Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

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TO: Maine Drug Utilization Review Board
DATE: 12/11/24
RE: Maine DUR Board Meeting minutes from December 10, 2024

ATTENDANCE	UNEXCUSED	EXCUSED	IN-PERSON	REMOTELY
Linda Glass, MD	X			
Kathleen Polonchek, MD		X		
Erin Ackley, PharmD.		X		
John Deason, PharmD.				X
Caitlin Morrow, PharmD.	X			
Non –Voting				
Mike Ouellette, R.Ph., Optum			X	
Roberta Capp, MD, Optum			X	
Anne-Marie Toderico, PharmD MaineCare			X	
Jan Wright, MaineCare			X	

Guests of the Board: Gavin Gillespie PharmD, Optum

CALL TO ORDER: 6:00PM

The meeting was called to order at 6:00 PM.

PUBLIC COMMENTS

Jonathan Jones from Bristol Myers Squibb: Highlighted the attributes of Cobenfy.

Hoa Pham from BeiGene: Highlighted the attributes of Tevimbra.

Elena Fernandez from Vertex: Highlighted the attributes of Casgevy.

Alain Nguyen from Gilead: Highlighted the attributes of Livdelzi.

Andrea Ligler from HypoPARathyroidism Association: Highlighted the attributes of Yorvipath.

Joseph Jones from ARS Pharma: Highlighted the attributes of Neffy.

MAINECARE UPDATE- ANNE-MARIE TODERICO

- Jan Wright will be Acting Associate Director of Pharmacy, Anne-Marie's last day in state service is 12/18/24
- MaineCare updated the standing order for naloxone to include prescription and over the counter naloxone
- With the ending of the PREP act - influenza and COVID vaccines will now only be covered by MaineCare under the Vaccine For Children program

OLD BUSINESS

CONSENT AGENDA

DUR MINUTES

Approval of November DUR meeting minutes

Board Decision: Due to a lack of quorum a vote will be taken by email.

NEW CANCER MEDICATIONS

Recommendations: Add Lazcluze, Tecelra, Tecentriq Hybreza, Tevimbra, and Voranigo to non-preferred.

Criteria: All non-preferred: A clinical PA is required to confirm appropriate clinical indication for the individual drug request. Specific to each drug all age, clinical testing requirements, previous step therapies, adjunctive drug therapy requirements, and response without disease progression will be also be evaluated for clinical appropriateness. The standard for the appropriate indication will include the FDA label as well as current NCCN guidelines

Board Decision: Due to a lack of quorum a vote will be taken by email.

BIOSIMILARS

Recommendations: Add Adalimumab- aacf and Tofidence to non-preferred.

Board Decision: Due to a lack of quorum a vote will be taken by email.

NEW BUSINESS

RETRODUR

Introduce Co- Administration of PPIs and Bisphosphonates

Proton pump inhibitors are the most efficient therapeutic class currently available for suppressing gastric acid secretion and are the most extensively prescribed medications worldwide.1 PPIs are indicated for the treatment of gastro-duodenal ulcers, gastroesophageal reflux disease (GERD), heartburn, and other conditions related to gastric acid. However, long term PPI use has been linked to significant adverse drug events (ADE), including, but not limited to kidney disease, dementia, and osteoporosis.1

A recent systematic review highlighted the relationship between PPIs, bone mineral density, and increased risk of fractures.2,3 A significant number of studies showed increased risk of hip and spine fractures associated with long term use of PPI, defined as use of PPI for longer than 12 months.3

Despite study results outlining the risks associated with long term PPI use, several studies reported overtreatment with PPI and prescriptions at higher doses or longer duration than required, and without a clear indication.1 There is recognition from the medical community on the risks associated with PPI overuse and some provider groups successfully piloted the use of clinical decision support to identify guideline concordant vs. guideline non-concordant prescriptions to help providers decrease PPI overuse.4 Finally, global choosing wisely campaign promoting appropriate PPI use and an ask of providers and patients to re-assess PPI use at least once a year. 5

Patients taking bisphosphonates may be at even high risk for fractures while on long term use of PPIs and this retro DUR will evaluate current use of episodic (prescription for less than 2 months), short term (≥ 2 months -12 months), and long term (>12 months) use of PPIs in those with highest risk for fractures, or those taking bisphosphonates.

Recommendation: We will use paid, non-reversed Medicaid pharmacy and medical claims from SFY 2024, excluding members with Part D, TPL and Maine RX coverage. This analysis will identify members with continuous Medicaid membership from SFY 2024 (July 2023-July 2024) with overlapping claims of PPI and bisphosphonates and look at duration and dose of PPI where possible. We will stratify the data by episodic, short term, and long-term use of PPI and identify the proportion of patients who also use bisphosphonates (for the same amount of time as the PPI within the same time frames). We will further stratify the data by different age groups. Finally, will identify the proportion of prescriptions in each subgroup: episodic, short term, and long term that originated from a hospital admission vs. outpatient setting and provider taxonomy associated with the original prescription.

