

P&T Committee Meeting Minutes
Commercial/Marketplace/GHP Kids E-vote
March 17, 2020

Review and Approval of Minutes:

The January 21, 2020 minutes were approved as written by a unanimous vote. None were opposed.

DRUG REVIEWS

ENHERTU (fam-trastuzumab)

Review: Patients with unresectable or metastatic HER2-positive breast cancer who progress on first line-treatment regimens which typically include the HER2-antibody trastuzumab, have few treatment options for subsequent therapy. Enhertu, which combines trastuzumab with a topoisomerase inhibitor (DXd), binds the HER2 receptor causing the internalization and release of membrane permeable DXd which leads to DNA damage and cell death. The efficacy of Enhertu was evaluated in DESTINY-Breast01, a single-arm, open-label study in 184 adult female patients with HER2-positive unresectable and/or metastatic breast cancer who have received two or more prior HER2-directed therapies. Part 1 of the study investigated pharmacokinetics and dosing, finding that 5.4 mg/kg provided the best balance between efficacy and safety. This was continued in patients until disease progression or unacceptable toxicity. Part 2 of the study evaluating efficacy showed a 60.9% overall response rate, including confirmed complete (6%) and partial responses (54.9%) (RECIST v 1.1.). Secondary endpoints showed a median duration of response of 14.8 months and progression free survival of 16.4 months. The estimated overall survival was 93.9% at 6 months and 56.2% at 12 months, but the median overall survival was not reached at the time of analysis.

Enhertu contains black box warnings for both interstitial lung disease (ILD) and the possibility of fetal embryo harm. In clinical trials, interstitial lung disease occurred in 9% of patients leading to fatal outcomes due to ILD and/or pneumonitis in 2.6% of patients. Enhertu should be discontinued in any patients with Grade 2 or higher symptomatic interstitial lung disease. In clinical trials of Enhertu, serious adverse reactions were reported in 20% of patients. Permanent discontinuation due to adverse reactions occurred in 9% of patients, 6% resulting from ILD. The most common adverse reactions were nausea, vomiting, fatigue, alopecia, constipation, decreased appetite, anemia, neutropenia, diarrhea, leukopenia, cough and thrombocytopenia.

For patients with recurrent or metastatic HER2 positive breast cancer, NCCN prefers a first-line treatment regimen of trastuzumab (Herceptin or biosimilars) and pertuzumab (Perjeta) along with a taxane. For patients who progress on first-line treatment, NCCN continues to recommend HER2 directed therapy which includes other treatment regimens containing trastuzumab, single-agent treatment with ado-trastuzumab (Kadcyla), or single agent treatment with Enhertu. They do not appear to prefer one agent over another for second-line treatment, but their recommendations for Enhertu are consistent with the FDA approved indication for patients who have received two or more prior anti-HER2-based regimens in the metastatic setting.

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

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

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

Outcome: Enhertu is a medical benefit that should not be added to the Commercial/Exchange/CHIP pharmacy formularies. The following prior authorization criteria will apply:

- Medical record documentation that prescription is written by a hematologist or oncologist **AND**
- Medical record documentation of patient age greater than or equal to 18 years **AND**
- Medical record documentation of unresectable or metastatic HER2-positive breast cancer **AND**
- Medical record documentation of two or more prior anti-HER2 based therapies in the metastatic setting

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.

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

PADCEV (enfortumab vedotin-ejfv)

Review: Padcev is an antibody-drug conjugate consisting of human IgG1-kappa antibody, anti-Nectin-4, attached to a microtubule disrupting agent, monomethyl auristatin E (MMAE), by a cleavable maleimidocaproyl valine-citrulline linker. The antibody-drug conjugate binds Nectin-4, an adhesion protein found on the cell surface which is overexpressed in many cancer cells. This complex is then internalized and MMAE is cleaved from the complex resulting in microtubule disruption and leading to cell cycle arrest and cell death. NCCN recommends Padcev as a preferred subsequent-line regimen for patients who have failed the preferred first- (platinum-based chemotherapy) and second-line (PD-L1 or PD-1 inhibitors) treatment options.

The efficacy of Padcev is demonstrated in Cohort 1 of EV-201, a Phase II, single-arm, open-label trial in 125 adult patients with locally advanced or metastatic urothelial carcinoma previously treated with both platinum chemotherapy and an anti-PD-1/L1 therapy. Patients included had progressed on their most recent therapy and had an ECOG performance status of < 1 and adequate organ function. Patients with motor or sensory neuropathy, CNS metastases, and uncontrolled diabetes were excluded. Patients received treatment with Padcev 1.25 mg/kg (maximum dose of 125 mg) by IV infusion on days 1, 8, and 15 of 28 day cycles until disease progression or unacceptable toxicity. The primary efficacy endpoint assessing confirmed objective response rate showed that 44% of patients had achieved a response with 12% achieving a full response and 32% achieving a partial response. The median duration of response was 7.6 months, which ranged from 3.6 to 11.3 months in patients who had achieved a complete response. Secondary endpoints showed 5.8 months for progression free survival and 11.7 months for overall survival.

Padcev includes warnings and precautions for hyperglycemia (in patients with or without existing diabetes), peripheral neuropathy, ocular disorders, and skin or skin and soft tissue reactions. During clinical trials, serious adverse reactions occurred in 46% of patients, most commonly urinary tract infection, cellulitis, febrile neutropenia, diarrhea, sepsis, acute kidney injury, dyspnea, and rash. Fatal adverse reactions resulting from acute respiratory failure, aspiration pneumonia, cardiac disorder, and sepsis occurred in 3.4% of patients. The most common adverse event leading to discontinuation was peripheral neuropathy and the most common adverse events leading to dose interruption were peripheral neuropathy, rash, and fatigue. Other adverse events that commonly occurred were altered taste, dry eye, pruritis, and dry skin.

For patients with metastatic bladder cancer, the standard of care is platinum-based chemotherapy resulting in an estimated overall survival of 9 to 15 months. For patients who relapse or don't respond to initial therapy, the

median survival is reduced to 5 to 7 months. NCCN recommends PD-L1 or PD-1 inhibitors for second line treatment after platinum based therapy as these have been shown to extend overall survival. For subsequent-line therapy, NCCN recommends Padcev or Balversa as preferred treatment options. Although Balversa has shown efficacy in this population, it is limited to patients whose tumors have susceptible FGFR3 or FGFR2 genetic alterations.

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

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

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

Outcome: Padcev is a medical benefit and should not be added to the Commercial, Exchange, or GHP Kids pharmacy formularies. The following prior authorization criteria will apply:

- Medical record documentation that prescription is written by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of locally advanced or metastatic urothelial cancer **AND**
- Medical record documentation that member has received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting

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.

