P&T Committee Meeting Minutes
Commercial, Exchange, CHIP
December 2024 e-Vote

DRUG REVIEWS

DUOPA (carbidopa and levodopa enteral suspension)

Review: Duopa is indicated to treat motor fluctuations in patient with advance Parkinson's disease who have bothersome and/or increased "Off" periods on the current standard of care therapy due to fluctuating drug levels. Duopa is also indicated as a second line treatment for patients. These patients will require placement of a PEG-J tube and medication is dispensed through an infusion pump.

Duopa is supplied as an enteral suspension containing 4.63 mg of carbidopa and 20 mg of levodopa per mL in a single-use cassette, with each cassette containing approximately 100 mL of suspension.

The maximum recommended daily dose of Duopa is 2000 mg of levodopa, one cassette per day, administered over 16 hours. Prior to initiating Duopa, patients should be converted from all forms of levodopa to an oral immediate-release carbidopa-levodopa tablets in a ratio of 1:4. The daily dose is determined by individualized patient titration and is composed of a morning dose, continuous dose and extra doses. Daily dose should be titrated based on patient's clinical response. The administration of Duopa is into the jejunum through a percutaneous endoscopic gastrostomy with jejunal tube (PEG-J) with the CADD®-Legacy 1400 portable infusion pump. At the end of the daily 16-hour infusion, patient will disconnect pump from the PEG-J and take their night-time dose of oral immediate-release carbidopa-levodopa tablets.

Efficacy of Duopa was established in a randomized, double-blind, double-dummy, active-controlled, parallel group, 12-week study in patients with advanced Parkinson's disease who were levodopa-responsive and had persistent motor fluctuations while on treatment with oral immediate-release carbidopa-levodopa and other Parkinson's disease medications. Patients eligible for study participation have had to experience 3 or more hours of "Off" time on their current Parkinson's disease drug treatment and demonstrated a clear responsiveness to treatment with levodopa. Patients selected had a mean age of 64 years and a disease duration of 11 years. 89% of patients were taking at least one concomitant medication for Parkinson's disease, e.g., dopaminergic agonist, COMT-inhibitor, MAO-B inhibitor, in addition to oral immediate release carbidopa-levodopa. 39% of patients were taking two or more concomitant medications. Seventy-one patients were enrolled and randomized 1:1 to either Duopa and placebo or placebo suspension and immediate-release carbidopa-levodopa 25/100 mg tablets with both groups having a PEG-J device in place. The mean daily levodopa dose was 1117 mg/day in the Duopa group and 1351 mg/day in the oral immediate-release carbidopa-levodopa group.

The clinical outcome was the mean change from baseline to week 12 in the total daily mean "Off" time based on a Parkinson's disease diary. The "Off" time was normalized to 16-hours awake period based on the person's waking day and daily infusion duration of 16 hours. The mean score decreases in "Off" time from baseline to week 12 was greater patients in the Duopa group ($p=0.0015$) than patients receiving oral immediate-release carbidopa-levodopa. The mean score increases of "On" time without dyskinesia from baseline to week 12 was greater for the Duopa group ($p=0.0059$) compared to the oral immediate-release carbidopa-levodopa group. The treatment differences for both "Off" and "On" times were approximately 1.9 hours.

Duopa is contraindicated in patients who are currently taking a nonselective monoamine oxidase (MOA) inhibitor, e.g., phenelzine and tranylcypromine, or who have recently, within the last 2 weeks, taken a nonselective MAO inhibitor. Precaution is needed in patient with existing peripheral neuropathy, which can be worsen with Duopa due to hyperhomocysteinaemia associated with higher doses of levodopa required when discontinuing other dopamine sparing therapies.

The most common adverse reactions seen in clinical trials for Duopa include gastrointestinal and gastrointestinal procedure-related risks, falling asleep during activities of daily living and somnolence, orthostatic hypotension, hallucinations/psychosis/confusion, impulse control/compulsive behaviors, depression and suicidality, withdrawal-emergent hyperpyrexia and confusion, dyskinesia, neuropathy, cardiovascular ischemic events, melanoma, laboratory test abnormalities, and glaucoma.

In patients 65 years of age and older, there was an increased risk for elevated BUN and CPK (above the upper limit of the normal reference range for these laboratory analytes) during treatment with Duopa compared to the risk for patients less than 65 years of age.

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

Outcome: Duopa is a pharmacy benefit and must be dispensed through a specialty pharmacy. It will be not added to the Commercial/Exchange/CHIP formularies. The following prior authorization criteria will apply:

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of treatment of motor fluctuations in advanced Parkinson disease **AND**
- Medical record documentation that Duopa is prescribed by or in consultation with a neurologist **AND**
- Medical record documentation of refractory tremor **AND**
- Medical record documentation of levodopa responsiveness with clearly defined “On” periods **AND**
- Medical record documentation of persistent motor complications with disabling “Off” periods such as muscle stiffness, slow movements, or difficulty starting movements **AND**
- Medical record documentation that member has undergone or has planned placement of a PEG-J tube **AND**
- Medical record documentation that the member was assessed for and determined for and determined to have no other secondary causes of Parkinson’s Disease **AND**
- Medical record documentation of therapeutic failure, intolerance to, or contraindication to carbidopa-levodopa, and at least two other classes of anti-Parkinson’s therapy

GPI LEVEL: GPI-12

QUANTITY LIMIT: 100 mL per day

AUTHORIZATION DURATION: 12 months

REAUTHORIZATION CRITERA:

- Medical record documentation of clinical improvement or maintenance of condition. Reauthorization will be for a 12-month period

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

KISUNLA (donanemab-azbt)

Review: Kisunla is indicated for the treatment of Alzheimer’s disease. Treatment with Kisunla should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in the clinical trials. The presence of amyloid beta pathology needs to be confirmed prior to initiating treatment.

Kisunla is the third amyloid-targeting mAb approved for the treatment of AD and the second agent in this class to have full FDA approval. Aduhelm is no longer available. The same registry requirements outlined in CMS' national coverage determination (NCD)/coverage with evidence development (CED) that apply to Medicare patients receiving Leqembi apply to Kisunla.

Donanemab-azbt is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against insoluble N-truncated pyroglutamate amyloid beta. The accumulation of amyloid beta plaques in the brain is a defining pathophysiological feature of Alzheimer's disease. Biologically, AD is defined by the presence of Aβ plaques and neurofibrillary tau deposits. While this understanding of the pathology of AD has formed the basis for therapeutic targeting of Aβ, it is understood that AD's underlying mechanisms are likely multifactorial (e.g. amyloid, tau, inflammation, and other processes).

As patients present with signs of dementia, one of the initial diagnosis is confirmed via cognitive tests. Doctors may conduct one or several short cognitive tests. Example cognitive tests include mini-mental state exam (MMSE), clinical dementia rating scale (CDR-SB or CDR-GS), Montreal cognitive assessment (MoCA), Quick Dementia Rating System (QDRS). The CDR-SB or CDR-GS measures six domains that are divided into cognitive domains (memory, orientation, judgement, and problem-solving) and functional domains (community affairs, home and hobbies, and personal care). The MoCA checks language, memory, visual and spatial thinking, and orientation skills. The QDRS is used in the context of comprehensive diagnosis and staging. Brain imaging with MRI is important in the evaluation of patients with suspected AD. Along with MRI, measurement of the CSF amyloid levels have become standard in the diagnosis of AD when a provider is considering the use of anti-amyloid monoclonal antibody therapy. Prior to the approval of Aduhelm, measurements were only conducted in clinical trials. There are two currently accepted methods to measure amyloid: a PET scan or analysis of CSF from a lumbar puncture. The use of amyloid PET in routine practice is very limited because it is expensive, not typically reimbursed by insurance and not widely available. CSF biomarker tests are also limited in use because some patients or providers consider lumbar punctures risky or invasive. Blood biomarkers can help increase patient access to AD biomarker testing and early treatment. These tests can significantly reduce the burden on specialists and reduce wait times for diagnosis and treatment. Blood biomarkers have been studied and are in development for AD and are starting to be used in clinical practice, some examples include reduced plasma Aβ42/Aβ40, assays for tau phosphorylated at amino acid 181 (p-tau181), 217 (p-tau217), or 231 (p-tau231), plasma NfL, and plasma GFAP. NfL is a biomarker of neuroaxonal damage, which is not specific for AD and therefore is unlikely to be used on its own for AD diagnosis. In 2022, the Alzheimer's Association released recommendations regarding biomarkers: Aβ levels decrease in CSF and Aβ buildup can be seen in the amyloid-based PET scans, tau levels increase in CSF and PET scans, synaptic dysfunction- hypometabolism seen on FDG-PET, and atrophy seen on brain MRI and can be measured with MRI volumetrics. According to the 2018 NIA-AA, it is also now widely accepted that CSF Aβ42 (or the Aβ42/ Aβ40 ratio) is a valid indicator of the abnormal pathologic state associated with cerebral Aβ deposition. Also, plasma amyloid beta (Aβ)1-42 and phosphorylated tau (p-tau) predict high amyloid status from Aβ PET.

Kisunla is available as 350 mg/20 mL (17.5 mg/mL) single dose vial. The recommended dose is 700 mg every four weeks for three doses, then 1400 mg every four weeks. Kisunla is administered every four weeks as an intravenous infusion over 30 minutes. In contrast, Leqembi is administered every 2 weeks. Providers should consider stopping dosing with Kisunla based on reduction of amyloid plaques to minimal levels on amyloid PET imaging. In the clinical trials, dosing was stopped based on reduction of amyloid plaques below predefined thresholds on PET imaging. If an infusion is missed, administration should be resumed every 4 weeks at the same dose as soon as possible.

During Kisunla therapy, it is recommended to monitor for amyloid related imaging abnormalities- edema (ARIA-E) and -hemosiderin deposition (ARIA-H). A recent baseline brain magnetic resonance imaging (MRI) prior to initiating treatment with Kisunla needs to be obtained. Also, an MRI prior to the 2nd, 3rd, 4th, and 7th infusion needs to be obtained. If a patient experiences symptoms suggestive of ARIA, a clinical evaluation should be performed, including an MRI if indicated.

While Kisunla's finite dosing and monthly administration are positive differentiators compared to Leqembi, the agent's safety profile is viewed less favorably. Note that Leqembi's label requires four brain MRIs prior to drug infusion, whereas Kisunla requires five. From a competitive perspective, Leqembi is likely to benefit from a first-mover advantage over Kisunla as well as from having a lower rate of ARIA-related AEs in clinical trials. Kisunla may have an initial competitive advantage based on once-monthly dosing versus every-2-week dosing for Leqembi.

The efficacy of Kisunla was evaluated in a double-blind, placebo-controlled, parallel-group study (Study 1) in patients with Alzheimer's disease. Patients included in the trial had confirmed presence of amyloid pathology and mild cognitive impairment or mild dementia stage of disease, consistent with Stage 3 and Stage 4 Alzheimer's disease. Patients were enrolled with a Mini-mental state examination (MMSE) score of ≥20 and ≤28 and had a progressive change in memory function for at least 6 months. MMSE score of 10-20 is classified as moderate dementia due to AD. MMSE score of 21-26 is classified as mild dementia due to AD. MMSE of 27-28 is MCI due to AD. Patients were included in the study based on visual assessment of tau PET imaging and standardized uptake value ratio. Patients were enrolled with or without concomitant approved therapies for Alzheimer's disease. Patients were excluded if they had a contraindication to MRIs or PET scans, history of current significant neurological disease affecting CNS other than AD or current psychiatric diagnosis likely to affect participation or interpretation of study results, current serious or unstable illness or life expectancy < 24 months, history of certain cancers in the last 5 years, significant suicide risk, history of alcohol or drug abuse disorder in the last 2 years, sensitivity to florbetapir or flortaucipir, received donanemab in any prior investigational study, presence of ARIA-E on MRI scans, > 4 cerebral microhemorrhages, > 1 area of superficial siderosis, any cerebral hemorrhage > 1 cm or severe white matter disease on MRI, and poor venous access. Patients could enroll in an optional, long-term extension. A total of 1,736 patients were included in the trial. Patients were randomized 1:1 to receive 700 mg of Kisunla every 4 weeks for the first 3 doses and then 1400 mg every 4 weeks (N=860) or placebo (N=876) for a total of up to 72 weeks. The amyloid PET levels were measured at Week 24, Week 52, and Week 76. If amyloid plaque level was < 11 Centiloids on a single PET scan or 11 to < 25 Centiloids on 2 consecutive PET scans, the patient was eligible to switch to placebo. Also, dose adjustments were allowed for treatment emergent ARIA or symptom that then showed ARIA-E or ARIA-H on MRI. Patients included in the trial had a mean age of 73 years, with a range of 59 to 86 years. Of those randomized, 68% had low/medium tau level and 32% had high tau level; 71% were ApoE ε4 carriers and 29% were ApoE ε4 noncarriers. The primary efficacy endpoint was change in the integrated Alzheimer's Disease Rating Scale (iADRS) score from baseline to 76 weeks. The iADRS is a combination of two scores: the Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog13) and the Alzheimer's Disease Cooperative Study – instrumental Activities of Daily Living (ADCSiADL) scale. The total score ranges from 0 to 144, with lower scores reflecting worse cognitive and functional performance. Other efficacy endpoints included Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB), ADAS-Cog13, and ADCS-iADL. There were two primary analysis populations based on tau PET imaging: 1) low/medium tau level population and 2) combined population of low/medium plus high tau population. Patients treated with Kisunla demonstrated a statistically significant reduction in clinical decline on iADRS compared to placebo at Week 76 in the combined population (2.92, $p < 0.0001$) and the low/medium tau population (3.25, $p < 0.0001$). Patients treated with Kisunla demonstrated a statistically significant reduction in clinical decline on CDR-SB compared to placebo at Week 76 in the combined population (-0.70, $p < 0.0001$). There were also statistically significant differences ($p<0.001$) between treatment groups as measured by ADAS-Cog13 and ADCS-iADL at Week 76. The percentage of patients eligible for switch to placebo based on amyloid PET levels at Week 24, Week 52, and Week 76 were 17%, 47%, and 69%, respectively. Amyloid PET values may increase after treatment with donanemab is stopped. There is no data beyond 76 weeks to guide whether additional dosing may be needed for longer-term clinical benefit.

