Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

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TO: Maine Drug Utilization Review Board
DATE: 06/13/24
RE: Maine DUR Board Meeting minutes from June 11, 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	
Jacquelyn Hedlund, MD, Optum			X	
Anne-Marie Toderico, PharmD MaineCare Pharmacy Director			X	

Guests of the Board:

CALL TO ORDER: 6:00PM

Erin Ackley called the meeting to order at 6:00 PM.

PUBLIC COMMENTS

Erin Booth from Vertex: Highlighted the attributes of Casgevy.
Daniel Shan from UCB: Highlighted the attributes of Bimzelx.
Paul Isikwe from Biogen: Highlighted the attributes of Zurzuvea.
Nicole Trask from J&J: Highlighted the attributes of Opsynvi.
Terry Dettling from Alexion: Highlighted the attributes of Voydeya.
Dr. Irwin Brodsky from MaineHealth: Highlighted the attributes of glucagon nasal spray.
Sandra Baldinger from Merck: Highlighted the attributes of Winrevair.
Omer Aziz from Teva: Highlighted the attributes of Simlandi.

Board Discussion: Follow-up on glucagon nasal spray will be discussed at the September DUR board meeting.

MAINECARE UPDATE- ANNE-MARIE TODERICO

- The MaineCare PDL has been moved to MaineCare's website www.maine.gov/dhhs/oms/providers/pharmacy-services
- Updates on the state's recovery from the Change Healthcare cyber attack can be found on the MaineCare listserv www.maine.gov/dhhs/oms/about-us/mainecare-bulletins
- MaineCare has a Standing Order that pharmacists can use to create prescriptions for OTC oral contraceptives.

OLD BUSINESS

DUR MINUTES

Approval of December DUR meeting minutes

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

NEW CANCER MEDICATIONS

Recommendations: Add Augtyro, Fruzaqla, Iwilfin, Loqtorzi and Truqap 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: The Board unanimously approved all the above recommendations.

NEW DRUG REVIEW

Agamree® (vamorolone oral suspension); **PDL category-** Muscular Dystrophy Agents

Vamorolone, the active ingredient of Agamree®, is a corticosteroid. It acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. The exact mechanism by which vamorolone exerts its effect in patients with Duchenne muscular dystrophy is not known. It is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older. The efficacy of Agamree® for the treatment of DMD was assessed in a multicenter, randomized, double-blind, parallel-group, placebo- and active-controlled study of 24 weeks in duration which included male patients (N=121) with DMD. The primary endpoint being the change from baseline to week 24 in Time to Stand Test (TTSTAND) velocity for Agamree® 6mg/kg/day as compared to placebo. Statistically significant differences in favor of Agamree® 6mg/kg/day were observed as compared to placebo for the primary endpoint, as well as key secondary endpoints of 6MWT distance and TTRW velocity. There is some evidence to suggest that Agamree® may be safer than prednisone when used as treatment for males with DMD in a phase 3 efficacy trial; however, there is no evidence at this time to support that Agamree® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Agamree® to non-preferred.

Criteria:

- Add For the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older.
- 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.

Board Decision: The Board unanimously approved all the above recommendations.

