-111 were encouraged to enroll in a long-term follow-up trial for an additional follow-up for a total of 15 years (Trial 3 - NCT04208529).

At the time of interim analysis, 59 patients enrolled in the trial in which 59 patients started mobilization. A total of 52 patients received Casgevy infusion and formed the full analysis set (FAS). Thirty-five patients from FAS had adequate follow-up to allow inclusion in the primary efficacy analysis and formed the primary efficacy set (PFS).

At interim analysis, the median duration of follow-up was 23.8 months from time of infusion. There were no cases of graft failure or graft rejection. The primary outcome was proportion of patients achieving transfusion independence for 12 months (TI12), defined by weighted average Hb ≥ 9 g/dL without RBC transfusions for at least 12 consecutive months any time within the first 24 months after Casgevy infusion, evaluated starting 60 days after the last RBC transfusions for post-transplant support or TDT disease management.

The TI12 responder rate was 32/35. All patients achieved TI12 remained transfusion-independent, with a median duration of transfusion-independence of 20.8 months and normal mean weighted average total Hb levels. The median time to last RBC transfusion for patients who achieved TI12 was 30 days following Casgevy infusion. Three patients did not achieve TI12. These patients had reductions in annualized RBC transfusion volume requirements of 79.8%, 83.9%, and 97.9% and reductions in annualized transfusion frequency of 78.6%, 67.4%, and 94.6%, respectively, compared to baseline requirements.

There are no black box warnings for Casgevy. Warnings include neutrophil engraftment failure, delayed platelet engraftment, hypersensitivity reactions, and off-target genome editing risk. In clinical trials, all

treated patients achieved neutrophil engraftment and no patients received rescue CD34+ cells. In the event of neutrophil engraftment failure, patients should be infused with rescue CD34+ cells. Delayed platelet engraftment has been observed with Casgevy, resulting in an increased risk of bleeding until platelet engraftment is achieved. In clinical trials, there was no association observed between incidence of bleeding events and time to platelet engraftment. Hypersensitivity reactions, including anaphylaxis, can occur due to dimethyl sulfoxide (DMSO) or dextran 40 in the cryopreservative solution. Although off-target genome editing was not observed in the edited CD34+ cells evaluated from healthy donors and patients, the risk of unintended, off-target edited in an individuals CD34+ cells cannot be ruled out due to genetic variants. The clinical significance of potential off-target editing is unknown.

The most common Grade 3 and 4 non-laboratory adverse reactions were mucositis and febrile neutropenia in patients with SCD and patients with TDT and decreased appetite in patients with SCD. All (100%) of the patients with TDT and SCD experienced Grade 3 or 4 neutropenia and thrombocytopenia. Other common Grade 3 or 4 lab abnormalities (≥ 50%) include leukopenia, anemia, and lymphopenia. The safety of efficacy in SCD was evaluated in 44 adolescent and adult patients with SCD treated with Casgevy undergoing myeloablative conditioning with busulfan. The adverse event profile was generally consistent with busulfan myeloablative conditioning and HSC transplant. Serious adverse reactions were observed in 45% of patients, most commonly cholelithiasis, pneumonia, abdominal pain, constipation, pyrexia, upper abdominal pain, non-cardiac chest pain, oropharyngeal pain, pain, and sepsis. One patient died to COVID-19 infection and subsequent respiratory failure and was found to be unrelated to Casgevy. Other clinically relevant reactions are veno-occlusive liver disease, and infusion related reactions, including abdominal pain, nausea, non-cardiac chest pain, pruritis, sinus tachycardia, and vomiting.

In patients with SCD, median time to platelet engraftment (3 consecutive platelet counts ≥ 50 x 109/L, obtained 3 different days after Casgevy infusion, without administration of platelet transfusions for 7 days) was 35 days. The median time to neutrophil engraftment (3 consecutive ANC ≥ 500 cells/μL on 3 different days after Casgevy infusion, without use of unmodified rescue CD34+ cells) was 27 days.

The safety of efficacy in TDT was evaluated in 52 adolescent and adult patients with SCD treated with Casgevy undergoing myeloablative conditioning with busulfan. The adverse event profile was generally consistent with busulfan myeloablative conditioning and HSC transplant. Serious adverse reactions after myeloablative conditioning and Casgevy infusion were observed in 33% of patients with TDT. The most common serious adverse reactions were veno-occlusive liver disease, pneumonia, hypoxia, thrombocytopenia, viral infection, and upper respiratory infection. Other clinically relevant adverse reactions included hemophagocytic lymphohistiocytosis, cerebral hemorrhage, and infusion related reactions (abdominal pain and nausea, pruritis and vomiting, lower abdominal pain, chills, sinus tachycardia, and tachycardia).

In patients with TDT, the median time to platelet engraftment was 44 days. Patients without a spleen had an earlier median time to platelet engraftment than patients with an intact spleen. The median time to neutrophil engraftment was 29 days. There was no association observed between infections and time to neutral engraftment.

Drug interactions include G-CSF (which must not be used for CD34+ HSC mobilization of patients with SCD); hydroxyurea, voxelotor (Oxbryta), and crizanlizumab (Adakveo) (use must be discontinued 8 weeks prior to each mobilization and conditioning cycle); iron chelators (discontinue at least 7 days prior to myeloablative conditioning due to potential interactions and use of non-myelosuppressive iron chelators should be avoided for at least 3 months and use of myelosuppressive iron chelators for at least 6 months); live vaccines have not been studied during and following Casgevy treatment.

The efficacy and safety of Casgevy has been established in pediatric patients with SCD and TDT aged 12 years and older, supported by data from 12 patients in CLIMB SCD-121 and 18 patients in CLIMB THAL-111. The efficacy and safety profile in pediatric patients was consistent with efficacy and safety in adult patients. Median times to platelet engraftment and neutrophil engraftment in pediatric patients with SCD and TDT were generally slightly longer than those in adult patients.

Casgevy has not been studied in patients over 65 years of age. HSC transplantation must be appropriate for patients to be treated with Casgevy.

Casgevy has not been studied in patients with renal impairment or hepatic impairment and patients should be assessed for impairment to ensure that HSC transplantation is appropriate. Casgevy has not been studied in patients with active HIV-1, HIV-2, HBV, or HCV and should not be used in patients.

Casgevy has not been studied in patients with prior allogeneic or autologous HSC transplant and is not recommended in these 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. Yarczower suggested that we look into prevalence within the GHP population to assist with projections. Kim Reichard will look into it. Aubrielle did previously love into prevalence for β-thalassemia and we will see if we can start with that. No comments or questions. The committee unanimously voted to accept the recommendations as presented. None were opposed.

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

Outcome: Casgevy will be a medical benefit and will be added to the medical benefit cost share list. Casgevy will not be dispensed by specialty pharmacies. It will require a prior authorization with the following criteria:

Sickle Cell Disease

- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of severe sickle cell disease with all of the following:
    - Documentation of a βS/βS, βS/β0 or βS/β+ genotype **AND**
    - Documentation of greater than or equal to two (2) vaso-occlusive crises (VOCs) or events (VOEs)** per year in the previous two years **AND**
    - Documentation of therapeutic failure, contraindication, or intolerance to hydroxyurea **AND**
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Lyfgenia) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV)

Transfusion-Dependent β-thalassemia

- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of transfusion-dependent β-thalassemia **AND** medical record documentation of a history of ≥ 100 mL/kg/year or 10 units/year of packed red blood cell (RBC) transfusions in the prior 2 years **AND**
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e.Zynteglo) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family

donor* **AND**

- Medical record documentation that the member has a negative serology test for Human Immunodeficiency Virus (HIV)

NOTES:

- The package insert recommends confirming that hematopoietic stem cell transplantation (HSCT) is appropriate prior to Casgevy since patients will be going through similar steps (mobilization, apheresis, and myeloablative) required for a HSCT. However, the clinical trials excluded patients who had a known and available HLA-matched related donor. Considering that HSCT has been available for longer and has more evidence supporting its use, it may be appropriate to require HSCT as an alternate to Casgevy. While it is possible for patients to have a matched unrelated donor, outcomes are best with matched related donors.
- In clinical trials, VOCs were defined as:
  - Acute pain event requiring a visit to a medical facility and administration of pain medications (opioids or intravenous [IV] non-steroidal anti-inflammatory drugs [NSAIDs]) or RBC transfusions
  - Acute chest syndrome
  - Priapism lasting > 2 hours and requiring a visit to a medical facility
  - Splenic sequestration

AUTHORIZATION DURATION: One (1) time approval per lifetime; Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

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.

LYFGENIA (lovotibeglogene autotemcel)

Review: Lyfgenia is an autologous hematopoietic stem cell-based gene therapy indicated for the treatment of patients 12 years of age and older with sickle cell disease and a history of vaso-occlusive events. Following Lyfgenia, patient with α-thalassemia trait (-α3.7/-α3.7) may experience anemia with erythroid dysplasia that may require chronic red blood cell transfusions. Lyfgenia has not been studied in patients with more than two α-globin gene deletions. Lyfgenia is a $\beta^{A\text{-}T87Q}$-globin gene therapy consisting of autologous CD34+ cells from patients with sickle cell disease, containing hematopoietic stem cells (HSCs) collected via apheresis, enriched for CD34+ cells, then transduced with BB305 LVV encoding $\beta^{A\text{-}T87Q}$-globin, suspended in cryopreservation solution. After Lyfgenia infusion, then transduced CD34+ HSCs engraft in the bone marrow and differentiate to produce red blood cells containing biologically active βA-T87Q-globin that will combine with α-globin to produce functional Hb containing βA-T87Q-globin (HbA^{T87Q}). HbA^{T87Q} has similar oxygen-binding affinity and oxygen hemoglobin dissociation curve to wild type HbA, reduces intracellular and total hemoglobin S (HbS) levels, and is designed to sterically inhibit polymerization of HbS thereby limiting the sickling of red blood cells.