Kisunla is contraindicated in patients with known serious hypersensitivity to donanemab-azbt or to any of the excipients. Reactions have included anaphylaxis. Kisunla has a boxed warning for amyloid related imaging abnormalities (ARIA). In the labeling, Kisunla has warning and precautions for ARIA and infusion-related reactions. Monoclonal antibodies directed against aggregated forms of beta amyloid, including Kisunla, can cause ARIA. ARIA can occur spontaneously in patients with Alzheimer's disease, particularly in patients with MRI findings suggestive of cerebral amyloid angiopathy, such as pretreatment

microhemorrhage or superficial siderosis. ARIA usually occurs early in treatment and is usually asymptomatic. When symptoms are present, reports include but are not limited to headache, confusion, visual changes, dizziness, nausea, and gait difficulty. Symptoms of ARIA usually resolve overtime. In addition to ARIA, intracerebral hemorrhages greater than 1 cm in diameter have occurred in patients treated with Kisunla. The risk of ARIA, including symptomatic and serious ARIA, is increased in apolipoprotein E ε4 (ApoE ε4) homozygotes, radiographic findings of cerebral amyloid angiopathy, and concomitant antithrombotic or thrombolytic medication. Approximately 15% of Alzheimer's disease patients are ApoE ε4 homozygotes. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. An FDA-authorized test for the detection of ApoE ε4 alleles to identify patients at risk of ARIA is currently not available. Current available tests used to identify ApoE ε4 alleles may vary in accuracy and design. Neuroimaging findings that indicate cerebral amyloid angiopathy (CAA) are at an increased risk for intracerebral hemorrhage. The presence of ApoE ε4 allele is associated with cerebral amyloid angiopathy. For infusion reactions, pre-treatment with antihistamines, acetaminophen, or corticosteroids prior to subsequent dosing may be considered. The most common adverse reactions (at least 10% and higher incidence compared to placebo): ARIA-E, ARIA-H microhemorrhage, ARIA-H superficial siderosis, and headache. There are no adequate data on Kisunla use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are no data on the presence of donanemab-azbt in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. The safety and effectiveness in pediatric patients have not been established. No overall differences in safety or effectiveness of Kisunla have been observed between patients 65 years and older and younger adult patients.

Dr. Glen Finney, director of neurology, provided his feedback on the initial criteria for Kisunla. He said that "enrollment in a prospective study or registry, and the specific listing of ALZ-NET, ideally would be removed for all patients other than CMS patients. We do have a Geisinger Registry that we will continue to use to enroll all our monoclonal antibodies against amyloid patients (dual entry into CMS registry as well for CMS patients) as there are also outside private insurers that require registry or comparative study, but so far I've seen this lead to more confusion and delays in care when there's been misunderstanding of the requirement (I've had some people think that CMS patients could ONLY be enrolled in one registry, I've had preauthorization staff think that patient HAD to be enrolled in ALZ-NET, etc)."

"I would adjust the biomarker section for initial approval to place amyloid PET, CSF biomarkers, and blood-based biomarkers on the same footing. The most recent generation of blood-based biomarkers are proving in good clinical studies to be equivalent to the amyloid PET and CSF biomarkers and will likely be easier to obtain for patients and less expense to the system. Geisinger laboratory services is actively working to get those as a regular option (restricted at this time to the same providers who are proposed to be able to order amyloid PET and also monoclonal antibodies against amyloid). I strongly advise that all three now be considered equal options for evidence of Alzheimer's disease pathology. Note that CMS is allowing all three as well."

"I would add to the cognitive screening line for RBANS the following, "or other similar neuropsychology testing demonstrating minor neurocognitive disorder or mild stage dementia level major neurocognitive disorder."

"For the reauthorization I would recommend removing the medical benefit part (it slows rate of decline in groups, no one will be unable to attest to clinical efficacy in individuals reliably since we don't know what their personal rate of decline would have been absent the treatment) and instead focus on tolerability. I would also remove the requirement of an Amyloid PET for reauthorization as I think that the decision of when and if to get an amyloid PET scan should for the foreseeable future remain a clinical judgment made with the patient and family."

"For the reauthorization I would remove the limit of no history of stroke, TIA, or seizures – whether to continue the infusions at that point should be a clinical decision made in consultation with the patient and family."

“Maybe clarify for the MRI requirement that the patient does not have ARIA-E (and/or ARIA-H) on the MOST RECENT MRI Brain scan (since some patients with minor ARIA on a prior MRI may resume treatment after demonstrating interval resolution on a repeat MRI Brain).”

“There will be patients who start in mild stage and at a year mark may be entering moderate stage but not necessarily having lack of meaningful clinical efficacy. A MMSE score of 20 is literally on the cusp between mild and moderate stage dementia for example, so it would be easy and to a degree expected to see a patient after a year to be a bit lower enough to technically fall into the moderate dementia stage but still could be only in the very start of moderate stage with effective treatment.”

“Requiring monitoring of the patient every 3 months is onerous in a patient who is tolerating a treatment that is not expected to show much clinical change. To give you a comparison to what the standards for follow up are in these patient populations are in regular practice, if the patient is on stable doses of medications and not experiencing any new symptoms or problems, mild cognitive impairment patients are seen yearly, and mild stage dementia patients every 6 months. Requiring they be seen every 3 months will be a major burden on patients and families and on the clinics slowing access for other patients.”

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

Outcome: Kisunla will be a medical benefit and it will be excluded from pharmacy coverage for Commercial, Exchange, and CHIP lines of business. The following prior authorization criteria will apply to requests through the medical benefit:

- Medical record documentation of enrollment in a prospective comparative study and/or a registry that collects information regarding treatment with Kisunla **AND**
- Medical record documentation that Kisunla is prescribed by or in consultation with a dementia specialist (e.g. neurologist, psychiatrist, geriatric psychiatrist, neuropsychiatrist, geriatrician, or gerontologist) **AND**
- Medical record documentation that the dementia specialist will monitor the beneficiary at appropriate intervals (prescribing information states MRI is to be obtained at baseline and prior to the 2nd, 3rd, 4th, and 7th infusion) **AND**
- Medical record documentation of a diagnosis of Mild Cognitive Impairment (MCI) due to Alzheimer’s Disease (AD) or mild dementia due to Alzheimer’s Disease (AD) [diagnosis codes may include G30, G30.0, G 30.1, G30.8, G 30.9, G31.84] **AND**
- Medical record documentation of no medical or neurological conditions (other than Alzheimer’s disease) that might be a significant contributing cause of the beneficiary’s cognitive impairment **AND**
- Medical record documentation of no contraindications to Magnetic Resonance Imaging (MRI) (e.g. cardiac pacemaker/defibrillator or ferromagnetic metal implants) **AND**
- Medical record documentation of positron emission tomography (PET) scan positive for brain amyloid plaques OR cerebrospinal fluid (CSF) biomarker testing positive for beta-amyloid plaques (as indicated by reduced amyloid beta 42 [Aβ42] levels **OR** reduced amyloid beta 42 amyloid beta 40 ratio [Aβ42/Aβ40 ratio] in CSF OR elevated total tau amyloid beta 1-42 ratio [t-tau/Aβ1-42]) OR blood based biomarker testing positive for beta-amyloid plaques (as indicated by reduced amyloid beta 42 amyloid beta 40 ratio [Aβ42/Aβ40 ratio] in plasma OR assays for tau phosphorylated at amino acid 181 (p-tau 181), 217 (p-tau217), or 231 (p-tau231) **OR** high NfL concentrations OR plasma GFAP) **AND**
- Medical record documentation of at least two (2) of the following:
    - Mini-Mental State Examination (MMSE) score of ≥20 to ≤28
    - Montreal Cognitive Assessment (MoCA) score greater than or equal to 17
    - Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 or 1
    - Clinical Dementia Rating-Sum of Boxes (CDR-SB) score less than or equal to 9
    - Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) score less than or equal to 85 OR other similar neuropsychology testing demonstrating minor neurocognitive disorder or mild stage dementia level major neurocognitive disorder and/or

    - Quick Dementia Rating System (QDRS) score less than or equal to 12 **AND**
- Medical record documentation that the member does not have history of stroke, transient ischemic attack (TIA), or seizures in the past year **AND**
- Medical record documentation that the member does not have a bleeding disorder that is not under adequate control (e.g. a platelet count <50,000 or international normalized ratio [INR] > 1.5) AND
- Medical record documentation that the member does not have a presence of ARIA-E (and/or ARIA-H) on the most recent MRI scan (brain edema or sulcal effusions) **AND**
- Do not see significant pathological findings on a pre-treatment MRI:
    - More than 4 microhemorrhages (defined as 10 millimeter [mm] or less at the greatest diameter,
    - A single macrohemorrhage > 10 mm at greatest diameter,
    - An area of superficial siderosis,
    - Evidence of vasogenic edema,
    - Evidence of cerebral contusion, encephalomalacia, aneurysms, vascular malformations, or infective lesions,
    - Evidence of multiple lacunar infarcts or stroke involving a major vascular territory, severe small vessel, or white matter disease,
    - Space occupying lesions, and
    - Brain tumors (excludes lesions diagnosed as meningiomas or arachnoid cysts and less than 1 cm at their greatest diameter) **AND**
- Medical record documentation of a dose that is consistent with FDA-approved package labeling

GPI LEVEL: GPI-12

AUTHORIZATION DURATION: Approval will be given for an initial duration of twelve (12) months or less if the reviewing provider feels it is medically appropriate. After the initial approval, subsequent approvals will be for a duration of twelve (12) months or less if the reviewing provider feels it is medically appropriate, and will require:

- Provider attestation that Kisunla is still medically necessary to continue **AND**
- Medical record documentation that the member is tolerating Kisunla **AND**
- Medical record documentation of continued enrollment in a prospective comparative study and/or a registry that collects information regarding treatment with Kisunla **AND**
- Medical record documentation Kisunla is prescribed by or in consultation with a dementia specialist (e.g. neurologist, psychiatrist, geriatric psychiatrist, neuropsychiatrist, geriatrician, or gerontologist) **AND**
- Medical record documentation that the member was, and will continue to be monitored and assessed by the prescribing dementia specialist at appropriate intervals **AND**
- Medical documentation of no medical or neurological conditions (other than Alzheimer's disease) that might be a significant contributing cause of the beneficiary's cognitive impairment **AND**
- Medical record documentation of no contraindications to Magnetic Resonance Imaging (MRI) (e.g. cardiac pacemaker/defibrillator or ferromagnetic metal implants) **AND**
- Medical record documentation of repeat testing AND documented results of at least two of the following:
    - Mini-Mental State Examination (MMSE),
    - Montreal Cognitive Assessment (MoCA),
    - Clinical Dementia Rating-Global Score (CDR-GS),
    - Clinical Dementia Rating-Sum of Boxes (CDR-SB),
    - Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) OR other similar neuropsychology testing and/or,
    - Quick Dementia Rating System (QDRS) **AND**
- One of the following:
    - Medical record documentation that the member does not have history of stroke, transient ischemic attack (TIA), or seizures in the past year **OR**

    - Medical record documentation of rationale for use in members that have a history of stroke, transient ischemic attack (TIA), or seizures in the past year **AND**
- Medical record documentation that the member does not have a bleeding disorder that is not under adequate control (e.g. a platelet count <50,000 or international normalized ratio [INR] > 1.5) **AND**
- Medical record documentation that the member does not have a presence of ARIA-E (and/or ARIA-H) on the most recent MRI scan (brain edema or sulcal effusions) **AND**
- Do not see significant pathological findings on a recent MRI:
    - More than 4 microhemorrhages (defined as 10 millimeter [mm] or less at the greatest diameter,
    - A single macrohemorrhage > 10 mm at greatest diameter,
    - An area of superficial siderosis,
    - Evidence of vasogenic edema,
    - Evidence of cerebral contusion, encephalomalacia, aneurysms, vascular malformations, or infective lesions,
    - Evidence of multiple lacunar infarcts or stroke involving a major vascular territory, severe small vessel, or white matter disease,
    - Space occupying lesions, and
    - Brain tumors (excludes lesions diagnosed as meningiomas or arachnoid cysts and less than 1 cm at their greatest diameter) **AND**
- Medical record documentation of a dose that is consistent with FDA-approved package labeling

RPH SIGNOFF REQUIRED: Yes

Additional Recommendation for Leqembi: Based on the feedback we received from Dr. Glen Finney, we are making updates to the Leqembi policy to match Kisunla. The rationales for the following are listed in the Kisunla review above.

The following changes are recommended to the Commercial/Exchange/CHIP policy:

- Medical record documentation of enrollment in a prospective comparative study and/or a registry that collects information regarding treatment with Leqembi, ~~which can include, but is not limited to, the Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)~~ **AND**
- Medical record documentation Leqembi (lecanemab-irmb) is prescribed by or in consultation with a dementia specialist (e.g., neurologist, psychiatrist, geriatric psychiatrist, neuropsychiatrist, geriatrician, or gerontologist) **AND**
- Medical record documentation that the dementia specialist will monitor the beneficiary at appropriate intervals (prescribing information states MRI is to be obtained prior to the 5th, 7th, and 14th infusions) **AND**
- Medical record documentation of a diagnosis of Mild Cognitive Impairment (MCI) due to Alzheimer's Disease (AD) or mild dementia due to Alzheimer's Disease (AD) [diagnosis codes may include: G30, G30.0, G30.1, G30.8, G30.9, G31.84] **AND**
- Medical record documentation of no medical or neurological conditions (other than Alzheimer's disease) that might be a significant contributing cause of the beneficiary's cognitive impairment **AND**
- Medical record documentation of no contraindications to Magnetic Resonance Imaging (MRI) (e.g. cardiac pacemaker/defibrillator or ferromagnetic metal implants) **AND**
- Medical record documentation of MRI obtained within one year prior to initiating treatment with Leqembi (lecanemab-irmb) **AND**
- Medical record documentation of positron emission tomography (PET) scan positive for brain amyloid plaques OR cerebrospinal fluid (CSF) biomarker testing positive for beta-amyloid plaques (as indicated by reduced amyloid beta 42 [Aβ42] levels OR reduced amyloid beta 42 amyloid beta 40 ratio [Aβ42/Aβ40 ratio] in CSF OR elevated total tau amyloid beta 1-42 ratio [t-tau/Aβ1-42]) OR blood based biomarker testing positive for beta-amyloid plaques (as indicated by reduced amyloid beta 42 amyloid beta 40 ratio [Aβ42/Aβ40 ratio] in plasma OR assays for tau phosphorylated at amino acid 181 (p-tau 181), 217 (p-tau217), or 231 (p-tau231) OR high NfL concentrations OR plasma GFAP) **AND**

- Medical record documentation of at least two (2) of the following:
    - Mini-Mental State Examination (MMSE) score of greater than or equal to 22,
    - Montreal Cognitive Assessment (MoCA) score greater than or equal to 17,
    - Clinical Dementia Rating-Global Score (CDR-GS) of 0.5 or 1,
    - Clinical Dementia Rating-Sum of Boxes (CDR-SB) score less than or equal to 9,
    - Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) score less than or equal to 85 OR other similar neuropsychology testing demonstrating minor neurocognitive disorder or mild stage dementia level major neurocognitive disorder and/or,
    - Quick Dementia Rating System (QDRS) score less than or equal to 12 AND
- Medical record documentation that member does not have any exclusions to treatment with Leqembi (lecanemab-irmb), including all of the following:
    - A history of stroke, transient ischemic attack (TIA), or seizures in the past year AND
    - A bleeding disorder that is not under adequate control (e.g. a platelet count <50,000 or international normalized ratio [INR] >1.5) AND
    - A brain MRI at screening showing any of the following significant pathological findings
        - More than 4 microhemorrhages (defined as 10 millimeter [mm] or less at the greatest diameter),
        - A single macrohemorrhage >10 mm at greatest diameter,
        - An area of superficial siderosis,
        - Evidence of vasogenic edema,
        - Evidence of cerebral contusion, encephalomalacia, aneurysms, vascular malformations, or infective lesions,
        - Evidence of multiple lacunar infarcts or stroke involving a major vascular territory, severe small vessel, or white matter disease,
        - Space occupying lesions, and
        - Brain tumors (excludes lesions diagnosed as meningiomas or arachnoid cysts and less than 1 cm at their greatest diameter) **AND**
- Medical record documentation of a dose that is consistent with FDA-approved package labeling.

