Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

Maine Department of Health and Human Services
Office of MaineCare Services - Pharmacy Unit
11 State House Station
Augusta, Maine 04333-0011
Toll Free: (866) 796-2463; TTY: Dial 711 (Maine Relay)
Fax: (207) 287-8601

TO: Maine Drug Utilization Review Board
DATE: 12/16/21
RE: Maine DUR Board **Meeting** minutes from December 14, 2021

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

CALL TO ORDER: 6:30PM

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

PUBLIC COMMENTS

Timothy Birner from Alkermes: Highlighted the attributes of Lybalvi.
Kris Washington from Vertice: Highlighted the attributes of Thyquidity.
Nicole Trask from Janssen: Highlight the attributes of Hafyera.
Praneeta Nagraj from Albireo: Highlighted the attributes of Bylvay.
Amy Tomasello from Abbvie: Highlighted the attributes of Qulipta.
Christine Dube from AstraZeneca: Highlighted the attribute of Saphnelo.

OLD BUSINESS

DUR MINUTES

Approval of October 14,2021 DUR meeting minutes.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE- ANNE-MARIE TODERICO

- In corporation with CDC as have put in place a standing order for nicotine replacement therapy, As of October 5% of claims were processed from that standing order and we have seen it steadily increasing.

- Effective 12/10/2021, MaineCare will expand access to Food and Drug Administration (FDA) approved and FDA Emergency Use Authorized (EUA) over the counter (OTC), direct to consumer (DTC), and prescription COVID-19 at-home tests and home collection kits through a Standing Order for MaineCare beneficiaries. These tests and collection kits will be covered with no member cost sharing.The Standing Order authorizes licensed pharmacists to create a prescription for the OTC, DTC, or prescription COVID-19 at home tests and home collection kits for eligible MaineCare members.

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

- None at this time

NEW BUSINESS

INTRODUCE: 2022 POTENTIAL RETRODUR INITIATIVES

CONCURRENT USE OF GLP-1 RECEPTOR AGONISTS, DPP-4 INHIBITORS AND SGLT-2 INHIBITORS

Purpose: Combination therapy provides only modest improvement in glycemic control with minimal weight loss benefits, which is similar to monotherapy with either agent. Combination is unlikely to provide synergistic effects and is not cost effective.

- Evaluate dispensing of GLP-1 Receptor Agonists, DPP-4 Inhibitors and SGLT-2 inhibitors looking for overlapping dates of service.
- Consider therapy edit to prevent combination therapy without prior authorization.

LETROZOLE USE FOR INFERTILITY

Purpose: Medicaid does not provide coverage for infertility treatment. However, since letrozole has multiple clinical indications and is a preferred agent, there may be unintended use.

- Evaluate pharmacy claims for Letrozole and evaluate medical claims for a diagnosis of breast cancer, polycystic ovary syndrome, and endometriosis.
- The expectation is that 2.5mg daily use for 30 or more days will be associated with a breast cancer diagnosis whereas 2.5mg-5mg daily for 5 days is more likely for ovulation induction.

BLOOD GLUCOSE TEST STRIPS IN CGM USERS

Purpose: The expectation is that blood glucose test strip (BGS) utilization will decrease after a member starts on a continuous glucose monitor (CGM) system.

- Identify new users of CGM and look at BGS pre and post CGM.
- Consider quantity limits for testing strips.

OPIOID USE FROM MULTIPLE PROVIDERS

Purpose: Asses potentially high-risk opioid prescribing practices and/or provider “shopping.”

- Identify the proportion of members receiving opioid prescriptions from 4 or more different prescribers in a 1-year timeframe.

- Identify the proportion of members receiving opioid prescriptions from 4 or more different pharmacies in a 1-year timeframe.
- Can also evaluate members that have multiple prescribers AND multiple pharmacies.

APPROPRIATE USE OF ASTHMA CONTROLLER MEDICATIONS

Purpose: To evaluate use of short term beta-adrenergic (SABA) inhalers since increased use of SABA has been associated with increased risk of acute asthma exacerbation and death. GINA guidelines were updated in 2019 and recommend that all adults and adolescents should receive ICS-containing controller treatment, including patients with mild asthma. The goal is to assess compliance with these guidelines.

- Identify members using a SABA and determine if there is also use of a controller medication.