Board Decision: None needed.

Data Presentation: Use of Stimulants in Children

Use of stimulants in children has significantly improved the quality of life of those with Attention Deficit and Hyperactivity Disorder. However, use of the medications has grown substantially in the last decade and monitoring is necessary to ensure that there is not inappropriate use. Concerns include incorrect diagnosis, treatment not including behavioral therapy along with drug therapy, inadequate monitoring, treatment noncompliance, co-prescribing of incompatible behavioral health medications, use of stimulants in patients with substance use disorder and medication diversion.

While stimulants are the mainstay of treatment and have been shown to improve a child's functional status and behavior, there is a role for non-stimulant drugs such as norepinephrine uptake inhibitors atomoxetine and viloxazine, and the alpha-2 adrenergic agonists, clonidine and guanfacine HCL, are used when there is intolerance or lack of effectiveness with stimulants. Augmentation therapy with non-stimulant drugs is sometimes used along with stimulants when the effectiveness of stimulants alone is not optimal.2 Guidelines exist for determining who should be offered stimulants and how those on stimulants should be monitored.

We will use paid, non-reversed Medicaid pharmacy and medical claims from SFY 2024, excluding members with Part D, TPL and Maine RX coverage. This analysis will identify children ages 1-18 on stimulants, norepinephrine uptake inhibitors and alpha-2 adrenergic agonists. The parameters used will include age, sex, diagnoses, doses of medications used, co-prescribing of the drugs in this study, uninterrupted duration of use of the medications (considering eligibility limitations) and concurrent use of drugs for depression or anxiety.

Recommendation: In April 2024, a systematic review on ADHD treatment published in Pediatrics suggested that stimulants significantly improve ADHD symptom severity, broadband measures, and functional impairment compared to non-stimulants, but not appetite suppression. In this retrospective DUR analysis, we evaluated stimulant vs. non-stimulant (norepinephrine reuptake inhibitors and alpha-2 adrenergic agonists) ADHD medication use. Over the past year, most prescriptions were for stimulants (84.2%), followed by alpha-2 adrenergic agonists (32.5%), and selective norepinephrine reuptake inhibitors (8.3%). Clinical guidelines recommend starting treatment for youth over 6 years old with FDA-

approved medications, supported by the recent review.5 Stimulants were most used for children aged 6-12 (53.9%) compared to adolescents aged 13-18 (43.3%), except for Lisdexamfetamine dimesylate, which was more used in adolescents (53.0%). Overall, 3.6% of all stimulant and non-stimulant users were pre-school children (ages 6 or less). For school-age children, guidelines suggest parent training and behavior interventions as first-line therapy.5 In the event of medication requirements, prior research showed improvement in preschool children on either alpha-2 adrenergic agonists or stimulants, with different adverse effect profiles.6 In this study, 20.5% of preschool children received alpha-2 adrenergic therapy, lower than previously reported (23%-35%).6 In summary, prescription of stimulant and non-stimulants for pre-school age children were low, suggesting uptake of AAP clinical guidelines. Guanfacine HCL was the most used alpha-2 adrenergic agonist (79.9%) compared to clonidine HCL (20.1%), likely due to side effect profiles. These therapies were most prescribed for children aged 6-12. A small number of patients (16.8%) had augmentation ADHD drug therapy (more than one drug prescribed for greater than 2 months). Based on prior literature, augmentation therapy can be effective for certain patients. When evaluating gender and use of ADHD therapy, a higher proportion of males [10977 (65.7%)] received ADHD treatment, regardless of drug class (stimulant alpha-2 adrenergic, or norepinephrine re-uptake inhibitors). Based on this RetroDUR review we do not recommend any changes to the current PDL.

Board Decision: Due to a lack of quorum a vote will be taken by email.

NEW DRUG REVIEW

Alyglo® (immune globulin intravenous, human-stwk)); **PDL category-** Immune Globulin

Alyglo® (immune globulin intravenous, human-stwk) is a ready-to-use, sterile liquid preparation of highly purified and concentrated human immunoglobulin G (IgG) antibodies. The active ingredient is human immunoglobulin G purified from human Source Plasma and processed using a modified Cohn-Oncley fractionation process, as well as anion and cation exchange chromatography. It contains 100mg/ml protein, of which not less than ≥96% is human IgG obtained from human Source Plasma. It is formulated with glycine targeted at 18.8mg/mL as a stabilizer and water for injection as a solvent with pH in the range of 4.5-5.5. In addition, Alyglo® contains ≤100mcg/mL of IgA. It is indicated for the treatment of primary humoral immunodeficiency (PI) in adults. This includes, but is not limited to, the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiency (SCID). Its efficacy was assessed in a prospective, open-label, single-arm study that was conducted in North America, with a primary efficacy analysis of annualized rate of acute serious bacterial infections (SBIs). During the 12-month study period, the acute SBI rate was 0.03, which met the predefined success rate of less than one acute SBI per subject per year. Per the manufacturing site, "Alyglo® is manufactured with cation exchange (CEX) chromatography, which is proven to reduce factor XIa (FXIa) to undetectable levels." There is no evidence at this time to support that Alyglo® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Alygo® to non-preferred.

Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Aqneursa® (levacetylleucine granule, for suspension); **PDL category-** Niemann-Pick Disease Agents

Levacetylleucine, the active ingredient of Aqneursa®, is a modified amino acid. The distinct molecular target for levacetylleucine in the treatment of Niemann-Pick disease type C is not known. It is indicated for the treatment of neurological manifestations of Niemann-Pick disease type C (NPD-C) in adults and pediatric patients weighing ≥15kg. Aqneursa® is the first standalone treatment indicated for the treatment of neurological manifestations of Niemann-Pick disease type C (NPD-C) in adults and pediatric patients weighing ≥15kg. NPD-C is a rare autosomal recessive disorder that results in progressive neurological symptoms and organ dysfunction. On average, individuals affected by this disease live on average for about 13 years.2 To date, there is supportive treatment for physical manifestations of the disease through physical therapy. The current treatment comparator for Aqneursa® is a combination therapy of Miplyffa® given in conjunction with miglustat, which was recently approved by the FDA (09/24). To date, there is no comparator trial studies between Aqneursa® and Miplyffa®. Each drug trial also looked at different functional scoring criteria outcomes. The safety and efficacy of Aqneursa® were assessed in a randomized, double-blind, placebo-controlled, two-period crossover study, with the primary efficacy outcome assessed using a modified version of the Scale for Assessment and Rating of Ataxia (SARA), referred to as the functional SARA (fSARA). The estimated treatment difference for the fSARA total score was -0.4, which was statistically significant ($p<0.001$). Results on the fSARA were supported by consistent results demonstrated on the original SARA.

Recommendation: Aqneursa® to non-preferred.

Criteria:

- Clinical PA required for appropriate diagnosis

Cobenfy® (xanomeline and trospium chloride); **PDL category-** Antipsychotics- Atypicals

Cobenfy® is a combination of xanomeline (a muscarinic agonist) and trospium chloride (a muscarinic antagonist). The mechanism of action of xanomeline for its approved indication is not clear; however, its efficacy is thought to be due to its agonist activity at M1 and M4 muscarinic acetylcholine receptors in the CNS. Trospium chloride antagonizes the muscarinic receptors primarily in the peripheral tissues. It is indicated for the treatment of schizophrenia in adults. Use of Cobenfy® is contraindicated in patients with moderate or severe hepatic impairment, as well as urinary and gastric retention and untreated narrow-angle glaucoma. The efficacy of Cobenfy® was assessed in phase 3, multicenter, double-blind, randomized studies that included patients diagnosed with schizophrenia per DSM-5 criteria. The primary efficacy measure of the two studies discussed above was the change from baseline in PANSS total score at week 5, and results suggested that the Cobenfy® group demonstrated a statistically significant reduction from baseline to week 5 in the PANSS Total Score compared to the placebo group. The drug demonstrated better tolerability than existing antipsychotics, with fewer side effects like weight gain and extrapyramidal symptoms.3 A meta-analysis of the EMERGENT trials revealed that about 51% of participants were excluded from the analysis due to various reasons, including, but not limited to: treatment discontinuation, protocol withdrawal, and adverse events.4 Cobenfy® is a first-in-class combination muscarinic agonist/muscarinic antagonist that provides another treatment option for schizophrenia. Head-to-head active comparator studies were not currently found.

Recommendation: Cobenfy® to non-preferred.

Criteria:

- Cobenfy: Patient must be 18 – 65 years old AND meet criteria for the diagnosis of severe Schizophrenia, defined as PANSS total score of 80 or higher, with at least 4 or more two positive symptom item or 5 or more one positive symptoms item AND Recent history of acute exacerbation of psychotic symptoms necessitating hospitalization in the past two months AND Trial of 2 prior preferred Second Generation Antipsychotics showing minimal response in control of symptoms of schizophrenia (PANSS score less than 20% from baseline) AND Trial of SGA that have yielded side effects of weight gain which has not been responsive to lifestyle & medication augmentation AND Patient must have baseline tests including heart rate, liver enzymes, kidney function tests and bilirubin prior to starting treatment.