GPI Level: GPI-12
Authorization Duration & Reauthorization Criteria: Approval will be given for an initial duration of twelve (12) months or less if the reviewing provider feels it is medically appropriate. After the initial twelve (12) month approval, subsequent approvals will be for a duration of twelve (12) months or less if the reviewing provider feels it is medically appropriate, and will require:

- ~~Medical record documentation that member continues to experience medical benefit from and tolerability to Leqembi (lecanemab-irmb) based on the prescriber's assessment AND~~
- Provider attestation that Leqembi is still medically necessary to continue AND
- Medical record documentation that the member is tolerating Leqembi AND
- Medical record documentation of continued enrollment in a prospective comparative study and/or a registry that collects information regarding treatment with Leqembi, ~~which can include, but is not limited to, the Alzheimer's Network for Treatment and Diagnostics (ALZ-NET)~~ AND
- Medical record documentation Leqembi (lecanemab-irmb) is prescribed by or in consultation with a dementia specialist (e.g., neurologist, psychiatrist, geriatric psychiatrist, neuropsychiatrist, geriatrician, or gerontologist) AND
- Medical record documentation that the member was, and will continue to be, monitored and assessed by the prescribing dementia specialist at appropriate intervals AND
- Medical record documentation of no medical or neurological conditions (other than Alzheimer's disease) that might be a significant contributing cause of the beneficiary's cognitive impairment AND
- Medical record documentation of no contraindications to Magnetic Resonance Imaging (MRI) (e.g. cardiac pacemaker/defibrillator or ferromagnetic metal implants) AND
- Medical record documentation of continuing treatment with Leqembi (lecanemab-irmb) based on recent MRI results as recommended in the FDA-approved package labeling (e.g. MRI to be obtained prior to the 5th, 7th, and 14th infusions) AND

- Medical record documentation of repeat testing AND documented results of at least two of the following:
    - Mini-Mental State Examination (MMSE),
    - Montreal Cognitive Assessment (MoCA),
    - Clinical Dementia Rating-Global Score (CDR-GS),
    - Clinical Dementia Rating-Sum of Boxes (CDR-SB),
    - Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) OR other similar neuropsychology testing and/or,
    - Quick Dementia Rating System (QDRS) AND
- Medical record documentation that member does not have any exclusions to treatment with Leqembi (lecanemab-irmb), including all of the following:
    - One of the following:
        - Medical record documentation of a history of stroke, transient ischemic attack (TIA), or seizures in the past year OR
        - Medical record documentation of rationale for use in members that have a history of stroke, transient ischemic attack (TIA), or seizures in the past year AND
    - A bleeding disorder that is not under adequate control (e.g. a platelet count <50,000 or international normalized ration [INR] >1.5) AND
    - A recent brain MRI showing any of the following significant pathological findings:
        - Evidence of cerebral contusion, encephalomalacia, aneurysms, vascular malformations, or infective lesions,
        - Evidence of multiple lacunar infarcts or stroke involving a major vascular territory, severe small vessel, or white matter disease,
        - Space occupying lesions, and
        - Brain tumors (excludes lesions diagnosed as meningiomas or arachnoid cysts and less than 1 cm at their greatest diameter); AND
- Medical record documentation of a dose that is consistent with FDA-approved package labeling.

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

RYTELO (imetelstat)

Review: Rytelo is an oligonucleotide telomerase inhibitor indicated for the treatment of adult patients with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia requiring 4 or more red blood cell units over 8 weeks who have not responded to or have lost response to or are ineligible for erythropoiesis-stimulating agents (ESA). The recommended dose of Rytelo is 7.1mg/kg every 4 weeks, to be administered over 2 hours. Rytelo is supplied in either a 47mg single dose vial (82959-112-01) or a 188mg single dose vial (82959-111-01). The prescribing information recommends to discontinue therapy if the patient does not experience a decrease in red blood cell (RBC) transfusion burden after 24 weeks of therapy (6 doses). Premedication to be given at least 30 minutes prior to Rytelo includes diphenhydramine and hydrocortisone, intravenous or oral for both. The dose may be delayed, reduced or entirely discontinued for Grade 3 or Grade 4 hematologic adverse reactions and for Grade 2 through 4 non-hematologic adverse reactions.

MDS is a group of rare bone marrow disorders characterized by abnormal differentiation, morphology, and maturation of myeloid cells. Cytopenia is a result of MDS, including anemia, neutropenia, leukopenia, and thrombocytopenia. About 66% of patients with MDS present with lower-risk MDS (LR-MDS), and about 50% of these patients develop transfusion-dependent (TD) anemia. Estimates report that approximately 10,000-40,000 new diagnoses of MDS are made each year, with a current total of 70,000-160,000 people living with MDS in the United States now.

Per UpToDate, for lower-risk MDS and serum erythropoietin (EPO) <200mU/mL, first line treatment is with an ESA. Reblozyl is another option for first line therapy in these patients. Per NCCN, Rytelo (first in

class medication) is preferred in the second line setting after either ESA or Reblozyl is tried. Rytelo is also a recommended therapy in the first line setting in a particular scenario.

There are currently no head-to-head trials between Reblozyl and Rytelo, however IPD Analytics did complete an indirect comparison of the sperate clinical trials for the medications. The comparison is summarized in Table 1. There is limited data to support the efficacy of Rytelo in patients previously on Reblozyl, however the results of IMerge showed that these patients, although the percentage in trial was low (6%), may respond to Rytelo after Reblozyl.

Rytelo was evaluated in a randomized, double-blind, placebo-controlled, multicenter trial (IMerge, NCT02598661) with 178 patients who had low or intermediate risk, transfusion-dependent MDS. Risk was determined using the International Prognostic Scoring System (IPSS) and transfusion-dependence was defined as requiring ≥4 RBC units over an 8-week period during the 16 weeks prior to randomization. Patients were required to have failed to respond, loss response to, or be ineligible for ESAs. Patient also had to have an absolute neutrophil count of 1.5 x 109/L or greater, platelets 75 x 109/L or greater, and no del(5q) cytogenetic abnormalities. The median age of patients was 72 years (range: 39-87 years).

Patients were randomized 2:1 to receive with Rytelo (n=118) or placebo (n=60) in 28 day treatment cycles until disease progression, unacceptable toxicity or withdrawal from the study. All patients did receive supportive care, which included RBC transfusions.

The primary efficacy outcome was the proportion of patients who achieved ≥8 week or ≥24 week RBC-transfusion independence, defined as the absence of RBC transfusion during any consecutive 8 week period and during any consecutive 24 week period from randomization to the start of subsequent anti-cancer therapy (if any), respectively.

Rytelo does not have any black boxed warnings or contraindications. Rytelo does carry warnings and precautions for thrombocytopenia, neutropenia, infusion related reactions, and embryo-fetal toxicity. It is recommended to monitor complete blood cell counts prior to initiation and weekly for the first 2 cycles, then once before every cycle thereafter. It is recommended to delay, reduce or discontinue therapy and administer growth factor, platelet transfusions, or anti-infective therapies as appropriate.

Serious adverse reactions occurred in 32% of patients receiving Rytelo, including sepsis, fracture, cardiac failure, and hemorrhage. Fatal adverse reaction occurred in 0.8% of patients and included sepsis. Patients who discontinued due to an adverse reaction was 15%, interruptions due to adverse reaction was 80%, and reductions due to adverse reactions 49%. Grade 3 or 4 decreased platelets occurred in 65% of patients treated with Rytelo, and Grade 3 or 4 decreased neutrophils occurred in 72% of patients treated with Rytelo. Safety and effectiveness of Rytelo in pediatric patients has not been studied. 77.1% of patients in the trial were 65 years or older and no differences in safety or efficacy were observed between older and younger patients.

The Oncologic Drugs Advisory Committee (ODAC) met on March 14, 2024 to discuss Rytelo. Prior to the meeting the FDA released a briefing document that highlighted the lack of overall survival benefit given the magnitude and duration of the RBC transfusion independence, the concern for the high rate of Grade 3 and 4 cytopenia, and the initial outcome data at 8-weeks. The ODAC voted 12-2 in favor of approving Rytelo, but did determine longer-term data would help to better define the population that will benefit, given the lack of overall survival and high rate of side effects.

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

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

- Medical record documentation of age greater than or equal to 18 years **AND**

- Medical record documentation of myelodysplastic syndromes (MDS) **AND**
- Medical record documentation of low to intermediate-1 risk disease per the Revised International Prognostic Scoring System (IPSS-R)* **AND**
- Medical record documentation that patient requires an average of at least four (4) red blood cell units per 8 weeks **AND**
- Medical record documentation of baseline number of transfusions and red blood cell (RBC) units required for the previous six (6) months **AND**
- Medical record documentation of therapeutic failure, intolerance to, contraindication to, or ineligibility for an erythropoiesis stimulating agent (ESA) **OR** medical record documentation that an ESA is not indicated per FDA labeling and NCCN guidelines **AND**
- Medical record recommendation that Rytelo is being dosed consistent with FDA-approved labeling** **AND**
- Medical record documentation of therapeutic failure, intolerance to, or contraindication to Reblozyl (luspatercept-aamt) **OR** medical record documentation that Reblozyl is not indicated per FDA labeling and NCCN guidelines

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

- A decrease in red blood cell (RBC) transfusion burden from baseline **AND**
- Rytelo being dosed consistent with the FDA-approved labeling**

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

- A sustained reduction of red blood cell (RBC) transfusion burden from baseline **AND**
- Rytelo being dosed consistent with the FDA-approved labeling**

LIMITATIONS: Rytelo will no longer be covered if the patient does not experience a decrease in transfusion burden after twenty four (24) weeks of treatment (administration of 6 doses) or if unacceptable toxicity occurs at any time.

***Note:** Per NCCN guidelines, Intermediate-Risk MDS may be managed as lower risk if the IPSS-R score is less than or equal to 3.5 (versus higher risk if the score is >3.5).

****Note:** Per FDA labeling, the dose of Rytelo is 7.1mg/kg every 4 weeks, with dose reductions allowed for Grade 3 or Grade 4 adverse reactions.

*****Note:** Per NCCN guidelines, ESA and Reblozyl are not recommended prior to Rytelo when member has: ring sideroblasts (RS) <15% (or RS <5% with a SF3B1 mutation) AND serum EPO >200 mU/mL AND a poor probability to respond to immunosuppressive therapy (IST). Patients with poor probability to respond generally have any of the following: >60 years old, >5% marrow blasts, No hypocellular marrows, No paroxysmal nocturnal hemoglobinuria (PNH) clone positivity, No STAT3-mutant cytotoxic T-cell clones.

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

FAST FACTS

ABRYSVO (respiratory syncytial virus vaccine)

Clinical Summary: Abrysvo is now indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in individuals 18 through 59

years of age who are at increased risk for LRTD caused by RSV. Abrysvo was previously indicated for active immunization of pregnant individuals at 32 through 36 weeks gestational age for the prevention of LRTD and severe LRTD caused by RSV in infants from birth through 6 months of age and active immunization for the prevention of LRTD caused by RSV in individuals 60 years of age and older.

The dose of Abrysvo has remained the same with the addition of the new indication, which is 0.5mL given as a single dose. Abrysvo was previously supplied in a kit that included a vial, prefilled syringe, and vial adapter. Now Abrysvo is supplied as either an Act-O-Vial, a vial and prefilled syringe presentation, or a vial and vial presentation. The storage and handling recommendations remained the same.

The updated indication is supported by a Phase 3, multicenter, randomized, double-blind placebo-controlled trial which assessed the safety and immunogenicity of Abrysvo in the updated population (Study 4, NCT05842967). Patients ages 18 to 59 years of age considered to be at risk of LRTD caused by RSV due to medical conditions were included in the study. Medical conditions considered to be high risk were chronic pulmonary (including asthma), cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, hematologic or metabolic disorders (including diabetes and hyper/hypothyroidism).

Efficacy was assessed by comparison of the RSV neutralizing geometric mean titers and seroresponse rates in the Study 4 population to that of the Study 3 (NCT05035212) population (Study 3 evaluated efficacy of Abrysvo in patients 60 years of age and older).

Non-inferiority was demonstrated for the ratio of neutralizing geometric mean titers for RSV A and RSV B (Study 4/Study 3 subgroup) and the percentage difference in neutralizing titer seroresponse rates for RSV A and RSV B (Study 4 minus Study 3).

The contraindication section has remained the same and includes a history of severe allergic reaction to any component of Abrysvo. The warnings and precautions have remained the same and are significant for potential risk of preterm birth, management of acute allergic reactions, syncope, altered immunocompetence and limitations of vaccine effectiveness. A section has been added in the adverse reactions section for individuals 18 through 59 at increased risk of LRTD caused by RSV. Solicited reactions included injection site pain, redness, swelling, fever, fatigue, headache, muscle pain, joint pain, nausea, vomiting, diarrhea and had a median duration of 1-2 days. Unsolicited adverse events within 1 month of vaccination were reported in 7.1% and 7.6% of patients with Abrysvo and placebo, respectively. Serious adverse events were reported in 1.1% and 3.1% of patients with Abrysvo and placebo, respectively.

A section was also added regarding concomitant administration of Abrysvo with a seasonal inactivated influenza vaccine. There were no notable differences reported in solicited local and systemic adverse reactions within 7 days following Abrysvo and Fluad quadrivalent compared to Abrysvo alone. No serious adverse reactions were considered related to vaccination.

Current Formulary Status: Abrysvo is a medical or pharmacy benefit and on the Commercial, Exchange, and GHP Kids formulary as preventive vaccines. Abrysvo does not require a prior authorization for patients 60 years of age and older. For members under 60 years of age, the following prior authorization criteria applies.

MBP 296.0 Abrysvo (Respiratory Syncytial Virus Vaccine (Recombinant) Injection)

- Medical record documentation that Abrysvo will be used for active immunization of pregnant individuals at 32 through 36 weeks gestational age

Pharmacy Benefit: Age limit: 60 to 999 years old

Recommendation: For the medical benefit, it is recommended that no prior authorization for Abrysvo be required for all members 18 years and older. It is recommended to retire MBP 296.0 Abrysvo. It is recommended to add an age limit of 18 years and older for the medical benefit. For the pharmacy benefit, it is recommended the age limit be changed.