Lyfgneia is supplied as a single dose infusion containing a suspension of CD34+ cells in one to four infusion bags. The minimum recommended dosage of Lyfgenia is 3×10^6 CD34+ cells/kg.

Prior to Lyfgenia infusion, patients should prepare for mobilization with at least 2 cycles of scheduled transfusions (one each month), to reach a target Hb of 8-10 g/dL, not to exceed 12 g/dL, and HbS of less than 30% to reduce the risk of SCD-related complications. For mobilization, patients should receive plerixafor to mobilize stem cells, then apheresis approximately 4-6 hours. For patients undergoing more than 1 mobilization cycle, cycles should be separated by at least 14 days. The minimum target for

collection is 16.5 x 10^6 CD34+ cells/kg for manufacturing and back-up. At least 1.5 x 10^6 cells/kg should be retained and cryopreserved as back-up if rescue treatment is needed.
Myeloablative conditioning can be started once the complete set of infusion bags of Lyfgenia has been received and stored. Myeloablative conditioning with busulfan must be administered prior to Lyfgenia infusion. After myeloablative conditioning, a minimum 48 hours of washout is recommended before Lyfgenia infusion.

Lyfgenia is for autologous use only. It must be administered within 4 hours after thawing. Each infusion bag is administered via intravenous infusion over a period of less than 30 minutes and each bag should be administered completely before proceeding to thaw and infuse the next infusion bag if applicable. Standard procedures for patient management after HSC transplantation should be followed after Lyfgenia infusion.

The efficacy and safety of Lyfgenia in sickle cell disease was evaluated in HGB-206, a single-arm, 24-month, open label Phase 1/2 study and continued in a long-term follow-up study. In HGB-206, 43 patients underwent apheresis after which 36 underwent myeloablative conditioning. Thirty-six patients received intravenous infusion of Lyfgenia with a median dose of 6.4 x 10^6 CD34+ cells/kg. No patients experienced graft failure or graft rejection.

The transplant population for VOE efficacy outcomes include patients with at least 4 VOEs in the 24 months prior to informed consent. Efficacy outcome were complete resolution of VOEs (VOE-CR) and severe VOEs (sVOE-CR) between months 6 and 18 after infusion of Lyfgenia.

VOEs were defined as any of the following requiring evaluation at a medical facility:

- An acute pain episode with no medically determined cause other than vaso-occlusion, lasting more than 2 hours
- Acute chest syndrome (ACS)
- Acute hepatic sequestration
- Acute splenic sequestration

Severe VOEs were defined as either of the following:

- VOE requiring hospitalization or multiple ER/urgent care visits over 72 hours and requiring IV medications at each visit
- Priapism requiring any level of medical attention.

Patients were also evaluated for Globin response (GR) defined as meeting the following criteria for a continuous period of at least 6 months following Lyfgenia infusion:

- Weighted average hemoglobin A^{T87Q} percentage of non-transfused total Hb ≥ 30 % AND
- Weighted average non-transfused total Hb (HbS+HbF+HbA2+HbAT87Q) increase of ≥ 3 g/dL compared to baseline total Hb OR weighted average non-transfused total Hb ≥ 10 g/dL

Efficacy results evaluating VOEs showed that 28 of 32 (88%) experienced VOE-CR and 30/32 (94%) of patients achieved sVOE-CR. All 36 patients were evaluated for globin response and 31/36 (86%) achieved globin response which was maintained in all patients. The median duration of follow-up was 38 months post Lyfgenia infusion. After primary evaluation period to last follow-up, 4 of 32 patients who achieved VOE-CR experienced VOEs while maintaining GR. After the primary evaluation period, 17 of 35 (49%) were prescribed opioids for sickle cell and non-sickle cell-related pain.

Five patients with history of stroke or vasculopathy were treated with Lyfgenia. All were at least 18 years old and on chronic transfusion therapy prior to infusion. At 44-60 months follow-up, all 5 subjects remained transfusion independent without recurrent stroke.

Lyfgenia has a black box warning for the risk of hematologic malignancy which may be increased by the additional hematopoietic stress associated with mobilization, conditioning, and infusion of Lyfgenia. At the time of initial product approval, two patients treated with an earlier version of Lyfgenia (different

manufacturing process and transplant procedure) developed acute myeloid leukemia (AML). One patient with α-thalassemia trait has been diagnosed with myelodysplastic syndrome. Patients with sickle cell disease have an increased risk of hematologic malignancy compared to the general population. Patients treated with Lyfgenia should have lifelong monitoring. Prescribing information recommends monitoring with a complete blood count (with differential) at least every 6 months for at least 15 years after treatment, and integration site analysis at months 6, 12, and as needed.

Other warnings include delayed platelet engraftment, neutrophil engraftment failure, insertional oncogenesis (lentiviral vector-mediated), hypersensitivity reactions, and interference with PCR-based testing (possible false HIV-positive results for PCR assay test due to integrated BB305 LVV pro-viral DNA. Delayed platelet engraftment has been observed with Lyfgenia and 2 (4%) patients required more than 100 days post-treatment with Lyfgenia to achieve platelet engraftment. Bleeding risk is increased prior to platelet engraftment and may continue after engraftment in patients with prolonged thrombocytopenia. There is potential failure of neutrophil engraftment after treatment of Lyfgenia, defined as failure to achieve 3 consecutive ANC ≥ 0.5 x 10^9 cells/L obtained on different days by Day 43 after infusion. Patients experiencing neutrophil engraftment should be provided with the back-up collection of CD34+ cells.

Safety was based on HGB-206 and one long-term follow-up study. Median duration of follow-up was 42 months. Mobilization and apheresis triggered SAEs of sickle cell crisis in 6 patients who initiated mobilization. All patients who initiated conditioning experienced at least one adverse event contributed to conditioning. Thirty-three (73%) patients who received Lyfgenia experienced at least one serious adverse event, most related to conditioning or underlying disease (Table 8).

Table 8. Adverse Reactions ≥ Grade 3 (> 5%) Following Treatment with LYFGENIA from Day 1 to Month 24 (N = 45)*

Adverse Reaction	Grade 3 or Higher n (%)
Blood and lymphatic system disorders	--
Thrombocytopenia	31 (69)
Neutropenia	27 (60)
Febrile neutropenia	20 (44)
Anemia[a]	15 (33)
Leukopenia	15 (33)
Sickle cell anemia with crisis[b]	7 (16)
Gastrointestinal disorders	--
Stomatitis	32 (71)
Nausea	4 (9)
General disorders and administration site conditions	--
Pyrexia	3 (7)
Infections and infestations	--
Bacteremia	3 (7)
Investigations	--
Aspartate aminotransferase increased	8 (18)
Alanine aminotransferase increased	6 (13)
Gamma-glutamyl transferase increased	6 (13)
Blood bilirubin increased	3 (7)
Metabolism and nutrition disorders	--
Decreased appetite	5 (11)
Respiratory, thoracic, and mediastinal disorders	--
Pharyngeal inflammation	5 (11)

* Includes adverse events associated with busulfan myeloablative conditioning and underlying sickle cell disease. a Includes a patient with α-thalassemia trait who was diagnosed with myelodysplastic syndrome after Month 24.b Includes events prior to Month 6 and non-adjudicated occurrences.

Three patients died during Lyfgenia clinical trials, one from sudden cardiac death due to underlying disease and two from acute myeloid leukemia who were treated with an earlier version of Lyfgenia. Two patients developed anemia following Lyfgenia treatment. One patient continues to require monthly packed

red blood cell (pRBC) transfusions and the other has been diagnosed with MDS. Both subjects had α-thalassemia trait.
Infusion related reactions were observed in 2 patients on the day of the Lyfgenia infusion. Both reactions were Grade 1 and resolved. Events included hot flush and decreased diastolic blood pressure.

Platelet engraftment was achieved in all patients (median Day 37). Two patients achieved platelet engraftment after Day 100, one of these patients were administered eltrombopag until Day 234. All patients achieved neutrophil engraftment by Day 43 (median Day 20) after Lyfgenia infusion.

Drug interactions with Lyfgenia include anti-retrovirals (at least one-month prior to mobilization and until all cycles of apheresis are completed), hydroxyurea (at least 2 months prior to mobilization and until all cycles of apheresis are completed), iron chelation (discontinue at least 7 days prior to mobilization and condition, restart non-myelosuppressive iron chelators no sooner than 3 months and restart myelosuppressive iron chelators no sooner than 6 months following Lyfgenia infusion).

The safety and efficacy of Lyfgenia has been established in pediatric patients 12 years of age and older with sickle cell disease, including 8 adolescents. No clinically meaningful differences were observed between adult and pediatric subgroups.

Lyfgenia has not been studied in patients 65 years and older. Autologous hematopoietic stem cell (HSC) transplantation must be appropriate for patients to be treated with Lyfgenia.

Lyfgenia has not been studied in patients with HIV-1 and HIV-2. A negative HIV test is necessary prior to apheresis. Patients positive for HIV will not be accepted for Lyfgenia treatment.

Lyfgenia has not been studied in patients with renal and hepatic impairment. Patients should be assessed to ensure that renal and hepatic function is appropriate for HSC transplantation.