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

VUMERITY (diroximel fumarate)

Review: Vumerity is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Vumerity produces the same active metabolite as Tecfidera. Vumerity has been shown to reduce adverse reactions and discontinuation with comparable efficacy to Tecfidera. Gastrointestinal adverse reactions may occur with Tecfidera, especially in the first month. It is unlikely that providers will switch patients from Tecfidera to Vumerity in those currently stable. Most utilization will come from new starts or those early in therapy with tolerability issues.

The starting dose for Vumerity is 231 mg twice daily, orally. After 7 days, the dosage should be increased to the maintenance dose of 462 mg (administered as two 231 mg capsules) twice daily. Temporary dosage reductions to 231 mg twice daily may be considered for patients with intolerance to the maintenance dose. However, within 4 weeks, 462 mg twice daily should be resumed. Vumerity should be discontinued in those who cannot tolerate the maintenance dose.

The efficacy of Vumerity is based upon bioavailability studies in patients with relapsing forms of MS and healthy subjects comparing oral dimethyl fumarate to Vumerity. The clinical studies in the package insert were conducted using dimethyl fumarate. Vumerity was compared to Tecfidera in the EVOLVE-MS trial which was a 5-week trial of 504 patients with relapse-remitting multiple sclerosis. Patients were administered diroximel fumarate 462 mg (231 mg twice daily for 1 week) or dimethyl fumarate 240 mg twice daily (120 mg twice daily for 1 week). Patients used two eDiary symptom scales to evaluate GI symptoms daily. The primary study endpoint was the number of days, with any Individual Gastrointestinal Symptom and Impact Scale (IGISIS) intensity score ≥ 2 in the overall study population. Patients rated the severity as 0 (did not have any) to 10 (extreme) within 9 hours of taking the drug. The number of days with a patient-assessed event was significantly less with diroximel fumarate. An additional endpoint evaluated the symptom intensity and frequency using the Global Gastrointestinal Symptom and Impact Scale (GGISIS) intensity score of ≥ 2 . Patients completed a daily questionnaire to rate the GI symptoms as 0 (did not have) to 10 (extreme). There were fewer days of events with diroximel fumarate compared with dimethyl fumarate, however the difference did not meet statistical significance. . GI symptom severity scores with diroximel fumarate and dimethyl fumarate seem to be similar by week 5.

Vumerity is contraindicated in patients with known hypersensitivity to diroximel fumarate, dimethyl fumarate, or any of the excipients of Vumerity or those taking dimethyl fumarate. Vumerity may be initiated the day following discontinuation of Tecfidera. Vumerity has warnings for anaphylaxis and angioedema, progressive multifocal leukoencephalopathy (PML), decreased lymphocyte counts, liver injury, and flushing. The most common adverse reactions (incidence for dimethyl fumarate [which has same active ingredient as Vumerity] $\geq 10\%$ and $\geq 2\%$ more than placebo) were flushing, abdominal pain, diarrhea, and nausea.

I spoke with Amanda Sharry-Rogers, MTDM neurology pharmacist. Vumerity would likely only be prescribed for patients who were intolerant to Tecfidera or who have a history of GI issues and are not comfortable starting one of the other oral disease modifying therapies. She believes that patients who are stable on Tecfidera will remain on Tecfidera.

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

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

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

Outcome: Vumerity is a pharmacy benefit and will be added to the Specialty tier or the Brand Preferred tier for members with a three tier benefit. The following quantity limits will apply:

QUANTITY LIMIT: 4 capsules per day, 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.

AKLIEF (trifarotene)

Review: Akliel is a topical retinoid indicated for the treatment of acne vulgaris in patients 9 years and older. It is dosed as 1 pump daily to cover the face and 2 pumps daily to cover the trunk. Trifarotene is a retinoic acid receptor (RAR) agonist which may modulate target genes involved cell differentiation and mediation of inflammation, but

the exact mechanism in the treatment of acne is unknown. Akliel falls into the same class (topical retinoid) as adapalene, tretinoin, tazarotene, and isotretinoin, however it is the only formulation that selectively targets the retinoic acid receptors.

Akliel was studied in two identical twin studies called PERFECT1 and PERFECT2 that demonstrated efficacy against a vehicle cream at 12 weeks follow up with statistically significant improvement in Investigator's Global Assessment (IGA) of facial acne and Physician's Global Assessment (PGA) of truncal acne.

Akliel has demonstrated a milder adverse event profile when compared to other similar medications such as tretinoin or tazarotene with skin irritation and photosensitivity being the most prominent effects. Warnings include skin irritation and photosensitivity with ultraviolet light exposure.

The American Academy of Dermatology has not yet updated its guidelines to include Akliel. According to the American Academy of Dermatology, acne treatment depends on if the acne is mild, moderate, or severe. Classification is defined by multiple factors including number of lesions, type of lesions, inflammation, and location. Treatment trials typically range from 2 to 3 months and then are assessed for progress. Mild acne is typically treated with benzoyl peroxide then a topical retinoid. Moderate acne can be treated with benzoyl peroxide in combination with a topical antibiotic, benzoyl peroxide in combination with a topical retinoid, or a combination of the three. An oral antibiotic may be added on if adequate treatment response is not obtained. Severe acne is treated with an oral antibiotic with topical combination therapy consisting of benzoyl peroxide and a topical antibiotic, a topical retinoid plus benzoyl peroxide, or a topical retinoid, antibiotic, and benzoyl peroxide. If adequate response is obtained oral isotretinoin can be added on.

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

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

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

Outcome: Akliel is a pharmacy benefit and will not be added to the Commercial, Exchange, or GHP Kids formularies. It will be added to the Commercial Policy 476.0 for Non-Preferred Acne Medications:

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

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

AYVAKIT (avapritinib)

Review: Gastrointestinal stromal tumors (GIST) are the most common soft tissue sarcoma in the gastrointestinal tract with an annual incidence of 4000 to 6000 cases per year in the United States. There is an overall survival rate of 76% in patients with GIST. Surgical resection is the only potentially curative treatment for patients and is typically followed by treatment with a tyrosine kinase inhibitor (TKI) in high-risk patients. For patients with unresectable or metastatic disease, the overall 5-year survival rate decreases to 48%.

A majority of GIST have a KIT mutation (80%), while 5 to 10% have a mutation in the gene for platelet-derived growth factor receptor alpha (PDGFRA) and 10 to 15% have no detectable KIT or PDGFRA mutations (wild-type GIST). For patients with unresectable or metastatic disease, patients will initially be treated with KIT-directed tyrosine kinase inhibitors including imatinib (Gleevec), sunitinib (Sutent), or regorafenib (Stivarga). Imatinib can improve progression free survival and overall survival, achieving disease control in approximately 85% of cases, but acquired secondary mutations can lead to drug resistance and progression on imatinib. NCCN recommends sunitinib for patients who are resistant to or can't tolerate imatinib and regorafenib for patients who experience disease progression on both imatinib and sunitinib. There are no standard treatments for patients who progress following treatment with imatinib, sunitinib, and regorafenib and options include sorafenib, nilotinib, dasatinib, pazopanib, and everolimus with a TKI.

