Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

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TO: Maine Drug Utilization Review Board
DATE: 03/10/22
RE: Maine DUR Board Meeting minutes from March 8, 2022

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD	X		
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR	X		
Kathleen Polonchek, MD	X		
Kenneth McCall, PharmD	X		
Erin Ackley, PharmD.			X
Corinn Normandin, PharmD.	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Laureen Biczak, DO, Change Healthcare	X		
Anne-Marie Toderico, PharmD MaineCare Pharmacy Director	X		

Guests of the Board: Ed Bosshart, PharmD, Fran Jensen, OMS Medical Director

CALL TO ORDER: 6:30PM

Anne- Marie Toderico called the meeting to order at 6:30 PM.

PUBLIC COMMENTS

Vijay Rao from Argenx: Highlighted the attributes of Vyvgart.
Paul Amato from Viiv Healthcare: Highlighted the attributes of Apretude.
Matt Ackerman from ChemoCentryx: Highlighted the attributes of Taveos.
Gene Muise from Amgen: Highlighted the attributes of Tezspire.
Mariola Vazquez from Leo Pharma: Highlighted the attributes of Adbry.
Jane Guo from Novartis: Highlighted the attributes of Leqvio.
Nitin Berri from Genetech: Highlighted the attributes of Susvimo.
Bethany Zanrucha from Sarepta: Highlighted the attributes of Amondys45, Exondys51, and Vyondys53.

OLD BUSINESS

DUR MINUTES

Approval of December 14, 2021 DUR meeting minutes.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE- ANNE-MARIE TODERICO

- On 12/10/2021 MaineCare authorized a Standing Order for licensed pharmacist to create a prescription for over the counter (OTC), direct to consumer (DTC), and prescription COVID-19 at-

home test collection kits for MaineCare members. The Standing Order is found at Office of MaineCare Services Home Page> About Us>Projects and Initiatives>COVID-19>Information by Provider Type>Pharmacies>MaineCare Standing Order For COVID-19 At Home Tests and Collection Kits. As a result, 6700 claims have been processed.

- As a result of providers reaching out, MaineCare is now allowing concomitant use of varenicline and nicotine replacement therapies for tobacco cessation. The member can receive prescriptions for both products, in accordance with the clinical judgement of their prescriber and regardless of their prescription fill history.
- As a result of providers reaching out, MaineCare will cover Humulin and Novolin NPH for gestational diabetes when pregnancy is indicated either in eligibility or on the prescription. If a prescription for Humulin or Novolin NPH is denied for prior authorization when processing a claim and pregnancy is indicated on the prescription, please contact the Change Healthcare Pharmacy Helpdesk for a pregnancy override.
- The Office of MaineCare Services (OMS), in coordination with their Pharmacy Benefits Manager, Change Healthcare (CHC), review data from the National Respiratory and Enteric Virus Surveillance System (NREVSS) to track the epidemic season for respiratory syncytial virus (RSV). With the PCR positivity percent < 3% for 5 consecutive weeks, MaineCare will no longer accept PA requests for palivizumab starting March 11, 2022. Scheduled doses will be covered through March 31, 2022.

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

MUSCULAR DYSTROPHY AGENTS

- Clinical criteria:

  Amondy 45 and Exondys®51: •The patient must be > 14 years of age AND • The prescriber is, or has consulted with, a neuromuscular disorder specialist AND • The dose does not exceed 30mg/kg once weekly AND • The patient is currently on a stable corticosteroid dose for at least 6 months.

  Vyondys® 53: •The patient must be > 16 years of age AND • The prescriber is, or has consulted with, a neuromuscular disorder specialist AND • The dose does not exceed 30mg/kg once weekly AND • The patient is currently on a stable corticosteroid dose for at least 6 months.