Bimzelx® (bimekizumab-bkzx); **PDL category-** Psoriasis Biologicals

Bimekizumab-bkzx, the active ingredient of Bimzelx®, is an interleukin (IL)-17 A and F antagonist. It is a recombinant humanized immunoglobulin G1 (IgG1) monoclonal antibody with two identical antigen binding regions that selectively bind to human IL-17A, IL-17F, and interleukin 17-AF cytokines, and inhibits their interaction with the IL-17 receptor complex. IL-17A and IL-17F are naturally occurring cytokines that are involved in normal inflammatory and immune responses. Bimekizumab-bkzx inhibits the release of proinflammatory cytokines and chemokines. It is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. There are 3 multicenter, randomized, double-bind trials (Trial-Ps-1, Trial-Ps-2, and Trial-Ps-3) that assessed the safety and efficacy of Bimzelx® and included adults 18 years of age and older (N=1480) with moderate to severe plaque psoriasis who had a body surface area (BSA) involvement of ≥10%, an Investigator's Global Assessment (IGA) score of ≥3 ('moderate') in the overall assessment of psoriasis on a severity scale of 0 to 4, and a Psoriasis Area and Severity Index (PASI) score ≥12. There is some evidence in a phase 3 study to suggest that Bimzelx® may be more effective than ustekinumab and may be more effective than adalimumab for the endpoints of PASI 90 response and an IGA score of 0 or 1 (with at least a 2-grade improvement from baseline) at week 16. There is also some evidence that Bimzelx® may be more effective than secukinumab in a double-blind study for PASI 100 response; however, there is no evidence at this time to support that Bimzelx® is safer or more effective than all currently preferred, more cost-effective medications.

Recommendation: Bimzelx® to non-preferred.

Criteria:

- Add For the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Board Decision: The Board unanimously approved all the above recommendations.

Cabtreo® Gel (adapalene,benzol peroxide,clindamycin topical gel); **PDL category-** Topical Acne Agents

Cabtreo® is a combination product that contains clindamycin (a lincosamide antibacterial), adapalene (binds to specific retinoic acid nuclear receptors; a modulator of cellular differentiation, keratinization, and inflammatory processes) and benzoyl peroxide (an oxidizing agent with bactericidal and keratolytic effects). It is indicated for the topical treatment of acne vulgaris in adult and pediatric patients 12 years of age and older. The efficacy of Cabtreo® was assessed in two multicenter, randomized, double-blind clinical trials (Trial 1 and Trial 2) in adult and pediatric subjects 10 years of age and older (N=363) with facial acne vulgaris. Note that while subjects aged 10 to less than 12 years of age were included in these trials, Cabtreo® is not approved for use in patients less than 12 years of age. The co-primary efficacy endpoints of success on the EGSS, absolute change in non-inflammatory lesion count, and absolute change in inflammatory lesion count were assessed at week 12. More achieved success on the EGSS in the Cabtreo® group vs the vehicle group, while also having a greater mean percent reduction and mean absolute reduction in both non-inflammatory and inflammatory facial lesions. Cabtreo® is the first triple-combination gel FDA approved for facial acne.

Recommendation: Cabtreo® Gel to non-preferred.

Criteria:

- Add Not approved for use in children <12 years of age
- 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.

Board Decision: The Board unanimously approved all the above recommendations.

Casgevy® (exagamglogene autotemcel (exa-cell)); **PDL category**- Sickle Cell Disease

Casgevy® (exagamglogene autotemcel) is a cellular gene therapy consisting of autologous CD34+ hematopoietic stem cells (HSCs) edited by CRISPR/Cas9-technology at the erythroid specific enhancer region of the BCL11A gene to reduce BCL11A expression in erythroid lineage cells, leading to increased fetal hemoglobin (HbF) protein production. The formulation contains 5% dimethyl sulfoxide (DMSO) and dextran 40. It is indicated for the treatment of patients aged 12 years and older with: Sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs). Transfusion-dependent β-thalassemia (TDT). The safety and efficacy of Casgevy® were assessed in Trial 1, an ongoing single-arm, multicenter trial that included adults and adolescent patients with sickle cell disease (SCD) who received a single dose of Casgevy®. In an ongoing single-arm study for TDT, an interim analysis was conducted. In the interim analysis, the TI12 responder rate was 91.4% (32 out of 35). All patients who achieved TI12 remained transfusion-independent, with a median duration of transfusion-independence of 20.8 months and normal mean weighted average total Hb levels. Casgevy® is the first approval of a CRISPR-based therapy approved in the US, and is one of two gene therapies approved for patients with SCD.

Recommendation: Casgevy® to non-preferred.

Criteria:

- Add For the treatment of patients ≥ 12 years of age.
- Add PA required to confirm FDA approved indication.

Board Decision: The Board unanimously approved all the above recommendations.