Most patients with PDGFRA mutations will initially respond to therapy with imatinib with the notable exception of D842V, the most common exon 18 mutation which responds poorly to all TKI treatment options. Prior to the approval of Ayvakit, Sprycel (dasatinib) was the only treatment option that demonstrated some efficacy in patients with PDGFRA D842V mutation and was associated with median progression free survival of 2 months and overall survival of 19 months in imatinib-resistant disease.

NCCN recommends Ayvakit for treatment of metastatic or unresectable gastrointestinal stromal tumors (GIST) with disease progression after therapy with imatinib, sunitinib, and regorafenib (category 2A) and for treatment of GIST with PDGFRA exon 18 mutations (including PDGFRA D842V) as primary treatment for unresectable, recurrent, or metastatic disease, postoperative treatment following persistent gross residual disease (R2 resection), or continued treatment for limited progression (category 2A).

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

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

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

Outcome: Ayvakit is a pharmacy benefit and will be added to the Oral Oncology Brand Non-preferred tier (\$0 copay) of the Commercial, Exchange, and GHP Kids pharmacy formularies. The following prior authorization criteria will apply:

- Medical record documentation that prescription is written by a hematologist or oncologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of unresectable or metastatic gastrointestinal stromal tumor (GIST) **AND**
- Medical record documentation of a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation

QUANTITY LIMIT: 1 tablet per day

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.

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

BEOVU (brolucizumab)

Review: Beovu is a human vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of Neovascular (Wet) Age-Related Macular Degeneration (AMD). Beovu is the 5th VEGF antagonist used for nAMD, joining Eylea (aflibercept), Lucentis (ranibizumab), Macugen (pegaptanib), and the off-label, bevacizumab. Beovu is the first VEGF agent to have demonstrated efficacy up to every 12 week dosing frequency without mention in its FDA label regarding a loss of efficacy when utilizing this frequency, though some patients may require every 8 week dosing. Although some may require every 4 week dosing, Eylea's recommended frequency is every 8 weeks, with label permissions up to every 12 weeks, noting patients must have had one year of effective therapy. The Lucentis label also allows for extension from every 4 week frequency to every 12 weeks but notes a loss of efficacy may occur. Off-label bevacizumab is generally dosed every 4 weeks with varying degrees of usage among providers and current literature.

Beovu is available as a 6mg vial given as an ophthalmic intravitreal injection administered by a qualified physician monthly (approximately every 25-31 days) for the first three doses, followed by 6mg (0.05mL) by intravitreal injection every 8-12 weeks.

The efficacy of Beovu was assessed in two randomized, multi-center, double-masked, active-controlled studies (HAWK and HARRIER) in patients with nAMD. A total of 1,817 patients were treated for two years (1,088 on Beovu and 729 on active control). In HAWK, patients were randomized 1:1:1 to Beovu 3mg, 6mg, or aflibercept 2mg. In HARRIER, patients were randomized 1:1 to Beovu 6mg or aflibercept 2mg. Both studies demonstrated efficacy in the primary endpoint defined as the change from baseline in Best Corrected Visual Acuity (BCVA) at Week 48, measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) Letter Score. In both studies, Beovu treated patients had a similar mean change from baseline in BCVA as the patients treated with aflibercept 2 mg (fixed every 8 weeks). Through Week 48, 56% (HAWK) and 51% (HARRIER) of patients remained on Beovu every 12 weeks. The proportion of patients who were maintained on every 12 week dosing through week 96 was 45% and 39% in HAWK and HARRIER, respectively. Treatment effects in evaluable subgroups (e.g., age, gender, race, baseline visual acuity) in each study were generally consistent with the results in the overall populations.

The most common adverse reactions ($\geq 5\%$) in patients receiving Beovu are vision blurred (10%), cataract (7%), conjunctival hemorrhage (6%), eye pain (5%), and vitreous floaters (5%). Beovu has no boxed warnings, but does have contraindications for ocular or periocular infections, active intraocular inflammation, and hypersensitivity. Similar to other VEGF inhibitors, additionally, Beovu has warnings and precautions for the time period following intravitreal injections including endophthalmitis and retinal detachments (therefore patients should be instructed to watch for and report any symptoms immediately), increases in intraocular pressure (IOP) within 30 minutes, and the potential risk of arterial thromboembolic events (ATE). The safety and efficacy of Beovu in pediatric patients has not been established.

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

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

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

Outcome: Beovu will be a medical benefit for Commercial, Exchange, and GHP Kids members. Beovu will not require a prior authorization.

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

WAKIX (pitolisant)

Review: Wakix is a histamine-3 (H₃) receptor antagonist/inverse agonist indicated for the treatment of excessive daytime sleepiness (EDS) in adult patients with narcolepsy. It is a first medication to target the histamine-3 receptor and is thought to modulate the release of neurotransmitters that play a role in wakefulness, including acetylcholine, norepinephrine and dopamine. It is the first non-controlled substance indicated for the treatment of excessive daytime sleepiness.

The efficacy of Wakix was shown in the HARMONY1 and HARMONY1bis two randomized, double-blind, placebo-controlled clinical trials in adult patients for the treatment of excessive daytime sleepiness who met the International Classification of Sleep Disorders (ICSD-2) criteria for narcolepsy with or without cataplexy and had an Epworth Sleepiness Scale (ESS) score ≥ 14 . Patients were randomized to Wakix, modafinil, or placebo. During a 3 week titration period, patients who received Wakix were titrated based on efficacy and tolerability from 8.9 to 35.6 mg in HARMONY1 and from 4.45 to 17.8 in HARMONY1bis.

The primary efficacy endpoint for both studies was clinically relevant reduction in the Epworth Sleepiness Scale (ESS) compared to placebo at week 8 (at least 3 points). HARMONY1 met the primary efficacy endpoint with a mean 3.1 point reduction in ESS, while HARMONY1bis did not meet the primary endpoint but still had a significant reduction in ESS over placebo (2.2 points). HARMONY1 showed a significant improvement in rate of cataplexy and Maintenance of Wakefulness test (MWT), while HARMONY1bis showed an increase from baseline in the rate of cataplexy and no significant difference in MWT. In both studies, a non-inferiority analysis to modafinil was conducted and in both studies, Wakix did not demonstrate non-inferiority to modafinil.

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

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

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

Outcome: Wakix is a pharmacy benefit that will not be added to the Commercial, Exchange, or GHP Kids formularies. The following prior authorization criteria will apply:

- Medical record documentation of diagnosis of excessive daytime sleepiness associated with narcolepsy **AND**
- Medical record documentation of the member being ≥ 18 years of age **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to: modafinil* or armodafinil* **AND** methylphenidate IR or amphetamine/dextroamphetamine IR

QUANTITY LIMIT: 2 tablets per day

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

TAZVERIK (tazemetostat)

Review: Tazverik is indicated for the treatment of adults and pediatric patients age 16 years or older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection. Most epithelioid sarcoma tumor cells have a loss of INI1 protein expression which results in uncontrolled oncogenic activity of the histone methyltransferase EZH2 enzyme. Tazverik is the first FDA-approved treatment for epithelioid sarcoma and is a novel, first-in-class methyltransferase inhibitor selective for EZH2.