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

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

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

Outcome: Lyfgenia is a medical benefit and will be added to the medical benefit cost share list. Lyfgenia will not be dispensed by specialty pharmacies. It will require a prior authorization with the following criteria:

- Prescription written by a hematologist and/or stem cell transplant specialist **AND**
- Medical record documentation of age greater than or equal to 12 years and less than or equal to 65 years **AND**
- Medical record documentation of a diagnosis of severe sickle cell disease with all of the following:
    - Documentation of a βS/βS, βS/β0 or βS/β+ genotype **AND**
    - Documentation of greater than or equal to two (2) vaso-occlusive crises (VOCs) or events (VOEs)** per year in the previous two years **AND**
    - Documentation of therapeutic failure, contraindication, or intolerance to hydroxyurea **AND**
- Medical record documentation that the member has not had a prior hematopoietic stem cell transplant or hematopoietic stem-cell based gene therapy (i.e. Casgevy) **AND**
- Medical record documentation the member is a candidate for a hematopoietic stem cell transplant but ineligible due to absence of Human Leukocyte Antigen (HLA)-matched family donor* **AND**
- Medical record documentation that the member has a negative serology test for Human

Immunodeficiency Virus (HIV)

NOTES:

- The package insert recommends confirming that hematopoietic stem cell transplantation (HSCT) is appropriate prior to Lyfgenia since patients will be going through similar steps (mobilization, apheresis, and myeloablative) required for a HSCT. However, the clinical trials excluded patients who had a known and available HLA-matched related donor. Considering that HSCT has been available for longer and has more evidence supporting its use, it may be appropriate to require HSCT as an alternate to Lyfgenia. While it is possible for patients to have a matched unrelated donor, outcomes are best with matched related donors.
- In clinical trials, VOCs were defined as:
    - An event with no medically determined cause other than a vaso-occlusion, requiring a ≥ 24-hour hospital or Emergency Room (ER) observation unit visit OR
    - At least 2 visits to a day unit or ER over 72 hours with both visits requiring intravenous treatment OR
    - 4 priapism episodes that require a visit to a medical facility (with or without inpatient admission)

AUTHORIZATION DURATION: One (1) time approval per lifetime; Requests for authorizations exceeding these limits will require the following medical record documentation of peer-reviewed literature citing well-designed clinical trials to indicate that the member's healthcare outcome will be improved by dosing beyond the FDA-approved treatment duration.

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.

CLASS REVIEWS

PULMONARY ARTERIAL HYPERTENSION CLASS REVIEW

Agents for PAH			
Brand Name	**Generic**	**Generic Available**	**Manufacturer**
Prostanoid analogues			
Flolan, Veletri	epoprostenol	Yes	GlaxoSmithKline & Actelion Pharmaceuticals US, Inc
Ventavis	iloprost	No	Bayer Intellectual Property GmbH
Remodulin, Tyvaso, Tyvaso DPI, Orenitram	treprostinil	Product Dependent	United Therapeutics Corporation
Prostacyclin receptor agonists			
Uptravi	selexipag	No	Actelion Pharmaceuticals US, Inc
Endothelin receptor antagonist (ERA)			
Letairis	ambrisentan	Yes	Gilead
Opsumit	macitentan	No	Actelion Pharmaceuticals US, Inc.
Tracleer	bosentan	Product dependent	Actelion Pharmaceuticals, Ltd
Phosphodiesterase-type 5 pathway-active Inhibitors (PDE5-I)			
Revatio, Liqrev	sildenafil	Product dependent	
Adcirca	tadalafil	Product dependent	Eli Lilly and Company
Soluble guanylate cyclase stimulator (sGC)			
Adempas	riociguat	No	Bayer HealthCare Pharmaceuticals

Background of Disease State: Pulmonary arterial hypertension (PAH) includes a heterogeneous group of disorders, where the common feature is elevated artery pressure. Pulmonary hypertension is a rare disorder found in 15 to 50 persons per million across the United States and Europe. PAH is divided into five group, based on pathophysiology, clinical features, and management. Pulmonary hypertension is a result of increased blood pressure in the lungs from blood vessels becoming thicker, narrowed or blocker which makes blood flow to the lungs more difficult. Cause of PAH include genetic mutations, drug, toxins, and disease associations. If left untreated pulmonary hypertension can lead to shortness of breath, right ventricular dysfunction/right heart failure, ascites and tachyarrhythmias.

Pharmacology/Place in Therapy: European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

- PAH is diagnosed with a right heart catheterization. After right heart catheterization patients with a mean pulmonary arterial pressure decrease of more than 10 mm Hg to less than 40 mm Hg and with an unchanged or increased cardiac output when challenged are considered responders. They should be started on calcium channel blockers (nifedipine, diltiazem, and amlodipine) and reassessed after 3-6 months, if no cardiac abnormalities continue therapy for 6-12 months
- Patients who are non-responder should be treated using the following potent vasodilating medication: ERA (ambrisentan, bosentan, macitentan), PDE5i (sildenafil, tadalafil, vardenafil), soluble guanylate cyclase stimulator (riociguat), prostanoid analogues (epoprostenol, iloprost, treprostinil) and prostacyclin receptor agonists (selexipag)

- Patients who do not have a sustained response to calcium channel blockers should be started on more potent vasodilating medication
- Initial combination therapy with PDE5-i plus ERA typically indicated for patients in low or intermediate risk category
- For high-risk PAH, consider initial triple therapy with PDE5-i, ERA, plus either IV epoprostenol or treprostinil (subcutaneous or IV)

Summary of Clinical Trials:

- **Comparative Effectiveness of medications for pulmonary arterial hypertension (PAH): A systematic review and network meta-analysis** of 53 randomized controlled trials assessing over 10 anti-pulmonary hypertension medications from 5 drug classes. Medications and their classes include biologics (imatinib, selonsertib, sotatercept), endothelin receptor antagonist {ERAs} (ambrisentan, bosentan, macitentan), NO-cyclic GMP-phosphodiesterase-type 5 pathway-active medications {PDE5i} (sildenafil, tadalafil, vardenafil), soluble guanylate cyclase stimulator (riociguat), oral/inhaled (OR/INH) prostanoid analogues (epoprostenol, iloprost, treprostinil) and prostacyclin receptor agonists (ralinepag, selexipag). Results were presented in separate networks including clinical worsening (41 trials), mortality (48 trials), hospitalization (26 trials), 6-min walk distance {6MWD} (49 trials), serious adverse effects (38 trials) and change in New York Hospital Association (NYHA)/WHO functional class (22 trials)
  - Clinical Worsening - Several PAH medications reduced the risk of clinical worsening compared to placebo
    - Riociguat = 133.6 fewer events per 1000
    - ERA+PDE5i = 120.7 fewer events per 1000
    - PDE5i = 85.3 fewer events per 1000
    - ERA = 75.7 fewer events per 1000
  - Mortality - Reduction in mortality as compared to placebo
    - Riociguat 29.1 fewer deaths per 1000
    - PDE5I = 24.9 fewer deaths per 1000
    - Prostanoid analogues 18.3 fewer deaths per 1000
  - Hospitalizations
    - Riociguat reduced hospitalizations with a high certain as compared to placebo (77.3 fewer events)
    - No other PAH met the pre-specified minimally important difference (MID) set for hospitalization
      - MID of 5%
  - 6MWD
    - Combination therapy with ERA+PDE5i and Riociguat monotherapy increased 6MWD as compared to placebo
      - ERA+PDE5i 49.9 m
      - Riociguat monotherapy 49.5 m
  - Change in New York Hospital Association (NYHA)/WHO Functional Class
    - No treatment individually or in combination improved NYHA/WHO FC with moderate- to high-certainty evidence
  - Serious Adverse Events
    - None of the United States Food and Drug Administration (FDA)-approved PAH treatments appeared to increase SAEs.
- **Comparative Effectiveness of medications for pulmonary arterial hypertension (PAH): A systematic review and network meta-analysis** of 31 randomized controlled trials assessing over 10 anti-pulmonary hypertension medications from 5 drug classes. Results were presented in separate networks including clinical worsening, hospitalizations, all-cause mortality assessment, Improvement in NYHA/WHO functional class and adverse events leading to discontinuation
  - Clinical Worsening (Median Percent)
    - ERA group had a median of 7.7 %
    - PDE5i group had a median of 5.7%
    - The combination of ERA + PDE5i group had a median of 3.9%

        - Riociguat group had a median of 2.8%
        - Compared the placebo group a median of 14.5%
    - Hospitalizations
        - Only the ERA + PDE5i combination was associated with improvement compared with placebo
    - All-cause Mortality
        - Events rates were low across trials, and between-group differences were not significant
    - Improvement in NYHA/WHO Functional Class (Median Percent)
        - A median 25.2% of in ERA group
        - A median 24.8% of in PDE5i group
        - A median 82.8% of in IV/SC prostanoids group
        - A median 16.2% of in placebo group
    - Adverse Events Leading to Discontinuation
        - Risk of discontinuation for PO/INH prostanoids was significantly higher compared with placebo (RR, 2.92; 95% CI, 1.68-5.06) but was also higher than ERA (RR, 2.78; 95% CI, 1.41-5.50), PDE5i (RR, 3.79; 95% CI, 1.72-8.34), riociguat (RR, 5.92; 95% CI, 1.85-18.94), and ERA + PDE5i (RR, 3.00; 95% CI, 1.16-7.81)
- **Comparative effectiveness of pulmonary arterial hypertension drugs in treatment-naive patients: a network meta-analysis** 21 randomized controlled trials assessing drug therapies specific for treatment of pulmonary arterial hypertension in treatment-naive patients only. Medications included epoprostenol, Treprostinil, iloprost, ambrisentan, bosentan, beraprost, macitentan, sildenafil, tadalafil, riociguat and selexipag. Efficacy outcomes included the 6-min walking distance (6MWD) and all-cause mortality. Safety outcome was discontinuation due to adverse events.
    - Efficacy Outcomes
        - The combination of tadalafil and ambrisentan was statistically significantly better at improving 6-min walk distance. Combination of tadalafil and ambrisentan performed better than 125 mg bosentan (43 m, 95% CrI: 19, 65), oral treprostinil or beraprost (42 m, 95% CrI: 21, 63), iloprost (32 m, 95% CrI: 3, 62), 40 mg tadalafil (26 m, 95% CrI: 12, 39) and ambrisentan (22 m, 95% CrI: 7, 37).
        - Of the eight PAH treatment used in this study, none showed statistically significant reduction in mortality compared with placebo. PAH treatments can be rank ordered as follows: epoprostenol = ERA = iv. treprostinil (high dose) = iloprost > PDE-5i and ERA combined = sc. treprostinil = PDE-5i > oral treprostinil or beraprost.