Eohilia® (budesonide oral suspension); **PDL category-** GI- Eosinophilic Esophagitis

Budesonide, the active ingredient of Eohilia®, is a synthetic corticosteroid; it is an anti-inflammatory corticosteroid and has a high glucocorticoid effect and a weak mineralocorticoid effect. Corticosteroids have a wide range of inhibitory activities against multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukocytes, and cytokines) involved in allergic inflammation. However, the exact mechanism of action for its approved indication is not known. It is indicated for 12 weeks of treatment in adult and pediatric patients 11 years of age and older with eosinophilic esophagitis (EoE). A limitation of use includes that Eohilia® has not been shown to be safe and effective for the treatment of EoE for longer than 12 weeks. The safety and efficacy of Eohilia® were assessed in two multicenter, randomized, double-blind, placebo-controlled, parallel-group studies. Both studies assessed efficacy endpoints of histologic remission (defined as a peak eosinophil count of ≤6/hpf across all available esophageal levels) and the

absolute change from baseline in subject-reported DSQ combined score after 12 weeks of treatment. er the full text study by Dellon et al (Study 2), significantly more in the Eohilia® group achieved histologic response endpoint as compared with placebo ($p<0.0001$). Per the full-text study by Hirano et al (Study 1), significantly more achieved histologic response with Eohilia® ($p<0.001$). While dietary modification, PPIs, and topical glucocorticoids are generally utilized for this diagnosis as initial treatment, Eohilia® is the first FDA approved oral treatment for EoE, to be used for 12 weeks in patients 11 years and older. Budesonide oral suspension is suggested if topical glucocorticoid therapy is to be utilized.

Recommendation: Eohilia® to non-preferred. Clinical

Criteria:

- Add new sub-category GI- Eosinophilic Esophagitis
- Approvals will not be longer than 12 weeks of treatment in adult and pediatric patients 11 years of age and older
- 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.
- Eohilia: Dietary modification, PPIs, and topical glucocorticoids are required as initial therapy.

Board Decision: The Board unanimously approved all the above recommendations.

Fabhalta® (iptacopan); **PDL category-** Monoclonal Antibody

Iptacopan, the active ingredient of Fabhalta®, is a complement Factor B inhibitor. Iptacopan binds to Factor B of the alternative complement pathway and regulates the cleavage of C3, generation of downstream effectors, and the amplification of the terminal pathway. In paroxysmal nocturnal hemoglobinuria, intravascular hemolysis (IVH) is mediated by the downstream membrane attack complex (MAC), while extravascular hemolysis (EVH) is facilitated by C3b opsonization. Iptacopan acts proximally in the alternative pathway of the complement cascade to control both C3b-mediated EVH and terminal complement-mediated IVH. It is indicated for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH). The efficacy of Fabhalta® in adults with PNH was assessed in a multicenter, open-label, 24-week, active comparator-controlled trial (APPLY-PNH) that included adults with PNH and residual anemia (hemoglobin <10g/dl) despite previous treatment with a stable regimen of anti-C5 treatment (either eculizumab or ravulizumab) for at least 6 months prior to randomization. fficacy was established based on demonstration of superiority of switching to Fabhalta® compared to continuing on anti-C5 therapy in achieving hematological response after 24 weeks of treatment, without a need for transfusion, by assessing the proportion of patients demonstrating a sustained increase of ≥2g/dL in hemoglobin levels from baseline (hemoglobin improvement), as well as sustained hemoglobin levels ≥12g/dL. Results suggested that Fabhalta® was statistically significantly more effective than continuing anti-C5 treatment for the primary endpoints, as well as the various secondary endpoints assessed. There is some evidence in a phase 3 study to suggest Fabhalta® may be more effective than anti-C5 treatment (eculizumab or ravulizumab) for the primary endpoints of proportion of patients demonstrating sustained increase of ≥2g/dL in hemoglobin levels from baseline and sustained hemoglobin levels ≥12g/dL. However, there is no evidence at this time to support that Fabhalta® is safer or more effective than the other currently available medications. I

Recommendation: Fabhalta® to non-preferred. Clinical

Criteria:

- Add Fabhalta and Ultomiris is recommended for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH).