Tazverik is available as 200 mg tablets and dosed at 800mg orally twice daily until disease progression or unacceptable toxicity. The recommended dose for patients that require a dose reduction due to adverse effects is 600mg twice daily for the first dose reduction and 400mg twice daily if a second dose reduction is required.

The approval of Tazverik was based on data from a single cohort (Cohort 5) in an open-label, single-arm phase 2 trial (EZH-202). Cohort 5 consisted of 62 patients with histologically confirmed, metastatic or locally advanced epithelioid sarcoma. During the review of the Tazverik application, the FDA also requested data from the manufacturer regarding another patient cohort (Cohort 6) in study EZH-202. Enrolled patients (Cohort 5) were required to have INI1 loss. At baseline 15% had Stage I/II disease, 71% had Stage III/IV disease and the remainder had an unknown stage of disease. More than half (61%) had received one or more lines of prior systemic chemotherapy and 77% had prior surgery. A major difference between study Cohort 5 and Cohort 6 was that patients in Cohort 6 could enroll regardless of INI1 status. Cohort 6 consisted of 44 patients. All patients received treatment with Tazverik 800mg orally twice daily until disease progression or unacceptable toxicity. In Cohort 5, 15% (CI 7,76) had an overall response rate (ORR) to therapy, including 25% in the treatment-naïve group and 8% in the relapsed/refractory group. The ORR for Cohort 6 was calculated to be 11% (CI 4, 25) and the ORR for the pooled analysis of Cohorts 5 and 6 was 13% (CI 7,21).

Tazverik does not carry any black box warnings or contraindications. Warnings and precautions for Tazverik include increased risk of secondary malignancies and embryo-fetal toxicity. The most common adverse reactions that occurred in 20% or more of patients treated with Tazverik included pain, fatigue, nausea, decreased appetite, vomiting and constipation. Tazverik should not be coadministered with cytochrome P450 CYP3A inducers or moderate to strong CYP3A inhibitors. A dose reduction of Tazverik should be considered if co-administration with a moderate CYP3A4 inhibitor cannot be avoided. The safety and effectiveness of Tazverik in pediatric patients aged less than 16 years have not been established.

The mainstay of treatment for localized disease is surgical resection; radiation can also be used. However, epithelioid sarcoma will recur in more than half of cases following surgery or radiation. For patients with advanced stage disease, systemic chemotherapy can be offered. The NCCN recommends Tazverik as single agent treatment of metastatic or locally advanced epithelioid sarcoma not eligible for complete resection (2A recommendation).

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

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

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

Outcome: Tazverik will be a pharmacy benefit. Tazverik be added to the Commercial, Exchange, and GHP Kids formularies at the OralOncBrandNP tier. Tazverik will require a prior authorization with the following criteria:

- Prescription written by or in consultation with an oncologist or hematologist **AND**
- Medical record documentation of age greater than or equal to 16 years **AND**
- Medical record documentation of metastatic or locally advanced epithelioid sarcoma **AND**
- Medical record documentation that member is not eligible for complete resection

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

QUANTITY LIMIT: 240 tablets per 30 days

Pharmacist note to CSR: Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).

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

NOURIANZ (istradefylline)

Review: Nourianz is an adenosine A_{2A} antagonist approved for adjunctive treatment to levodopa/carbidopa in adult patients with Parkinson's disease (PD) experiencing "OFF" episodes. Inhibition of the A_{2A} receptor reduces the overactivation of the indirect pathway thought to play a role in the abnormal movements of Parkinson's disease. It is used in combination with levodopa, which affects both the indirect and direct pathway, and helps to reduce "OFF" periods associated with long term levodopa use. It has been available in Japan since 2013 but was not approved with the initial submission in the US due to efficacy concerns. Additional clinical trials included in the subsequent submission, supported its efficacy as adjunctive treatment to carbidopa/levodopa in patients with Parkinson's disease experiencing "OFF" episodes.

Study 1 and 2, which were included in the original submission, were randomized, double-blind, placebo controlled 12-week trials in adult patients with Parkinson's disease who had received at least one year of treatment with levodopa and were experiencing at least 2 hours of "OFF" episodes per day. In Study 1, Nourianz 40 compared to placebo produced a statistically significant reduction for the primary endpoint assessing the percentage change of daily awake "OFF" hours, as well as secondary endpoints measuring change from baseline in total hours of "OFF" time and "ON" time with non-troublesome dyskinesia. There was numerically higher but not statistically significant increase in the amount of "ON" time without dyskinesia for the Nourianz treatment group compared to placebo. In Study 2, Nourianz 20 compared to placebo produced a statistically significant reduction in the percentage change of daily awake "OFF" hours, as well as change from baseline in total hours of "OFF" time but did not show any significant differences in "ON" hours with or without dyskinesia.

Study 3 and 4 were randomized double-blind, placebo-controlled 12-week trials in which patients received Nourianz 20 mg, Nourianz 40 mg, or placebo. In both Study 3 and 4, both Nourianz 20 mg and 40mg achieved the primary endpoint with a statistically significant decrease in total "OFF" time compared to placebo. Compared to placebo, Nourianz 40 significantly increased the amount of "ON" time with non-troublesome dyskinesia for both Study 3 and 4, while Nourianz had significant results in Study 4, but not Study 3.

Safety concerns for Nourianz are consistent with those of other Parkinson's disease adjuvant treatments and included warnings for dyskinesia, hallucinations, psychotic behavior, and impaired impulse control. In clinical trials, the most commonly reported adverse reactions were dyskinesia, dizziness, constipation, nausea, hallucinations, and insomnia.

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

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

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

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

- Medical record documentation that the prescription is written by or in consultation with a neurologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of Parkinson's disease with "OFF" episodes or motor fluctuations **AND**
- Medical record documentation that Nourianz will be used as adjunctive treatment to carbidopa/levodopa **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three formulary alternatives.

QUANTITY LIMIT: 1 tablet per day

Other Recommendations: Tolcapone is available on the generic tier without a prior authorization. Tolcapone has more risk of adverse reactions and the cost is significantly greater compared to entacapone and should be reserved for patients who can't tolerate entacapone. It is recommended to add the following step therapy requirements to tolcapone:

- Electronic step therapy of on-line prescription drug claims history showing 15 days use of entacapone or carbidopa/levodopa/entacapone within the previous 180 days. If this electronic step is met, the claim with automatically adjudicate **OR**
- If the electronic step therapy criteria are not met, prescribing provider should request an exception for coverage indicating therapeutic failure on, intolerance to, or contraindication to entacapone or carbidopa/levodopa/entacapone

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

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

INBRIJA (levodopa)

Review: Inbrija is an inhaled form of levodopa indicated for the intermittent treatment of "OFF" episodes in patients with Parkinson's disease treated with carbidopa/levodopa. It is administered using a breath-actuated inhaler designed for competent use in patients with Parkinson's disease even during periods of diminished dexterity. It is

only the second medication available to be used as on-demand treatment to quickly reverse “OFF” episodes in patients with Parkinson’s disease. Although it does not appear to reverse symptoms as rapidly as Apokyn injections (20 minutes vs. 30 minutes), it may offer some advantages in ease of administration and the side effect profile which is generally consistent with oral levodopa.