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

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

Outcome:

Medications	Current Policy	Recommendations
Prostanoid Analogues (PCA)		
epoprostenol (Flolan, Veletri)	• Must be prescribed by a pulmonologist or cardiologist **AND** • Physician provided documentation of a diagnosis of class 4 pulmonary arterial hypertension **OR** • Physician provided documentation of a diagnosis of class 2 or 3 pulmonary arterial hypertension with therapeutic failure on, intolerance to or contraindication to one (1) formulary preferred agent which is approved or medically accepted for the beneficiary's diagnosis or indication, from any of the following classes of medications: ○ Endothelin Receptor Antagonist ○ Phosphodiesterase-5 Enzyme Inhibitor ○ Prostacyclin **OR**	• Must be prescribed by a pulmonologist or cardiologist **AND** • Physician provided documentation of a diagnosis of class 4 pulmonary arterial hypertension **OR** • Physician provided documentation of a diagnosis of class 2 or 3 pulmonary arterial hypertension with therapeutic failure on, intolerance to or contraindication to one (1) formulary preferred agent which is approved or medically accepted for the beneficiary's diagnosis or indication, from any of the following classes of medications: ○ Endothelin Receptor Antagonist ○ Phosphodiesterase-5 Enzyme Inhibitor ○ Prostacyclin **OR** • In patient without cardiopulmonary comorbidities who have a vasoreactivity test of negative and high risk or increase risk of mortality allow, documentation of use in combination of sildenafil AND bosentan.
Ventavis	• Medical record documentation that Ventavis is prescribed by a pulmonologist or cardiologist **AND** • Medical record documentation of a diagnosis of functional class 3 or 4 pulmonary arterial hypertension **AND** • Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to sildenafil AND bosentan.	• Medical record documentation that Ventavis is prescribed by a pulmonologist or cardiologist **AND** • Medical record documentation of a diagnosis of functional class 3 or 4 pulmonary arterial hypertension **AND** • Medical record documentation of one of the following: ○ Medical record documentation of a therapeutic failure on, intolerance to, or contraindication to sildenafil AND bosentan **OR** ○ In patient without cardiopulmonary comorbidities who have a vasoreactivity test of negative and high risk or increase risk of mortality allow, medical record documentation of use in combination of sildenafil AND bosentan.

Remodulin	• Medical record documentation that treprostinil is prescriber by a pulmonologist or cardiologist **AND** • Medical record documentation that treprostinil is being administered subcutaneously **AND** • Medical record documentation of a diagnosis of functional class 2, 3, or 4 pulmonary arterial hypertension **AND** • Medical record documentation of therapeutic failure on, intolerance to or contraindication to, or use in combination with sildenafil (generic Revatio) AND an appropriate second line agent (an endothelin receptor antagonist or Uptravi) used with sildenafil (generic Revatio).	No changes recommended.
Orenitram	• Medical record documentation that Orenitram 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 **AND** • 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 on, intolerance to, or contraindication to Uptravi.	No changes recommended.

Tyvaso/Tyvaso DPI	**Class III of IV Pulmonary Arterial Hypertension** • Medical record documentation that Tyvaso DPI is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a diagnosis of functional class III or IV pulmonary arterial hypertension **AND** • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to, or use in combination with sildenafil OR bosentan. **Pulmonary Hypertension associated with Interstitial Lung Disease** • Medical record documentation that Tyvaso DPI is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a diagnosis of pulmonary hypertension associated with interstitial lung disease (World Health Organization Group 3 Pulmonary Hypertension).	No changes recommended.
Prostacyclin Receptor Agonists (PRA)		
Uptravi	• Medical record documentation that Uptravi is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a diagnosis of World Health Organization (WHO) Group I, functional class II or III pulmonary hypertension **AND** • Medical record documentation of use in combination with, or failure on, intolerance to, or contraindication to sildenafil and/or an endothelin receptor antagonist (Tracleer [bosentan], Letairis [ambrisentan], or Opsumit [macitentan]).	No changes recommended.

Endothelin Receptor Antagonist		
ambrisentan (Letairis)	• Medical record documentation that ambrisentan is prescribed by a pulmonologist or cardiologist **AND** • Medical record documentation of a diagnosis of functional class 2 or 3 pulmonary arterial hypertension **AND** • Medical record documentation of one of the following: ○ Therapeutic failure on, intolerance to, or contraindication to sildenafil (generic Revatio) **OR** ○ Use as first line therapy in combination with tadalafil (generic Adcirca) in patients with WHO Group 1, function class II or III symptoms.	• Medical record documentation that ambrisentan is prescribed by a pulmonologist or cardiologist **AND** • Medical record documentation of a diagnosis of functional class 2 or 3 pulmonary arterial hypertension **AND** • Medical record documentation of a negative pregnancy test in females of childbearing potential **AND** • Medical record documentation of one of the following: ○ Therapeutic failure on, intolerance to, or contraindication to sildenafil (generic Revatio) **OR** Use as first line therapy in combination with tadalafil (generic Adcirca) in patients with WHO Group 1, function class II or III symptoms.
Opsumit	• Medical record documentation that Opsumit 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 **AND** • Medical record documentation that Opsumit will be used in combination with (or therapeutic failure on, intolerance to, or contraindication to) sildenafil.	No changes recommended.
Tracleer	• Medical record documentation that bosentan is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a diagnosis of functional class II, III, or IV pulmonary arterial hypertension.	• Medical record documentation that bosentan is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a diagnosis of functional class II, III, or IV pulmonary arterial hypertension **AND** • Medical record documentation of a negative pregnancy test in females of childbearing potential
PDE5-I		
sildenafil (Revatio) & Liqrev	• Medical record documentation that sildenafil is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a diagnosis of functional class 2, 3, or 4 pulmonary arterial hypertension **AND** • See no medical record documentation of organic nitrate therapy **AND** • If request is for sildenafil 10 mg/mL (generic Revatio): Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Liqrev.	No changes recommended.

Adcirca	• Medical record documentation that tadalafil is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a diagnosis pulmonary arterial hypertension (PAH) **AND** • Medical record documentation that tadalafil will not be used concomitantly with organic nitrate therapy.	No changes recommended.
sCG		
Adempas	• Medical record documentation that Adempas is prescribed by a cardiologist or pulmonologist **AND** • Medical record documentation of a baseline 6-minute walking distance **AND** • Medical record documentation of World Health Organization (WHO) functional class II, III, or IV symptoms **AND** • Medical record documentation of <u>one</u> of the following: ○ Medical record documentation of chronic thromboembolic pulmonary hypertension (CTEPH) (World Health Organization Group 4), which is inoperable or previously treated surgically **OR** ○ All of the following: ▪ Medical record documentation of a diagnosis of World Health Organization (WHO) Group I pulmonary arterial hypertension **AND** ▪ Medical record documentation of therapeutic failure on, intolerance to, or contraindication to, or use in combination with bosentan.	No changes recommended.

There are no changes recommended to formulary placement at this time.

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

UPDATES

RINVOQ UPDATE

Background: Based on feedback from Expion Health, reference to specific alternatives in the atopic dermatitis section must be removed to qualify for rebates.

Recommendations: The following changes are recommended for Commercial Policy 605.0 for Rinvoq:

For treatment of atopic dermatitis (AD)

An exception for coverage of Rinvoq may be made for members who meet the following criteria:

- Medical record documentation of a diagnosis of moderate to severe atopic dermatitis AND
- Medical record documentation that Rinvoq is prescribed by an allergist, dermatologist, or immunologist AND
- Medical record documentation of age greater than or equal to 12 years AND
- Medical record documentation of one of the following:
  - Therapeutic failure on an adequate trial of at least one medium (or higher) potency topical corticosteroid OR
  - For members with an intolerance or contraindication to topical corticosteroids or for members in whom topical corticosteroids are inadvisable (use on sensitive areas, age between 2 and 15 years): Therapeutic failure on, intolerance to, or contraindication to a topical calcineurin inhibitor AND
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure to one systemic therapy [e.g., Dupixent, Adbry] AND
- Medical record documentation of contraindication to, intolerance to, or therapeutic failure on an adequate trial of phototherapy (UVA/UVB treatment) AND
- Medical record documentation that Rinvoq will not be used in combination with another Janus kinase (JAK) inhibitor, biologic immunomodulator, or with other immunosuppressants including but not limited to azathioprine and cyclosporine

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

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

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

WEGOVY & ZEPBOUND QUANTITY LIMIT UPDATE

Background: Wegovy once weekly doses of 0.25 mg, 0.5 mg, and 1 mg are for initiation and escalation doses only and are not approved as maintenance doses. The approved maintenance doses are 2.4 mg or 1.7 mg once weekly for adults and 2.4 mg once weekly for pediatric patients 12 years and older. Table 1 and 2 shows the titration schedule for Wegovy for adult and pediatric patients, respectively.