Board Decision: The Board unanimously approved all the above recommendations.

Furoscix® (furosemide injection); **PDL category-** Diuretics

Furosemide, the active ingredient of Furoscix®, is a loop diuretic, which is an anthranilic acid derivative. It mainly inhibits the reabsorption of sodium and chloride in the proximal and distal tubules and in the loop of Henle. The high degree of diuresis is mainly due to the unique site of action. The action on the distal tubule is independent of any inhibitor effect on carbonic anhydrase and aldosterone. It is indicated for the treatment of congestion due to fluid overload in adult patients with New York Heart Association (NYHA) Class II and Class III chronic heart failure. Limitations of use include that Furoscix® is not indicated for use in emergency situations or in patients with acute pulmonary edema. The On-Body Infusor will deliver only an 80mg-dose of Furoscix®. There was no clinical trial section found in the prescribing information for Furoscix®. Furoscix® is not indicated for use in emergency situations or in patients with acute pulmonary edema. There is no evidence at this time to support that Furoscix® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Furoscix® to non-preferred.

Criteria:

- Add The indication for use is the treatment of congestion due to fluid overload in adults with NYHA Class II or Class III chronic heart failure AND the medication is being prescribed by or in consultation with a cardiologist AND the patient is experiencing symptoms despite compliance with oral loop diuretic therapy AND oral loop diuretic therapy will be resumed as soon as practical AND medical reasoning beyond convenience is provided for not pursuing therapy in an outpatient infusion setting. PA approval will be authorized for 1 month.

Board Decision: The Board unanimously approved all the above recommendations.

Jylamvo® (methotrexate oral solution); **PDL category-** Rheumatoid Arthritis

Methotrexate, the active ingredient of Jylamvo®, inhibits dihydrofolic acid reductase. Dihydrofolates must be reduced to tetrahydrofolates by this enzyme before they can be utilized as carriers of one-carbon groups in the synthesis of purine nucleotides and thymidylate. Thus, methotrexate interferes with DNA synthesis, repair, and cellular replication. The mechanism of action in RA and psoriasis is not known. It is indicated for the treatment of adults: with neoplastic diseases. With acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen. With mycosis fungoides (cutaneous T-cell lymphoma) as a single agent or as part of a combination chemotherapy regimen. With relapsed or refractory non-Hodgkin lymphomas as part of a metronomic combination chemotherapy regimen. With rheumatoid arthritis (RA). With severe psoriasis. There were no clinical trials included in the Jylamvo® prescribing information. Methotrexate tablets, oral solution in a different dose, and injectable methotrexate have been available for many years and have the same indications as Jylamvo®.

Recommendation: Jylamvo® to non-preferred.

Criteria:

- Update sub-category to say Rheumatoid Arthritis/Ulcerative Colitis
- Jylamvo will require using preferred methotrexate if unable please provide clinical rational as why inappropriate.

Board Decision: The Board unanimously approved all the above recommendations.

Likmez® (metronidazole); **PDL category-** Antibiotics, Misc

Metronidazole, the active ingredient of Likmez®, is a nitroimidazole antimicrobial. Once metronidazole enters the organism by passive diffusion and activated in the cytoplasm of susceptible anaerobic bacteria, it is reduced. Because of this alteration of the metronidazole molecule, a concentration gradient is created and maintained, which promotes the drug's intracellular transport. The reduced form of metronidazole and free radicals can interact with DNA, leading to inhibition of DNA synthesis and DNA degradation leading to death of the bacteria. The exact mechanism of action of metronidazole is not clear. It is indicated for the treatment of:

- Trichomoniasis:
  - Symptomatic trichomoniasis caused by *Trichomonas vaginalis* in adult females and males when the diagnosis is confirmed by appropriate laboratory procedures.
  - Asymptomatic trichomoniasis caused by *Trichomonas vaginalis* in adult females when the organism is associated with endocervicitis, cervicitis, or cervical erosion.
  - Because trichomoniasis is a sexually transmitted disease with potentially serious sequelae, treat sexual partners of patients simultaneously to prevent re-infection.
- Amebiasis:
  - For the treatment of acute intestinal amebiasis (amoebic dysentery) and amebic liver abscess in adults and pediatric patients. In amebic liver abscess, treatment with Likmez® does not obviate the need for aspiration or drainage of pus.
  - Anaerobic Bacterial Infections: Likmez® is indicated in the treatment of the following serious infections caused by susceptible anaerobic bacteria in adults:
  - Intra-abdominal infections, including peritonitis, intra-abdominal abscess, and liver abscess
  - Skin and skin structure infections
  - Gynecologic infections, including endometritis, endomyometritis, tubo-ovarian abscess, and postsurgical vaginal cuff infection.
  - Bacterial septicemia
  - Bone and joint infections (as adjunctive therapy)
  - Central nervous system (CNS) infections, including meningitis and brain abscess
  - Lower respiratory tract infections, including pneumonia, empyema, and lung abscess
  - Endocarditis

There was no clinical trials section in the Likmez® prescribing information. Metronidazole tablets and brand Flagyl® (metronidazole) capsules have been available for many years and have the same indications as Likmez® suspension.

Recommendation: Likmez® to non-preferred.

Criteria:

- Add Likmez: patient has a medical necessity for a non-solid oral dosage form.

Board Decision: The Board unanimously approved all the above recommendations.

Lyfgenia® (lovotibeglogene autoemcel); **PDL category- Sickle** Cell Disease

Lyfgenia® (lovotibeglogene autotemcel) is a βA-T87Q-globin gene therapy consisting of autologous CD34+ cells from patients with sickle cell disease containing hematopoietic stem cells (HSCs) transduced with BB305 lentiviral vector (LVV) encoding βA-T87Q-globin, suspended in cryopreservation solution. Lyfgenia® is to be administered one-time to add functional copies of a modified form of the β-globin gene (βA-T87Q-globin gene) into the patient's own HSC. It is indicated for he treatment of patients 12 years of age or older with sickle cell disease (SCD) and a history of vaso-occlusive (VOC) events. A limitation of use includes that following treatment with Lyfgenia®, patients with α-thalassemia trait (-α3.7/-α3.7) may experience anemia with erythroid dysplasia that may require chronic red blood cell (RBC) transfusions. Lyfgenia® has not been studied in patients with more than two α-globin gene deletions. The efficacy of Lyfgenia® was assessed in a single-arm, 24-month, open-label, multicenter Phase 1/2 study (Study 1-C) and continued on a long-term follow-up study. In this Study 1-C, patients (N=43) underwent apheresis after mobilization with plerixafor, of which 36 received myeloablative busulfan conditioning. The efficacy of Lyfgenia® was assessed in a single-arm, 24-month, open-label study. The efficacy outcome of complete resolution of VOEs (VOE-CR) between 6 and 18 months after Lyfgenia® infusion was achieved by 88% (N=28/32), while the efficacy outcome of complete resolution of severe VOEs (sVOE-CR) was achieved by 94% (N=30/32).

Recommendation: Lyfgenia® to non-preferred.

Criteria:

- Add For the treatment of patients ≥ 12 years of age.
- Add PA required to confirm FDA approved indication.

Board Decision: The Board unanimously approved all the above recommendations.