Medical Benefit: **Age limit:** 18 years and older
Pharmacy Benefit: Age limit: ~~60 to 999 years old~~ 18 years to 999 years old

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

BRINEURA (cerliponase alfa)

Clinical Summary: Brineura is a hydrolytic lysosomal N-terminal tripeptidyl peptidase indicated to slow the loss of ambulation in pediatric patients with neuronal ceroid lipofuscinosis type 2 (CLN2 disease), also known as tripeptidyl peptidase 1 (TPP1) deficiency.

The age was recently updated from age 3 and older to include the pediatric population from birth up. Recommended Brineura dosage is 300 mg administered once every other week as an intraventricular infusion. In patients less than 2 years of age, lower doses are recommended and updated dosing is listed below by dose, volume, and infusion rate by age.

The safety and effectiveness of Brineura have been established in pediatric patients at birth based on the following trial: Trial 3 (NCT02678689) which was a Phase 2, open label clinical study designed to enroll symptomatic and presymptomatic CLN2 patients less than 18 years of age. The trial enrolled 14 patients ranging in age from 1 to 6 years of age at baseline, including 8 patients less than 3 years of age with the median age of 2.7 years.

Patients received Brineura at the recommended dose every 2 weeks by intraventricular infusion for 144 weeks (1 patient withdrew to receive treatment commercially). Fifty-seven percent of patients were female and 43% were male. All patients were White; for ethnicity, 14% identified as Hispanic/Latino, 86% as non-Hispanic/Latino.

The mean baseline CLN2 Motor score was 2.3 (standard deviation (SD) 0.83) with a range from 1 to 3. Thirteen of the 14 Brineura treated patients were matched with up to 3 natural history comparators based on age within 3 months, equal CLN2 Motor score, and genotype (0, 1, or 2 key mutations). None of the Brineura treated patients (N=14) had a 2-point decline or score of zero in the Motor scale by Week 169. Among the matched natural history comparators (N=31), 20 subjects (65%) had an unreversed 2-point decline or score of zero by last assessment. The median time to an unreversed 2-point decline in Motor score or score of 0 was 133 weeks among the natural history comparators and was not reached by last assessment (Week 169) in patients treated with Brineura. In patients below 3 years of age, none (0%) of the Brineura treated patients (N=8) had a 2-point decline or score of zero in the Motor score by Week 169. Among the 8 treated patients, 7 were matched to 18 untreated patients from the natural history cohort. Among the matched natural history comparators (N=18), 11 subjects (61%) had an unreversed 2-point decline or score of zero in the Motor score by last assessment. All seven of the treated patients below 3 years of age with a motor score of 3 at baseline remained at a motor score of 3 at the last measured timepoint, which represents grossly normal gait. In this population Brineura treated patients showed a delay in disease onset.

Hypersensitivity reactions were reported in 5 of 8 (63 %) of patients less than 3 years of age at baseline with a single anaphylactic reaction occurring in this population.

Brineura should be administered by a healthcare provider knowledgeable in management of hypersensitivity reactions including anaphylaxis. The medication should be initiated in a healthcare setting with appropriate medical monitoring and support measures. Premedication of patients with antihistamines, antipyretics and/ or corticosteroids is recommended 30 to 60 minutes prior to the start of the infusion and patients should be closely observed during and after infusion.

Current Formulary Status: Medical Benefit, Formulary, Prior Authorization required, QL.

Recommendation: It is recommended to update policy MBP 157.0 by removing the age bullet since the FDA approved age is now from birth and up instead of 3 years of age and up.

Medical Benefit Policy for Brineura: MBP 157.0
DESCRIPTION:
Brineura (cerliponase alfa) is a proenzyme that, once activated, cleaves tripeptides from the N-terminus of proteins. This leads to the breakdown of lysosomal storage materials that otherwise accumulate in patients with late infantile neuronal ceroid lipofuscinosis type 2 (CLN2), leading to progressive decline in motor function.
CRITERIA FOR USE: Requires Prior Authorization by Medical Director or Designee
Brineura (cerliponase alfa) will be considered medically necessary for the commercial, exchange, and CHIP lines of business when ALL the following criteria are met:

- Medical record documentation that the prescription is written by a pediatric neurologist AND
- ~~Medical record documentation that the patient is 3 years of age or older AND~~
- Medical record documentation of a diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (LINCL) confirmed by the following test results:
    - Deficient TPP1 activity in leukocytes on the enzyme activity test AND
    - Pathogenic variant/mutation in the TPP1/CLN2 gene (note- may be absent in up to 20% of patients, but if present is confirmatory of diagnosis) AND
- Medical record documentation of the baseline score on the motor domain of the CLN2 clinical rating scale AND
- Medical record documentation that the patient is ambulatory (e.g. able to walk with assistance, not wheelchair bound, does not have full-time dependence on motorized wheelchairs or scooters for mobility)

  QUANTITY LIMIT: 2 doses per month (24 doses per year)

  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 Reauthorization criteria are met:
    - Medical record documentation that patient remains to be ambulatory (e.g. able to walk with assistance, not wheelchair bound, does not have full-time dependence on motorized wheelchairs or scooters for mobility)

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

FABHALTA (iptacopan)

Clinical Summary: Fabhalta is now approved for the reduction of proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio ≥ 1.5g/g. Previously, this medication was approved for the treatment of paroxysmal nocturnal hemoglobinuria in adult patients.

There is no change to the dosing for the new indication. There is also no change or update to the safety considerations as result of the new indication.

Fabhalta was evaluated in a multicenter, randomized, double-blind study in adults with biopsy-proven IgAN, eGFR ≥ 20mL/min/1.73m2 and urine protein-to-creatinine ratio (UPCR) ≥ 1g/g on a stable dose of maximally tolerated RAS inhibitor therapy. Patients were randomized 1:1 to either Fabhalta 200mg or placebo twice daily. The primary endpoint was the percent reduction in UPCR at month 9 relative to baseline.

Current Formulary Status: Fabhalta is on the specialty tier requiring prior authorization.

Recommendation: No formulary placement changes recommend. It is recommended to update the PA criteria.

Primary Immunoglobulin A Nephropathy

- Medical record documentation of a diagnosis of primary immunoglobulin A nephropathy (IgAN) confirmed by biopsy **AND**
- Medical record documentation that Fabhalta will be used for reduction of proteinuria in members at risk of rapid disease progression defined as a urine protein-to-creatinine ratio (UPCR) of ≥1.5 g/g or proteinuria ≥ 1g/day **AND**
- Medical record documentation that Fabhalta is prescribed by a nephrologist **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 eGFR ≥ 30 mL/min/1.73 m2 **AND**
- Medical record documentation that member has received a stable dose of a RAS inhibitor (ACE inhibitor or ARB) at a maximally tolerated dose for ≥ 90 days **AND**
- Medical record documentation that patient has received ≥ 90 days of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification

Auth duration for PNH: Initial approval will be for 6 months. Subsequent authorizations will be for 6 months and will require:

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

Auth duration for IgAN: Initial approval will be for 9 months. Subsequent authorizations will be for 12 months and will require:

- Medical record documentation of continued diseases improvement or lack of disease progression according to prescriber (i.e., decreased levels of proteinuria from baseline or decreased urine protein-to-creatinine ratio (UPCR) from baseline).

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

FASENRA (benralizumab)

Clinical Summary: Fasenra is now indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA). Previously, Fasenra was only indicated for add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma and an eosinophilic phenotype.

The dosing for the new indication is 30 mg every 4 weeks.

This updated indication for Fasenra was based on positive results from the MANDARA Phase III trial, a randomized, double-blinded, active-controlled trial which compared the efficacy and safety of Fasenra to the only approved EGPA treatment, mepolizumab (Nucala), in adult patients with relapsing or refractory EGPA. In the trial, 140 patients were randomized 1:1 to receive either a single 30mg subcutaneous injection of Fasenra, or three separate 100mg subcutaneous injections of Nucala, once every four weeks. The primary endpoint was the proportion of patients who were in remission at both weeks 36 and 48. Remission is defined as Birmingham Vasculitis Activity Score (BVAS)=0 and oral corticosteroid (OCS) dose less than or equal to 4 mg/day. A secondary endpoint was the proportion of patients who were able

to fully taper off OCS at weeks 48 through 52. The primary statistical analysis was to demonstrate non-inferiority of Fasenra versus Nucala based on the primary endpoint.

Full results showed that Fasenra met the primary endpoint of the trial and demonstrated non-inferior rates of remission compared to Nucala. The primary endpoint of adjusted rate of remission was 59% for Fasenra-treated patients at weeks 36 and 48, compared with 56% for Nucala (difference in rates: 3%; 95% CI:, –13,18). Additionally, a higher proportion of Fasenra-treated patients were able to fully taper off OCS during weeks 48 through 52 (41% in the Fasenra arm vs. 26% in the comparator arm (difference: 16%; 95% CI: 1,31). Fasenra was well tolerated with no new safety signals, which is consistent with the known profile of the medicine.

Current Formulary Status: Pharmacy Benefit on the Brand Preferred Tier or Medical Benefit that requires a prior authorization.

Recommendation: No changes are recommended to the formulary placement of Fasenra. The following changes are recommended to incorporate the new indication to the existing policies:

Medical Benefit Policy 173.0 Fasenra Prefilled Syringes (benralizumab):
Fasenra Prefilled Syringes (benralizumab) will be considered medically necessary for the commercial, exchange, and CHIP lines of business when ALL of the following criteria are met:
Eosinophilic Granulomatosis (EGPA)

- Medical record documentation that Fasenra is prescribed by an allergist/immunologist, pulmonologist, and/or rheumatologist **AND**
- Medical record documentation that patient is ≥18 years of age **AND**
- Medical record documentation of eosinophilic granulomatosis (EGPA) confirmed by biopsy evidence of vasculitis AND at least four (4) of the following criteria:
    - Asthma (a history of wheezing or the finding of diffuse high-pitched wheezes on expiration)
    - Eosinophilia (blood eosinophil level of ≥10% or ≥1500 cells/microL on differential white blood cell count)
    - Mononeuropathy (including multiplex) or polyneuropathy
    - Migratory or transient pulmonary opacities detected radiographically
    - Paranasal sinus abnormality
    - Biopsy containing a blood vessel showing the accumulation of eosinophils in extravascular areas

  AND
- For nonsevere disease:
    - Medical record documentation of use in combination with, or of a therapeutic failure on, contraindication to, or intolerance to systemic glucocorticoid therapy **OR**
- For severe* disease:
    - Medical record documentation of a therapeutic failure on, contraindication to, or intolerance to systemic glucocorticoid therapy AND at least one immunosuppressant therapy (e.g. cyclophosphamide, rituximab)

  AND
- Medical record documentation that the medication will not be used in combination with Nucala (mepolizumab), Cinqair (reslizumab), Dupixent (dupilumab), Xolair (omalizumab), or Tezspire (tezepelumab)

*Note: Severe disease is defined by the American College of Rheumatology (ACR) guidelines as: Vasculitis with life- or organ-threatening manifestations (e.g., alveolar hemorrhage, glomerulonephritis, central nervous system vasculitis, mononeuritis multiplex, cardiac involvement, mesenteric ischemia, limb/digit ischemia)

Severe Eosinophilic Asthma

- Medical record documentation that Fasenra is prescribed by an allergist/immunologist or pulmonologist **AND**
- Medical record documentation of age greater than or equal to 6 years **AND**
- Medical record documentation of a diagnosis of severe eosinophilic asthma AND that Fasenra is being used as add-on maintenance treatment **AND**
- Medical record documentation of blood eosinophil count >150 cells/microL (0.15 x 10E3/uL) within the past 3 months **AND**
- Medical record documentation of ONE of the following:
    - Intolerance to or not well controlled or very poorly controlled symptoms* despite at least a 3-month trial of high-dose inhaled corticosteroids and/or oral systemic corticosteroids plus a long-acting beta agonist **OR**
    - Two or more exacerbations in the previous 12 months requiring additional medical treatment (oral corticosteroids, emergency department or urgent care visits, or hospitalization) despite current therapy with high-dose inhaled corticosteroids plus a long-acting beta agonist

  AND
- Medical record documentation that individual is adherent to current therapeutic regimen and has demonstrated appropriate inhaler technique **AND**
- Medical record documentation that known environmental triggers within the member's control have been eliminated **AND**
- Medical record documentation that the medication will not be used in combination with another biologic medication indicated for asthma treatment (e.g. Xolair (omalizumab), Nucala (mepolizumab), Dupixent (dupilumab), Cinqair (reslizumab), Tezspire (Tezepelumab))

Limitations:

~~• Fasenra is not indicated for treatment of other eosinophilic conditions.~~

• Fasenra is not indicated for the relief of acute bronchospasm or status asthmaticus.

AUTHORIZATION DURATION: *Recommend updating current reauthorization criteria to match reauthorization criteria for Nucala medical benefit policy [removal of below (in red) and addition of highlighted section]*

*Initial approval will be for **12 months** or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional **12 months** or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of the following:*

- *Documentation that patient is not experiencing toxicity or worsening of disease **AND***
- *Medical record documentation of at least one of the following:*
    - *o Medical record documentation of continued disease improvement or lack of disease progression **as evidenced by a reduction in asthma exacerbations (e.g. reduced use of rescue medications, reduced urgent care visits, reduced hospitalizations) OR***
    - ***o Medical record documentation of decreased oral corticosteroid use (if on maintenance treatment prior to Fasenra initiation)***

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

QUANTITY LIMITS:

- **Severe Eosinophilic Asthma:** Enter a 3-month auth for QL of 1 syringe (1mL for Fasenra 30 mg/mL, 0.5 mL for Fasenra 10 mg/0.5 mL) per 28 days. Remainder of the 12-month authorization duration and subsequent renewals, QL of 1 syringe (1mL for Fasenra 30 mg/mL, 0.5 mL for Fasenra 10 mg/0.5 mL) per 56 days.
- **Eosinophilic Granulomatosis**: Fasenra 30mg/mL: 1 mL per 28 days.