Board Decision: After board discussion, on Topic concurrent use of glp-1 receptor agonists, dpp-4 inhibitors and sglt-2 inhibitors we really need to look at evaluate dispensing of glp-1 receptor agonists, dpp-4 inhibitors. the board felt that letrozole use for infertility was not a priority for the RetroDUR. Discussion on doing a RetroDUR on the changes that were made to streamline the PA process for buprenorphine. It was decided to bring back an initiative to the March meeting. Included the Buprenorphine topic that will be brought back to the board in March, the board will also do the following topics: appropriate use of asthma controller medications, opioid use from multiple providers, concurrent use of glp-1 receptor agonists, dpp-4 inhibitors.

PRESENTATION: ZOSTER VACCINATION RATES

Vaccination to prevent reactivation of the varicella -zoster virus is recommended in people age 50 and older. Vaccination has been shown to decrease reactivation of the virus, which causes rash and neuropathic pain that can range from mild to severe. Unfortunately, many infections are severe, and the discomfort can linger for many months, sometimes never completely resolving. Zostavax was the first vaccine available. It was a live, attenuated virus, but was removed from the market in the US in July 2020. Because it was a live virus, concerns existed around causing infection in immunocompromised hosts. Shingrix, which is a recombinant vaccine, where the virus glycoprotein E is combined with an adjuvant (AS01B). While it has proven safe to give to just about any patient, there are concerns that an immune reaction to the adjuvant could case flares of autoimmunity or transplant graft rejection in some patients. Zostavax was one injection, Shingrix is two. Additionally, there are side effects that occur in a number of patients, which include local reactions/pain (78%), myalgias (44%), fatigue (44%), headache (38%), chills (26%), fever (20%) and GI symptoms (17%). There have been rare reports of Guillain-Barre syndrome in those over 65 who got the Shingrix vaccine. The timing of the Shingrix doses should be no closer than 4 weeks apart and should be within 6 months of each other. Immunity with Shingrix has been shown to be at least 4 years in most people, with limited studies showing humoral (b-cell) and t-cell immune responses at 9 years in patients with long-term follow-up. Additionally, it is safe to vaccinate those who previously had shingles. We used paid, non-reversed Medicaid pharmacy and medical claims date from January 2020 – December 2020 excluding members with Part D, MaineRX and TPL. We looked at all members over the age of 50 and identified those who were administered Zostavax or at least one dose of Shingrix. We determined the rate of vaccination per all eligible donors and assessed if those who received Shingrix also got their second dose 1 to 6 months after the first dose, to assess compliance with recommendations. We could not determine if some members were vaccinated under medical coverage in provider offices/facilities and were not able to look at the number of eligible who were previously vaccinated.

Recommendation: The percentage of members vaccinated in 2020 does not consider those who may have been previously vaccinated, and this was a COVID year, in which many members delayed routine care. It would be worth repeating this analysis in a future year once the effect of COVID on preventive care has waned. If more intervention is necessary, then a general educational message to PCPs may be an effective remind er to get members vaccinated. Public service announcements to the public may also be effective, as well as direct mailings to members.

Board Decision: The Board unanimously approved the above recommendation.

PRESENTATION: HPV VACCINATION RATES

Human papilloma virus (HPV) infection is recognized as a major contributor to morbidity and mortality in the US. Chronic infection is tied to cervical, vaginal and vulvar carcinomas in females, penile cancers in males and oropharyngeal and anal carcinomas in both sexes. Additionally, cutaneous and genital warts are associated with HPV infections. Approximately 80% of sexually active individuals worldwide are exposed to HPV once in their lifetime, although some experts put this at 100%. Around the world, anogenital HPV is the most common sexually transmitted disease. Most infections in the western world occur in people in the 15- to 25- year age range. Since the development of the HPV vaccine, infection rates have plummeted, as have the complications of infections. As an example, cervical samples of HPV serotypes 6, 11, 16 and 18 (those in the quadrivalent vaccine) have decreased 88% from pre-vaccine levels (11.5 % down to 1.1%). This was in a population where only 55% of the eligible adolescent females received the vaccine. Herd protection has helped decrease the incidence of the disease in the unvaccinated population as well. The current CDC recommendation is that vaccination begin routinely in children of both sexes at age 11-12 but can begin in those as young as 9 years old. Two doses are recommended in those starting the series before age 15, and the second dose should be given 6-12 months after the first. If the second dose was administered within 5 months of the first dose, a third dose should be administered. For those ages 15-26, the 3- dose series should be administered at 0, 1-2 and 6- month intervals. All those aged patients who are immunocompromised should receive 3 doses. There is less benefit to vaccinating those between the ages of 27-45, as many will have been exposed, but it is appropriate in some situations. We used paid, non-reversed Medicaid medical, and pharmacy claims for the NDCs and from calendar year 2019 (pre-COVID), excluding members with Part D, MaineRX and TPL. We looked at 2019 claims that included the NDC for Gardasil and the 2 administration codes (first and subsequent injections) to determine the rate of vaccination in children 11-18 years of age.