Omvoh® (mirikizumab-mrkz); **PDL category-** Rheumatoid Arthritis

Mirikizumab-mrkz, the active ingredient of Omvoh®, is a humanized immunoglobulin G4 (IgG4) variant monoclonal antibody that is directed against the p19 subunit of IL-23 and does not bind IL-12. It selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor. Note that IL-23 is involved in mucosal inflammation and affects the differentiation, expansion, and survival of T cell subsets, and innate immune cell subsets, which represent sources of pro-inflammatory cytokines. Mirikizumab-mrkz inhibits the release of pro-inflammatory cytokines and chemokines. It is indicated for the the treatment of moderately to severely active ulcerative colitis (UC) in adults. The safety and efficacy of Omvoh® were assessed in 2 randomized, double-blind, placebo-controlled studies, with one being an induction study (UC-1) and one being a maintenance study (UC-2), that included adults with moderately to severely active ulcerative colitis who had inadequate response, loss of response, or failed to tolerate any of the following, including corticosteroids, 6-mercaptopurine, azathioprine, biologic therapy (TNF blocker, vedolizumab), or tofacitinib. The primary endpoint of study 1 was clinical remission at week 12, and significantly more in the Omvoh® 300mg IV group achieved

clinical remission compared with placebo (p<0.001). The primary endpoint in study 2 was clinical remission at week 40, and significantly more in the Omvoh® 200mg SC group achieved clinical remission as compared with placebo (p<0.001). Head-to-head comparator studies with other active ingredients were not currently found.

Recommendation: Omvoh® to non-preferred.

Board Decision: The Board unanimously approved all the above recommendations.

Opsynvi® (macitentan & tadalafil); **PDL category-** Pulmonary Antihypertensives

Opsynvi® is a single tablet combination containing two oral components used to treat pulmonary arterial hypertension (PAH), including macitentan (an endothelin receptor antagonist [ERA]) and tadalafil (a phosphodiesterase 5 [PDE5] inhibitor). It is indicated for the chronic treatment of adults with pulmonary arterial hypertension (PAH, WHO Group I and WHO Functional Class (FC) II-III). The safety and efficacy of Opsynvi® were assessed in a multinational, multicenter, double-blind, adaptive, randomized, active-controlled, parallel-group study that included patients (N=187) with PAH (WHO FC II-III). The study was designed to compare the safety and efficacy of Opsynvi® to each monotherapy macitentan or tadalafil. he primary endpoint was the change from baseline in PVR (expressed as the ratio of geometric means of end of double-blind treatment to baseline) vs the individual component monotherapies after 16 weeks. Results suggested that Opsynvi® demonstrated greater reduction in PVR after 16 weeks. Regarding tadalafil efficacy, the primary efficacy endpoint of a randomized, 16-week, placebo-controlled study was the change from baseline at week 16 in the 6-minute walk distance. esults suggested that Opsynvi® demonstrated greater reduction in PVR after 16 weeks. Treatment with Opsynvi® resulted in a statistically significant treatment effect of 0.71 (p<0.0001) representing a 29% reduction in PVR as compared to macitentan and of 0.72 (p<0.0001) representing a 28% reduction in PVR as compared to tadalafil. Opsynvi® is the first FDA approved once-daily single-tablet combination treatment for PAH.

Recommendation: Opsynvi® to non-preferred.

Criteria:

- Add Require WHO Group 1 diagnosis of primary PAH (Primary Pulmonary Hypertension) and NYHA (WHO) functional class 2 or 3.

Board Decision: The Board unanimously approved all the above recommendations.

Velsipity® (etrasimond); **PDL category-** Rheumatoid Arthritis

Etrasimod, the active ingredient of Velsipity®, is a sphingosine 1-phosphate (S1P) receptor modulator that binds with high affinity to S1P receptors 1, 4, and 5. It partially and reversibly blocks the capacity of lymphocytes to egress from lymphoid organs, reducing the number of lymphocytes in peripheral blood. The mechanism of action by which etrasimod exerts its therapeutic effects for its approved indication is not known, but may involve the reduction of lymphocyte migration into the intestines. It is indicated for the treatment of moderately to severely active ulcerative colitis (UC) in adults. The efficacy of Velsipity® was assessed in 2 randomized, double-blind, placebo-controlled studies (UC-1 and UC-2) in adults with moderately to severely active ulcerative colitis (UC) who had an inadequate response, loss of response, or intolerance to one or more of the following treatment options, including oral aminosalicylates, corticosteroids, thiopurines, Janus kinase (JAK) inhibitors, or biologic therapies (e.g., TNF blocker, anti-