  Amondy 45, Exondys®51, Vyondys® 53, Note: Initial approval will be granted for 6 months. For re-approval after 6 months, the patient must demonstrate a response to therapy

NEW BUSINESS

INTRODUCE: CONCOMITANT USE OF GLP-1 AGONISTS AND DPP-4 INHIBITORS IN TYPE II DM

Treatment for Type 2 DM has improved substantially in the last decade. Several effective classes of medications are now available, including glucagon-like peptide-1 receptor agonists (GLP-1 agonists), sodium-glucose co-transporter 2 inhibitors (SGLT-2 inhibitors) and dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors, also called gliptins), along with older medications, such as sulfonylureas and insulin. Recent guidelines from the American Diabetes Associate and the American Society of Endocrinology

incorporate these newer agents into treatment algorithms, often recommending considering these drugs before starting insulin therapy. Some of these agents have beneficial effects on other risks, such as heart failure and other cardiovascular diseases and determining which drugs to use depends on an individual's health profile. GLP-1 receptor agonists work by stimulating insulin secretion and decreasing glucagon production. DPP-4 inhibitors prevent the degradation of GLP-1. Both have shown benefit in lowering blood glucose, however comparative trials have shown GLP-1 receptor agonists to be superior in improving glycemic control and inducing weight loss. Studies have shown that combining a GLP-1 agonist with a DPP-4 inhibitor provides minimal improvement in glycemic control and weight loss compared with either monotherapy and is not cost effective. Guidelines do not support combined therapy with these drugs. We will use paid, non-reversed Medicaid pharmacy and medical claims date from January 2021 – December 2021 excluding members with Part D, MaineRX and TPL. We will look at all members with a diagnosis of Type II DM and look to see if any are being prescribed both a DDP-4 inhibitor and GLP-1 agonist to determine if the practice is widespread or isolated among a few providers. This will determine if there should be adjustment to the PDL, PA process or if provider education is warranted.

Board Decision: None at this time

PRESENTATION: CODEINE USE IN PEDIATRIC POPULATION

Codeine use in children has come under scrutiny within the last few years due to the recent attention paid to complications of opiate use, including death. Codeine has been historically considered safe for treating pain in children, being used often to treat acute pain after surgical procedures and to suppress cough associated with respiratory infections. In 2013, the FDA restricted use in children younger than 18 to those who have acute pain after tonsillectomy/adenoidectomy. In a 2015 Drug Safety Communication, the public was warned about children who were ultra-rapid metabolizers of codeine, leading to high concentrations of the active metabolite too quickly, resulting in breathing difficulties. From 1969 – 2015, 64 cases of serious breathing problems, including 24 deaths in children under 18 were reported to the FDA Adverse Event Reporting System. This is likely is an underreporting of the incidence of these complications. An FDA safety alert was issued in April 2017 stating the use of codeine was contraindicated in the pediatric population younger than 12 years old and issued a warning about use in those ages 12-18 who are obese or have conditions such as obstructive sleep apnea or severe lung disease In February 2018, codeine was removed from over the counter pain and cough medications. The purpose of this retroDUR is to investigate the practice patterns of use of codeine in children, including as a cough suppressant, as well as pain management among providers who care for pediatric patients. We will look at use in the outpatient and inpatient settings, to evaluate both acute and chronic use for pain. We used paid, non-reversed Medicaid medical, and pharmacy claims from calendar year 2020 and 2021, excluding members with Part D, MaineRX and TPL. For 2020 and 2021, we identified members, stratified by age cohort (less than 12, 12-18) with at least one prescription for a codeine containing product. We identified the diagnosis and number of days prescribed by both medical and dental providers and determined if codeine was being used for acute or chronic pain management. We looked for providers who repeatedly prescribed codeine in order to do a targeted intervention. If the practice is widespread, general education will be provided to the provider community.

Recommendation: There was an increase in the use of codeine in children in 2021 compared with 2020, however usage in 2020 may have been unusually low due to procedures being delayed due to covid. It appears that most members received only 1 prescription for pain and the days supplied was no more

than 4 days, most often 3 days. Additionally, other than particular specialties, such as oral surgery, where we would expect to see higher pain management utilization, the prescriber data does not suggest that there is over-prescribing by providers. Continued monitoring of codeine usage in children is warranted however given the increased usage in 2021 over 2020, to be sure there is not a trend toward increasing usage of codeine in children.

Board Decision: The Board unanimously approved the above recommendation.