Crexont® (carbidopa & levodopa capsules, ER); **PDL category-** Parkinsons- Dopaminergic/Carbidopa/ Levodopa

Crexont® is a combination of carbidopa (an inhibitor of aromatic amino acid decarboxylation) and levodopa (an aromatic amino acid), in an extended-release capsule. It contains immediate-release granules consisting of carbidopa and levodopa and extended-release pellets consisting of levodopa. When levodopa is administered orally, it is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the CNS. Carbidopa inhibits the decarboxylation of peripheral levodopa, making more levodopa available for delivery to the brain. Levodopa is the metabolic precursor of dopamine, does cross the blood-brain barrier, and presumably is converted to dopamine in the brain. This is thought to be the mechanism whereby levodopa treats symptoms of Parkinson's disease. It is indicated for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication in adults. Crexont® is contraindicated in patients currently taking a non-selective MAO inhibitor or have recently (within 2 weeks) taken a non-selective MAO inhibitor. The efficacy of Crexont® was assessed in double-blind, double-dummy study, with IR carbidopa-levodopa as the active comparator. The primary efficacy measure was the mean change from baseline in "On" time without troublesome dyskinesia in hours per day at the end of the study. Patients reported an improvement in "On" time without troublesome dyskinesia with Crexont® compared to IR carbidopa-levodopa, which was statistically significant (p=0.019). In addition, Crexont®-treated patients also reported less "Off" time compared to IR carbidopa-levodopa, which was statistically significant

Recommendation: Crexont® to non-preferred.

Criteria:

- Approvals will require trials of preferred medications including extended release levodopa/carbidopa tablet.

Ebglyss® (lebrikizumab-lbkz); **PDL category**- Topical- Atopic Dermatitis

Lebrikizumab-lbkz, the active ingredient of Ebglyss®, is an interleukin (IL)-13 antagonist, an immunoglobulin G4 (IgG4) monoclonal antibody that binds to IL-13 and inhibits IL-13 signaling. It is an IgG4 monoclonal antibody that binds with high affinity and slow off-rate to IL-13 and allows IL-13 to bind to IL-13Rα1 but inhibits human IL-13 signaling through the IL-4Rα/IL-13Rα1 receptor complex. IL-13 is a naturally occurring cytokine that is involved in Type 2 inflammation, which is an important component in the pathogenesis of atopic dermatitis. Lebrikizumab-lbkz inhibits IL-13 induced responses including the

release of proinflammatory cytokines, chemokines and IgE. Lebrikizumab-lbkz-bound IL-13 can still bind IL-13Rα2 allowing subsequent internalization and natural clearance of IL-13. It is indicated for the treatment of adults and pediatric patients 12 years of age and older who weigh at least 40 kg with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Ebglyss® can be used with or without topical corticosteroids. Three studies assessed the safety and efficacy of Ebglyss® in patients with moderate-to-severe atopic dermatitis, two of which were monotherapy studies and one was a concomitant therapy trial where both Ebglyss® and placebo treatment groups also utilized TCS. All three trials assessed the primary endpoint of the proportion of subjects who achieved an IGA score of 0 (clear) or 1 (almost clear) and at least a 2-point improvement from baseline at week 16. More in the Ebglyss® groups achieved the primary endpoint as compared to the placebo groups. Per the full-text study by Silverberg et al2 (of ADvocate 1 and ADvocate 2), the results of the primary endpoint were statistically significant for both studies, in favor of the Ebglyss® group ($p<0.001$ for both studies). Per the full-text study by Simpson et al3 of the ADhere study, significantly more in the lebrikizumab plus TCS group achieved IGA score of 0 or 1 with 2 or more points improvement from baseline as compared with the placebo plus TCS group at week 16 (41.2% vs 22.1%, respectively; $p=0.01$). Direct head-to-head active comparator studies were not currently found.

Recommendation: Ebglyss® to non-preferred.

Criteria:

- Clinical PA required.
- For the treatment of patients ≥ 12 years of age.

Livdelzi® (seladelpar lysine); **PDL category-** Primary Biliary Cholangitis Agents