Fasenra Prefilled Syringes (benralizumab) will be considered medically necessary for the Medicare line of business when ALL of the following criteria are met:

Eosinophilic Granulomatosis (EGPA)

- Medical record documentation that Fasenra is prescribed by an allergist/immunologist, pulmonologist, and/or rheumatologist **AND**
- Medical record documentation that patient is ≥18 years of age **AND**
- Medical record documentation of eosinophilic granulomatosis (EGPA) confirmed by biopsy evidence of vasculitis AND at least four (4) of the following criteria:
    - Asthma (a history of wheezing or the finding of diffuse high-pitched wheezes on expiration)
    - Eosinophilia (blood eosinophil level of ≥10% or ≥1500 cells/microL on differential white blood cell count)
    - Mononeuropathy (including multiplex) or polyneuropathy
    - Migratory or transient pulmonary opacities detected radiographically
    - Paranasal sinus abnormality
    - Biopsy containing a blood vessel showing the accumulation of eosinophils in extravascular areas

  AND
- For nonsevere disease:
    - Medical record documentation of use in combination with, or of a therapeutic failure on, contraindication to, or intolerance to systemic glucocorticoid therapy **OR**
- For severe* disease:
    - Medical record documentation of a therapeutic failure on, contraindication to, or intolerance to systemic glucocorticoid therapy AND at least one immunosuppressant therapy (e.g. cyclophosphamide, rituximab)

  AND
- Medical record documentation that the medication will not be used in combination with Nucala (mepolizumab), Cinqair (reslizumab), Dupixent (dupilumab), Xolair (omalizumab), or Tezspire (tezepelumab)

*Note: Severe disease is defined by the American College of Rheumatology (ACR) guidelines as: Vasculitis with life- or organ-threatening manifestations (e.g., alveolar hemorrhage, glomerulonephritis, central nervous system vasculitis, mononeuritis multiplex, cardiac involvement, mesenteric ischemia, limb/digit ischemia)

Severe Eosinophilic Asthma

- Medical record documentation that Fasenra is prescribed by an allergist/immunologist or pulmonologist **AND**
- Medical record documentation of age greater than or equal to 6 years **AND**
- Medical record documentation of a diagnosis of severe eosinophilic asthma AND that Fasenra is being used as add-on maintenance treatment **AND**
- Medical record documentation of blood eosinophil count ≥150 cells/microL (0.15 x 10E3/uL) within the past 3 months **AND**
- Medical record documentation of ONE of the following:
    - Intolerance to or not well controlled or very poorly controlled symptoms* despite at least a 3-month trial of high-dose inhaled corticosteroids and/or oral systemic corticosteroids plus a long-acting beta agonist **OR**
    - Two or more exacerbations in the previous 12 months requiring additional medical treatment (oral corticosteroids, emergency department or urgent care visits, or hospitalization) despite current therapy with high-dose inhaled corticosteroids plus a long-acting beta agonist

  AND

- Medical record documentation that the medication will not be used in combination with another biologic medication indicated for asthma treatment (e.g. Xolair (omalizumab), Nucala (mepolizumab), Dupixent (dupilumab), Cinqair (reslizumab), Tezspire (Tezepelumab))

Limitations:
~~• Fasenra is not indicated for treatment of other eosinophilic conditions.~~
• Fasenra is not indicated for the relief of acute bronchospasm or status asthmaticus.

AUTHORIZATION DURATION: Recommend updating current reauthorization criteria to match reauthorization criteria for Nucala medical benefit policy [removal of below (in red) and addition of highlighted section]
*Initial approval will be for **12 months** or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional **12 months** or less if the reviewing provider feels it is medically appropriate and will require medical record documentation of the following:*
- *Documentation that patient is not experiencing toxicity or worsening of disease **AND***
- *Medical record documentation of at least one of the following:*
  - *Medical record documentation of continued disease improvement or lack of disease progression **as evidenced by a reduction in asthma exacerbations (e.g. reduced use of rescue medications, reduced urgent care visits, reduced hospitalizations) OR***
  - ***Medical record documentation of decreased oral corticosteroid use (if on maintenance treatment prior to Fasenra initiation)***

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

QUANTITY LIMITS:
- **Severe Eosinophilic Asthma:** Enter a 3-month auth for QL of 1 syringe (1mL for Fasenra 30 mg/mL, 0.5 mL for Fasenra 10 mg/0.5 mL) per 28 days. Remainder of the 12-month authorization duration and subsequent renewals, QL of 1 syringe (1mL for Fasenra 30 mg/mL, 0.5 mL for Fasenra 10 mg/0.5 mL) per 56 days.
- **Eosinophilic Granulomatosis**: Fasenra 30mg/mL: 1 mL per 28 days.

Commercial Policy 593.0 Fasenra for Self-Administration
Eosinophilic Granulomatosis (EGPA)
- Medical record documentation that Fasenra is prescribed by an allergist/immunologist, pulmonologist, and/or rheumatologist **AND**
- Medical record documentation that patient is ≥18 years of age **AND**
- Medical record documentation of eosinophilic granulomatosis (EGPA) confirmed by biopsy evidence of vasculitis AND at least four (4) of the following criteria:
  - Asthma (a history of wheezing or the finding of diffuse high-pitched wheezes on expiration)
  - Eosinophilia (blood eosinophil level of ≥10% or ≥1500 cells/microL on differential white blood cell count)
  - Mononeuropathy (including multiplex) or polyneuropathy
  - Migratory or transient pulmonary opacities detected radiographically
  - Paranasal sinus abnormality
  - Biopsy containing a blood vessel showing the accumulation of eosinophils in extravascular areas

  AND
- For nonsevere disease:

    - Medical record documentation of use in combination with, or of a therapeutic failure on, contraindication to, or intolerance to systemic glucocorticoid therapy **OR**
- For severe* disease:
    - Medical record documentation of a therapeutic failure on, contraindication to, or intolerance to systemic glucocorticoid therapy AND at least one immunosuppressant therapy (e.g. cyclophosphamide, rituximab)

AND

- Medical record documentation that the medication will not be used in combination with Nucala (mepolizumab), Cinqair (reslizumab), Dupixent (dupilumab), Xolair (omalizumab), or Tezspire (tezepelumab)

*Note: Severe disease is defined by the American College of Rheumatology (ACR) guidelines as: Vasculitis with life- or organ-threatening manifestations (e.g., alveolar hemorrhage, glomerulonephritis, central nervous system vasculitis, mononeuritis multiplex, cardiac involvement, mesenteric ischemia, limb/digit ischemia)

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

MEDISPAN AUTHORIZATION LEVEL: GPI-10

QUANTITY LIMITS:

- **QL FOR LETTER & AUTHORIZATION:**
    - 30 mg every 4 weeks: 1 mL per 28 days

Severe Eosinophilic Asthma

- Medical record documentation that Fasenra is prescribed by an allergist/immunologist or pulmonologist **AND**
- Medical record documentation of age greater than or equal to 6 years **AND**
- Medical record documentation of a diagnosis of severe eosinophilic asthma AND that Fasenra is being used as add-on maintenance treatment **AND**
- Medical record documentation of a blood eosinophil count greater than 150 cells/mcL (0.15 x 10E3/uL) within the past 3 months **AND**
- Medical record documentation of one of the following:
    - Intolerance to or not well controlled or very poorly controlled symptoms* despite at least a 3-month trial of: high-dose inhaled corticosteroids and/or oral systemic corticosteroids plus a long-acting beta agonist **OR**
    - Two or more exacerbations in the previous 12 months requiring additional medical treatment (oral corticosteroids, emergency department or urgent care visits, or hospitalization) despite current therapy with high-dose inhaled corticosteroids plus a long-acting beta agonist **AND**
- Medical record documentation that member is adherent to current therapeutic regimen and must demonstrate appropriate inhaler technique **AND**
- Medical record documentation that known environmental triggers within the member's control have been eliminated **AND**
- Medical record that Fasenra will not be used in combination with another biologic medication indicated for asthma treatment (e.g., Xolair, Dupixent, Nucala, Cinqair, or Tezspire)

MEDISPAN AUTHORIZATION LEVEL: GPI-10

QUANTITY LIMIT:

- **Initial Approval –** *Two authorizations must be entered.*
    - Fasenra 30 mg every 4 weeks for the first 3 doses, then once every 8 weeks
      1. In PA Hub: Treat as "Include" Process Modifier.
      2. In NCRx Next: Add Treat as "Include" Process Modifier, Ignore Misc Handler, Max Scripts 3, Max Script Quantity 1, Max Script Days 28, with a duration of 3 months.
        - QL FOR LETTER: Loading dose: 1 mL per 28 days; Maintenance dose: 1 mL per 56 days
    - Fasenra 10 mg every 4 weeks for the first 3 doses, then once every 8 weeks
      1. In PA Hub: Treat as "Include" Process Modifier.
      2. In NCRx Next: Add Treat as "Include" Process Modifier, Ignore Misc Handler, Max Scripts 3, Max Script Quantity 0.5, Max Script Days 28, with a duration of 3 months.
        - QL FOR LETTER: Loading dose: 0.5 mL per 28 days; Maintenance dose: 0.5 mL per 56 days

- **Renewal –** *No QLs need to be entered within the authorization unless the requested quantity exceeds the QL.*
    - QL FOR LETTER ONLY:
        - 30 mg every 8 weeks: 1 mL per 56 days
        - 10 mg every 8 weeks: 0.5 mL per 56 days

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

- Documentation that patient is not experiencing toxicity or worsening of disease **AND**
- Medical record documentation of at least ONE of the following:
    - Medical record documentation of continued disease improvement or lack of disease progression as evidenced by a reduction in asthma exacerbations (e.g. reduced use of rescue medications, reduced urgent care visits, reduced hospitalizations) **OR**
    - Medical record documentation of decreased oral corticosteroid use (if on maintenance treatment prior to Fasenra initiation)

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

FUROSCIX (furosemide injection)

Clinical Summary: Furoscix is indicated for the treatment of congestion due to fluid overload in adults with chronic heart failure. Previously, it was indicated for the treatment of congestion due to fluid overload in adults with NYHA Class II/III chronic heart failure.

No new updates in dosing. The single-use, on-body Infusor with prefilled cartridge is pre-programed to deliver 30mg of Furoscix over the first hour followed by 12.5mg per hour for the subsequent 4 hours.

There were no new updates to clinical studies or safety considerations.

Current Formulary Status: Non-formulary medication requiring a prior authorization

Recommendation: There are no changes to the formulary status or authorization duration. It is recommended that the following changes be made to commercial policy 770.0:

Policy 770.0

- Medical record documentation that Furoscix is prescribed by or in consultation with a cardiologist **AND**

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of ~~New York Heart Association (NYHA) Class II or Class III~~ chronic heart failure **AND**
- Medical record documentation of congestion due to fluid overload **AND**
- Medical record documentation that member is stable on background loop diuretic therapy **AND**
- Medical record documentation of provider attestation that member will use Furoscix for short-term use only and will be transitioned to oral diuretics as soon as practical

MEDISPAN AUTHORIZATION LEVEL: GPI-12

AUTHORIZATION DURATION: 1 month

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

LIVMARLI (maralixibat)

Clinical Summary: Livmarli is now indicated for the treatment of cholestatic pruritus in patients 12 months of age and older with progressive familial intrahepatic cholestasis (PFIC). Livmarli is not recommended in a subgroup of PFIC type 2 patients with specific ABCB11 variants resulting in non-functional or complete absence of bile salt export pump (BSEP) protein. Previously, Livmarli was indicated for the treatment of Alagille syndrome (ALGS) in patients 3 months of age and older. Livmarli is the second drug indicated for PFIC after Bylvay which is also indicated in the treatment of ALGS and PFIC.

There are two strengths of Livmarli available. The 9.5 mg/mL strength is indicated for ALGS and the 19 mg/mL strength is indicated for the treatment of PFIC. The two strengths should not be substituted for one another – particularly in patients less than 5 years of age as Livmarli oral solution contains propylene glycol as an excipient. The recommended dosage of Livmarli for PFIC is 570 mcg/kg twice daily 30 minutes before a meal. The starting dose is 285 mcg/kg orally once daily in the morning, should be increased to 285 mcg/kg twice daily, 428 mcg/kg twice daily, and then to 570 mcg/kg twice daily, as tolerated. The maximum daily dose should not exceed 38 mg (2 mL) per day.

The efficacy of Livmarli for the treatment of PFIC was evaluated in the MARCH-PFIC trial, a 26-week randomized, placebo-controlled trial in 64 patients with documented PFIC with presence of biallelic known pathogenic variants, including 31 non-truncated PFIC2 patients (i.e. excluding patients with BSEP3) and 33 patients with PFIC1 (n=13), PFIC3 (n=9), PFIC4 (n=7), or PFIC6 (n=4). Additional patients with BSEP3 (n=9), prior surgical diversion (n=8), heterozygous subjects (n=2), or no variants associated with cholestasis (n=8) were included for evaluation in a supplemental cohort.

Given the patients' young age, a single-item observer-reported outcome was used to measure patients' pruritus symptoms as observed by their caregiver twice daily (once in the morning and once in the evening) on the Itch Reported Outcome Instrument (ItchRO[Obs]). Pruritus symptoms were assessed on a 5-point ordinal response scale, with scores ranging from 0 (none observed or Reference ID: 5475379 reported) to 4 (very severe). Patients were included in Trial 2 if their average pruritus score was greater than or equal to 1.5 in the 4 weeks prior to baseline.

Patients were randomized to receive Livmarli orally 570 mcg/kg (n=33) or placebo (n=31) twice daily. Most patients were on stable ursodeoxycholic acid (89.1%) or rifampicin (51.6%) therapy at baseline.

Table 2 shows the results of the comparison between Livmarli and placebo on the mean change in average morning ItchRO[Obs] severity score between baseline and Weeks 15-26. For Weeks 15-26 the average morning severity score was calculated by averaging the morning scores within a week and

then averaging 4 weekly morning scores to yield a single 4 week score and then averaging the three 4-week average morning scores. Patients treated with Livmarli showed a greater improvement in pruritic compared to placebo.

Although the number of patients with BSEP3 in the trial were limited, improvement in pruritic was no observed in 5 patients with BSEP3 who received Livmarli compared to 4 patients with BSEP3 who received placebo for 26 weeks.

No new safety signals were identified for Livmarli for the new indication. The most common adverse reactions of Livmarli for the new indication were diarrhea, fat-soluble vitamin deficiency, abdominal pain, liver test abnormalities, hematochezia, and bone fractures.

Current Formulary Status: Livmarli is a non-formulary medication requiring prior authorization.

Recommendation: Livmarli 19.0 mg/mL is a pharmacy benefit and will not be added to the Commercial, Marketplace, or GHP Kids formulary. The following prior authorization criteria will be added to Commercial Policy 694.0 to incorporate the new indication.