NEW DRUG REVIEW

Adbry® (tralokinumab-ldrm); **PDL category-** Topical- Atopic Dermatitis

Tralokinumab-ldrm, the active ingredient of Adbry®, is an interleukin-13 antagonist, a human IgG4 monoclonal antibody that specifically binds to human interleukin-13 (IL-13) and inhibits its interaction with the IL-13 receptor α1 and α2 subunits (IL-13Rα1 and IL-13Rα2). IL-13 is a naturally occurring cytokine of the Type 2 immune response. Tralokinumab-ldrm inhibits the bioactivity of IL-13 by blocking IL-13 interaction with IL-13Rα1/IL-4Rα receptor complex. Tralokinumab-ldrm inhibits IL-13 induced responses including the release of proinflammatory cytokines, chemokines, and IgE. It is indicated for the treatment of moderate-to-severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Adbry® can be used with or without topical corticosteroids. The safety and efficacy of Adbry® were assessed in three double-blind, randomized, placebo-controlled trials (ECZTRA 1, ECZTRA 2, ECZTRA 3) that included adult subjects 18 years of age and older (N=1934 total) with moderate-to-severe atopic dermatitis not adequately controlled by topical medication(s). In one study, Adbry® was used in combination with TCS and compared with placebo plus TCS and as needed topical calcineurin inhibitors. All three trials assessed the primary endpoints of the proportion of subjects with an IGA 0 or 1 at week 16 and the proportion of subjects with EASI-75 at week 16. However, there is no evidence to suggest that Adbry® is safer or more effective than other currently preferred, more cost effective medications.

Recommendation: Adbry® to non-preferred.

Clinical criteria:

- Preferred drugs also indicated for this condition, including topical steroids, cyclosporin AND calcineurin inhibitors 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
- Additionally, after trials above for Mild Atopic Dermatitis: 1. Eucrisa, 2. Opzelura. For Moderate Atopic Dermatitis: 1. Dupixent, 2. Rinvoq. For Moderate/Severe Atopic Dermatitis: 1. Dupixent, 2. Rinvoq Note: If unable to use TCIs then a trial of Eucrisa is required before Dupixent.

Apretude® (cabotegravir extended-rlease injectable suspension); **PDL category-** Antiretroviral Agents

Cabotegravir, the active ingredient of Apretude®, is an HIV-1 integrase strand transfer inhibitor (INSTI). It inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral DNA integration that is essential for the HIV replication cycle. It is indicated in at-risk adults and adolescents weighing at least 35kg for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 infection. Individuals must have a negative HIV-1 test prior to initiating Apretude® (with or without an oral lead-in with oral cabotegravir) for HIV-1 PrEP. The safety and efficacy of Apretude® to reduce the risk of acquiring HIV-1 infection were assessed in 2 randomized, double-blind, controlled, multinational trials, including HPTN 083 (in HIV-1 uninfected men and transgender women who have sex with men and have evidence of high-risk behavior for HIV-1 infection) and HPTN 084 (in HIV-1 uninfected cisgender women at risk of acquiring HIV-1). In clinical trials, it was compared with oral Truvada® and the primary analysis demonstrated the superiority of Apretude® compared with Truvada® with an 88% reduction in the risk of acquiring incident HIV-1 infection (study HPTN 084) and with a 66% reduction in the risk of acquiring HIV-1 infection (study HPTN 083).

Recommendation: Apretude® to preferred.

Besremi® (ropeginterferon alfa-2b); **PDL category**- Polycythemia Vera Treatments

Ropeginterferon alfa-2b-njft, an interferon alfa-2b, is an N-terminal mono-pegylated covalent conjugate of proline interferon alfa-2b, produced in E. coli cells by recombinant DNA technology, with a methoxy polyethylene glycol (mPEG) moiety. Interferon alfa belongs to the class of type I interferons, which exhibit their cellular effects in polycythemia vera in the bone marrow by binding to a transmembrane receptor termed interferon alfa receptor (IFNAR). Binding to IFNAR initiates a downstream signaling cascade through the activation of kinases, in particular Janus kinase I (JAK1) and tyrosine kinase 2 (TYK2) and activator of transcription (STAT) proteins. Nuclear translocation of STAT proteins controls distinct gene-expression programs and exhibits various cellular effects. The actions involved in the therapeutic effects of interferon alfa in polycythemia vera are not fully elucidated. It is indicated for the treatment of adults with polycythemia vera. The safety and efficacy of Besremi® were assessed in a prospective, multicenter, single-arm study of 7.5 years in duration (PEGINVERA) that included adults with polycythemia vera. s life-threatening or fatal neuropsychiatric reactions have occurred in patients receiving interferon alfa products, including Besremi®, closely monitor patients for any symptoms of psychiatric disorders and consider psychiatric consultation and treatment if such symptoms emerge. Treatment should be avoided in patients with severe or unstable cardiovascular disease or recent stroke or MI. CBC should be monitored regularly, including at baseline, every 2 weeks during the titration phase and every 3-6 months during the maintenance phase. In a small prospective, single-arm study that included adults with polycythemia vera (N=51), the efficacy of Besremi® was evaluated by assessing complete hematological response (CHR). Results indicated that the CHR in the treated population during the treatment period was 61%, and the median duration of response was 14.3 months.