Recommendation: It appears that both males and females are appropriately receiving immunizations for HPV. We cannot know how many eligibles were previously vaccinated and think that assuming some older members were likely vaccinated, a 9% vaccination rate is reasonable. A general educational strategy targeting PCPs and members could be done to increase awareness of the benefits of vaccination.

Board Decision: The Board unanimously approved the above recommendation.

NEW DRUG REVIEW

Aemcolo® (rifamycin, delayed release); **PDL category-** Antibiotics- Misc

Rifamycin, the active ingredient of Aemcolo®, is an antibacterial drug that belongs to the ansamycin class of antibacterial drugs. It acts by inhibiting the beta-subunit of the bacterial DNA-dependent RNA polymerase, blocking one of the steps in DNA transcription. This results in inhibition of bacterial synthesis and consequently growth of bacteria. It is indicated for the treatment of traveler's diarrhea (TD) caused by non-invasive strains of Escherichia coli in adults. It is not indicated in patients with diarrhea complicated by fever or bloody stool or due to pathogens other than noninvasive strains of Escherichia coli. The safety and efficacy of Aemcolo® were assessed in a multicenter, randomized, double-blind, placebo-controlled study that included adults with traveler's diarrhea. n a multicenter, randomized, double-blind, placebo-controlled trial that included adults with TD, Aemcolo® significantly reduced the time to last unformed (watery or soft) stool (TLUS) compared to placebo (p=0.0008), with a difference of 22 hours. In addition, significantly more subjects achieved clinical cure with Aemcolo® compared with placebo (NNT calculated by CHC of 5). In the full-text study by Steffen et al2 that compared rifamycin with ciprofloxacin 500mg BID for the treatment of TD in a randomized, double-blind, phase 3 study (ERASE), the primary outcome was TLUS, after which clinical cure was declared. The study was designed to demonstrate non-inferiority of rifamycin to ciprofloxacin. Results of the per-protocol (PP) analysis suggest that the median TLUS was 42.8 hours in the rifamycin group as compared with 36.8 hours with ciprofloxacin, which indicated non-inferiority of rifamycin to ciprofloxacin (p=0.0035). Results from the ITT analysis confirmed the PP analysis (median TLUS was 44.3 hours with rifamycin vs 40.3 hours with ciprofloxacin, with p=0.0011 for non-inferiority in the ITT population). The incidence of adverse events and adverse drug reactions was similar in both treatment groups.

Recommendation: Aemcolo® to non-preferred.

Clinical 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.

Invega® Hafyera (paliperidone palmitate injection, suspension, extended-release); **PDL category-** Antipsychotics- Atypicals

Paliperidone palmitate, the active ingredient of Invega® Hafyera, is hydrolyzed to paliperidone, which is the major active metabolite of risperidone. It is an atypical antipsychotic and while its mechanism of action is unclear, its efficacy in the treatment of schizophrenia may be mediated through a combination of central dopamine D2 and serotonin 5HT2A receptor antagonism. It is indicated as an every-six-month injection, indicated for the treatment of schizophrenia in adults after they have been adequately treated with: A once-a-month paliperidone palmitate extended-release injectable suspension (e.g. Invega® Sustenna) for at least four months, or An every-three-month paliperidone palmitate extended-release injectable suspension (e.g. Invega® Trinza) for at least one three-month cycle. The safety and efficacy of Invega® Hafyera were assessed in a randomized, double-blind, active-controlled, interventional, parallel-group, multicenter, non-inferiority study that included patients with schizophrenia who had previously been stably treated with either PP1M for at least 4 months or PP3M for at least one 3-month injection cycle. In a double-blind, active-controlled, multicenter, non-inferiority study, a relapse event was experienced by 7.5% of the Invega® Hafyera group as compared with 4.9% of the PP3M group, which demonstrated non-inferiority of Invega® Hafyera to PP3M.

Recommendation: Invega® Hafyera to non-preferred.

Clinical 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. Non preferred atypicals will be approved for patients with FDA-approved indications, and for specific conditions supported by at least two published peer-reviewed double-blinded, placebo-controlled randomized trials that are not contradicted by other studies of similar quality and as long as all first line preferred therapies have been tried and failed at full therapeutic doses for adequate durations (at least two weeks).