Table 1. Recommended dosage Regimen for Adults

Treatment	Weeks	Once weekly Subcutaneous Dosage
Initiation	1 through 4	0.25 mg
Escalation	5 through 8	0.5 mg
	9 through 12	1 mg
	13 through 16	1.7 mg
Maintenance	17 and onward	1.7 mg or 2.4 mg

Table 2. Recommended dosage Regimen for Pediatrics

Treatment	Weeks	Once weekly Subcutaneous Dosage
Initiation	1 through 4	0.25 mg[a]
Escalation	5 through 8	0.5 mg[a]
	9 through 12	1 mg[a]
	13 through 16	1.7 mg[b]
Maintenance	17 and onward	2.4 mg

Z n and ent. After 4 weeks of the 2.5 mg starting dose, the dose is increased to 5 mg once weekly.

Recommendations: It is recommended that the quantity limits for Wegovy and Zepbound be updated for the initiation and escalation doses to ensure titration to appropriate doses for glycemic control.

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

- QL FOR LETTER ONLY:
  - Wegovy 0.25 mg, 0.5 mg, and 1 mg: 2 mL per 180 days
  - Wegovy 1.7 mg and 2.4 mg : 3 mL per 28 days
  - Zepbound 2.5 mg: 2 mL per 180 days
  - Zepbound 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg: 2 mL per 28 days

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

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

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

YCANTH UPDATE

Background: DHS required removal of the dermatologist criteria from the Ycanth medical benefit policy. The GHP P&T Committee had included the dermatologist prescriber requirement to ensure appropriate and judicious use of Ycanth.

Recommendations: With the removal of the prescriber requirement, it is recommended that failure of other first-line treatments commonly used upon initial diagnosis be added to the Policy. The following changes are recommended to be added to the Ycanth Medical Benefit Policy:

- Medical record documentation of age greater than or equal to 2 years **AND**
- ~~Medical record documentation that Ycanth is prescribed by a dermatologist **AND**~~
- Medical record documentation of a diagnosis of molluscum contagiosum (MC) **AND**
- Medical record documentation of treatment failure of at least one other treatment modality (including but not limited to cryotherapy, curettage, or podofilox) or reason why other treatments cannot be used

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

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

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

XALKORI ORAL PELLETS UPDATE

Background: Xalkori is now available as 20 mg, 50 mg, and 150 mg oral pellets. Xalkori pellets are supplied encapsulated in shells which can be administered by 2 options:

1. Open shell(s) containing Xalkori pellets and empty the contents directly into the patient's mouth.
2. Open shell(s) containing Xalkori pellets and empty the contents into a consumer -supplied oral dosing aid (e.g., spoon, medicine cup). Administer Xalkori pellets via the dosing aid directly into the patient's mouth.

Immediately after administration, give a sufficient amount of water to ensure that all medication is swallowed.

The recommended dosages for the indications and populations of Xalkori oral pellets are shown below:

Recommended Dosage for Adult Patients with ALK- or ROS1-Positive Metastatic NSCLC

For adults who cannot swallow capsules, the recommended dosage of XALKORI pellets is 250 mg (2 x 50 mg + 1 x 150 mg) orally, twice daily, with or without food until disease progression or unacceptable toxicity occurs.

Recommended Dosage for Pediatric and Young Adult Patients with ALK-Positive ALCL

The recommended dosage for Xalkori capsules or pellets is based on body surface area (Table 1) and given twice daily, with or without food until disease progression or unacceptable toxicity occurs.

Table 1. Recommended XALKORI Dosage for Pediatric Patients 1 Year of Age and Older and Young Adults With ALK-Positive ALCL Using Either XALKORI Capsules or Pellets

Body Surface Area (BSA)	Recommended XALKORI Dosage to Achieve 280 mg/m^2 Twice Daily	Dose Strength Combinations of XALKORI Pellets to Administer[a]	Dose Strength Combinations of XALKORI Capsules to Administer
0.38 to 0.46 m^2	120 mg twice daily	1 x 20 mg + 2 x 50 mg	---
0.47 to 0.51 m^2	140 mg twice daily	2 x 20 mg + 2 x 50 mg	---
0.52 to 0.61 m^2	150 mg twice daily	1 x 150 mg	---
0.62 to 0.80 m^2	200 mg twice daily	1 x 50 mg + 1 x 150 mg	---
0.81 to 0.97 m^2	250 mg twice daily	2 x 50 mg + 1 x 150 mg	---
0.98 to 1.16 m^2	300 mg twice daily	2 x 150 mg	---
1.17 to 1.33 m^2	350 mg twice daily	1 x 50 mg + 2 x 150 mg	---
1.34 to 1.51 m^2	400 mg twice daily	2 x 50 mg + 2 x 150 mg	2 x 200 mg
1.52 to 1.69 m^2	450 mg twice daily	3 x 150 mg	1 x 200 mg + 1 x 250 mg
1.7 m^2 or greater	500 mg twice daily	1 x 50 mg + 3 x 150 mg	2 x 250 mg

[a] No more than 4 oral pellet shells are to be used for a single dose.

Recommended Dosage for Pediatric and Adult Patients with ALK-Positive IMT

The recommended dosage for Xalkori capsules or pellets is based on body surface area (Table 1) and given twice daily, with or without food until disease progression or unacceptable toxicity occurs.

Table 2. Recommended XALKORI Dosage for Pediatric Patients 1 Year of Age and Older with ALK-positive IMT Using Either XALKORI Capsules or Pellets

Body Surface Area (BSA)	Recommended XALKORI Dosage to Achieve 280 mg/m² Twice Daily	Dose Strength Combinations of XALKORI Pellets to Administer[a]	Dose Strength Combinations of XALKORI Capsules to Administer
0.38 to 0.46 m^2	120 mg twice daily	1 x 20 mg + 2 x 50 mg	---
0.47 to 0.51 m^2	140 mg twice daily	2 x 20 mg + 2 x 50 mg	---
0.52 to 0.61 m^2	150 mg twice daily	1 x 150 mg	---
0.62 to 0.80 m^2	200 mg twice daily	1 x 50 mg + 1 x 150 mg	---
0.81 to 0.97 m^2	250 mg twice daily	2 x 50 mg + 1 x 150 mg	---
0.98 to 1.16 m^2	300 mg twice daily	2 x 150 mg	---
1.17 to 1.33 m^2	350 mg twice daily	1 x 50 mg + 2 x 150 mg	---
1.34 to 1.51 m^2	400 mg twice daily	2 x 50 mg + 2 x 150 mg	2 x 200 mg
1.52 to 1.69 m^2	450 mg twice daily	3 x 150 mg	1 x 200 mg + 1 x 250 mg
1.7 m^2 or greater	500 mg twice daily	1 x 50 mg + 3 x 150 mg	2 x 250 mg

[a] No more than 4 oral pellet shells are to be used for a single dose.

Recommendations: Xalkori oral pellets should be added to Oral Oncology Brand NP tier. It will require a prior authorization and will be reviewed with Commercial Policy 255.0. The following quantity limits should be added:

MEDISPAN AUTHORIZATION LEVEL: GPI-10 to include both oral pellet and capsule formulations

QUANTITY LIMIT:

- 20 mg oral pellets: 4 pellets per day, 30 day supply per fill
- 50 mg oral pellets: 4 pellets per day, 30 day supply per fill
- 150 mg oral pellets: 6 pellets per day, 30 day supply per fill

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

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

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

MEDICAL BENEFIT POLICY UPDATE

Background: The following policies were modified following PARP review:

Recommendations:

Policy	DHS Identified Issue	Changes to Policy
MBP 23.0 Velcade (bortezomib)	How can a member have therapeutic failure to the inactive ingredients?	Updated policy criteria to eliminate “therapeutic failure on”
MBP 36.0 Abraxane (paclitaxel protein bound particles)	How can a member have therapeutic failure to the inactive ingredients?	Updated policy criteria to eliminate “therapeutic failure on”
MBP 38.0 Clolar (clofarabine)	How can a member have therapeutic failure to the inactive ingredients?	Updated policy criteria to eliminate “therapeutic failure on”

MBP 62.0 Remodulin IV (treprostinil)	How can a member have therapeutic failure to the inactive ingredients?	Updated policy criteria to eliminate “therapeutic failure on”
MBP 90.0 Benlysta (belimumab)	Please revise to reflect the wording in the package labeling: "The efficacy of BENLYSTA has not been evaluated in patients with severe active central nervous system (CNS) lupus. Use of BENLYSTA is not recommended in this situation."	Updated policy to accurately reflect labeling
MBP 132.0 Avycaz (cetfazidime/avibactam)	HABP and VABP should be an “or” instead of “and”	Updated policy to accurately reflect labeling/indication
MBP 233.0 Pepaxto (melphalan flufenamide)	The FDA announced withdrawal of approval of Pepaxto. There are no eligible NDC’s of Pepaxto available and CMS terminated their labeler agreement effective 1/1/22 and the NDC is obsolete as of 10/22/21.	Policy Retired (FDA withdrew approval effective 2/23/24 [published in federal register on 4/18/24]).
MBP 307.0 Elevidys (delandistrogene moxeparvovec-rokl)	While extremely rare, female patients may have defective genes in both x chromosomes that result in DMD.	At DHS’ direction, “male based on assigned sex at birth” requirement was deleted; however, diagnostic criteria was updated to appropriately confirm a DMD diagnosis in female patients

MBP 23.0, MBP 36.0, MBP 38.0, and MBP 62.0 were updated to reflect the following changes:

AND

- If a brand drug is being requested when a therapeutically equivalent generic drug exists:
  - Medical record documentation of a therapeutic failure on, or intolerance to the generic formulary agent(s) **OR**
  - Medical record documentation of an ~~therapeutic failure on,~~ intolerance to~~,~~ or contraindication to the inactive ingredients of the generic formulary agent(s)