The efficacy of Inbrija was evaluated in a 12-week, randomized double-blind, placebo controlled study in patients aged 30 to 85 years with Parkinson’s disease on a stable regimen containing no more than 1600 mg of levodopa, who experienced at least 2 hours of motor fluctuations daily. Patients receiving Inbrija 84 mg compared to placebo had statistically significant response from pre-dose to 30 minutes post-dose in USPRDS part III motor score which assesses the severity of motor function symptoms. There were also a statistically significant greater proportion of patients maintaining an “ON” state at 60 minutes post-dose in the Inbrija treatment group compared to placebo.

A 12-month, randomized, controlled, open label study in patients without underlying lung disease compared pulmonary function in patients with Parkinson’s disease who received Inbrija to those maintained on oral regimens alone. At one year, the average reduction in FEV₁ were comparable between treatment groups. A double-blind placebo controlled crossover study in patients with mild or moderate asthma showed that patients had an increased incidence in cough (60%) and temporary reductions in FEV₁ (40%) when receiving Inbrija compared to placebo. Due to this increased risk of bronchospasm, Inbrija is not recommended in patients with underlying lung disease. During clinical trials, the most commonly reported adverse reactions were cough and fall. Other adverse events reported during clinical trials were consistent with the known safety profile of oral levodopa.

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

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

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

Outcome: Inbrija is a pharmacy benefit that will be added to the Commercial, Marketplace, and GHP Kids formularies at the Specialty tier, or the Brand Non-Preferred tier for members with a three-tier benefit. No prior authorization criteria will apply.

QUANTITY LIMIT: 10 capsules per day (5 boxes per month)

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

CLASS REVIEW

SGLT2 Inhibitor Class Review

Trade Name	Generic Name	FDA Approved Indication
Invokana Invokamet/ Invokamet XR	canagliflozin, canagliflozin/metformin, canagliflozin/metformin ER	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults Canagliflozin is indicated for risk reduction of major adverse cardiovascular events in adults with Type 2 Diabetes Mellitus and established cardiovascular disease NEW – Canagliflozin is indicated for risk reduction for end stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with Type 2 Diabetes Mellitus and diabetic nephropathy with albuminuria > 300 mg per day
Jardiance	empagliflozin	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults Risk reduction of major adverse cardiovascular events in adults with Type 2 Diabetes Mellitus and established cardiovascular disease
Synjardy/ Synjardy XR Glyxambi	empagliflozin /metformin, empagliflozin /metformin ER, empagliflozin/linagliptin	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults The effect of Synjardy/ Synjardy XR/Glyxambi on the risk of cardiovascular death in patients with Type 2 Diabetes Mellitus and established cardiovascular disease has not been established
Farxiga, Xigduo XR	Dapagliflozin dapagliflozin/metformin ER	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control NEW – Dapagliflozin is indicated to reduce the risk of hospitalization for heart failure in adults with type 2 DM and established cardiovascular disease or multiple cardiovascular risk factors
Qtern	dapagliflozin/saxagliptan	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults
Steglatro	ertugliflozin	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults
Segluromet	ertugliflozin/metformin	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults
Steglujan	ertugliflozin/sitagliptan	Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults
NEW - Qternmet	dapagliflozin/saxagliptan/metformin	NEW – Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults
NEW - Trijardy XR	empagliflozin/linagliptin/metformin	NEW - Type 2 Diabetes Mellitus, as an adjunct to diet and exercise to improve glycemic control in adults Empagliflozin is indicated for risk reduction of major adverse cardiovascular events in adults with Type 2 Diabetes Mellitus and established cardiovascular disease

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

Current Formulary Status/Prior Authorization Criteria:

	Commercial/GHP Kids	Exchange
Preferred Generic		
Generic		
Brand Preferred	Invokana, Invokamet, Invokamet ER, Jardiance, Synjardy, Synjardy XR, Glyxambi,	Invokana, Invokamet, Invokamet ER, Jardiance, Synjardy, Synjardy XR, Glyxambi,
Brand Non-Preferred		
Specialty		
Non-Formulary	Farxiga, Qtern, Steglatro, Segluromet, Steglujan, Xigduo XR	Farxiga, Qtern, Steglatro, Segluromet, Steglujan, Xigduo XR

Commercial/Exchange/GHP Kids	
Medication	Current Policy
Invokana	No current policy
Invokamet	No current policy
Invokamet XR	No current policy
Jardiance	No current policy
Synjardy	No current policy
Synjardy XR	No current policy
Glyxambi	No current policy
Farxiga	<ul style="list-style-type: none"> • Medical record documentation of a diagnosis of type II diabetes mellitus AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Invokana AND Jardiance
Xigduo XR	<ul style="list-style-type: none"> • Medical record documentation of a diagnosis of type II diabetes mellitus AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Jardiance in combination with metformin, Synjardy, or Synjardy XR AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Invokana in combination with metformin, Invokamet, or Invokamet XR
Qtern	<ul style="list-style-type: none"> • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of a diagnosis of type II diabetes mellitus AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Glyxambi OR

	<ul style="list-style-type: none"> • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Tradjenta AND one formulary SGLT2 inhibitor
Steglatro	<ul style="list-style-type: none"> • Medical record documentation of a diagnosis of type II diabetes mellitus AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Invokana AND Jardiance
Segluromet	<ul style="list-style-type: none"> • Medical record documentation of a diagnosis of type II diabetes mellitus AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Jardiance in combination with metformin, Synjardy OR Synjardy XR AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Invokana in combination with metformin, Invokamet, OR Invokamet XR
Steglujan	<ul style="list-style-type: none"> • Medical record documentation of a diagnosis of type II diabetes mellitus AND • Medical record documentation of age greater than or equal to 18 years AND • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Glyxambi OR • Medical record documentation of therapeutic failure on, intolerance to, or contraindication to Tradjenta AND one formulary SGLT2 inhibitor

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

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

Outcome: Invokana, Invokamet, and Invokamet XR are currently our preferred SGLT2 agents available without a prior authorization. Because current guidelines don't recommend the use of one particular SGLT2 inhibitor over another, the new indication for risk reduction for renal failure supports its formulary placement. There were no changes in the dosage with the new indication, so no changes are needed to our current quantity limit.