Lybalvi® (olanzapine and samidorphan L-malate); **PDL category**- Antipsychotics- Atypicals

Lybalvi® is a combination of olanzapine (an atypical antipsychotic) and samidorphan (as samidorphan L-malate; an opioid antagonist). The mechanism of action of olanzapine is not clear; however, its efficacy in the treatment for its approved indications could be mediated through a combination of dopamine and serotonin type 2 (5HT2) antagonism. The mechanism of action of samidorphan may be mediated through opioid receptor antagonism. It is indicated for the for the treatment of Schizophrenia in adults, Bipolar I disorder in adults: Acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate, Maintenance monotherapy treatment. The safety and efficacy of Lybalvi® for the treatment of schizophrenia in adults is based, in part, upon adequate and well-controlled studies of orally administered olanzapine. The efficacy of Lybalvi® was also assessed in a 4-week, randomized, double-blind, placebo- and active-controlled study (study 1). In this study, adults met DSM-5 criteria for schizophrenia and were randomized to Lybalvi®, olanzapine, or placebo for 4 weeks of daily dosing. The study was designed to compare Lybalvi® with placebo, not with olanzapine. In a double-blind, placebo- and active controlled study that included adults who met DSM-5 criteria for schizophrenia, adults were randomized to Lybalvi®, olanzapine, or placebo; however, the study was designed to compare Lybalvi® with placebo, not with olanzapine. Results suggested that compared with placebo, a statistically significant improvement in the change from baseline in PANSS total score at week 4 was observed in patients treated with Lybalvi®. The inclusion of samidorphan in Lybalvi® did not appear to negatively impact the antipsychotic efficacy of olanzapine. Furthermore, in a second study that compared Lybalvi® with olanzapine in patients with schizophrenia, weight gain was assessed. Treatment with Lybalvi® was associated with statistically significantly less weight gain than olanzapine alone and with a smaller proportion of patients who gained ≥10% body weight.

Recommendation: Lybalvi® to non-preferred.

Clinical 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. Non preferred atypicals will be approved for patients with FDA-approved indications, and for specific conditions supported by at least two published peer-reviewed double-blinded, placebo-controlled randomized trials that are not contradicted by other studies of similar quality and as long as all first line preferred therapies have been tried and failed at full therapeutic doses for adequate durations (at least two weeks).

Loreev® XR (lorazepam capsule, extend release) **PDL category-** Anxiolytics- Benzodiazepines

Lorazepam, the active ingredient of Loreev® XR, is a benzodiazepine that exerts its effect for the treatment of anxiety disorders through binding to the benzodiazepine site of the gamma-aminobutyric acid-A (GABA-A) receptors in the brain and enhances GABA-mediated synaptic inhibition. It is indicated for the treatment of anxiety disorders in adults who are receiving stable, evenly divided, three times daily dosing with lorazepam tablets. There were no clinical trials in the Loreev® XR prescribing information. The safety of Loreev® XR is based on studies with lorazepam tablets. Lorazepam tablets, available both generically and under the brand name Ativan®, have been available for many years and have been found to be effective in the treatment of anxiety disorders or for the short-term relief of the symptoms of anxiety or anxiety associated with depressive symptoms. The effectiveness of Loreev® XR use for more than 4 months has not been assessed in clinical studies; thus, healthcare providers should periodically re-evaluate longer term use of Loreev® XR. There were no clinical trials in the Loreev® XR prescribing information, but the safety of Loreev® XR in adults is based on studies with lorazepam tablets. Lorazepam tablets have been available for many years. This formulation provides physicians a treatment option that allows for once daily dosing.

Recommendation: Loreev® XR to non-preferred.

Clinical 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.

Exkivity® (mobovertinib); **PDL category**- Cancer

Mobocertinib, the active ingredient of Exkivity®, is a kinase inhibitor. It is a kinase inhibitor of the epidermal growth factor receptor (EGFR) that irreversibly binds to and inhibits EGFR exon 20 insertion mutations at lower concentrations than wild type (WT) EGFR. It is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). The safety and efficacy of Exkivity® were assessed in a pooled subset of patients with EGFR exon 20 insertion mutation-positive metastatic or locally advanced NSCLC whose disease had progressed on or after platinum-based chemotherapy enrolled in an international, open-label, multicohort trial. Patients had histologically or cytologically confirmed locally advanced or metastatic disease and a documented EGFR exon 20 insertion mutation based on local testing. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). In a pooled subset of patients with EGFR exon 20 insertion mutation-positive metastatic or locally advanced NSCLC whose disease had progressed on or after platinum-based chemotherapy enrolled in an open-label, multicohort clinical trial, the overall response rate was 28%. All responses were partial responses.