integrin, anti-IL12/23). In both studies, subjects were randomized to Velsipity® or placebo and continued on treatment for the entire duration of the study, being 52 weeks with study UC-1 and 12 weeks with study UC-2. The primary endpoint was the proportion of subjects achieving clinical remission at week 12. The secondary endpoints included the proportion of subjects achieving endoscopic improvement and histologic-endoscopic mucosal improvement at week 12. Head-to-head comparator studies with other active ingredients were not currently found.

Recommendation: Velsipity® to non-preferred.

Board Decision: The Board unanimously approved all the above recommendations.

Vevye® (cyclosporine ophthalmic solution 0.1%); **PDL category-** OP. – Of Interest

Cyclosporine, the active ingredient of Vevye®, is a calcineurin inhibitor. It is a relatively selective immunomodulatory drug. It is indicated for the treatment of the signs and symptoms of dry eye disease. The safety and efficacy of Vevye® were assessed in a total of 1,369 patients with dry eye disease, of which 738 received Vevye®. In two multicenter, randomized, adequate and well-controlled studies, patients with dry eye disease were treated with Vevye® or vehicle. Its efficacy was assessed in two randomized controlled studies where Vevye® was compared with vehicle. At day 29, there was a statistically significant higher percentage of eyes with increases of ≥10mm from baseline in Schirmer's wetting with Vevye® as compared with vehicle (NNT 13 study 1, NNT 26 study 2). There are other cyclosporine ophthalmic products available that are also indicated for dry eye disease, including Cequa® (solution 0.9mg/ml, 0.09%) and Restasis® (emulsion 0.05%). Vevye® is the only water-free cyclosporine dissolved in a semi fluorinated alkane, for dry eye disease. Per the manufacturer, this product spreads uniformly over the ocular surface. This product offers prescribers another treatment option.

Recommendation: Vevye® to non-preferred.

Criteria:

- Add Must fail adequate trials of multi agents from artificial tears and lubricant category and a preferred cyclosporine alternative.

Board Decision: The Board unanimously approved all the above recommendations.

Voquezna® (vonoprazan); **PDL category-** GI- Proton Pump Inhibitor

Vonoprazan, the active ingredient of Voquezna®, is a potassium-competitive acid blocker. It suppresses basal and stimulated gastric acid secretion at the secretory surface of the gastric parietal cell through inhibition of the H+, K+ -ATPase enzyme system in a potassium competitive manner. Because this enzyme is regarded as the acid (proton) pump within the parietal cell, vonoprazan has been characterized as a type of gastric proton-pump inhibitor (PPI), in that it blocks the final step of acid production. Vonoprazan does not require activation by acid. It may selectively concentrate in the parietal cells in both the resting and stimulated states. Vonoprazan binds to the active pumps in a non-covalent and reversible manner. It is indicated for healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults. To maintain healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults. In combination with amoxicillin and clarithromycin for the treatment of Helicobacter pylori (H. pylori) infection in adults. In combination with amoxicillin for the treatment of H. pylori infection in adults. The safety and efficacy of Voquezna® for the healing of erosive

esophagitis and relief of heartburn were assessed in a randomized, active-controlled, double-blind, eight-week study conducted in the US and Europe that included adults (N=1024) with endoscopically confirmed erosive esophagitis. There is some evidence at this time from a phase 3 study to suggest that Voquezna® (as triple or dual therapy) may be more effective than lansoprazole (as triple therapy) for treatment of H. pylori infection, and that Voquezna® may be more effective than lansoprazole in maintenance of healed erosive esophagitis.

Recommendation: Voquezna® Tablet to non-preferred GI- Proton Pump Inhibitors category. Add VOQUEZNA DUAL PAK and VOQUEZNA TRIPLE PAK to non-preferred in GI-Ulcer Anti-Infective category.

Board Decision: The Board unanimously approved all the above recommendations.