Farxiga and Xigduo XR are both non-formulary agents requiring a prior authorization. Because the risk reduction of major adverse cardiovascular events is indicated in patients with Type 2 diabetes, no changes are needed to our current prior authorization criteria. There were no changes to the dosage with the new indication, so no changes are needed to our current quantity limit.

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

FAST FACTS

KEYTRUDA (pembrolizumab)

Updated Indication: Keytruda is now indicated for the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy.

Previously in urothelial carcinoma, Keytruda was indicated in patients with PD-L1 CPS \geq 10 tumors or in patients who have progressed on or after platinum-containing chemotherapy or are not eligible for platinum-containing chemotherapy.

Current formulary status: NF (Medical benefit requiring PA)

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

- Prescription written by a hematologist/oncologist **AND**
 - Medical record documentation that patient is \geq 18 years of age **AND**
 - Medical record documentation of locally advanced or metastatic urothelial carcinoma **AND**
 - Medical record documentation of one of the following:
 - Disease progression during or following platinum-containing chemotherapy
- OR**
- Disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- OR**
- Patient is not eligible cisplatin-containing chemotherapy* **AND**
 - Tumors express PD-L1 (combined positive score [CPS] greater than or equal to 10) as determined by an FDA-approved test
- OR**
- Patient is not eligible for any platinum-containing chemotherapy (regardless of PD-L1 status)
- OR**
- Patient has high-risk, non-muscle invasive bladder cancer (NMIBC)** **AND**
 - Patient's disease is unresponsive to an adequate trial of Bacillus Calmette-Guerin (BCG) therapy**
 - AND**
 - Patient is ineligible for or has elected not to undergo cystectomy

****Note:**

- BCG-unresponsive high-risk NMIBC is defined as persistent disease despite adequate BCG therapy, disease recurrence after an initial tumor-free state following adequate BCG therapy, or T1 disease following a single induction course of BCG.
- Adequate BCG therapy was defined as administration of at least five of six doses of an initial induction course plus either of: at least two of three doses of maintenance therapy or at least two of six doses of a second induction course.

Discussion: No comments or questions.

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

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

WILATE (von Willebrand Factor/Coagulation Factor VIII Complex, Human)

Updated Indication: In addition to patients with von Willebrand disease (VWD), Wilate is now indicated in adolescents and adults with hemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes and on-demand treatment and control of bleeding episodes.

Previously, Wilate was only indicated in children and adults with VWD for on-demand treatment and control of bleeding episodes and perioperative management of bleeding.

Current formulary status: Wilate is a pharmacy benefit or medical benefit. It does not require a prior authorization on the medical benefit. It is available at the Specialty tier or Brand Non-Preferred Tier for members with a three tier benefit requiring a prior authorization. There is no policy in place for Alphanate, Humate-P, and Wilate at this time.

Recommendation: There are no changes recommended to formulary status at this time. Also, it is not recommended to add a policy at this time for VWF/FVIII products.

Discussion: No comments or questions.

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

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

ENTRESTO (sacubitril/valsartan)

Updated Indication: Entresto is now indicated for the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older. Entresto reduces NT-proBNP and is expected to improve cardiovascular outcomes.

Previously, Entresto was indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure and reduced ejection fraction and the safety and efficacy in pediatric patients was not established.

Current formulary status: Brand Preferred, requiring a prior authorization

Recommendation: Entresto currently requires prior authorization to ensure appropriate utilization. The cost of Entresto remains high compared to alternatives, however based on the most recent prior authorization case volume data the prior authorization is not adding any value to overall treatment of this population as it once did since Entresto is appropriate (approved) in a large majority of patients. Because of this, it is recommended that the prior authorization and associated criteria be removed for Entresto. Entresto will continue to process at its designated tier without prior authorization.

It is recommended to update the quantity limits to the following to incorporate the updated dosing for the new indication in pediatric patients:

QUANTITY LIMITS:

Entresto 24/26 mg tablets: 6 tablets per day
Entresto 49/51 mg tablets: 3 tablets per day
Entresto 97/103 mg tablets: 2 tablets per day

Discussion: No comments or questions.

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

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

XARELTO (rivaroxaban)

Updated Indication: Xarelto is now indicated for the prophylaxis of venous thromboembolism (VTE) and VTE related death during hospitalization and post hospital discharge in adult patients admitted for acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE and are not at high risk of bleeding.

Previously Xarelto was indicated in treatment of VTE, treatment and prophylaxis of deep-vein thrombosis (DVT), to reduce the risk of stroke or systemic embolism with atrial fibrillation, and to reduce the risk of major cardiovascular events in patients with chronic coronary artery disease or peripheral artery disease

Current formulary status: Brand Preferred tier, not requiring a prior authorization.

QUANTITY LIMITS: 2.5 mg tablets – 2 tablets/day, 10 mg tablets – 1 tablet/day, 15 mg tablets – 2 tablets/day, 20 mg tablets – 1 tablet/day

Recommendation: The current quantity limit is applicable to the new indication and no changes are recommended. Although there is risk to certain populations with the use of Xarelto for the prophylaxis of VTE in acutely ill patients, the indication and package insert clearly outline the population at greatest risk in whom Xarelto should not be used. Because these risks are addressed, no changes need to be made to the formulary status of Xarelto at this time.

Discussion: No comments or questions.

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

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

DYSPORT (abobotulinumtoxin A)

Updated Indication: Dysport is now indicated for the treatment of upper limb spasticity in pediatric patients 2 years of age and older, excluding spasticity caused by cerebral palsy.

Dysport maintains its cervical dystonia, spasticity in adults, lower limb spasticity in pediatric patients, and cosmetic glabellar lines indications.

Current formulary status: Medical benefit requiring PA

Recommendation: No changes are recommended to the formulary placement of Dysport at this time. It is recommended that the criteria outlined in MBP 11.0 be updated to account for the new pediatric upper limb spasticity indication as outlined below:

MBP 11.0

Geisinger Health Plan approved FDA labeled indications for Botulinum Toxin Type A (Dysport) are:

1. Cervical dystonia
OR
2. Upper Limb Spasticity
 - Medical record documentation that Dysport is being used for the treatment of upper limb AND
 - Documentation that the patient is >18 2 years of age.OR
3. Lower Limb Spasticity

Discussion: No comments or questions

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

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

LYNPARZA (olaparib)

Updated Indication: Lynparza is now indicated for the maintenance treatment of adult patients with deleterious or suspected deleterious *gBRCA*m metastatic pancreatic adenocarcinoma whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

Previously Lynparza was indicated in ovarian cancer and metastatic breast cancer.