Recommendation: Exkivity® to non-preferred.

Clinical 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

Welireg® (belzutifan); **PDL category**- Cancer

Belzutifan, the active ingredient of Welireg®, is an inhibitor of hypoxia-inducible factor-2α (HIF-2α). HIF-2α is a transcription factor that plays a role in oxygen sensing by regulating genes that promote adaptation to hypoxia. Under normal oxygen levels, HIF-2α is targeted for ubiquitin-proteasomal degradation by VHL protein. Lack of functional VHL protein results in stabilization and accumulation of HIF-2α. Upon stabilization, HIF-2α translocates into the nucleus and interacts with hypoxia-inducible factor 1 beta (HIF-1β) to form a transcriptional complex that induces expression of downstream genes, including genes associated with cellular proliferation, angiogenesis, and tumor growth. Belzutifan binds to HIF-2α, and in conditions of hypoxia or impairment of VHL protein function, belzutifan blocks the HIF-2α-HIF-1β interaction, leading to reduced transcription and expression of HIF-2α target genes. In vivo, belzutifan demonstrated anti-tumor activity in animal models of renal cell carcinoma. it is indicated for the treatment of adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery. he safety and efficacy of Welireg® were assessed in an open-label clinical trial (Study 004) that included patients with VHL-associated RCC (N=61) diagnosed based on a VHL germline alteration and with at least one measurable solid tumor localized to the kidney as defined by response evaluation criteria in solid tumors (RECIST) v1.1. Included patients had other VHL-associated tumors including CNS hemangioblastomas and pNET. In an open-label study that included a small population with VHL-associated RCC diagnosed based on a VHL germline alteration and with at least one measurable solid tumor localized to the kidney, the overall response rate (the major efficacy endpoint) was 49%.

Recommendation: Welireg® to non-preferred.

Clinical 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

Bylvay® (odevixibat); **PDL category**- GI- IBAT Inhibitors

Odevixibat, the active ingredient of Bylvay®, is a reversible inhibitor of the ileal bile acid transporter (IBAT). It decreases the reabsorption of bile acids (primarily the salt forms) from the terminal ileum. Although the complete mechanism by which odevixibat improves pruritus in progressive familial intrahepatic cholestasis (PFIC) patients is not known, it may involve inhibition of the IBAT, which results in decreased reuptake of bile salts, as observed by a decrease in serum bile acids. It is indicated for the treatment of pruritus in patients 3 months of age and older with progressive familial intrahepatic cholestasis. Bylvay® may not be effective in PFIC type 2 patients with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3). The safety and efficacy of Bylvay® were assessed in a randomized, double-blind, placebo-controlled trial of 24 week duration that included pediatric patients (Trial 1, N=62) aged 6 months to 17 years, with a confirmed molecular diagnosis of PFIC type 1 or type 2 and the presence of pruritus at baseline. Bylvay® may not be effective in PFIC type 2 patients with ABCB11 variants resulting in non-functional or complete absence of bile salt export pump protein (BSEP-3). Obtain

baseline liver tests and monitor during treatment with Bylvay®. In addition, obtain serum fat-soluble vitamin (FSV) levels at baseline and monitor during treatment, along with any clinical manifestations. If FSV deficiency is diagnosed, supplement with FSV. In a 24-week, randomized, double-blind, placebo-controlled trial that included pediatric patients aged 6 months to 17 years with a confirmed molecular diagnosis of PFIC type 1 or type 2 and presence of pruritus at baseline (N=62), patients treated with Bylvay® demonstrated greater improvement in pruritus compared with placebo.

Recommendation: Bylvay® to non-preferred.

Clinical criteria:

- For the treatment of patients ≥ 3months of age.
- Clinical PA required for appropriate diagnosis.

Livmarli® (maralixibat); **PDL category**- GI- IBAT Inhibitors

Maralixibat, the active ingredient of Livmarli®, is a reversible inhibitor of the ileal bile acid transporter (IBAT). It decreases the reabsorption of bile acids (primarily the salt forms) from the terminal ileum. Pruritus is a common symptom in patients with Alagille syndrome (ALGS) and the pathophysiology of pruritus in patients with ALGS is not completely understood. While the complete mechanism by which maralixibat improves pruritus in ALGS patients is not known, it may involve inhibition of the IBAT, which results in decreased reuptake of bile salts, as observed by a decrease in serum bile acids. It is indicated for the treatment of cholestatic pruritus in patients with ALGS 1 year of age and older. The safety and efficacy of Livmarli® were assessed in Trial 1, which consisted of an 18-week, open-label treatment period; a 4-week randomized, double-blind, placebo-controlled, drug-withdrawal period; a subsequent 26-week, open-label treatment period; and a long-term open-label extension period. In one small study that included pediatric ALGS patients with cholestasis and pruritus, on average, patients administered Livmarli® for 22 weeks maintained pruritus reduction whereas those in the placebo group who were withdrawn from Livmarli® after 18 weeks returned to baseline pruritus scores by week 22.