Seladelpar lysine, the active ingredient of Livdelzi®, is a peroxisome proliferator-activated receptor (PPAR)-delta agonist. However, the mechanism by which seladelpar exerts its therapeutic effects in patients with PBC is not well understood. Pharmacologic activity that is potentially relevant to therapeutic effects includes inhibition of bile acid synthesis through activation of PPAR-delta, which is a nuclear receptor expressed in most tissues, including the liver. Published studies demonstrate that PPAR-delta activation by seladelpar reduces bile acid synthesis through Fibroblast Growth Factor 21 (FGF21)-dependent downregulation of CYP7A1, the main enzyme for the synthesis of bile acids from cholesterol. It is indicated for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have had an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. This indication is approved under accelerated approval based on a reduction of alkaline phosphatase (ALP). Improvement in survival or prevention of liver decompensation events have not been demonstrated. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). A limitation of use includes that use of Livdelzi® is not recommended in patients who have or develop decompensated cirrhosis (e.g., ascites, variceal bleeding, hepatic encephalopathy). The efficacy of Livdelzi® was assessed in a randomized, double-blind, placebo-controlled study of 12 months duration that included adults with PBC with an inadequate response or intolerance to UDCA. The primary endpoint was biochemical response at month 12, and results suggested that Livdelzi® demonstrated greater improvement on biochemical response (and ALP normalization) at month 12 as compared to placebo. Per the full text by Hirschfield et al2, the results of this primary endpoint were statistically significant in favor of Livdelzi®

(p< 0.001), as was ALP normalization (p<0.001). Head-to-head trials with other active comparators were not found, but this provides patients with another treatment option.

Recommendation: Livdelzi® to non-preferred.

Criteria:

- Clinical PA is required for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults who have had an inadequate response to UDCA, or as monotherapy in patients unable to tolerate UDCA. Patients who do not have a diagnosis of decompensated cirrhosis.

Miplyffa® (arimoclomol); **PDL category-** Niemann-Pick Disease Agents

The mechanism(s) by which arimoclomol, the active ingredient of Miplyffa®, exerts its clinical effects is not known. Miplyffa® is indicated for use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPD-C) in adult and pediatric patients 2 years of age and older. NPD-C is a rare autosomal recessive disorder that results in progressive neurological symptoms and organ dysfunction. On average, individuals affected by this disease live on average for about 13 years.4 To date, there is supportive treatment for physical manifestations of the disease through physical therapy. The current treatment comparator treatment is Aqneursa®, which was recently approved by the FDA (09/24). To date, there is no comparator trial studies between Aqneursa® and Miplyffa®. Each drug trial also looked at different functional scoring criteria outcomes. The efficacy of Miplyffa® was established in a randomized, double-blind, placebo-controlled, 12-month trial that included 50 patients with a molecularly confirmed diagnosis of NPD-C. Efficacy assessments included the R4DNPCCSS score, with higher scores representing greater severity of disease. The least square mean change from baseline to month 12 was -0.2 with Miplyffa® plus miglustat as compared with 2 with placebo plus miglustat. Per the full-text study by Mengel et al2, the primary endpoint of the trial discussed above was the change from baseline in NPD-C severity at 12 months as assessed by the 5-domain NPD-C Clinical Severity Scale (5DNPCCSS). The fully validated 5-domain NPCCSS includes the domains determined to be most clinically relevant to patients, caregivers, and clinicians: ambulation, cognition, fine motor skills, speech, and swallowing. The total score ranges from 0 to 25, with a higher score indicating more severe clinical impairment. Results suggested for this primary endpoint, at month 12, the mean change was 0.76 for arimoclomol as compared with 2.15 for placebo, corresponding to a significant treatment effect in favor of arimoclomol of -1.40 (p=0.046). Furthermore, in the subgroup analysis of patients ≥4 years of age (N=44) and patients receiving concomitant miglustat (N=39), the treatment effect within each subgroup was increased (p<0.05). Per the manufacturer, due to recommendations from the FDA, the 5DNPCCSS was amended to a R4DNPCCSS by making two functional changes. The cognition domain was removed from the scoring, due to concerns relating to cognition assessment in as 12-month study timeframe. In addition, the swallow domain was updated. The scoring system thus ranges from 0-20 for the R4DNPCCSS.

Recommendation: Miplyffa to non-preferred. Add Roflumilast to preferred.

Criteria:

- Clinical PA required for appropriate diagnosis.

Myhibbin® (mycophenolate mofetil suspension); **PDL category-** Immunosppressant

Mycophenolate mofetil (MMF), the active ingredient of Myhibbin®, is an antimetabolite immunosuppressant. It is the 2-morpholinoethyl ester of mycophenolic acid (MPA), an

immunosuppressive agent; an inosine monophosphate dehydrogenase (IMPDH) inhibitor. It is indicated for the prophylaxis of organ rejection, in adult and pediatric recipients 3 months of age and older of allogeneic kidney, heart, or liver transplants, in combination with other immunosuppressants. No new clinical trials were found in the Myhibbin® prescribing information, but rather were the same as found in the Cellcept® prescribing information, another mycophenolate product. Cellcept® is available as a power for reconstitution for oral suspension (200mg/ml upon reconstitution). Myhibbin® is the only FDA approved ready-to-use mycophenolate mofetil oral suspension.