Current formulary status: ORALONCBRANDNP tier requiring a prior authorization

Recommendation: No changes are recommended to the current formulary placement, authorization duration, or quantity limits of Lynparza. It is recommended the criteria for Commercial Policy 362.0 Lynparza be updated as outlined below to incorporate the new indication:

Part D Policy 617.0D Lynparza

For Advanced Ovarian Cancer

- Medical record documentation that Lynparza is prescribed by an oncologist or hematologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of deleterious or suspected deleterious germline *BRCA*-mutated advanced ovarian cancer as verified by a Food and Drug Administration (FDA) approved test **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to three or more prior lines of chemotherapy

For Recurrent Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancer

- Medical record documentation that Lynparza is prescribed by an oncologist or hematologist **AND**

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer **AND**
- Medical record documentation of Lynparza being used as maintenance therapy after a complete or partial response to platinum-based chemotherapy

For Metastatic Breast Cancer

- Medical record documentation that Lynparza is prescribed by an oncologist or hematologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of a diagnosis of deleterious or suspected deleterious *gBRCAm*, HER2-negative metastatic breast cancer **AND**
- Medical record documentation that member has been previously treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting **AND**
- If hormone receptor (HR)-positive, medical record documentation that prior treatment included endocrine therapy or documentation that endocrine therapy would be considered inappropriate

For Metastatic Pancreatic Adenocarcinoma

- Medical record documentation that Lynparza is prescribed by an oncologist or hematologist **AND**
- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation of diagnosis of deleterious or suspected deleterious *gBRCAm* metastatic pancreatic adenocarcinoma **AND**
- Medical record documentation that member has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen.

NOTE: The FDA approved test is the BRACAnalysis Cdx™

Discussion: No comments or questions.

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

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

NPLATE (romiplostim)

Updated Indication: Nplate is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in:

- Adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
- Pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Limitations of Use:

- Nplate is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than ITP.
- Nplate should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding.

- Nplate should not be used in an attempt to normalize platelet counts.

Previously, Nplate was indicated for the treatment of thrombocytopenia in:

- Adult patients with **chronic** immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy
- Pediatric patients 1 year of age and older with ITP for at least 6 months who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Current formulary status: Nplate is a medical benefit and requires a prior authorization.

Recommendation: There is no change to formulary status at this time. It is recommended to update the prior authorization criteria to the following:

- Physician supplied documentation of a diagnosis of immune thrombocytopenia (ITP); **AND**
- Physician supplied documentation of a therapeutic failure on, intolerance to, or contraindication to corticosteroids, immunoglobulins, rituximab*, splenectomy, and eltrombopag (Promacta)*; **AND**
- Physician supplied documentation of:
 - symptomatic ITP with platelets less than 30,000/ μ L and bleeding symptoms; **OR**
 - a platelet count of less than 20,000/ μ and an increased risk of bleeding

AUTHORIZATION DURATION:

If an exception is made, Nplate will be authorized for an initial period of three (3) months. Subsequent authorizations will be for a period of six (6) months and will require medical record documentation of platelet count greater than or equal to 50,000/microL and continued or sustained reduction in bleeding events.

Discussion: No comments or questions.

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

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

BAXDELA (delafloxacin)

Updated Indication: Baxdela is indicated in adults for the treatment of community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin susceptible [MSSA] isolates only), *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Chlamydia pneumoniae*, *Legionella pneumophila*, and *Mycoplasma pneumoniae*.

Previously Baxdela was indicated for the treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) caused by designated susceptible bacteria.

Current formulary status:

Baxdela 300 mg vials: Medical Benefit requiring a prior authorization

Baxdela 450 mg tablets: Specialty tier or Brand Non-Preferred tier for members with a three tier benefit requiring a prior authorization

Recommendation: No changes are recommended to the formulary placement or current quantity limits of Baxdela. The following changes are recommended the prior authorization criteria and authorization duration:

Commercial Policy 494.0 Baxdela

- Medical record documentation of age greater than or equal to 18 years **AND**
- Medical record documentation that Baxdela is prescribed by or in consultation with infectious disease **AND**
- Medical record documentation of one of the following:
 - Documentation of a diagnosis of acute bacterial skin and skin structure infections (ABSSSI)* caused by susceptible isolates of the following: *Staphylococcus aureus* (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), *Staphylococcus haemolyticus*, *Staphylococcus lugdunensis*, *Streptococcus agalactiae*, *Streptococcus anginosus Group* (including *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*), *Streptococcus pyogenes*, *Enterococcus faecalis*, *Escherichia coli*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, or *Pseudomonas aeruginosa* **OR**
 - Documentation of community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin susceptible [MSSA] isolates only), *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Chlamydia pneumoniae*, *Legionella pneumophila*, and *Mycoplasma pneumoniae*

AND

- Medical record documentation of culture and sensitivity showing the patient's infection is not susceptible to alternative antibiotic treatments **OR** a documented history of previous intolerance to or contraindication to other antibiotics shown to be susceptible on the culture and sensitivity **OR**
- Medical record documentation that Baxdela therapy was started during an inpatient setting

QUANTITY LIMIT: Pharmacist note to CSR: *Authorization should be entered by HICL and only checking the Formulary PA required box (no QLs need to be entered within the authorization).*

- 2 tablets per day

AUTHORIZATION DURATION:

ABSSSI: one-time, 14-day authorization

CABP: one-time, 10-day authorization

Discussion: No comments or questions.

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

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

UPDATES

TRUXIMA (rituximab) UPDATE

Updated Indication: Truxima is now indicated for treatment of adult patients with moderately-to-severely- active rheumatoid arthritis (RA) in combination with methotrexate who have inadequate response to one or more TNF antagonist therapies. In addition, Truxima is now indicated for the treatment of adult patients with Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in combination with glucocorticoids. Previously, Truxima was only indicated for the treatment of Rituxan's oncology indications. Of note, Truxima is not yet able to be marketed for RA or GPA due to legal issues and Truxima does not yet carry Rituxan's Pemphigus Vulgaris (PV) indication.

Recommendations: During the initial Truxima P&T review, available literature from the Truxima AMCP Dossier was reviewed, including the RA clinical trials, and it was decided that, based on the available literature, the clinical policy for Truxima should match that of Rituxan. No additional information is available regarding Truxima's updated indications that has not already been reviewed previously. No changes to the Truxima or Rituxan policies are recommended at this time.

Discussion: No comments or questions.