Recommendation: Livmarli® to non-preferred.

Clinical criteria:

- For the treatment of patients ≥ 3months of age.
- Clinical PA required for appropriate diagnosis.

Rezurock® (belumosudil); **PDL category**- Immunosuppressants

Belumosudil, the active ingredient of Rezurock®, is a kinase inhibitor. It is an inhibitor of rho-associated, coiled-coil containing protein kinase (ROCK) which inhibits ROCK2 and ROCK1. Belumosudil down-regulated proinflammatory responses via regulation of STAT3/STAT5 phosphorylation and shifting Th17/Treg balance in in-vitro human T cell assays. Belumosudil also inhibited aberrant pro-fibrotic signaling, in-vitro. It is indicated for the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (chronic GVHD) after failure of at least 2 prior lines of systemic therapy. The safety and efficacy of Rezurock® were assessed in a randomized, open-label, multicenter study that included patients with chronic GVHD who had received 2 to 5 prior lines of systemic therapy and required additional treatment. t is treatment that focuses on both inflammation and fibrosis. In a randomized, open-label, single-arm study that included patients with chronic GVHD who had received 2 to 5 prior lines

of systemic therapy and required additional treatment (N=65), results of the primary endpoint of overall response rate was 75%.

Recommendation: Rezurock® to non-preferred.

Clinical criteria: For the treatment of adult and pediatric patients 12 years and older with chronic graft-versus-host disease (chronic GVHD) after failure of at least 2 prior lines of systemic therapy.

Trudhesa® (dihydroergotamine mesylate spray); **PDL category**- Diuretics

Dihydroergotamine, the active ingredient of Trudhesa®, binds with high affinity to 5-HT1Dα and 5-HT1Dβ receptors. The therapeutic activity of dihydroergotamine in migraine is generally attributed to the agonist effects at 5-HT1D receptors. It is indicated for the acute treatment of migraine with or without aura in adults. It is not indicated for the preventive treatment of migraine. It is not indicated for the management of hemiplegic or basilar migraine. The efficacy of Trudhesa® is based on the relative bioavailability of Trudhesa® nasal spray compared to dihydroergotamine mesylate nasal spray in healthy subjects. The clinical studies described in the prescribing information for Trudhesa® were conducted using dihydroergotamine mesylate nasal spray, which is available under the brand name Migranal®. Migranal® is also available as a generic and has the same indication as Trudhesa®. Neither treatments are approved for use in the pediatric population. However, Trudhesa® uses a different technology, called POD, to deliver dihydroergotamine to the vascular-rich upper nasal area. Both Trudhesa® and Migranal® are manufactured by the same manufacturer (Mipharm, S.p.A. in Milano, Italy).

Recommendation: Trudhesa® to non-preferred.

Clinical 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.

Qulipta® (atogepant); **PDL category**- Migraine, Misc.

Atogepant, the active ingredient of Qulipta®, is a calcitonin gene-related peptide (CGRP) receptor antagonist. It is indicated for the preventive treatment of episodic migraine in adults. The safety and efficacy of Qulipta® for the preventive treatment of episodic migraine were assessed in two randomized, multicenter, double-blind, placebo-controlled studies that included adults with at least a 1-year history of migraine with or without aura, per the International Classification of Headache Disorders (ICHD-3) diagnostic criteria. In two randomized, double-blind, placebo-controlled trials, the primary efficacy endpoint assessed was the change from baseline in mean monthly migraine days (MMD) across the 12-week treatment period. In both studies, results suggested that there was a significantly greater reduction in mean monthly migraine days across the 12-week treatment period in all three Qulipta® treatment doses as compared with placebo. Qulipta® is now the second FDA approved oral CGRP receptor antagonist indicated for the preventive treatment of episodic migraine.

Recommendation: Qulipta® to non-preferred.

Clinical 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.