Recommendation: Besremi® to non-preferred.

Clinical Criteria:

- Add new category Polycythemia Vera Treatments
- PA required to confirm FDA approved indication.

Elyxyb® (celecoxib solution) **PDL category-** Migraine, Misc.

Celecoxib, the active ingredient of Elyxyb®, is a nonsteroidal anti-inflammatory drug with analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action by which celecoxib exerts therapeutic effects for its approved indication is not fully understood but may involve inhibition of prostaglandin synthesis, mainly via inhibition of COX-2. It indicated for the acute treatment of migraine with or without aura in adults. It is not indicated for the preventive treatment of migraine. The safety and efficacy of Elyxyb® for the acute treatment of migraine with or without aura was demonstrated in two randomized, double-blind, placebo-controlled clinical trials. Results suggested that in both studies, the percentage of patients achieving MBS freedom at 2 hours post-dose was significantly greater among patients receiving Elyxyb® compared to those receiving placebo. This endpoint in study 1 was not statistically significant between treatment groups. Elyxyb® allows providers another treatment option for patients needing acute treatment of migraine. There is no evidence at this time to support that Elyxyb® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Elyxyb® XR to non-preferred.

Eprontia® (topiramate); **PDL category**- Anticonvulsants

The mechanism by which topiramate, the active ingredient of Eprontia®, works is not known; however, preclinical studies have revealed 4 properties that may contribute to its efficacy for epilepsy and the preventive treatment of migraine. Electrophysiological and biochemical evidence suggests that topiramate, at pharmacologically relevant concentrations, blocks voltage-dependent sodium channels, augments the activity of the neurotransmitter gamma-aminobutyrate at some subtypes of the GABA-A receptor, antagonizes the AMPA/kainate subtype of the glutamate receptor, and inhibits the carbonic anhydrase enzyme, particularly isozymes II and IV. It is indicated for the following: Initial monotherapy for the treatment of partial-onset or primary generalized tonic-clonic seizures in patients 2 years of age and older, Adjunctive therapy for the treatment of partial-onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome in patients 2 years of age and older, The preventive treatment of migraine in patients 12 years and older. The safety and efficacy of Eprontia® are based on the relative bioavailability of Eprontia® compared to topiramate sprinkle capsules in healthy subjects. The safety and efficacy of Eprontia® are based on the relative bioavailability of Eprontia® compared to topiramate sprinkle capsules in healthy subjects. Topiramate sprinkle capsules have comparable bioavailability to topiramate tablets. The studies described in the prescribing information of Eprontia® were conducted using topiramate tablets or sprinkle capsules. The studies described in the prescribing information of Eprontia® were conducted using topiramate tablets or sprinkle capsules. Topiramate, under the brand name Topamax®, has been available for numerous years as both a brand and generic, with the same indications as Eprontia®. Eprontia® offers providers another treatment option with this new dosage form.

Recommendation: Eprontia® to non-preferred.

Clinical Criteria:

- Initial monotherapy for the treatment of partial-onset or primary generalized tonic-clonic seizures in patients 2 years of age and older. Adjunctive therapy for the treatment of partial-onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox Gastaut syndrome in patients 2 years of age and older. The preventive treatment of migraine in patients 12 years and older. Will require a step though topiramate.