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

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

BOTOX – CHRONIC MIGRAINE

Current PA criteria (for chronic migraine):

Botulinum toxin A for the treatment of chronic migraine headache may be considered medically necessary when all of the following criteria are met:

- Physician provided medical record documentation of a history of 15 or more migraine headache days per month that last 4 or more hours per day **AND**
- Physician provided medical record documentation of a completed Neurology consult and recommendation **AND**
- Physician provided medical record documentation of failure, intolerance or contraindication to an adequate trial of at least two different migraine prophylaxis medications (eg, beta-blockers, calcium channel blockers, tricyclic antidepressants or anticonvulsant medications) **AND**
- Medical record documentation that Botox will not be used in combination with a CGRP antagonist **OR**
- If the request is for use in combination with a CGRP antagonist, all of the following must be met:
 - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
 - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Recommendations:

Based on discussions with the Migraine Carepath team, it is recommended to make the following updates to the Botox policy for chronic migraine:

- Physician provided medical record documentation of a history of 15 or more migraine headache days per month that last 4 or more hours per day **AND**
- Medical record documentation that Botox is prescribed by or in consultation with a neurologist or headache specialist **AND**
- Medical record documentation of therapeutic failure on, intolerance to, or contraindication to at least three (3) of the following:
 - One (1) beta blocker (metoprolol, propranolol, timolol, atenolol, nadolol)
 - Topiramate
 - Divalproex/sodium valproate
 - Amitriptyline
 - Venlafaxine **AND**
- Medical record documentation that Botox will not be used in combination with a CGRP antagonist **OR**
- If the request is for use in combination with a CGRP antagonist, all of the following must be met:
 - Medical record documentation of a therapeutic failure on a minimum 3 month trial of at least one CGRP antagonists without the concomitant use of Botox **AND**
 - Medical record documentation of therapeutic failure on a minimum 6 month trial of Botox without the concomitant use of a CGRP antagonist

Discussion: No comments or questions.

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

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

MEDICAL BENEFIT POLICY UPDATES

The following policy updates were made to the following Medical Benefit Policies based on recommendations from the Department of Human Services (DHS) during policy review submissions. The recommended policy changes were suggested and/or required for further policy approval from DHS. These recommendations were made based on current treatment guidelines for each indication.

MBP 4.0 Intravenous Immune Globulin (IVIG)**• Post-transfusion purpura**

The following criteria must be met:

1. Medical record documentation of an onset of severe thrombocytopenia (platelet count less than 30,000/mm³) occurring 2-14 days post blood product transfusion.
- ~~2. Medical documentation of failure, intolerance, or contraindication to corticosteroids and plasmapheresis; **OR**~~
- ~~3. Platelet count less than 10,000/mm³ with bleeding~~

• Kawasaki Disease

The following criteria must be met:

1. Documentation of a diagnosis of Kawasaki disease.
2. Treatment with IVIG is begun within 10 days of the onset of fever. **OR**

3. Patient has a delayed diagnosis (i.e., later than day 10 of fever) with ongoing systemic inflammation as manifested by elevation of ESR or CRP (CRP>3.0mg/dL) together with either persistent fever without other explanation or coronary artery aneurysms.

- **Myasthenia Gravis (Acute use)**

The following criteria must be met:

1. Must be prescribed by a neurologist; AND
2. ~~Documentation of therapeutic failure on, intolerance to, or contraindication to at least two standard treatments (e.g. cholinesterase inhibitors, azathioprine, corticosteroids) and/or a combination of these treatments for a minimum of 3 months; AND~~

Medical documentation of one of the following indications:

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

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

- **Chronic Inflammatory Demyelinating Polyneuropathy**

All of the following criteria must be met:

1. Must be prescribed by a neurologist; AND
2. Documented evidence of focal or symmetric neurologic deficits that are slowly progressive or relapsing over **2 months** ~~12 weeks~~ or longer AND
3. Physician provided documentation of EMG abnormalities consistent with the diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy with the presence of at least ONE of the following: ~~(a minimum of 3 of the following must be documented):~~
 - a. Motor distal latency prolongation $\geq 50\%$ above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome), OR
 - b. Reduction of motor conduction velocity $\geq 30\%$ below LLN in two nerves, OR
 - c. Prolongation of F-wave latency $\geq 30\%$ above ULN in two nerves ($\geq 50\%$ if amplitude of distal negative peak CMAP $< 80\%$ of LLN values), OR
 - d. Absence of F-waves in two nerves if these nerves have distal negative peak CMAP amplitudes $\geq 20\%$ of LLN + ≥ 1 other demyelinating parameter in ≥ 1 other nerve, OR
 - e. Partial motor conduction block: $\geq 50\%$ amplitude reduction of the proximal negative peak CMAP relative to distal, if distal negative peak CMAP $\geq 20\%$ of LLN, in two nerves, or in one nerve + ≥ 1 other demyelinating parameter in ≥ 1 other nerve, OR
 - f. Abnormal temporal dispersion ($>30\%$ duration increase between the proximal and distal negative peak CMAP) in ≥ 2 nerves, OR
 - g. Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) increase in ≥ 1 nerve (median ≥ 6.6 ms, ulnar ≥ 6.7 ms, peroneal ≥ 7.6 ms, tibial ≥ 8.8 ms) + ≥ 1 other demyelinating parameter in ≥ 1 other nerve
 - h. ~~Partial conduction block of one or more motor nerves~~
 - i. ~~Decreased conduction velocity of two or more motor nerves~~
 - j. ~~Prolongation of distal latency of two or more motor nerves~~
 - k. ~~Prolongation or absence of F wave latencies in two or more motor nerves~~

Improvement should be apparent after **3 months** ~~8 weeks~~ of treatment; otherwise, requests for further treatment will require Medical Director review.

~~Relapses may require periodic isolated treatments with a single dose of IVIG.~~

- **Multifocal Motor Neuropathy**

The following criteria must be met:

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

~~Treatment is limited to one course of therapy defined as 3 months if approved. Requests for further treatment will require Medical Director review.~~

- **Catastrophic Antiphospholipid Syndrome (CAPS) (III/C)**

All of the following criteria must be met:

1. **Documentation of patient with antiphospholipid syndrome (APS) with multiorgan failure (evidence of involvement of three or more organs, systems, and/or tissues AND**
 2. **Development of manifestations simultaneously or in less than one week AND**
 3. **Confirmation by histopathology of small vessel occlusion in at least one organ or tissue AND**
 4. **Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, and/or anti-beta2-glycoprotein I antibodies)**
OR
 - o **All four criteria are met, except for only two organs, systems and/or sites of tissues involvement OR**
 - o **All four criteria are met, except for laboratory confirmation OR**
 - o **Criteria 1, 2, and 4 are met OR**
 - o **Criteria 1,3, and 4 and the development of a third event in more than a week but less than a month, despite anticoagulation**
- ~~5.— Documentation of a life threatening condition~~
~~6.— Documentation of severe thrombocytopenia and microangiopathic hemolytic anemia~~
~~7.— Documentation of failure on, contraindication to, or intolerance to conventional treatment with anticoagulation and steroids~~
~~8.— Should be used in combination with plasma exchange~~

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

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

Discussion: No comments or questions.

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

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

QUARTERLY CASE AUDIT RESULTS

The Quarterly Case Audit was held on March 5th utilizing data from 4th quarter 2019. No recommendations of formulary changes were made at this time. Will continue to look for opportunities to create more drug specific policies at future quarterly case audit meetings.

Future Scheduled Meetings

The next bi-monthly scheduled meeting will be held on Tuesday, May 19, 2020 at 1:00 HCN3A & 3B Conference room

All of these meetings are scheduled to be held at Geisinger Health Plan, Hughes Center North and South Buildings; 108 Woodbine Lane; Danville, PA 17821.