Commercial 694.0 Livmarli

ALGS

- Medical record documentation that Livmarli is prescribed by or in consultation with a hepatologist or gastroenterologist **AND**
- Medical record documentation of diagnosis of Alagille Syndrome (ALGS) **AND**
- Medical record documentation of the presence of moderate to severe pruritus **AND**
- Medical record documentation that the member is receiving an appropriate dose* based on the member's weight **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ursodiol **AND** one of the following: cholestyramine, rifampin, naltrexone, sertraline

NOTE:

Patient Weight (kg)	Days 1-7 (190 mcg/kg once daily)	Beginning Day 8 (380 mcg/kg once daily)
	9.5 mg/mL Solution (for ALGS) Volume per Dose (mL)	
5 to 6	0.1	0.2
7 to 9	0.15	0.3
10 to 12	0.2	0.45
13 to 15	0.3	0.6
16 to 19	0.35	0.7
20 to 24	0.45	0.9
25 to 29	0.5	1
30 to 34	0.6	1.25
35 to 39	0.7	1.5
40 to 49	0.9	1.75
50 to 59	1	2.25
60 to 69	1.25	2.5
70 or higher	1.5	3

PFIC

- Medical record documentation that Livmarli is prescribed by or consultation with a hepatologist or gastroenterologist AND
- Medical record documentation of a diagnosis of progressive familial intrahepatic cholestasis (PFIC) confirmed by genetic testing AND
- Medical record documentation of the presence of moderate to severe pruritus AND
- Medical record documentation of age greater than or equal to 12 months AND

- Medical record documentation that the member is receiving an appropriate dose* based on the member's weight AND
- Medical record documentation of concurrent use or therapeutic failure on, intolerance to, or contraindication to ursodiol

NOTE:

Patient Weight (kg)	285 mcg/kg (once daily titrated to twice daily)	428 mcg/kg (twice daily)	570 mcg/kg (twice daily as tolerated)
	19 mg/mL Solution (for PFIC) Volume per Dose (mL)		
5	0.1	0.1	0.15
6 to 7	0.1	0.15	0.2
8	0.1	0.2	0.25
9	0.15	0.2	0.25
10 to 12	0.15	0.25	0.3
13 to 15	0.2	0.3	0.4
16 to 19	0.25	0.4	0.5
20 to 24	0.3	0.5	0.6
25 to 29	0.4	0.6	0.8
30 to 34	0.45	0.7	0.9
35 to 39	0.6	0.8	1
40 to 49	0.6	0.9	1
50 to 59	0.8	1	1
60 or higher	0.9	1	1

MEDISPAN AUTHORIZATION LEVEL: GPI-14

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

- Livmarli 9.5 mg/mL: QL for letter only: 3 mL per day, 30 day supply per fill
- Livmarli 19 mg/mL: QL for letter only: 2 mL per day, 30 day supply per fill

RE-AUTHORIZATION CRITERIA: Initial approval will be for 6 months or less if the reviewing provider feels it is medically appropriate. Subsequent approvals will be for an additional 6 months or less if the reviewing provider feels it is medically appropriate and will require the following:

- Medical record documentation of improvement in pruritus from baseline **AND**
- Medical record documentation that the member is receiving an appropriate dose* based on the patient's weight

Formulary Alternatives: PFIC: ursodiol

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

PALFORZIA (peanut [Arachis hypogaea] allergen powder)

Clinical Summary: Palforzia is an oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut. Palforzia is approved for use in patients ages 1 through 17 years of age with a confirmed diagnosis of peanut allergy. Initial Dose Escalation may be administered to patients aged 1 through 17 years. Up-Dosing and Maintenance may be continued in patients 1 year of age and older. Palforzia is to be used in conjunction with a peanut-avoidant diet.

Treatment with Palforzia is administered in 3 sequential phases: Initial Dose Escalation, Up-Dosing, and Maintenance.

The efficacy of Palforzia for the mitigation of allergic reactions, including anaphylaxis, in subjects 1 through 3 years of age with peanut allergy was investigated in Study 3 (NCT03736447). Study 3 was a phase 3, international, randomized, double-blind, placebo-controlled study of the efficacy and safety of Palforzia in subjects with peanut allergy aged 1 through 3 years in the United States, and Europe. The primary analysis population consisted of 146 subjects (Palforzia, N = 98; placebo, N = 48) aged 1 through 3 years in the ITT population who received at least 1 dose of study treatment. After an Initial Dose Escalation ranging from 0.5 mg to 3 mg on Day 1 and confirmation of tolerability of the 1 mg dose on Day 2, subjects underwent Up-Dosing for 20-40 weeks starting at 1 mg until the 300 mg dose was reached. The Up-Dosing period varied for each subject depending on how the dose was tolerated. Subjects then underwent 12-24 weeks of Maintenance immunotherapy with 300 mg Palforzia until the end of the study. At the end of the Maintenance period, subjects completed an exit DBPCFC to approximate an accidental exposure to peanut and to assess their ability to tolerate increasing amounts of peanut protein with no more than mild allergic symptoms.

The primary efficacy endpoint was the percentage of subjects tolerating a single dose of 600 mg peanut protein in the exit DBPCFC with no more than mild allergic symptoms after 6 months of Maintenance treatment. The primary efficacy endpoint was considered met if the lower bound of the 95% confidence interval (CI) for the difference in response rates between the treatment and the placebo groups was greater than the prespecified margin of 15%. Key secondary endpoints included the comparisons of the response rates after single doses of 300 mg and 1000 mg peanut protein as well as a comparison of the maximum severity of symptoms at any challenge dose of peanut protein during the exit DBPCFC (up to 2000 mg). The key secondary endpoints were to be evaluated for statistical significance (two-sided $p < 0.05$) only if the primary endpoint and all the preceding tests in the hierarchy were statistically significant in favor of Palforzia.

The completer population consisted of all subjects aged 1 through 3 years in the ITT population who stayed on treatment and had an evaluable exit DBPCFC (83 Palforzia, 45 placebo). In the completer population, the proportion of subjects who tolerated single highest doses of 300 mg, 600 mg, and 1000 mg, with no more than mild symptoms at the exit DBPCFC were 94.0%, 86.7%, and 80.7%, respectively for Palforzia -treated subjects compared with 24.4%, 6.7%, and 4.4%, for placebo-treated subjects. There are no data available on the efficacy of Palforzia in individuals who did not progress onto Maintenance therapy.

Study 3 (NCT03736447) was a randomized, double-blind, placebo-controlled efficacy and safety study conducted in the United States and Europe evaluating Palforzia versus placebo in 146 subjects aged 1 through 3 years with peanut allergy. The primary efficacy analysis population consisted of 98 subjects who received at least one dose of study treatment. In this study, eligible subjects were those sensitive to > 3 mg and ≤ 300 mg of peanut protein at the screening DBPCFC. Of the subjects treated with Palforzia in the primary analysis population, 13.3% had a medical history of allergic rhinitis, 72.4% reported multiple food allergies, 63.3% had a medical history of atopic dermatitis, and 9.6% had a present or previous diagnosis of asthma. The median age of subjects was 2 years. More than half of the subjects were male (58.2%). Most subjects were White (67.3%), Asian (16.4%), or Black or African American (3.4%) and most were not Hispanic or Latino (72.6%). In Study 3, the most common adverse reactions in subjects treated with Palforzia (incidence ≥ 5%) were gastrointestinal, respiratory, and skin symptoms commonly associated with allergic reactions.

In Study 3, anaphylactic reaction was reported in 8 (8.2%) Palforzia -treated subjects (in no subjects during Initial Dose Escalation, 2 subjects during Up-Dosing, and 6 subjects during Maintenance) and 4 (8.3%) placebo-treated subjects (in no subjects during Initial Dose Escalation, 2 subjects during Up-Dosing, and 2 subjects during Maintenance). Out of the 9 total anaphylactic reaction events in 8 Palforzia -treated subjects, 3 were related to Palforzia, all during Up-Dosing, and 6 were to other food allergens.

A total of 15 (15.3%) Palforzia -treated subjects and 3 (6.3%) placebo-treated subjects discontinued for any reason in Study 3. Adverse reactions led to study discontinuation in 5.1% Palforzia -treated subjects and no placebo-treated subjects during Up-Dosing in Study 3, and 2.3% Palforzia-treated subjects and no placebo-treated subjects during Maintenance dosing in Study 3. Gastrointestinal reactions were the most common reason leading to discontinuation of study 14 product during Up-Dosing (3.1% Palforzia, none in placebo), followed by respiratory disorders (3.1% Palforzia, none in placebo) in Study 3. No Palforzia -treated subjects discontinued during IDE.

Current Formulary Status: Palforzia is a non formulary medication requiring prior authorization under commercial policy 630.0. Auth duration and quantity limits apply.

Recommendation: Recommend the following changes to commercial policy 630.0 to reflect the new age indication. Recommend no changes to the auth duration or quantity limits.

- Medical record documentation that Palforzia is prescribed by an allergist, immunologist, or a physician qualified to prescribe allergy immunotherapy **AND**
- If the request is for initial dose escalation: Medical record documentation that member is greater than or equal to 1 year of age to less than 18 years of age **OR**
- If the request is for up-dosing or maintenance dose: Medical record documentation that member is greater than or equal to 1 year of age.

AND

- Medical record documentation of confirmed diagnosis of peanut-allergy with history of allergic reaction from peanuts **AND** one of the following:
  - positive skin test **OR**
  - *in vitro* testing for peanut-specific IgE antibodies

AND

- Medical record documentation that Palforzia will be used in conjunction with peanut-avoidant diet **AND**
- Medical record documentation that the member has (or will receive) a prescription for an epinephrine auto-injector **AND**
- Medical record documentation that the member does not have severe, unstable, or uncontrolled asthma **AND**
  Medical record documentation that the member has no experienced severe or life-threatening anaphylaxis within 60 days of Palforzia initiation.

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

SIRTURO (bedaquiline)

Clinical Summary: Sirturo is a diarylquinoline antimycobacterial drug and has now received full approval for use as part of combination therapy in adult and pediatric patients (5 years and older and weighing at least 15 kg) with pulmonary tuberculosis (TB) due to Mycobacterium tuberculosis resistant to at least rifampin and isoniazid. It was previously approved for under accelerated approval as part of combination therapy in adult and pediatric patients (5 years and older and weighing at least 15 kg) with pulmonary multi-drug resistant tuberculosis (MDR-TB). A limitation of use for Sirturo remains that it should not be used for the treatment of latent, extra-pulmonary or drug-sensitive TB or for the treatment of infections caused by nontuberculous mycobacteria.

The recommended dosage for Sirturo in adults is 400 mg (4 of the 100 mg tablets OR 20 of the 20 mg tablets) once daily for 2 weeks followed by 200 mg (2 of the 100 mg tablets OR 10 of the 20 mg tablets) 3 times per week (with at least 48 hours between doses) for 22 weeks. The recommended dosage for Sirturo in pediatric patients 5 years and older and weighing at least 15 kg is based on body weight (see the table below). The total duration of treatment for adults and pediatric patients is 24 weeks. When

treatment is considered necessary beyond 24 weeks for adults and pediatric patients 16 years and older and weighing at least 30 kg, treatment may be continued at a dose of 200 mg three times per week.

The efficacy and safety of Sirturo in adult patients was evaluated in 4 studies. Study 1 (NCT00449644, Stage 2) was a placebo-controlled, double-blind, randomized trial conducted in patients with newly diagnosed sputum smear-positive pulmonary TB due to M. tuberculosis resistant to at least rifampin and isoniazid. Patients were randomized to receive a combination of Sirturo or placebo with five other antimycobacterial drugs (i.e., ethionamide, kanamycin, pyrazinamide, ofloxacin, and cycloserine/terizidone or available alternative) for a total duration of 18 to 24 months or at least 12 months after the first confirmed negative culture. Treatment was 24 weeks of treatment with Sirturo 400 mg once daily for the first two weeks followed by 200 mg three times per week for 22 weeks or matching placebo for the same duration. Seventy-nine patients were randomized to the Sirturo arm and eighty-one to the placebo arm. A final evaluation was conducted at Week 120. Time to sputum culture conversion was defined as the interval in days between the first dose of study drug and the date of the first of two consecutive negative sputum cultures collected at least 25 days apart during treatment. In this trial, the Sirturo treatment group had a decreased time to culture conversion and improved culture conversion rates compared to the placebo treatment group at Week 24. Median time to culture conversion was 83 days for the Sirturo treatment group compared to 125 days for the placebo treatment group.

Study 2 (NCT00449644, Stage 1) was a smaller placebo-controlled study designed similarly to Study 1 except that Sirturo or placebo was given for only eight weeks instead of 24 weeks. Patients were randomized to either Sirturo and other drugs used to treat pulmonary TB due to M. tuberculosis resistant to at least rifampin and isoniazid (Sirturo treatment group) (n=23) or placebo and other drugs used to treat TB (placebo treatment group) (n=24). Twenty-one patients randomized to the Sirturo treatment group and 23 patients randomized to the placebo treatment group had confirmed pulmonary TB due to M. tuberculosis resistant to at least rifampin and isoniazid based on patients' baseline M. tuberculosis isolate obtained prior to randomization. The Sirturo treatment group had a decreased time to culture conversion and improved culture conversion rates compared to the placebo treatment group at Week 8. At Weeks 8 and 24, the differences in culture conversion proportions were 38.9% [95% CI: (12.3%; 63.1%) and p-value: 0.004], 15.7% [95% CI (-11.9%; 41.9%) and p-value: 0.32], respectively.

Study 3 (NCT00910871) was a Phase 2b, uncontrolled study to evaluate the safety, tolerability, and efficacy of Sirturo as part of an individualized treatment regimen in 233 patients with sputum smear positive (within 6 months prior to screening) pulmonary TB due to M. tuberculosis resistant to at least rifampin and isoniazid, including patients with isolates resistant to second-line injectables and/or fluoroquinolones. Patients received Sirturo for 24 weeks in combination with antimycobacterial drugs. Upon completion of the 24-week treatment with Sirturo, all patients continued to receive their background regimen in accordance with national TB program (NTP) treatment guidelines. A final evaluation was conducted at Week 120. Treatment responses to Sirturo at Week 120 were generally consistent with those from Study 1.

Study 4 (NCT02409290) was a Phase 3, open-label, multicenter, active-controlled, randomized trial to evaluate the efficacy and safety of Sirturo, coadministered with other oral anti-TB drugs for 40 weeks in patients with sputum smear-positive pulmonary TB caused by M. tuberculosis that was resistant to at least rifampin. Patients in whom the M. tuberculosis strain was known to be resistant at screening to second-line injectable agents or fluoroquinolones were excluded from enrollment. When phenotypic susceptibility testing of the baseline isolates became available post randomization, patients infected with M. tuberculosis resistant to either second-line injectable agents or fluoroquinolones were kept in the study, however, those with M. tuberculosis resistant to both second-line injectables and fluoroquinolones were discontinued from the study. Patients were randomized to one of four treatment arms. Arm A (N=32) was the locally used treatment in accordance with 2011 WHO treatment guidelines with a recommended 20-month duration. Arm B (N=202) was a 40-week treatment of moxifloxacin (N=140) or levofloxacin (N=62), clofazimine, ethambutol, pyrazinamide, supplemented by injectable kanamycin, high-dose isoniazid and prothionamide in the first 16 weeks (intensive phase). Arm C (N=211) was a 40-week, all-oral treatment of Sirturo, levofloxacin, clofazimine, ethambutol, and pyrazinamide, supplemented by high-dose isoniazid and prothionamide in the first 16 weeks (intensive phase). Arm D (N=143) was a 28-week

treatment consisting of Sirturo, levofloxacin, clofazimine, and pyrazinamide, supplemented by kanamycin injectable and a higher isoniazid dose for the first eight weeks (intensive phase). Sirturo was administered 400 mg once daily for the first two weeks and 200 mg three times a week for the following 38 weeks (in Arm C) or 26 weeks (in Arm D). All patients were to be followed up until study completion at Week 132. During study conduct, enrollment in Arms A and D was stopped due to changes in the standard of care for TB treatment. Patients already randomized to these study arms were to complete their assigned treatment and follow-up. The primary objective was to assess whether the proportion of patients with a favorable efficacy outcome in Arm C was noninferior to that in Arm B at Week 76. The primary efficacy outcome measure was the proportion of patients with a favorable outcome at Week 76. A favorable outcome at Week 76 was defined as the last two consecutive cultures being negative and with no unfavorable outcome. An unfavorable outcome at Week 76 was assessed as a composite endpoint, covering both clinical and microbiological aspects such as changes in TB treatment, all-cause mortality, at least one of the last two culture results positive or no culture results within the Week 76 window. In case of treatment failure, recurrence or serious toxicity on the allocated treatment, salvage treatment that could include Sirturo was provided, based on investigator judgment. The modified intent-to-treat population (mITT) was the primary efficacy population and included all randomized patients with a positive sputum culture for M. tuberculosis that was resistant to at least rifampin and not resistant to both second-line injectables and fluoroquinolones, based on susceptibility results (taken prior to randomization). A total of 196 and 187 patients were included in the mITT population in Arm C and Arm B, respectively. For efficacy analyses beyond Week 76, data collection was stopped at the point when the last recruited patient was projected to reach Week 96. The long-term efficacy data therefore include data up to at least Week 96 for all patients, and up to Week 132 for 146/196 (74.5%) patients in Arm C and 145/187 (77.5%) patients in Arm B.