Leqvio® (inclisiran); **PDL category**- Familial Hypercholesterolemia

Inclisiran, the active ingredient of Leqvio®, is a double-stranded small interfering ribonucleic acid (siRNA), conjugated on the sense strand with triantennary N-Acetyl galactosamine (GalNAc) to facilitate uptake by hepatocytes. In hepatocytes, inclisiran utilizes the RNA interference mechanism and directs catalytic breakdown of mRNA for proprotein convertase subtilisin kexin type 9 (PCSK9). This increases LDL-C receptor recycling and expression on the hepatocyte cell surface, which increases LDL-C uptake and lowers LDL-C levels in the circulation. It is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C). The effect of Leqvio® on cardiovascular morbidity and mortality has not been determined. The safety and efficacy of Leqvio® were assessed in 3 randomized, double-blind, placebo-controlled trials that included adults with HeFH or clinical ASCVD who were taking maximally tolerated statin therapy and required additional LDL-C lowering. Its efficacy in lowering LDL-C was assessed in 3 multicenter, placebo-controlled, double-blind studies that included patients with clinical ASCVD or HeFH who were taking maximally tolerated statin therapy and required additional LDL-C lowering. In all studies, the difference between the Leqvio® and placebo groups in mean percentage change in LDL-C from baseline to day 510 was statistically significant.

Recommendation: Leqvio® to non-preferred.
Livtencity® (maribavir); **PDL category**- Cytomegalovirus Agents

Maribavir, the active ingredient of Livtencity®, is a benzimidazole riboside cytomegalovirus (CMV) pUL97 protein kinase inhibitor. It is an antiviral agent against human CMV, mediated by competitive inhibition of the protein kinase activity of human CMV enzyme pUL97, which results in inhibition of the phosphorylation of proteins. It is indicated for the treatment of adults and pediatric patients (12 years of age and older and weighing at least 35kg) with post-transplant cytomegalovirus (CMV) infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir, or foscarnet. A phase 3, multicenter, randomized, open-label, active-controlled, superiority trial was performed to assess the safety and efficacy of Livtencity® as compared to Investigator-Assigned Treatment (IAT; ganciclovir, valganciclovir, foscarnet, or cidofovir) in hematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT) recipients with CMV infections (N=352) that were refractory to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir, including CMV infections with or without confirmed resistance to 1 or more of the IATs. Subjects with CMV disease involving the CNS, including the retina, were excluded from the study. Subjects were randomized to treatment for up to 8 weeks; and, after completion of the treatment period, subjects entered a 12-week follow-up phase. The primary efficacy endpoint was confirmed CMV DNA level <LLOQ at the end of week 8, and results suggested that Livtencity® was statistically superior to IAT (56% vs 24%, respectively; NNT 4).

Recommendation: Livtencity® to non-preferred.

Clinical criteria:

- Add new category Cytomegalovirus Agents
- DDI: Livtencity is a substrate of CYP3A4. Coadministration of Livtencity® with strong inducers of CYP3A4 is not recommended, except for selected anticonvulsants.

Lofena® (diclofenac potassium); **PDL category**- NSAIDs

Diclofenac potassium, the active ingredient of Lofena®, is a benzene-acetic acid derivative that has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action of Lofena®, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2). Diclofenac is a potent inhibitor of prostaglandin synthesis. Because diclofenac is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues. It is indicated for careful consider the potential benefits and risks of Lofena® and other treatment options before deciding to use Lofena®. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. Lofena® is indicated for: Treatment of primary dysmenorrhea, Relief of mild to moderate pain, Relief of the signs and symptoms of osteoarthritis (OA), Relief of the signs and symptoms of rheumatoid arthritis (RA). There was no information in the prescribing information regarding clinical trials. Diclofenac potassium tablets, available as a 50mg strength, have been available for many years, have the same indication as Lofena® tablets, and have been found to be safe and effective.

Recommendation: Lofena® to non-preferred.