The following changes were made to MBP 90.0:

For active, autoantibody positive, Systemic Lupus Erythematosus (SLE)

- Medical record documentation of age greater than or equal to 5 years **AND**
- Physician provided documentation of a diagnosis of systemic lupus erythematosus **AND**
- Medical record documentation that patient has active disease OR recurrent flares OR inability to wean steroids in systemic lupus erythematosus **AND**
- Positive ANA/anti-dsDNA antibody **AND**
- Medical record documentation that Benlysta is being used in combination with, or patient has a contraindication or intolerance to, standard therapy (e.g. corticosteroid, NSAID, anti-malarial or immunosuppressant) **AND**
- No severe active CNS involvement **AND**
- Must be prescribed by a Rheumatologist **AND**

- Medical record documentation of a dose and duration of therapy that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

AUTHORIZATION DURATION:
Each authorization will be for a period of 12 months. Re-review is required with medical record documentation showing a clinical benefit of one of the following:

- Improvement in functional impairment
- Decrease in the number of exacerbations since the start of Benlysta
- Decrease in the daily required dose of oral corticosteroids such as Prednisone

AND

- Medical record documentation of a dose and duration of therapy that is consistent with FDA-approved package labeling, nationally recognized compendia, or peer-reviewed medical literature

The following changes were made to MBP 307.0:

- Medical record documentation of a diagnosis of Duchenne Muscular Dystrophy confirmed by a genetic mutation in the Duchenne Muscular Dystrophy gene **AND**
- One of the following:
    - Medical record documentation that the member is a male based on assigned sex at birth

    OR

    - Medical record documentation that the member is a female based on assigned sex at birth AND
    - Medical record documentation that the member has a confirmed X-inactivation of the unmutated X-chromosome OR confirmed biallelic variants in the *DMD* gene (cytogenetic or molecular) alteration involving the Xp21 locus

AND

- Medical record documentation of patient age of at least 4, but no older than 5, years of age **AND**
- Medical record documentation that the patient does NOT have a deletion in exon 8 and/or exon 9 in the Duchenne Muscular Dystrophy gene **AND**
- ~~Medical record documentation that the member is a male based on assigned sex at birth and is at least 4, but no older than 5 years of age **AND**~~
- Medical record documentation of provider attestation that the member is ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent) **AND**
- Medical record documentation that Elevidys is prescribed by a neurologist or pediatric neurologist **AND**
- Medical record documentation that patient has been initiated on corticosteroids for Duchenne muscular dystrophy one day prior to Elevidys infusion and medical documentation that patient will continue the regimen after for 60 days* **AND**
- Medical record documentation that the patient is on the appropriate weight-based dose **AND**
- Medical record documentation that the patient has never received Elevidys treatment in their lifetime **AND**
- Medical record documentation that the member has not received any previous gene therapy for Duchenne muscular dystrophy **AND**
- Medical record documentation that the patient will not receive exon-skipping therapies for Duchenne Muscular Dystrophy [e.g., Amondys (casimersen), Exondys 51 (eteplirsen), Viltepso (viltolarsen), Vyondys 53 (golodirsen)] concomitantly with Elevidys treatment. (Note: Any current authorizations for exon-skipping therapy will be terminated upon Elevidys approval.)

***** Deflazacort is <u>not</u> recommended for use as a peri-Elevidys infusion corticosteroid

The following changes were made to MBP 132.0:

- Prescribed by or in consultation with an infectious disease specialist **AND**
- Medical record documentation of one of the following:
    - A diagnosis of complicated intra-abdominal infection caused by caused by the following susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis,*

Enterobacter cloacae, Klebsiella oxytoca, Citrobacter freundii complex *and Pseudomonas aeruginosa* **OR**

- A diagnosis of complicated urinary tract infections (cUTI) including pyelonephritis caused by the following susceptible microorganisms: *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae, Citrobacter freundii* complex, *Proteus mirabilis*, and *Pseudomonas aeruginosa* **OR**
- A diagnosis of Hospital-acquired Bacterial Pneumonia ~~and~~ or Ventilator-associated Bacterial Pneumonia (HABP/VABP) caused by the following susceptible microorganisms: *Enterobacter cloacae, Escherichia coli, Haemophilus influenzae, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa and, Serratia marcescens*

AND

- Medical record documentation of culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity

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

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

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

MAY 2024 DUR/ADHERENCE UPDATE

Commercial/Exchange/TPAs (COMM, D6)

In Progress

- Pharmacotherapy for Opioid Use Disorder (POD) HEDIS measure report

Ongoing

- DPP-4/GLP-1 Diabetes Duplicate Therapy Report
  - We receive this report monthly for all LOBs (Star team addresses Medicare) from Adam Kelchner. This report identifies members who potentially have duplicate therapy on a DPP-4/GLP-1 combination. Calls are made to the prescribers to discuss the lack of clinical evidence of this combination and/or duplicate therapy. Recommendations are made to discontinue one agent (ex. the DPP-4 if member on both a GLP-1 and DPP-4).
    - For 2024 we have resolved the following number of **c**ases of therapeutic duplication:
    - **COMM: 1 case** of therapeutic duplication resulting in a projected savings of **$488.33 per script** (this is savings to both member and the health plan)
    - **D6: 1 case** of therapeutic duplication resulting in a projected savings of **$486.43 per script** (this is savings to both member and the health plan)
    - **TPN2: 1 case** of therapeutic duplication resulting in a projected savings of **$544.29 per script** (this is savings to both member and the health plan)
    - **SASN: 1 case** of therapeutic duplication resulting in a projected savings of **$486.75 per script** (this is savings to both member and the health plan)

- TNF and Oral Oncology Agent Report
    - We get this report monthly for the Commercial/Exchange, TPA, and CHIP LOBs from Adam Kelchner.
    - This report was generated in response to removing the renewal prior authorization requirement for these agents.
    - This report identifies members who are on a TNF or Oral Oncology agent and may not have been seen by their applicable specialist in the last 15 months.
    - We research these members and reach out to the offices/members as necessary to ensure the member has been seen within the last 15 months, an appointment has been scheduled or will be scheduled with the member to ensure the member continues to be able to receive their medication.
    - For 2024:
        - For COMM
            - Members Reviewed: **23**
            - Outreaches Made: **3**
            - Letters Sent: **1**
            - Negative Overrides Entered: **0**
        - For D6
            - Members Reviewed: **29**
            - Outreaches Made: **7**
            - Letters Sent: **3**
            - Negative Overrides Entered: **1**
        - For TG48
            - Members Reviewed: **22**
            - Outreaches Made: **1**
            - Letters Sent: **1**
            - Negative Overrides Entered: **0**
        - For TG51
            - Members Reviewed: **9**
            - Outreaches Made: **2**
            - Letters Sent: **0**
            - Negative Overrides Entered: **0**
        - For TGW2
            - Members Reviewed: **3**
            - Outreaches Made: **0**
            - Letters Sent: **0**
            - Negative Overrides Entered: **0**
        - For TP23
            - Members Reviewed: **1**
            - Outreaches Made: **0**
            - Letters Sent: **0**
            - Negative Overrides Entered: **0**
        - For TP45
            - Members Reviewed: **2**
            - Outreaches Made: **0**
            - Letters Sent: **0**
            - Negative Overrides Entered: **0**
        - For TP50

        - Members Reviewed: **1**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
    - For TP56
        - Members Reviewed: **2**
        - Outreaches Made: **1**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
    - For SASK
        - Members Reviewed: **1**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
    - For SASN
        - Members Reviewed: **2**
        - Outreaches Made: **0**
        - Letters Sent: **0**
        - Negative Overrides Entered: **0**
- Cystic Fibrosis Adherence Report
    - We get this report monthly for all LOBs from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.
        - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence
        - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
        - And for all members we send a letter discussing the importance of medication adherence
        - For 2024, please see below for the number of **members** an adherence letter was sent to:
            - Letters are only sent to members every 6 months
                - For COMM: 3
                - For D6: 3
                - For TG48: 4
                - TGW2: 1
                - For WF89: 1
        - Please see below for the number of letters sent to non-GHS pulmonologists
            - For D6: **0**
        - Please see below for the number of members referred to the CF coordinators:
            - For COMM: **1**
            - For D6: 3
            - For TG48: 4
            - For TGW2: 1
            - For WF89: 1
- Duplicate Anticoagulant Report

- We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
- For 2024:
  - For COMM (Commercial): **3 members** reviewed and **0 interventions** made
  - For D6 (Exchange): **6 members** reviewed and **0 interventions** made
  - For TG48/TG51: **1 members** reviewed and **0 intervention** made

- Duplicate Specialty Therapy
  - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Smith. These members are identified and written up and sent to a medical director if follow up is needed.
    - For Commercial/Exchange/TPA for 2024, **4 members** were reviewed by a pharmacist and **0 members** were referred to Medical Directors for additional follow-up.
      - For COMM: **0**
      - For D6: **1**
      - For TG48,TG51: **2**
      - For EMYD: **1**
- Duplicate Buprenorphine Therapy
  - We get this report **quarterly** with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows and Dr. Hossler for further outreach.
    - For Commercial/Exchange, TPAs for 2024, we have reviewed **1 member for COMM** and **0 members** were referred to Dr. Meadows
- Suboxone with an Opioid Report
  - We get this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each new member that flags on the report. These members are being discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both medical directors look into whether it is appropriate to end the opioid authorizations still in place or if further intervention is required.
  - For Commercial/Exchange/TPA for 2024, see below for the new members reviewed and those referred to the MDs:
    - For COMM: we have reviewed **0 new members** and **0 members** were referred to MDs
    - For D6: we have reviewed **0 new members** and **0 members** were referred to MDs
    - For EMYD: we have reviewed **1 new members** and **0 members** were referred to MDs
- Ending Opioid Authorizations
  - We are working on identifying members who have active opioid authorizations in place but have since started Buprenorphine therapy. The letter is sent to the members notifying them the opioid authorization has been ended due to the start of buprenorphine therapy.
  - For Commercial/Exchange/TPA for 2024, see below for the number of letters we sent to members notifying them that we are ending their opioid authorization(s):
    - For D6: **0**
    - For COMM: **0**