Nexviazyme® (avalglucosidase alfa-ngpt); **PDL category**- Pompe Disease Agents

Avalglucosidase alfa-ngpt, the active ingredient of Nexviazyme®, is a hydrolytic lysosomal glycogen-specific recombinant human α-glucosidase enzyme conjugated with multiple synthetic bis-mannose-6-phosphate (bis-M6P) -tetra-mannose glycans. It is indicated for the treatment of patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency). The safety and efficacy of Nexviazyme® were assessed in a randomized, double-blind, multicenter study that compared Nexviazyme® to alglucosidase alfa in treatment-naïve patients (N=100) with late-onset Pompe disease (LOPD) for 49 weeks. The trial included an open-label, long-term follow-up phase of up to 5 years, in which patients in the alglucosidase arm were switched to Nexviazyme® treatment. In a clinical study to assess for the safety and efficacy of Nexviazyme®, patients with late-onset Pompe disease were randomized to either Nexviazyme® or alglucosidase alfa (another hydrolytic lysosomal glycogen-specific enzyme indicated for patients with Pompe disease [both late-onset and infantile-onset] under the brand name Lumizyme® manufactured by Genzyme as well). The primary endpoint of the study was the change in FVC (% predicted) in the upright position from baseline to week 49, and the treatment difference of 2.4% favored Nexviazyme®. Statistical superiority of Nexviazyme® over alglucosidase alfa was not achieved.

Recommendation: Nexviazyme® to non-preferred.

Clinical Criteria: For patients 1 year of age and older with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency).

Saphnelo® (anifrolumab-fnia); **PDL category**- SLE

Anifrolumab-fnia, the active ingredient of Saphnelo®, is a type I interferon (IFN) receptor antagonist. It is a human IgG1k monoclonal antibody that binds to subunit 1 of the type I interferon receptor (IFNAR) with high specificity and affinity. This binding inhibits type I IFN signaling, thereby blocking the biologic activity of type I IFNs. Anifrolumab-fnia also induces the internalization of IFNAR1, thus reducing the levels of cell surface IFNAR1 available for receptor assembly. Blockade of receptor mediated type I IFN signaling inhibits IFN responsive gene expression as well as downstream inflammatory and immunological processes. Inhibition of type I IFN blocks plasma cell differentiation and normalizes peripheral T-cell subsets. It is indicated for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), who are receiving standard therapy. The efficacy of Saphnelo® has not been evaluated in patients with severe active lupus nephritis or severe active CNS lupus. Use of Saphnelo® is not recommended in these situations. The safety and efficacy of Saphnelo® were assessed in three 52-week treatment period, multicenter, randomized, double-blind, placebo-controlled trials that included patients diagnosed with SLE per the American College of Rheumatology (1982 reviewed) classification criteria. Three studies assessed the safety and efficacy of Saphnelo®. While in study 2 treatment with anifrolumab-fnia did not result in statistically significant improvements over placebo for the primary endpoint of SRI-4 responder analysis, anifrolumab-fnia 300mg demonstrated statistically significant and clinically meaningful efficacy in overall disease activity compared with placebo in trial 3 for the primary endpoint of BICLA responder analysis. This is the first FDA approval for a type 1 interferon receptor antagonist, offering physicians another treatment option in SLE.

Recommendation: Saphnelo® to non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved (in step order), 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

Azstarys® (serdexmthylphenidate and dexmethylphenidate); **PDL category**- Stimulant- Methylphenidate, Long- Acting

Azstarys® contains dexmethylphenidate (a CNS stimulant) and serdexmethylphenidate (a prodrug of dexmethylphenidate). Each capsule contains a fixed molar ratio of 30% dexmethylphenidate and 70% serdexmethylphenidate. The mode of therapeutic action in ADHD is not known. It is indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in patients 6 years of age and older. The efficacy of Azstarys® for the treatment of ADHD in pediatric patients 6 to 12 years of age was assessed in a randomized, double-blind, placebo-controlled, parallel group, analog classroom study. The pediatric patients (N=150) in this study met Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria for a primary diagnosis of ADHD (combined, inattentive, or hyperactive/impulsive presentation) confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). As with other CNS stimulants for ADHD, Azstarys® has a box warning regarding abuse and dependence. Assess the risk of abuse prior to prescribing and monitor for signs of abuse and dependence while on therapy. In a randomized, double-blind, placebo-controlled analog classroom study that included pediatric patients 6 to 12 years of age who met DSM-5 criteria for ADHD, the mean change from baseline in the SKAMP-Combined scores, averaged across the test day (primary outcome) was statistically significantly lower (improved) with Azstarys® compared to placebo. This product offers physicians another treatment option for ADHD.