Recorlev® (levoketoconazole); **PDL category**- Cushing Disease Agents

Levoketoconazole, the active ingredient of Recorlev®, is the 2S, 4R-enantiomer derived from racemic ketoconazole and is a cortisol synthesis inhibitor. In vitro, levoketoconazole inhibits key steps in the synthesis of cortisol and testosterone, mainly those mediated by CYP11B1 (11β hydroxylase), CYP11A1 (the cholesterol side-chain cleavage enzyme, the first step in the conversion of cholesterol to pregnenolone), and CYP17A1 (17α-hydroxylase). It is indicated for the treatment of endogenous hypercortisolemia in adult patients with Cushing's syndrome for whom surgery is not an option or has not been curative. Recorlev® is not approved for the treatment of fungal infections. The safety and effectiveness of Recorlev® for the treatment of fungal infections have not been established. The safety and efficacy of Recorlev® in patients with Cushing's syndrome were assessed in 2 studies. Levoketoconazole, the active ingredient of Recorlev®, is the 2S, 4R-enantiomer derived from racemic ketoconazole and in vitro levoketoconazole inhibits key steps in the synthesis of cortisol and testosterone. Recorlev® does have a box warning regarding increased risk of hepatotoxicity and QT prolongation. The number and percent of patients who had normal mUFC at the end of the randomized withdrawal phase in one phase 3 study was 11/21 (52.4%) in the Recorlev® group and 1/18 (5.6%) in the placebo group (NNT = 3). Recorlev® provides healthcare professionals a new treatment option for patients.

Recommendation: Recorlev® to non-preferred.

Clinical criteria:

- Recorlev® is associated with dose-related QT interval prolongation. QT interval prolongation may lead to life-threatening ventricular dysrhythmias such as Torsades de pointes.

Scemblix® (asciminib); **PDL category**- Cancer

Asciminib, the active ingredient of Scemblix®, is a kinase inhibitor. It is an ABL/BCR-ABL1 tyrosine kinase inhibitor. Asciminib inhibits the ABL1 kinase activity of the BCR-ABL1 fusion protein, by binding to the ABL myristoyl pocket. It is indicated for the treatment of adult patients with: Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs). This indication is approved under accelerated approval based on major molecular response (MMR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Ph+ CML in CP with the T315I mutation. The

efficacy of Scemblix® in the treatment of patients with Ph+ CML in chronic phase previously treated with 2 or more TKIs was assessed in a multicenter, randomized, active-controlled, and open-label study (ASCEMBL). In this study, patients (N=233) were randomized to receive either Scemblix® 40mg BID or bosutinib 500mg QD and patients continued treatment until unacceptable toxicity or treatment failure occurred. The MMR rate was significantly greater with Scemblix® as compared with bosutinib (NNT calculated by CHC 9). In a small, open-label study that included patients with Ph+ CML-CP with the T315I mutation, the MMR was achieved by 24 weeks in 42% of the 45 patients treated with Scemblix® and was achieved by 96 weeks in 49% of the 45 patients treated with Scemblix®.

Recommendation: Scemblix® to non-preferred.

Clinical Criteria:

- PA required to confirm appropriate diagnosis and testing
- Clinical PA required for appropriate diagnosis
- Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Ph+ CML in CP with the T315I mutation.
- Scemblix is for the treatment of adult patients with: Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs).

Skytrofa® (lonapegsomatropin-tcgd); **PDL category**- Growth Hormone

Lonapegsomatropin-tcgd, the active ingredient of Skytrofa®, is a long-acting prodrug of a human growth hormone (somatropin) produced by recombinant DNA technology using E. coli. It is a pegylated human growth hormone (somatropin). Somatropin binds to the growth hormone (GH) receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamic effects. It has direct tissue and metabolic effects, and indirect effects mediated by insulin-like growth factor-1 (IGF-1), including stimulation of chondrocyte differentiation and proliferation, stimulation of hepatic glucose output, protein synthesis, and lipolysis. Somatropin stimulates skeletal growth in pediatric patients with growth hormone deficiency (GHD) as a result of effects on the growth plates (epiphyses) of long bones. It is indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH). The safety and efficacy of Skytrofa® were assessed in a multicenter, randomized, open-label, active-controlled, parallel-group phase 3 study that was conducted in treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency (GHD). Treatment with once-weekly Skytrofa® for 52 weeks resulted in an annualized height velocity (primary efficacy endpoint) of 11.2 cm/year, while subjects treated with daily somatropin achieved an annualized height velocity of 10.3cm/year after 52 weeks of treatment. The rates of adverse events and serious adverse events were similar between groups. The authors concluded that this trial met its objective of non-inferiority in annualized height velocity and further demonstrated superiority of Skytrofa® to daily somatropin, with a similar safety profile.