- Opioid Overutilization Report **(Report was on hold for first quarter)**
    - We get this report **monthly** from Navitus and we write up each member that flags on the report. We have been monitoring the members that are continuously showing up on the report by any change in their MED. For those members we deem appropriate we will send a letter to their PCP.
    - For Commercial/Exchange/TPA for 2024, see below for the number of reviewed cases.
        - For COMM: we have reviewed **0 members** and sent **0 cases** to MDs for review
        - For EMYD: we have reviewed **0 members** and sent **0 cases** to MDs for review
        - For TG48: we have reviewed **0 members** and sent **0 cases** to MDs for review
- FWA Reports
    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For COMM for 2024, we have reviewed **10** cases and corrected claims, resulting in a potential **cost savings/avoidance of $1,428.55**
        - For D6 for 2024, we have reviewed **8** cases and corrected claims, resulting in a potential **cost savings/avoidance of $603.52**
        - For EMYD for 2024, we have reviewed **3** cases and corrected claims, resulting in a potential **cost savings/avoidance of $1,093.66**
        - For TG48, TG51 for 2024, we reviewed **2** cases and corrected claims, resulting in a potential **cost savings/avoidance of $14.21**
        - For SASE for 2024, we reviewed **1** cases and corrected claims, resulting in a potential **cost savings/avoidance of $0.00**
- Duplicate Antipsychotics (report on hold first quarter)
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - We have sent the following provider letters in 2024
            - For COMM: **0**
            - FOR D6: **0**
            - FOR TG48, TG51: **0**
- Severity Report (on hold for first quarter)
    - We get this report **monthly** for **all LOBs** on members who have filled a medication that has a level one interaction with another medication they have a claim for
        - For Commercial/Exchange/TPA for 2024 see below for the number of members identified and had sent letters to their MI attributed PCP:
            - For COMM: **0**
            - For D6: **0**
            - For EMYD: **0**
            - For SASF: **0**
            - For SASN: **0**
            - For SASE: **0**
            - For TG48: **0**
- Tobacco Cessation Program
    - We get this report **monthly** to identify members on prolonged tobacco cessation treatment. We send a letter and resource pamphlet to provide additional behavioral health support through Geisinger Health and Wellness.

- For Commercial/Exchange/TPA for 2024, we sent letters to the below number of members:
  - For COMM: **4**
  - For D6: **2**
  - For EMYD: **9**
  - For SASN: **3**
  - TG48**: 2**
  - TPI0: **1**

- <u>STENT Adherence Report (report on hold first quarter)</u>
  - We get this report **<u>monthly</u>** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
  - In 2024, we have sent letters encouraging adherence to the below number of members:
    - **Members for Antiplatelet:**
      - COMM: **0**
      - D6: **0**
      - EMYD: **0**
      - SASN: **0**
      - TG48, TG51: **0**
      - TGW2: **0**
      - TP41: **0**
      - TP23: **0**
      - TP33: **0**
      - TP45: **0**
      - TP46: **0**
      - TP50: **0**
      - TP56: **0**
      - TP64: **0**
      - TP74: **0**
    - **Members for Beta-Blocker:**
      - COMM: **0**
      - D6: **0**
      - EMYD: **0**
      - SASN: **0**
      - TG48, TG51: **0**
      - SASK: **0**
      - TPB3: **0**
      - TPI3: **0**
      - TPR1: **0**
      - TPT2: **0**
      - TPU1: **0**
      - TGW2: **0**
      - SASE: **0**
    - **Members for Statin:**
      - COMM: **0**
      - D6: **0**
      - EMYD: **0**
      - SASN: **0**
      - SASF: **0**
      - TG48, TG51: **0**
      - WF89: **0**
      - TP33: **0**
      - TP50: **0**
      - SASX: **0**
      - TPB3: **0**
      - TPH2: **0**
      - TPT2: **0**
      - TP41: **0**

        - *member may flag for more than one measure and are included in the count for each measure
    - In 2024, we have attempted telephonic outreach to the below number of members non-adherent in all 3 measures and reached the below members to encourage adherence.
        - COMM:
            - Attempted: **0**
            - Reached: **0**
        - D6:
            - Attempted: **0**
            - Reached:**0**
        - EMYD:
            - Attempted: **0**
            - Reached: **0**
        - SASN:
            - Attempted: **0**
            - Reached: **0**
- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR) (reports on hold first quarter)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.
        - For Commercial/Exchange for 2024, see below for the number of letters sent to members:
            - COMM: **0**
            - D6: **0**
- Asthma Medication Ratio (AMR) Member Calls
    - Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. The RPHs call Commercial/Exchange members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication.
    - For Commercial/Exchange for 2024, see below for the number of members we have outreached to and the number of members that have been reached:
        - COMM:
            - Outreached to: **20**
            - Reached: **10**
        - D6:
            - Outreached to: **12**
            - Reached: **9**
- Antidepressant Medication Management (AMM) (report on hold first quarter)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
        - For Commercial/Exchange for 2024, see below for the number of letters sent to members:
            - Effective Acute Phase:
                - COMM: **0**
                - D6: **0**
            - Effective Continuation Phase:
                - COMM: **0**
                - D6: **0**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA) (report on hold first qt)

- Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
    - For Commercial/Exchange for 2024, see below for the number of letters sent to members:
        - COMM: **0**
        - D6: **0**

- Statin Therapy for Patients with Cardiovascular Disease (SPC) (report on hold first quarter)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange in 2024, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **0**
            - D6: **0**
        - For Commercial/Exchange in 2024, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **0**
            - D6: **0**
- Statin Therapy for Patients with Diabetes (SPD) (report on hold first quarter)
    - We get this report **monthly** to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For Commercial/Exchange for 2024, see below for the number of letters sent to **providers** to encourage statin therapy initiation**:**
            - COMM: **0**
            - D6: **0**
        - For Commercial/Exchange for 2024, see below for the number of letters sent to **members** to promote statin adherence:
            - COMM: **0**
            - D6: **0**
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH) (report on hold first quarter)
    - We get this report **monthly** to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For Commercial/Exchange for 2024, see below for the number of letters sent to **members:**
            - COMM: **0**
            - D6: **0**
- Use of Opioids from Multiple Providers (UOP) (report on hold first quarter)
    - We get this report quarterly to identify members 18 years of age and older with a total day supply of all opioid claims to be 15 days or greater
        - See below for the number of members that were identified who were seeing 4 or more providers from different offices for their opioid prescriptions for 2024
            - **COMM: 0**
            - **D6: 0**
        - See below for the number of members that were identified who were seeing 4 or more providers within the same office for their opioid prescriptions for 2024
            - **COMM: 0**
            - **D6: 0**

        - We sent letters to the MI attributed PCP of each member with the respective medication fill history to encourage medication evaluation of the opioid medications

- **HEDIS PQA Initiatives:**
- HEDIS PQA- INR Report
    - We get this report **weekly** for the Exchange population from Adam Kelchner
    - This report looks at the percentage of members 18 years of age and older who had at least one 56-day interval of warfarin therapy and who received at least one international normalized ratio (INR) monitoring test during each 56-day interval with active warfarin therapy.
        - For Exchange for 2024, we have performed telephonic outreach to providers for **1 members** that had not had an INR level drawn.
- HEDIS PQA-AMO Report
    - We get this report **monthly** for the Exchange population from Adam Kelchner
    - This report looks at the percentage of members 18 years of age and older who are prescribed long-term opioid therapy and have not received a drug test at least once during the measurement year.
        - For Exchange for 2024, we have reviewed **108 members** that had not had a drug test completed and completed outreach to those without a drug test.
- HEDIS PQA-PDC Letters (report on hold)
    - We get this report **monthly** for the Exchange population from Adam Kelchner
    - This report looks at the percentage of members 18 years of age and older who have a PDC of less than 80% during the measurement year for the below medication classes who are past due for a medication refill:
        - Renin Angiotensin System Antagonists (PDC-RASA)
        - Diabetes All Class (PDC-DR)
        - Statins (PDC-STA)
        - For Exchange for 2024, we have identified the following number of members and sent letters:
            - Renin Angiotensin System Antagonists (PDC-RASA): **0**
            - Diabetes All Class (PDC-DR): **0**
            - Statins (PDC-STA): **0**

Fliers/Letters

- Commercial/Exchange DUR/FWA Program internal Fliers
    - Last updated 6/2023 next update 6/2024
- Current Provider Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Statin Use in Persons with Diabetes DUE
        - Opioid Overutilization
        - Duplicate Antipsychotic medication
        - Severity Report
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - SUPD/SPD Provider Letter
        - HEDIS: Asthma Medication Ratio (AMR)
        - HEDIS: Use of Opioids from multiple providers (UOP)

        - HEDIS: Use of Opioids at High Dosage (HDO)
- Current Member Letters
        - Exchange PQA Adherence Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Ending Opioid Authorizations
        - Tobacco Cessation Letter
        - STENT Adherence Report
        - HEDIS: Asthma Medication Ratio (AMR)
        - HEDIS: Antidepressant Medication Management (AMM)
        - HEDIS: Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - HEDIS: Statin Therapy for Patients with Diabetes (SPD)
        - HEDIS: Persistence of eta-Blocker Treatment After a Heart Attack (PBH)