Recommendation: Myhibbin® to non-preferred.

Criteria:

- Clinical PA is required.
- Myhibbin: For the prophylaxis of organ rejection, in adult and pediatric recipients 3 months of age and older of allogeneic kidney, heart, or liver transplants, in combination with other immunosuppressants.

Neffy® (epinephrine spray); **PDL category-** Anaphylactic Devices

Epinephrine, the active ingredient of Neffy®, is a sympathomimetic catecholamine. Epinephrine acts on both alpha and beta-adrenergic receptors. Through its action on alpha-adrenergic receptors, epinephrine lessens the vasodilation and increased vascular permeability that occurs during anaphylaxis, which can lead to loss of intravascular fluid volume and hypotension. Through its action on beta-adrenergic receptors, epinephrine causes bronchial smooth muscle relaxation and helps alleviate bronchospasm, wheezing, and dyspnea that may occur during anaphylaxis. It is indicated for emergency treatment of type I allergic reactions, including anaphylaxis, in adult and pediatric patients who weigh 30kg or greater. Each Neffy® nasal spray is for single use and delivers the entire dose upon activation. Epinephrine auto-injector is considered first line therapy for treatment of anaphylaxis. The rate of unintentional injections with epinephrine from autoinjectors is high but have complete resolution of symptoms that did not require surgery or hospitalization. Patients with elevated BMI may require more than one autoinjector dose secondary to low absorption of the medication. Neffy® nasal spray offers an alternative to an injectable epinephrine, being the first needle-free epinephrine nasal spray, while providing comparable systemic exposures as those achieved with needle injections. If obesity is a matter of concern, the nasal spray could be a suitable option.

Recommendation: Neffy® and Auvi-Q to non-preferred. Remove Symjepi from the PDL.

Ocrevus Zunovo® (ocrelizumab & hyaluronidase); **PDL category-** Multiple Sclerosis

Ocrevus® Zunovo contains ocrelizumab and hyaluronidase-ocsq. Ocrelizumab is a recombinant humanized monoclonal antibody directed against CD20-expressing B-cells. It is a glycosylated immunoglobulin G1 (IgG1), and the exact mechanism of its therapeutic effects in multiple sclerosis is unknown. However, it is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, ocrelizumab results in antibody-dependent cellular cytolysis and complement-mediated lysis. It 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 or Primary progressive MS, in adults. Ocrevus® Zunovo is for subcutaneous use in the abdomen only and should be administered by a

healthcare professional. Ocrevus® Zunovo has different dosage and administration instructions than IV ocrelizumab. There were three studies described in the clinical studies section of the Ocrevus® Zunovo prescribing information; these studies established the effectiveness of ocrelizumab for the treatment of RMS and PPMS in adults and were conducted with IV-administered ocrelizumab. Study 4 in the clinical trials section demonstrated comparable exposure of Ocrevus® Zunovo relative to ocrelizumab IV formulation, which established the efficacy of Ocrevus® Zunovo. Ocrevus® Zunovo is available as a subcutaneous injection to be administered over 10 minutes twice a year.

Recommendation: Ocrevus® Zunovo ® to non-preferred.

Criteria:

- Clinical PA is required to establish diagnosis and medical necessity.

Onyda® XR (clonidine HCl suspension, extended-release); **PDL category-** Stimulant- Stimulant Like

Clonidine, the active ingredient of Onyda® XR, is a centrally acting alpha2-adrenergic agonist. Clonidine is an imidazoline derivative and stimulates alpha2-adrenergic receptors in the brain. It is not a CNS stimulant. The mechanism of action of clonidine in attention deficit hyperactivity disorder (ADHD) is not known. It is indicated for the treatment of ADHD as monotherapy and as adjunctive therapy to central nervous system (CSN) stimulant medications in pediatric patients 6 years of age and older. The efficacy results of these adequate and well-controlled studies of clonidine HCl extended-release tablets are presented in the Onyda® XR prescribing information. Efficacy of clonidine HCl ER tablets in the treatment of ADHD was established in pediatric patients 6 to 17 years in one short-term, placebo-controlled monotherapy trial (Study 1), one short-term adjunctive therapy to psychostimulants trial (Study 2), and one randomized withdrawal trial as monotherapy (Study 3). Onyda® XR is the first liquid non-stimulant ADHD treatment.

Recommendation: Onyda® XR to non-preferred.