Recommendation: Skytrofa® to non-preferred.

Susvimo® (ranibizumab); **PDL category**- Op.- Of Interest

Ranibizumab, the active ingredient of Susvimo®, is a recombinant humanized IgG1 kappa isotype monoclonal antibody fragment for intraocular use. It binds to the receptor binding site of multiple biologically active forms of VEGF-A, including VEGF110. VEGF-A has been shown to cause

neovascularization and leakage in models of ocular angiogenesis and vascular occlusion and is thought to contribute to pathophysiology of neovascular age-related macular edema (AMD). The binding of ranibizumab to VEGF-A prevents the interaction of VEGF-A with its receptors (VEGFR1 and VEGFR2) on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation. It is indicated for the treatment of patients with Neovascular (wet) Age-related Macular Degeneration (AMD) who have previously responded to at least two intravitreal injections of a Vascular Endothelial Growth Factor (VEGF) inhibitor medication. In a randomized, visual assessor-masked, active treatment trial that included patients diagnosed with nAMD within the 9 months prior to screening and who received ≥3 doses of anti-VEGF intravitreal agents in the study eye within the last 6 months prior to screening, Susvimo® implant was compared with intravitreal ranibizumab injections every 4 weeks. The primary efficacy endpoint (change from baseline in distance Best Corrected Visual Acuity [BCVA] score averaged over week 36 and week 40) demonstrated that Susvimo® was equivalent to intravitreal ranibizumab injections administered every 4 weeks. As this is a continuous delivery of medication into the eye through the refillable implant, as few as two treatments per year of Susvimo® may benefit patents with nAMD.

Recommendation: Susvimo® to non-preferred.

Tavneos® (avacopan); **PDL category**- Complement Receptor Antagonists

Avacopan, the active ingredient of Tavneos®, is a complement 5a receptor (C5aR) antagonist that inhibits the interaction between C5aR and the anaphylatoxin C5a. Avacopan blocks C5a-mediated neutrophil activation and migration. The exact mechanism by which avacopan exerts a therapeutic effect in patients for its approved indication has not been definitively established. It is indicated as an adjunctive treatment of adult patients with severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (granulomatosis with polyangiitis [GPA] and microscopic polyangiitis [MPA]) in combination with standard therapy including glucocorticoids. Tavneos® does not eliminate glucocorticoid use. Due to the reports of serious cases of hepatic injury observed in patients taking Tavneos®, obtain a liver test panel before starting Tavneos®, every 4 weeks after the start of therapy for the first 6 months of treatment, and as clinically indicated thereafter. Hepatitis B virus reactivation was observed in the clinical program. Screen patients for HBV infection before starting treatment and monitor patients with evidence of current or prior HBV infection for clinical and laboratory signs of hepatitis, or HBV reactivation during and for 6 months following Tavneos® therapy. In a double-blind, active-controlled study comparing Tavneos® with prednisone, with both added to standard immunosuppressive regimens, remission at week 26 (a primary endpoint) was achieved by 72.3% of the Tavneos® group and 70.1% in the prednisone group. Per the full-text study by Jayne et al2, this met non-inferiority ($p<0.001$) but not superiority ($p=0.24$). At week 52, a significantly greater percentage of patients had sustained remission at week 52 (the second primary endpoint) in the Tavneos® group as compared with the prednisone group (65.7% vs 54.9%). Per the full-text study by Jayne et al2, this met non-inferiority ($p<0.001$) and superiority ($p=0.007$).

Recommendation: Tavneos® to non-preferred.