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

In Progress
- Pharmacotherapy for Opioid Use Disorder (POD) HEDIS measure report

Ongoing
- DPP-4/GLP-1 Diabetes Duplicate Therapy Report
    - We receive this report monthly for all LOBs (Star team addresses Medicare) from Adam Kelchner. This report identifies members who potentially have duplicate therapy on a DPP-4/GLP-1 combination. Calls are made to the prescribers to discuss the lack of clinical evidence of this combination and/or duplicate therapy. Recommendations are made to discontinue one agent (ex. the DPP-4 if member on both a GLP-1 and DPP-4).
        - For 2024 we have resolved **0 cases** of therapeutic duplication.
- Cystic Fibrosis Adherence Report
    - We get this report **monthly** for **all LOBs** from Adam Kelchner. The report identifies patients who have a specific diagnosis of Cystic Fibrosis & outpatient/office visits within the past 2 years. Further the report calls out medication fill history for specific CF medications and the corresponding PDC.
        - For those members who are seen by a GHS provider we send their information to the CF coordinators to discuss their medication adherence with the member
        - We send letters to non-GHS providers with the CF medication fill history for those members with a PDC less than 80%
        - And for all members we send a letter discussing the importance of medication adherence
        - For CHBQ for 2024, we sent **0 members** an adherence letter
            - Letters are only sent to members every 6 months
            - There were **0 members** who saw a non-GHS pulmonologist and a letter was sent to that pulmonologist
            - There were **0 members** who saw GHS pulmonologists and were sent to the CF coordinators for follow up
- Duplicate Anticoagulant Report

    - We get this report **weekly** for **all LOBs** flagging members filling duplicate anticoagulant medications. We personally reach out to the providers/members of the flagged members to confirm proper medication therapy.
        - For CHBQ in 2024, we have reviewed **0 members** and have made interventions for **0 members**
- Duplicate Specialty Therapy
    - We run an in-house retrospective report **quarterly** for **all LOBs** with help from Adam Kelchner and Aubrielle Smith. These members are identified and written up and sent to a medical director if follow up is needed.
        - For CHBQ for 2024, **0 members** were reviewed by pharmacists and **0 members** were referred to Medical Directors for additional follow-up.
- Duplicate Buprenorphine Therapy
    - We get this report **quarterly** with help from Adam Kelchner. The report works to identify members who have at least a 7 day overlap period of generic Buprenorphine and generic Buprenorphine/naloxone products. Members identified as being on both products are being forwarded to Dr. Meadows and Dr. Hossler for further outreach.
        - For CHBQ for 2024, we have reviewed **0 members** and **0 members** were referred to MDs
- Suboxone with an Opioid Report
    - We get this report **weekly** for **all LOBs** from Adam Kelchner and we are writing up each member that flags on the report. These members are being discussed at our weekly meeting with Dr. Meadows and Dr. Hossler. Both MDs look into whether it is appropriate to end the opioid authorizations still in place or if further intervention is required.
        - For CHBQ for 2024, we have reviewed **0 new members**, and **0 members** were referred to MDs
- Ending Opioid Authorizations
    - We are working on identifying members who have active opioid authorizations in place but have since started Buprenorphine therapy. The letter is sent to the members notifying them the opioid authorization has been ended due to the start of buprenorphine therapy.
        - For CHBQ for 2024, we sent **0 members** a letter notifying them of the end of their opioid authorization(s).
- Severity Report
    - This is a **monthly** report for **all LOBs** on members who have filled a medication that has a level one interaction with another medication they have a claim for
        - For CHBQ for 2024, letters have been sent to MI attributed providers of **0 CHIP members**
- FWA Reports
    - We get this report **weekly** for **all LOBs** from Jeremy Baker. We prepare this report by determining which claims need to be verified, and our GHP technician makes calls to pharmacies to correct/verify claims.
    - We review claims for anti-hypertensives, statins, 1-day supply, and inhalers
        - For CHBQ for 2024, we have reviewed **9** cases and corrected claims, resulting in a potential **cost savings/avoidance of $2,141.83**
- TNF and Oral Oncology Agent Report

    - We get this report monthly for the Commercial/Exchange, TPA, and CHIP LOBs from Adam Kelchner.
    - This report was generated in response to removing the renewal prior authorization requirement for these agents.
    - This report identifies members who are on a TNF or Oral Oncology agent and may not have been seen by their applicable specialist in the last 15 months.
    - We research these members and reach out to the offices/members as necessary to ensure the member has been seen within the last 15 months, an appointment has been scheduled or will be scheduled with the member to ensure the member continues to be able to receive their medication.
    - For 2024:
        - For CHBQ
            - Members Reviewed: **1**
            - Outreaches Made: **0**
            - Letters Sent: **0**
            - Negative Overrides Entered: **0**
- Tobacco Cessation Program
    - We get this report **monthly** to identify members on prolonged tobacco cessation treatment. We send a letter and resource pamphlet to provide additional behavioral health support through Geisinger Health and Wellness.
        - For CHBQ for 2024, we have not sent any letters
- STENT Adherence Report (report on hold first quarter)
    - We get this report **monthly** to identify members on an antiplatelet medication and then flag for betablocker and statin medication claims.
    - For CHBQ for 2024, we have sent letters encouraging adherence to:
        - Members for Antiplatelet:
            - CHBQ: **0**
        - Members for Beta-blocker:
            - CHBQ: **0**
        - Members for Statin:
            - CHBQ: **0**
        - *member may flag for more than one measure and are included in the count for each measure
- Antipsychotic with Opioid Report (report on hold first quarter)
    - We get this report **quarterly** to identify **CHIP** members with an overlap of 8 or more days between an opioid and antipsychotic medication.
    - We send a letter with claims data to both the opioid prescriber and the antipsychotic prescriber to encourage collaboration in medication management.
        - For CHBQ for 2024, we sent **0 letters** to **opioid and antipsychotic prescribers**
- Duplicate Antipsychotics (report on hold first quarter)
    - We get this report **quarterly**, and we send letters to the PCPs to address potential duplicate therapy issues.
        - For CHBQ in 2024, we have sent letters to **0 providers**
- **HEDIS Initiatives: *Using proactive HEDIS data***
- Asthma Medication Ratio (AMR) (report on hold first quarter)
    - Jesse Barsh runs this proactive HEDIS report **monthly,** and we send letters to the flagged members who have a ratio of controller to total asthma medications of < 0.5.

        - For CHBQ for 2024, we sent **0 letters** to members
- Asthma Medication Ratio (AMR) Member Calls
    - Adam Kelchner runs this report **weekly** based off of proactive HEDIS reporting. we send CHIP members who have had a controller or reliever medication filled in the past 3 months AND are past due for their controller medication to the Respiratory Therapists for direct telephonic outreach.
        - For CHBQ for 2024, we have referred **0 members** to the Respiratory Therapists for outreach.
        - For CHBQ for 2024, our pharmacy technician and the STAR reps have outreached to **0 members** and reached **0 members**
- Antidepressant Medication Management (AMM) (reports on hold first quarter)
    - Jesse Barsh runs this proactive HEDIS report **monthly,** and we send letters to the flagged members who appear non-adherent to their antidepressant medications.
        - For CHBQ for 2024, we sent **0 letters** to members in the **Effective Acute Phase**, and **0 letter** to members in the **Effective Continuation Phase**
- Adherence to Antipsychotics for Individuals with Schizophrenia (SAA) (reports on hold first quarter)
    - Jesse Barsh runs this report **monthly,** and we send letters to the flagged members who appear non-adherent to their antipsychotic medications.
        - For CHBQ for 2024, we have sent **0 letters** to members
- Statin Therapy for Patients with Cardiovascular Disease (SPC) (reports on hold first quarter)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ for 2024, we have sent **0 letters** to providers
        - For CHBQ for 2024, we have sent **0 letters** to members
- Statin Therapy for Patients with Diabetes (SPD) (reports on hold first quarter)
    - This is a **monthly** report to identify members with cardiovascular disease and who have not received a statin medication or who are non-adherent to statin therapy
        - For CHBQ for 2024, we have sent **0 letters** to providers
        - For CHBQ for 2024, we have sent **0 letters** to members
- Persistence of Beta-Blocker Treatment After a Heart Attack (PBH) (reports on hold first quarter)
    - This is a **monthly** report to identify members with a diagnosis of AMI who received beta-blocker treatment for 6 months after discharge and who are non-adherent to beta-blocker therapy
        - For CHBQ for 2024, we have sent **0 letters** to members

Fliers/Letters

- Chip DUR/FWA Program internal Fliers
    - Last updated 6/2023 next update 6/2024
- Current Provider Letters
        - Cystic Fibrosis Adherence Letter
        - TNF/Oral Oncology Letter
        - Duplicate Antipsychotic medication
        - Severity Report
        - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
        - SUPD/SPD Provider Letter
        - HEDIS: Asthma Medication Ratio (AMR)

- Current Member Letters
    - Cystic Fibrosis Adherence Letter
    - TNF/Oral Oncology Letter
    - Ending Opioid Authorizations
    - Tobacco Cessation Letter
    - STENT Adherence Report
    - HEDIS: Asthma Medication Ratio (AMR)
    - HEDIS: Antidepressant Medication Management (AMM)
    - HEDIS: Adherence to Antipsychotics for Individuals with Schizophrenia (SAA)
    - HEDIS: Statin Therapy for Patients with Cardiovascular Disease (SPC)
    - HEDIS: Statin Therapy for Patients with Diabetes (SPD)

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

Meeting adjourned at 4:06 pm.

The next bi-monthly scheduled meeting will be held on July 16th, 2024 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.