Criteria:

- For pediatric patients 6 years of age or older

Piasky® (crovalimab injection); **PDL category-** Monoclonal Antibody

Crovalimab-akkz, the active ingredient of Piasky®, is a complement C5 inhibitor. It is a humanized monoclonal antibody based on a human IgG1 framework produced in Chinese hamster ovary (CHO) cells. Crovalimab-akkz specifically binds with high affinity to the complement protein C5, inhibiting its cleavage into C5a and C5b, preventing the formation of the membrane attack complex (MAC). Crovalimab-akkz inhibits terminal complement-mediated intravascular hemolysis in patients with PNH. It is indicated for the treatment of adult and pediatric patients 13 years and older with paroxysmal nocturnal hemoglobinuria (PNH) and body weight of at least 40kg. The first-line treatment for symptomatic hemolytic PNH without severe bone marrow failure is C5 inhibitor (C5i) therapy, rather than supportive care or transfusions alone. Among complement inhibitors, ravulizumab requires less frequent administration compared to other C5 inhibitors.2 Currently, there are no head-to-head trials evaluating the efficacy of ravulizumab against Piasky®. Piasky® has a box warning regarding serious meningococcal infections, as Piasky® increases the risk of serious and life-threatening infections caused by Neisseria meningitidis. Because of this risk of serious meningococcal infections, Piasky® is available only through a restricted program under a REMS called Piasky® REMS. Vaccinate patients for

meningococcal infections per current ACIP recommendations at least 2 weeks prior to the start of treatment. If urgent Piasky® treatment is indicated in a patient who is not up to date with meningococcal vaccines per ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer these vaccines as soon as possible. The efficacy of Piasky® in patients with PNH was assessed in an active-controlled, open-label, non-inferiority study that randomized patients with PNH not previously treated with a complement inhibitor to receive either Piasky® or eculizumab. Efficacy was based on hemolysis control, as measured by the mean proportion of patients with LDH ≤1.5 X ULN from week 5 to week 25; and the proportion of patients who achieved transfusion avoidance, defined as patients who were pRBC transfusion-free, from baseline through week 25. Piasky® was non-inferior to eculizumab in the co-primary endpoints of hemolysis control (79.3% vs 79%; OR 1.02) and proportion with transfusion avoidance (65.7% vs 68.1%, weighted difference -2.8%).

Recommendation: Piasky® to non-preferred.

Tryvio® (aprocitentan); **PDL category-** Antihypertensives/Cardiacs, ERAs

Aprocitentan, the active ingredient of Tryvio®, is an endothelin receptor antagonist (ERA) that inhibits the binding of endothelin (ET)-1 to ET-A and ET-B receptors. ET-1, via its receptors (ET-A and ET-B) mediates a variety of deleterious effects such as vasoconstriction, fibrosis, cell proliferation, and inflammation. In hypertension, ET-1 can cause endothelial dysfunction, vascular hypertrophy and remodeling, sympathetic activation, and increased aldosterone synthesis. It is indicated in combination with other antihypertensive drugs, is indicated for the treatment of hypertension, to lower blood pressure (BP) in adult patients who are not adequately controlled on other drugs. Lowering blood pressure reduces the risk of fatal and non-fatal cardiovascular events, primarily strokes and myocardial infarctions. Tryvio® has a box warning regarding embryo-fetal toxicity. Because of the risk of birth defects, Tryvio® is only available through a restricted program called the Tryvio® REMS. The efficacy of Tryvio® was assessed in a multipart, phase 3 multicenter study. The primary endpoint was the change in sitting SBP (SiSBP) from baseline to week 4 during part 1, and Tryvio® 12.5mg was statistically superior to placebo in reducing SiSBP at week 4 (part 1). The treatment effect was consistent for sitting diastolic BP. Tryvio® is the first FDA approved ERA indicated to lower blood pressure when used in combination with other antihypertensive treatments for those with hypertension that is not adequately controlled on other drugs.

Recommendation: Tryvio® to non-preferred.

Criteria:

- Tryvio: In combination with other antihypertensive drugs, is indicated for the treatment of resistant hypertension, to lower blood pressure (BP) in adult patients who are not adequately controlled on other drugs. Resistant HTN is defined as a patient who takes at least 3 different class antihypertensive medications with complementary mechanisms including thiazide, ACE inhibitor, ARB, long-acting calcium channel blocker, with a trial of spironolactone, unless contra-indicated

Vigafyde® (vigabatrin solution); **PDL category-** Anticonvulsants

Vigabatrin, the active ingredient of Vigafyde®, is an antiepileptic drug. The exact mechanism of action is not known but it is believed to be the result of its action as an irreversible inhibitor of ɣ-aminobutyric acid transaminase (GABA-T), the enzyme responsible for the metabolism of the inhibitory

neurotransmitter GABA. This action results in increased levels of GABA in the CNS. No direct correlation between plasma concentration and efficacy has been established. The duration of drug effect is presumed to be dependent on the rate of enzyme re-synthesis, rather than on the rate of elimination of the drug from the systemic circulation. It is indicated as monotherapy for the treatment of infantile spasms in pediatric patients 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss. The efficacy of Vigafyde® is based upon a comparison of the compositional differences between vigabatrin for oral solution and Vigafyde® oral solution. The efficacy of vigabatrin as monotherapy was established for infantile spasms in two multicenter controlled studies. Both studies were similar in terms of disease characteristics and prior treatments of patients and all enrolled infants had a confirmed diagnosis of infantile spasms. The clinical studies included in the Vigafyde® prescribing information were with vigabatrin for oral solution. Vigabatrin for oral solution, under the brand name Sabril® is available as a powder to be mixed with water and has been available for several years. Vigafyde® is an oral solution ready for use.