Tezspire® (Tezepelumab-ekko); **PDL category**- Antiasthmatic- Anti-inflammatory Agents

Tezepelumab-ekko, the active ingredient of Tezspire®, is a thymic stromal lymphopoietin (TSLP) blocker, a human monoclonal antibody IgG2λ that binds to human TSLP with a dissociation constant of 15.8pM and blocks its interaction with the heterodimeric TSLP receptor. TSLP is a cytokine mainly derived from

epithelial cells and occupies an upstream position in the asthma inflammatory cascade. Blocking TSLP with tezepelumab-ekko reduces biomarkers and cytokines associated with inflammation including blood eosinophils, airway submucosal eosinophils, IgE, FeNO, IL-5, and IL-13; however, the mechanism of action in asthma has not been definitely established. It is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma. Tezspire® is not indicated for the relief of acute bronchospasm or status asthmaticus. The safety and efficacy of Tezspire® were assessed in two randomized, double-blind, parallel group, placebo-controlled studies of 52 weeks duration that included patients 12 years of age and older (N=1609) with severe asthma.

Recommendation: Tezspire® to non-preferred.

Clinical criteria:

- For adult and pediatric patients aged 12 years and older with severe asthma.

Voxzogo® (vosoritide); **PDL category**- Achondroplasia Treatments

Vosoritide, the active ingredient of Voxzogo®, is a human C type natriuretic peptide (CNP) analog, a 39 amino acid peptide. In patients with achondroplasia, endochondral bone growth is negatively regulated due to a gain of function mutation in fibroblast growth factor receptor 3 (FGFR3). Binding of vosoritide to natriuretic peptide receptor-B (NPR-B) antagonizes FGFR3 downstream signaling by inhibiting the extracellular signal-regulated kinases 1 and 2 (ERK1/2) in the mitogen-activated protein kinase (MAPK) pathway at the level of rapidly accelerating fibrosarcoma serine/threonine protein kinase (RAF-1). As a result, vosoritide, like CNP, acts as a positive regulator of endochondral bone growth as it promotes chondrocyte proliferation and differentiation. It is indicated to linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses. This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). The safety and efficacy of Voxzogo® were assessed in one multicenter, randomized, double-blind, placebo-controlled study of 52 weeks in duration that included patients with genetically confirmed achondroplasia (N=121) who were randomized to either Voxzogo® or placebo. Voxzogo® treatment for 52 weeks resulted in a treatment difference in the change from baseline in AGV of 1.57 cm/year.

Recommendation: Voxzogo® to non-preferred.

Clinical Criteria:

- Add new category Achondroplasia treatments.
- Pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses.
- Voxzogo: To increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses. This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Vyvgart® (efgartigimod alfa); **PDL category**- Myasthenia Gravis Treatments

Efgartigimod alfa-fcab, the active ingredient of Vyvgart®, is a human immunoglobulin G1 (IgG1)-derived Fc fragment of the za allotype. It is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG. It is indication for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

The safety and efficacy of Vyvgart® were assessed in a multicenter, randomized, double-blind, placebo-controlled study of 26 weeks in duration that included adults with generalized myasthenia gravis (gMG) who were AChR antibody positive (N=167). This study enrolled patients who met the following criteria at screening: Myasthenia Gravis Foundation of America (MGFA) clinical classification class II to IV, MG-Activities of Daily Living (MG-ADL) total score of ≥5, On stable dose of MG therapy prior to screening, that included acetylcholinesterase (AChE) inhibitors, steroids, or non-steroidal immunosuppressive therapies (NSISTs), either in combination or alone, IgG levels of at least 6g/L. Assess the need to administer age-appropriate immunizations according to immunization guidelines before initiation of a new treatment cycle with Vyvgart®. In a multicenter, randomized, double-blind, placebo-controlled study that compared Vyvgart® with placebo, the primary efficacy endpoint was the comparison of the percentage of MG-ADL responders during the first treatment cycle between treatment groups in the AChR-Ab positive population. Results suggested that a statistically significant difference favoring Vyvgart® was observed in the MG-ADL responder rate during the first treatment cycle (67.7% with Vyvgart® and 29.7% with placebo; NNT calculated by CHC- 3). Vyvgart® also reduced muscle weakness as measured by the percentage of QMG responders. This product gives patients another treatment option.

Recommendation: Vyvgart® to non-preferred.

Clinical Criteria:

- Add new category Myasthenia Gravis Treatments.
- For adult patients who are anti-acetylcholine receptor (AChR) antibody positive.

FDA SAFETY ALERTS

None at this time

Board Decision: No action.

ADJOURNMENT: 8:45PM

The next meeting will be held on **June 14, 2022** 530pm- 8:30pm virtually.