Recommendation: Azstarys® to preferred.

Winlevi® (clascoterone); **PDL category**- Topical- Acne Preparations

Clascoterone, the active ingredient of Winlevi®, is an androgen receptor inhibitor. The mechanism of action for its approved indication is not known. It is indicated for the topical treatment of acne vulgaris in patients 12 years of age and older. The safety and efficacy of Winlevi® cream were assessed in two identically-designed multicenter, randomized, double-blind, vehicle-controlled trials for the treatment of acne vulgaris that included subjects 12 years of age and older (N=1421) with facial acne vulgaris. Hypothalamic-pituitary-adrenal (HPA) axis suppression was observed and may occur during or after treatment with clascoterone. If HPA axis suppression develops, an attempt should be made to withdraw the drug. The safety and efficacy of Winlevi® cream were assessed in 2 identically-designed, randomized, double-blind trials that included subjects 12 years of age and older with facial acne vulgaris. More patients in the Winlevi® group obtained IGA success as compared with placebo in both studies, as well as a greater mean percent reduction in inflammatory and non-inflammatory lesions. Per the full-text study by Hebert et al2, more patients achieved IGA success with Winlevi® as compared with vehicle ($p<0.001$ for both studies) at week 12. Comparator studies with other active ingredients were not identified.

Recommendation: Winlevi® to non-preferred.

Clinical Criteria: Limited to 24 months due to the risk of continued bone loss, which may not be reversible.

Opzelura® (ruxolitinib); **PDL category**- Topical- Atopic Dermatitis

Ruxolitinib, the active ingredient of Opzelura®, is a Janus kinase (JAK) inhibitor that inhibits JAK1 and JAK2 which mediate the signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. JAK signaling involves recruitment of STATs (signal transducers and activators of transcription) to cytokine receptors, activation, and subsequent localization of STATs to the nucleus leading to modulation of gene expression. The relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known. It is indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Use of Opzelura® in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended. The safety and efficacy of Opzelura® were assessed in two double-blind, randomized, vehicle-controlled trials of identical design (Trial 1 and Trial 2) that included subjects 12 years of age and older (N=1249) with atopic dermatitis for ≥2 years. Opzelura® has a box warning regarding serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis. Two double-blind, vehicle-controlled studies of identical design assessed the safety and efficacy of Opzelura® in patients 12 years and older with atopic dermatitis. The primary efficacy endpoint, the proportion of subjects at week 8 achieving IGA treatment success was achieved by a larger percent of subjects treated with Opzelura® than with placebo (NNT calculated by CHC was 3 for study 1 and 3 for study 2). Per the full-text study by Papp et al2, the results were significantly different, with significantly more patients achieving IGA treatment success with Opzelura® as compared with placebo ($p<0.0001$) at week 8. The authors concluded that topical JAK and PDE4 inhibitors have promising treatment efficacy and safety for AD patients. Furthermore, tofacitinib 2% BID, ruxolitinib 1.5% BID, and delgocitinib 3% demonstrated superior efficacy over other JAK and PDE4 inhibitors. One network meta-analysis suggests that some topical JAK inhibitors, including ruxolitinib 1.5% BID, may be more effective than topical PDE4 inhibitors and tacrolimus; however, there is no head-to-head evidence at this time to support that Opzelura® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Opzelura® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

Recommendation: Opzelura® to non-preferred.

Clinical Criteria: For the treatment of patients ≥ 12 years of age.

Thyquidity® (levothyroxine sodium); **PDL category**- Thyroid Hormones

Thyquidity® contains synthetic levothyroxine (T4) sodium. Synthetic T4 is chemically identical to that produced in the human thyroid gland and is slightly soluble in water. Thyroid hormones exert their physiologic actions through control of DNA transcription and protein synthesis. Triiodothyronine (T3) and L-thyroxine (T4) diffuse into the cell nucleus and bind to thyroid receptor proteins attached to DNA. This hormone nuclear receptor complex activates gene transcription and synthesis of messenger RNA and cytoplasmic proteins. It is indicated for Hypothyroidism: As a replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism, Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression: As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer. Limitations of

use include: Thyquidity® is not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients as there are no clinical benefits and overtreatment with Thyquidity® may induce hyperthyroidism. Thyquidity® is not indicated for treatment of hypothyroidism during the recovery phase of subacute thyroiditis.

FDA SAFETY ALERTS

None at this time

Board Decision: No action.

ADJOURNMENT: 6:45PM

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