The pediatric trial, (NCT02354014), was designed as a single-arm, open-label, multi-cohort trial to evaluate the pharmacokinetics, safety and tolerability of Sirturo in combination with a background regimen in patients 5 to less than 18 years of age with confirmed or probable pulmonary TB due to M. tuberculosis resistant to at least rifampin.

For pediatric Patients (12 years to less than 18 years of age), fifteen patients 14 years to less than 18 years of age were enrolled in the first cohort. No patient 12 years to less than 14 years of age was enrolled in this cohort. Sirturo was administered as 400 mg once daily for the first two weeks and 200 mg three times/week for the following 22 weeks using the 100 mg tablet. In the subset of patients with culture positive pulmonary TB resistant to at least rifampin at baseline, treatment with Sirturo resulted in conversion to a negative culture in 75.0% (6/8 patients) at Week 24.

For pediatric Patients (5 years to less than 12 years of age), fifteen patients 5 years to 10 years of age were enrolled in the second cohort. No patient older than 10 years to less than 12 years of age was enrolled in this cohort. The body weight range was 14 kg to 36 kg; only one patient weighing 14 kg was enrolled. Sirturo was administered as 200 mg once daily for the first two weeks and 100 mg three times/week for the following 22 weeks using the 20 mg tablet. In the subset of patients with culture positive pulmonary TB resistant to at least rifampin at baseline, treatment with Sirturo resulted in conversion to a negative culture in 100% (3/3 patients) at Week 24.

Warnings and precautions of Sirturo have been updated. The QTc prolongation warning and precaution was updated to recommend an ECG be obtained before initiation of treatment, 2 weeks after initiation, during treatment, as clinically indicated and at the expected time of maximum increase in the QTc interval of the concomitantly administered QTc prolonging drugs (as applicable) and to recommend electrolytes be obtained at baseline and during treatment and correct electrolytes as clinically indicated. The mortality imbalance in clinical trials warning and precaution was updated to address deaths that had occurred in clinical trials. An increased risk of death was seen in the Sirturo treatment group (9/79, 11.4%) compared to the placebo treatment group (2/81, 2.5%) in one placebo-controlled trial in adults (Study 1; based on the 120 week visit window). One death occurred during the 24 weeks of administration of Sirturo. The imbalance in deaths is unexplained. No discernible pattern between death and sputum culture conversion, relapse, sensitivity to other drugs used to treat tuberculosis, HIV status, or severity of disease could be observed. In a subsequent active-controlled trial in adults (Study 4), deaths by Week 132

occurred in 11/211 (5.2%) patients in the 40-week Sirturo treatment group, 8/202 (4%) patients in the active-control treatment group including four of 29 patients who received Sirturo as part of a salvage treatment, and 2/143 (1.4%) patients in the 28-week Sirturo treatment group.

Current Formulary Status: Sirturo is a pharmacy benefit on the Specialty tier or Brand Non-Preferred for patients with a three-tier benefit, requiring a prior authorization. Quantity limits apply.

Recommendation: No changes recommended to the formulary placement, prior authorization criteria, quantity limit, and authorization duration of Sirturo at this time due to Sirturo receiving full approval of its indication.

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

TALZENNA (talazoparib)

Clinical Summary: Talzenna is now indicated in combination with enzalutamide for the treatment of adult patients with HRR gene-mutated metastatic castration-resistant prostate cancer (mCRPC).

The recommended dosage of Talzenna for mCRPC is 0.5 mg orally once daily until disease progression or unacceptable toxicity. Patients should also receive a gonadotropic-releasing hormone (GnRH) analog concurrently or should have had bilateral orchiectomy.

Dosage adjustments are also recommended for patients with renal impairment. A dosage of 0.35 mg once daily is recommended for patients with moderate renal impairment and a dosage of 0.25 mg once daily is recommended for patients with severe renal impairment.

The efficacy of Talzenna in combination with enzalutamide (Xtandi) was evaluated in the TALAPRO-2 trial, a randomized, double-blind, placebo-controlled, multi-cohort trial in 399 patients with HRR gene-mutated (HRRm) mCRPC. Patients with randomized 1:1 to received Xtandi 160 mg daily plus either Talzenna 0.5 mg or placebo daily until unacceptable toxicity or progression. All patients received a GnRH analog or had prior bilateral orchiectomy and needed to have progressed on prior androgen deprivation therapy. Patients were required to have a mutation in at least one of 12 genes involved in the HRR pathway (ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, or RAD51C).

The major efficacy outcome was radiographic progression-free survival (rPFS) evaluated according the RECIST v1.1 and Prostate Cancer Working Group (PCWG3)(bone) criteria assessed by BICR. Overall survival (OS) was also measured. There was a statistically significant improvement in rPFS demonstrated at the pre-specified interim analysis in patients treated with Talzenna + Xtandi compared to placebo + Xtandi (Table 2). Overall survival data was not mature at the time of the rPFS (24% of patients had died).

No new safety signals were identified during the TALAPRO-2 trial, and the adverse reaction profile was consistent with the known safety profile of Talzenna.

Current Formulary Status: Oral Onc Brand NP tier, PA new starts only, QL

Recommendation: It is recommended that Talzenna 0.1 mg and 0.35 mg capsules are added to the Commercial formulary to the Oral Oncology Brand NP tier ($0 copay) to match the placement of other Talzenna capsules. They will require a prior authorization for new starts only. The following changes are recommended to the prior authorization criteria in Commercial Policy 544.0 to incorporate the new indication. No changes are recommended to the quantity limit and no changes are recommended to the formulary placement of other Talzenna doses.

Breast Cancer:

- Medical record documentation that Talzenna is prescribed by or in consultation with a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) HER2-negative advanced or metastatic breast cancer as verified by a Food and Drug Administration (FDA)-approved test

Prostate Cancer:

- Medical record documentation that Talzenna is prescribed by or in consultation with an oncologist or hematologist AND
- Medical record documentation that member is 18 years of age or older AND
- Medical record documentation of a diagnosis of homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer AND
- Medical record documentation that Talzenna will be used in combination with enzalutamide (Xtandi) AND
- Medical record documentation that a gonadotropin-releasing hormone (GnRH) analog will be used concurrently **OR** member has had bilateral orchiectomy

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

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

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

NOTE: Information on the FDA-approved test for the detection of BRCA mutations is available at http://www.fda.gov/companiondiagnostics

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

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

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

VELPHORO (sucroferric oxyhydroxide)

Clinical Summary: Velphoro is a phosphate binder indicated for the control of serum phosphorus levels in adult and pediatric patients 9 years of age and older with chronic kidney disease (CKD) on dialysis. It was previously indicated for the control of serum phosphorus levels in patients with CKD disease on dialysis.

Chew or crush Velphoro tablets, do not swallow whole. The recommended starting dose for adults and pediatric patients 12 years of age and older is one 500 mg tablet three times daily with meals. The recommended starting dose for pediatric patients 9 to <12 years of age is one 500 mg tablet two times daily with meals. Adjust dosage by one 500 mg tablet per day as needed until an acceptable serum phosphorus level is reached, with regular monitoring afterwards. Titrate as often as weekly.

In an open-label, randomized study, with a 10-week dose titration period and 24-week safety extension, 60 patients 6 to 18 years of age received at least one dose of Velphoro, including 30 patients (50%) exposed for at least 19 weeks. The safety profile of Velphoro in pediatric patients was similar to that

observed in adult patients. Velphoro is not approved in pediatric patients 6 years to less than 9 years of age because of the lack of an appropriate dosage strength.

There are no changes to the safety considerations.

Current Formulary Status: Pharmacy benefit available at the Specialty Tier or the Brand Non-Preferred (NP) Tier for members with a three-tier benefit; Requires prior authorization

Recommendation: No recommended changes.

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

ZORYVE (roflumilast 0.15% cream)

Clinical Summary: Zoryve 0.15% cream has received FDA approval for the treatment of mild to moderate atopic dermatitis in patients aged 6 years and older. Zoryve is a selective, highly potent phosphodiesterase 4 (PDE4) inhibitor used as a once daily, steroid free topical treatment designed for long term disease control.

The approval of Zoryve 0.15% cream was based on findings from the INTEGUMENT-1 and INTEGUMENT-2 studies which included 1337 patients with mild to moderate AD aged 6 years and older. Patients were randomized to either roflumilast cream 0.15% (n = 884) or to vehicle cream (n = 453), applied once daily for 4 weeks. The primary endpoint was the proportion of subjects who achieved Validated Investigator Global Assessment-AD (vIGA-AD) success at Week 4. Success was defined as a score of “Clear” (0) or “Almost Clear” (1), plus a 2-grade improvement from baseline. The primary end point was achieved in 31.3% of the roflumilast group compared with 14.1% of the vehicle group.

The proportion of subjects who discontinued treatment due to an adverse reaction was 1.6% for subjects treated with Zoryve cream, 0.15%, and 1.1% for subjects treated with vehicle cream. The most common adverse reactions reported were headache, nausea, application site pain, diarrhea and vomiting.

Current Formulary Status: Pharmacy benefit requiring prior authorization, specialty tier or non-preferred brand tier for members with a 3 tier benefit currently, however Zoryve cream will be changing to non-formulary status in 2025.

Recommendation: The following criteria is recommended to be added to commercial Zoryve policy 744.0 effective 1/1/2025.

Atopic Dermatitis - Zoryve 0.15% Cream

1. Medical record documentation that Zoryve 0.15% cream is prescribed by or in consultation with a dermatologist, allergist, or immunologist AND
2. Medical record documentation of a diagnosis of mild to moderate atopic dermatitis AND
3. Medical record documentation of age greater than or equal to 6 years AND
4. Medical record documentation that member is immunocompetent AND
5. Medical record documentation of Body Surface Area (BSA) less than or equal to 20% AND
6. Medical record documentation of therapeutic failure on, intolerance to, or contraindication to ALL of the following:
    a. One formulary topical calcineurin inhibitor (tacrolimus ointment) AND
    b. One formulary topical corticosteroid unless deemed inadvisable due to potential risks such as (a) use on sensitive skin areas (face, axillae, or groin).

MEDISPAN AUTHORIZATION LEVEL: GPI-12
QUANTITY LIMIT: No QLs need to be entered within the authorization unless the requested quantity exceeds the QL. • QL FOR LETTER ONLY: 60 grams (1 tube) every 30 days

AUTHORIZATION DURATION: Initial approval will be for 6 months. Subsequent approvals will be for an additional 12 months and will require medical record documentation of the following:

- For Zoryve 0.3% topical cream: Medical record documentation of clinical improvement based on signs and symptoms of plaque psoriasis OR
- For Zoryve 0.3% topical foam: Medical record documentation of clinical improvements based on signs and symptoms of seborrheic dermatitis OR
- For Zoryve 0.15% topical cream: Medical record documentation of clinical improvement based on signs and symptoms of atopic dermatitis

FORMULARY ALTERNATIVES:

Calcineurin Inhibitors: tacrolimus ointment, pimecrolimus cream*
Low-potency topical corticosteroids: alclometasone dipropionate 0.5% cream and ointment (Aclovate); fluocinolone acetonide 0.01% soln. (Synalar); hydrocortisone 2.5% cream, ointment, and lotion (Hytone)
Medium-potency topical corticosteroids: betamethasone valerate 0.1% cream (Valisone); fluocinolone acetonide 0.025% cream and ointment (Synalar); fluticasone propionate 0.05% cream, ointment, and lotion (Cutivate); triamcinolone 0.1% cream, ointment and lotion (Kenalog); triamcinolone acetonide 0.025% cream, ointment and lotion (Kenalog); triamcinolone acetonide 0.147 mg/g aerosol (Kenalog Spray)
High-potency topical corticosteroids: augmented betamethasone dipropionate 0.05% cream (Diprolene AF); betamethasone valerate 0.1% ointment (Valisone); triamcinolone 0.5% cream (Kenalog); fluocinonide 0.05% cream, ointment and gel (Lidex)
Very high-potency topical corticosteroids: augmented betamethasone dipropionate 0.05% ointment, gel and lotion (Diprolene); clobetasol 0.05% cream, ointment, and scalp lotion (Temovate) diflorasone diacetate 0.05% cream and ointment (ApexiCon/Psorcon)

*prior authorization required

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

UPDATES

2025 FORMULARIES FOR APPROVAL

Background: The following 2025 formularies were submitted for annual approval:

- AON Exchange Formulary
- Commercial 4 Tier Formulary
- Commercial Traditional Formulary
- Commercial Triple Choice Formulary
- GHP Kids Formulary
- Marketplace Formulary

Formularies may also be accessed at:
https://www.geisinger.org/health-plan/find/covered-drug-pharmacy

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

DUVYZAT QUANTITY LIMIT UPDATE

Background: A quantity limit for Duvyzat of 12 milliliters per day was recommended at the November P&T Meeting. Duvyzat is dispensed in 140 milliliter bottles.

Recommendation: It is recommended that the quantity limit be updated as follows to allow Duvyzat to be dispensed in the supplied bottles:

- QL: 420 milliliters (3 bottles) per 30 days, 30 day supply per fill

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

POLICY UPDATED & FORMULARY CHANGES FOR JANUARY 1, 2025

<u>Farxiga & Xigduo Formulary Removal</u>
Background: Farxiga is indicated:

- To reduce the risk of sustained eGFR decline, end stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression
- To reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure
- To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors
- As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus

Xigduo XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus.