Recommendation: Vigafyda® to non-preferred.

Criteria:

- Vigafyde: Indicated as monotherapy for the treatment of infantile spasms in pediatric patients 1 month to 2 years of age for whom the potential benefits outweigh the potential risk of vision loss

Yorvipath® (palopegteriparatide); **PDL category-** Parathyroid Hormone

Palopegteriparatide, the active ingredient of Yorvipath®, is a parathyroid hormone analog (PTH(1-34)). Palopegteriparatide is a prodrug of teriparatide (PTH(1-34)), consisting of PTH(1-34) transiently conjugated to an inert carrier via a proprietary TransCon Linker. PTH(1-34) is identical to the 34 N-terminal amino acids (the biologically active region) of the 84-amino acid human parathyroid hormone. The carrier is a branched 40 kDa methoxy polyethylene glycol (mPEG) moiety. It is indicated for the treatment of hypoparathyroidism in adults. The efficacy of Yorvipath® was assessed in a randomized, double-blind, placebo-controlled, phase 3 study that included adults with hypoparathyroidism (N=82). Results suggested that at week 26, 68.9% of the Yorvipath® group met the efficacy endpoint as compared with 4.8% of the placebo group (CHC calculated NNT = 2). Yorvipath® is the only FDA-approved agent for the treatment of adults with hypoparathyroidism and may be a good agent to be used for patients with persistent hypocalcemia, hypercalciuria, or intolerance to conventional therapy.

Recommendation: Yorvipath® to non-preferred.

Criteria:

- Recommended only for those who cannot be well-controlled on calcium supplements and active forms of vitamin D alone.

Zituvimet® (sitagliptin and metformin); **PDL category-** Diabetic-DPP-4 Enzyme Inhibitor- Combinations

Zituvimet® combines two antihyperglycemic agents with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes mellitus, including sitagliptin (a dipeptidyl peptidase-4 [or DPP-4] inhibitor) and metformin (a member of the biguanide class). Sitagliptin is a DPP-4 inhibitor, which is believed to exert its action in patients with type 2 DM by slowing the inactivation of incretin hormones. Metformin is an antihyperglycemic agent which improves glucose tolerance in

patients with type 2 DM, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Limitations of use include that Zituvimet® is not recommended in patients with type 1 diabetes mellitus. In addition, Zituvimet® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Zituvimet®. The clinical studies included in the Zituvimet® prescribing information are the same as those found in the Janumet® prescribing information, which is a sitagliptin and metformin combination tablet with the same indication as Zituvimet®.

Recommendation: Zituviment® to non-preferred.

Criteria:

- Zituvimet®/ Zituvimet® XR: Approvals will require trial of preferred sitagliptin/metformin products or other preferred diabetic agents

Zituvimet® XR (sitagliptin and metformin extended- release); **PDL category-** Diabetic-DPP-4 Enzyme Inhibitor- Combinations

Zituvimet® XR combines two antihyperglycemic agents including sitagliptin (a dipeptidyl peptidase-4 [or DPP-4] enzyme inhibitor) and metformin extended-release (a member of the biguanide class). Sitagliptin is a DPP-4 inhibitor, which is believed to exert its action in patients with type 2 DM by slowing the inactivation of incretin hormones. Metformin improves glucose tolerance in patients with type 2 DM, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Limitations of use include that Zituvimet® XR is not recommended in patients with type 1 diabetes mellitus. In addition, Zituvimet® XR has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Zituvimet® XR. The clinical studies included in the Zituvimet® XR prescribing information are the same as those found in the Janumet® XR prescribing information, which is a sitagliptin and metformin extended-release combination tablet with the same indication as Zituvimet® XR. Zituvimet® XR offers providers another treatment option.

Criteria:

- Zituvimet®/ Zituvimet® XR: Approvals will require trial of preferred sitagliptin/metformin products or other preferred diabetic agents

Board Decision: Due to a lack of quorum a vote will be taken by email.

FDA SAFETY ALERTS

None at this time.

Board Decision: No action.

ADJOURNMENT: 8:30PM

The next meeting will be held on March 11 2025 6 – 8p hybrid.