Recommendation: It is recommended that a policy is devised for non-formulary Farxiga and Xigduo XR requests with the following criteria:

- Farxiga
    - Medical record documentation of use:
        - To reduce the risk of sustained eGFR decline, end stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression **OR**

        - To reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with heart failure **OR**
        - To reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors **OR**
        - As an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus **AND**
    - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Jardiance

- Xigduo XR
    - Medical record documentation of use as an adjunct to diet and exercise to improve glycemic control in adults and pediatric patients aged 10 years and older with type 2 diabetes mellitus **AND**
    - Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Jardiance in combination with metformin **OR** Synjardy **OR** Glyxambi

It is also recommended that failure of Farxiga be removed from the following policies:

- 784.0 Brenzavvy
- 502.2 Steglatro and Invokana
- 682.0 Kerendia

Psoriasis and Psoriatic Arthritis Criteria for Biologic Therapy

Background: The treatment algorithms for mild to moderate psoriasis (PsO) and psoriatic arthritis (PsA) have been updated to include Otezla as a treatment option earlier in the algorithm. Our current drug policy currently requires:

- Psoriasis:
    - Mild → 2 topicals **AND** failure of phototherapy
    - Mod-Severe → topical steroid **AND** systemic therapy or phototherapy
- PsA: 2 NSAIDs **OR** failure of one biologic

Recommendation: In order to align the drug policy with treatment algorithm it is recommended that the criteria be updated to:

- Psoriasis:
- Mild → ~~2~~ 1 topical~~s~~ ~~AND~~ **OR** failure of phototherapy
- Mod-Severe → topical steroid ~~AND~~, systemic therapy, or phototherapy (select 1)
- PsA → ~~2 NSAIDs OR~~ failure of one ~~biologic~~ conventional/non-biologic agent

In order to maintain parity across PsA and PsO biologics, it is recommended that the same updated is made to the following products:

- **Psoriasis:** Enbrel, adalimumab, Otezla, Skyrizi SC, Sotyktu, Stelara SC, Taltz, Tremfya, Bimzelx, Cimzia, Cosentyx SC, Ilumya, Siliq
- **PSA:** Enbrel, adalimumab, Otezla, Skyrizi SC, Stelara SC, Taltz, Tremfya, Rinvoq/Rinvoq LQ, Xeljanz/Xeljanz XR, Cimzia, Cosentyx SC, Orencia SC, Simponi SC

Criteria for Preferred GLP-1 Agents (Commercial/Exchange/CHIP)

Background: We have begun to see inappropriate utilization of GLP-1 therapies without members following the guideline recommendation of first line metformin.

Recommendation: In order to ensure appropriate utilization and effectiveness of therapy the following changes are recommended to the prior authorization criteria in policy 732.0 Preferred GLP-1 Agonists and Mounjaro

- Medical record documentation* of a diagnosis of type II diabetes mellitus **AND**
- Therapeutic failure on, intolerance to, or contraindication to metformin **OR** any other oral antidiabetic drug

*NOTE: Any one form of documentation is allowed (either ICD-10 code, medical records, chart notes, A1C or other lab confirming T2DM diagnosis). Multiple forms of documentation or any requirement of a specific lab value are not permitted.

AUTHORIZATION DURATION: 1 year

Victoza & Ozempic for Weight Loss (Geisinger Employee Plan)
Background: Effective January 1, 2025 Victoza and Ozempic when prescribed for weight loss will no longer be a covered service. Members established on therapy prior to January 1, 2025 can continue receiving Victoza or Ozempic as long as there is no break in coverage/therapy and they continue to meet established re-authorization requirements.

Recommendations: It is recommended that policy 782.0 Victoza or Ozempic for GHS Employees is updated as follows:

Ozempic or Victoza for Diabetes

- Medical record documentation* of a diagnosis of type II diabetes mellitus
- Therapeutic failure on, intolerance to, or contraindication to metformin **OR** any other oral antidiabetic drug

*NOTE: Any one form of documentation is allowed (either ICD-10 code, medical records, chart notes, A1C or other lab confirming T2DM diagnosis). Multiple forms of documentation or any requirement of a specific lab value are not permitted.

AUTHORIZATION DURATION: 1 year

MEDISPAN APPROVAL LEVEL: GPI-12, Brand Code = Trademarked if request is for Victoza

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

QL FOR LETTER ONLY:

- Victoza: 9 mL per 30 days
- Ozempic: 3 mL per 28 days

~~**Victoza for Weight Loss**~~

- ~~Medical record documentation of age greater than or equal to 18 years **AND**~~
- ~~Medical record documentation of one of the following:~~
  - ~~Victoza is managed by Geisinger Nutrition and Weight Management or Geisinger Endocrinology **OR**~~
  - ~~Member resides outside of Pennsylvania **AND**~~
- ~~Medical record documentation of body mass index (BMI) greater than or equal to 30 kg/m^2 **AND**~~
- ~~Medical record documentation of at least one of the following specific weight related comorbid conditions:~~
  - ~~Hemoglobin A1C (HgbA1c) between 6% - 6.4%~~
  - ~~Elevated aspartate aminotransferase (AST) or alanine transaminase (ALT)~~
  - ~~Obstructive sleep apnea requiring treatment with CPAP/BiPAP~~

~~**MEDISPAN APPROVAL LEVEL:** GPI-12, , Brand Code = Trademarked~~

~~**QUANTITY LIMIT:** *QLs need to be entered within the authorization.*~~
~~QL FOR LETTER ONLY: Victoza: 15 mL per 30 days~~

Ozempic for Weight Loss

- ~~Medical record documentation of age greater than or equal to 18 years **AND**~~
- ~~Medical record documentation of one of the following:~~
  - ~~Victoza is managed by Geisinger Nutrition and Weight Management or Geisinger Endocrinology **OR**~~
  - ~~Member resides outside of Pennsylvania **AND**~~
- ~~Medical record documentation of body mass index (BMI) greater than or equal to 30 kg/m^2 **AND**~~
- ~~Medical record documentation of therapeutic failure of Victoza defined as failure to achieve a 10% weight loss after 6 months of Victoza therapy~~

AUTHORIZATION DURATION: Initial approval will be for 6 months. Subsequent approvals will be indefinite. Reauthorization will require the following be met:

- Medical record documentation of 5% weight loss **AND**
- Medical record documentation of one of the following:
  - ~~Victoza~~ Ozempic is managed by Geisinger Nutrition and Weight Management or Geisinger Endocrinology **OR**
  - Member resides outside of Pennsylvania

MEDISPAN APPROVAL LEVEL: GPI-12

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

- QL FOR LETTER ONLY: Ozempic: 3 mL per 28 days

Formulary Additions/Changes

Recommendation: It is recommended that the following products are added to the formulary. Existing quantity limits should remain in place:

	Commercial 2 Tier/CHIP	Commercial 3 Tier	Commercial 4 Tier	Exchange	Medicare
Glatopa	Tier 1, no PA	Tier 1, no PA	Tier 4, no PA	Tier 6, no PA	Tier 5, no PA
Dabigatran	Tier 1, no PA	Tier 1, no PA	Tier 1, no PA	Tier 3, no PA	Tier 4, remove step therapy

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

LUTATHERA UPDATE

Background: Upon discussion with medical directors, it was decided that the prior authorization criteria point regarding discontinuation of long-acting somatostatin analogs did not completely assess the information in the package insert. The package insert notes that long-acting somatostatin analogs must be discontinued or held for 4 weeks prior to administration of Lutathera.

Recommendation: Criteria point #5 in the policy will be changed to include "/held" to clarify the appropriate measures that must be taken by providers prior to administration of Lutathera.

Revised Prior Authorization Criteria:
Lutathera (lutetium Lu 177 dotatate) will be considered medically necessary for all lines of business when ALL of the following criteria are met:

- Prescribed by a hematologist/oncologist **AND**
- Patient is 12 years of age or older **AND**
- Medical record documentation of a diagnosis of gastroenteropancreatic neuroendocrine tumor (GEP-NET) (including foregut, midgut, and hindgut tumors) **AND**
- Medical record documentation of presence of somatostatin receptors on all lesions (somatostatin receptor positive disease) **AND**
- Medical record documentation that long-acting somatostatin analogs have been (or will be) discontinued/held at least 4 weeks prior to initiation of treatment with Lutathera

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

MEDICAL BENEFIT POLICY UPDATES

Keytruda Update

Discussion: After review of the Keytruda medical benefit policy, it was determined that the criteria for NSCLC in combination with carboplatin and paclitaxel for first-line use can be updated to more closely reflect the package labeling (squamous cell) and what is recommended in NCCN guidelines (EGFR/ALK).

Recommendations: It is recommended to update the criteria for Keytruda NSCLC, specifically to add the specific indication that the carboplatin/paclitaxel combination is indicated for, and to add the EGFR/ALK monitoring requirement.

MBP 119.0 Keytruda (pembrolizumab)

1. **Metastatic Non-Small Cell Lung Cancer (NSCLC)**
   - Prescription written by a hematologist/oncologist **AND**
   - Medical record documentation that patient is ≥ 18 years of age **AND**
   - Medical record documentation of a diagnosis of metastatic NSCLC meeting one of the following situations:
     - Medical record documentation of stage III NSCLC, metastatic NSCLC, OR that the member is not a candidate for surgical resection or definitive chemoradiation **AND**
     - Medical record documentation that Keytruda is being used as first-line treatment **AND**
     - Medical record documentation that Keytruda is being given as monotherapy **AND**
     - Medical record documentation that tumors express PD-L1 (TPS) ≥1% as determined by an FDA-approved test **AND**
     - Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

     OR
     - Medical record documentation that Keytruda is being given as monotherapy **AND**
     - Medical record documentation that tumors express PD-L1 (TPS) ≥1% as determined by an FDA-approved test **AND**
     - Medical record documentation of disease progression on or after platinum-containing chemotherapy **AND**
     - For patients with EGFR or ALK genomic tumor aberrations: medical record documentation of disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda.

     OR
     - Medical record documentation of metastatic nonsquamous NSCLC **AND**
     - Medical record documentation that Keytruda will be given in combination with pemetrexed AND either carboplatin or cisplatin **AND**

- Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

OR

- Medical record documentation of metastatic squamous NSCLC **AND**
- Medical record documentation that Keytruda will be given in combination with carboplatin AND either paclitaxel or nab-paclitaxel **AND**
- Medical record documentation that Keytruda, carboplatin, and paclitaxel (or nab-paclitaxel) are being used as first-line treatment **AND**
- Medical record documentation that tumors do not have EGFR or ALK genomic tumor aberrations

Erwinaze Update

Discussion: After discussion with DHS and internal sources, it was determined that there is most likely no remaining Erwinaze product left on the market. The Labeler reported their NDC as obsolete on 7/31/2021, then terminated their CMS rebate agreement on 4/1/2022. An FDA file lists the market end date as 7/23/2021.

Recommendations: It is recommended to retire MBP 95.0 Erwinaze (asparaginase).

Drug Optimization Program Update

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

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

I. Policy:
Medical Benefit Drug Optimization Program

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

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

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

SKYRIZI & TREMFYA UPDATE

Recommendation: It is recommended that the following changes be made to the prior authorization criteria for Skyrizi and Tremfya to clarify the criteria regarding prior biologic therapy:

- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to one conventional systemic therapy* (e.g. corticosteroids, immunomodulators such as azathioprine, 6 mercaptopurine, cyclosporine, tacrolimus) OR medical record documentation of a therapeutic failure on or intolerance to one prior biologic therapy other than the requested agent

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

SOFDRA UPDATE

Background: At the November P&T Meetting, it was recommended that Sofdra be added to the Commercial formulary to match Qbrexa. Sofdra does not offer any clinical advantage over other available products and will require failure of two products, including Qbrexa prior to approval.

Recommendation: It is recommended that Sofdra remain non-formulary for Commercial, Marketplace, and GHP Kids to keep it in line with the Medicare Formulary.

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

Formulary Updates Based on Specialty Routing Tool Updates

Background: To have continuity when switching PBMs, Navitus identified specialty medications in the specialty drug list based on medications we had on our previous specialty list. However, some medications are listed as “TBD” (to be determined) in the specialty routing tool. Several of these medications Navitus classified as medical only and they do not contract them through specialty pharmacy. After reviewing the list of TBD medications and comparing to current formulary status, the following commercial, exchange, CHIP, and Medicaid formulary changes are recommended based on the specialty routing tool updates that were sent to Navitus.

Recommendation: For commercial plans, for a medication to process through specialty, it must be assigned a tier. If a medication is medical only, it should be excluded on the pharmacy formulary.

Drug Name	Current Formulary Status for Commercial Formulary	Specialty Routing Tool Update	Recommendations to Commercial Formulary
APHEXDA	Tier 3	Update routing tool with medical benefit language	Excluded

ARTESUNATE	Tier 3	Update routing tool with medical benefit language	Excluded
BEQVEZ	Non-formulary pending P&T	Update routing tool with medical benefit language	Excluded
CASGEVY	Non-formulary	Update routing tool with medical benefit language	Excluded
COLUMVI	Tier 3	Update routing tool with medical benefit language	Excluded
GLIADEL WAFER	Non-formulary	Update routing tool with medical benefit language	Excluded
HEMGENIX	Tier 3	Update routing tool with medical benefit language	Excluded
IDOSE TR	Non-formulary pending P&T	Update routing tool with medical benefit language	Excluded
IMLYGIC	Tier 3	Update routing tool with medical benefit language	Excluded
IXEMPRA KIT	Tier 3	Update routing tool with medical benefit language	Excluded
JESDUVROQ	Non-formulary	Update routing tool with medical benefit language	Excluded
KCENTRA	Tier 3	Update routing tool with medical benefit language	Excluded

LENMELDY	Non-formulary	Update routing tool with medical benefit language	Excluded
LYFGENIA	Non-formulary	Update routing tool with medical benefit language	Excluded
LUTATHERA	Tier 3	Update routing tool with medical benefit language	Excluded
METYROSINE	Non-formulary	Update routing tool with medical benefit language	Excluded
MITOMYCIN	Tier 1	Update routing tool with medical benefit language	Excluded
MUGARD	Non-formulary	Update routing tool with medical benefit language	Excluded
MUTAMYCIN	Tier 1	Update routing tool with medical benefit language	Excluded
NELARABINE	Tier 3	Update routing tool with medical benefit language	Excluded
PEMFEXY	Tier 3	Update routing tool with medical benefit language	Excluded
PLUVICTO	Tier 3	Update routing tool with medical benefit language	Excluded
PRAXBIND	Tier 3	Update routing tool with medical benefit language	Excluded

QALSODY	Tier 3	Update routing tool with medical benefit language	Excluded
SCENESSE	Tier 3	Update routing tool with medical benefit language	Excluded
TALVEY	Tier 3	Update routing tool with medical benefit language	Excluded
TECVAYLI	Tier 3	Update routing tool with medical benefit language	Excluded
UNITUXIN	Tier 3	Update routing tool with medical benefit language	Excluded
VYJUVEK	Tier 3	Update routing tool with medical benefit language	Excluded
ZEVALIN Y-90	Tier 3	Update routing tool with medical benefit language	Excluded

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

Voting responses were received from 32 of 49 members. The vote was unanimously approved.

The next bi-monthly scheduled meeting will be held on January 14th, 2025 at 1:00 p.m.

Meeting will be held virtually via phone/Microsoft Teams.