Voydeya® (danicopan); **PDL category-** Hematological- Monoclonal Antibody

Danicopan, the active ingredient of Voydeya®, is a small molecule complement Factor D inhibitor. It binds reversibly to complement Factor D and selectively inhibits the alternative complement pathway. Danicopan prevents the cleavage of complement Factor B into the Ba and Bb fragments, which are required for the formation of the alternative pathway (AP) complement component C3 convertase (C3bBb), the generation of downstream effectors including C3 fragment opsonization, and the amplification of the terminal pathway. It is indicated as an add-on therapy to ravulizumab or eculizumab for the treatment of extravascular hemolysis (EVH) in adults with paroxysmal nocturnal hemoglobinuria (PNH). A limitation of use includes that Voydeya® has not been shown to be effective as monotherapy and should only be prescribed as an add-on to ravulizumab or eculizumab. The safety and efficacy of Voydeya® were assessed in adults with PNH and clinically significant EVH in a multiple-region, randomized, double-blind, placebo-controlled study. It does have a box warning regarding serious infections caused by encapsulated bacteria. The primary outcome measure was the change in Hgb level from baseline to week 12. Efficacy was established based on the demonstration of superiority of Voydeya® in combination with ravulizumab or eculizumab compared to placebo in combination with ravulizumab or eculizumab in all efficacy measures, with statistically significant results.

Recommendation: Voydeya® to non-preferred.

Board Decision: The Board unanimously approved all the above recommendations.

Wainua® (eplontersen); **PDL category-** Neurologics- hATTR Agents

Eplontersen, the active ingredient of Wainua®, is a transthyretin-directed antisense oligonucleotide (ASO), covalently linked to a ligand containing three N-acetyl galactosamine (GalNAc) residues to enable delivery of the ASO to hepatocytes. It is an antisense oligonucleotide-GalNAc conjugate that causes degradation of mutant and wild-type transthyretin (TTR) mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. It is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. The efficacy of Wainua® was demonstrated in a randomized, open-label, multicenter trial that included adults with polyneuropathy caused by hereditary transthyretin-mediated amyloidosis. fficacy assessments were based on a comparison of Wainua® with an external placebo group in another study comprised of a comparable population of adults with polyneuropathy caused by hATTR amyloidosis. Results suggested that treatment with Wainua® resulted in statistically significant improvements in the mNIS+7 and the Norfolk QoL-DN total scores compared to the external placebo control (both $p<0.001$)

at week 35. Wainua® provides another treatment option for polyneuropathy of hereditary transthyretin-mediated amyloidosis, which can be administered by the patient once monthly and has no box warning.

Recommendation: Wainue® to non-preferred.

Criteria:

- Add PA required for appropriate diagnosis.

Board Decision: The Board unanimously approved all the above recommendations.

Winrevair® (sotatercept-csrk for injection); **PDL category-** Pulmonary Antihypertensives

Sotatercept-csrk, the active ingredient of Winrevair®, is a homodimeric recombinant fusion protein consisting of the extracellular domain of the human activin receptor type IIA (ActRIIA) linked to the human IgG1 Fc domain. Sotatercept-csrk, a recombinant activin receptor type IIA-Fc (ActRIIA-Fc) fusion protein, is an activin signaling inhibitor that binds to activin A and other TGF-β superfamily ligands. As a result, sotatercept-csrk improves the balance between the pro-proliferative and anti-proliferative signaling to modulate vascular proliferation. In animal models of PAH, a sotatercept-csrk analog reduced inflammation and inhibited proliferation of endothelial and smooth muscle cells in diseased vasculature. These cellular changes were associated with thinner vessel walls, partial reversal of right ventricular remodeling, and improved hemodynamics. It is indicated for the treatment of adults with pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group 1) to increase exercise capacity, improve WHO functional class (FC), and reduce the risk of clinical worsening events. The efficacy of Winrevair® was assessed in adult patients with PAH in the STELLAR study, a global, multicenter, double-blind, placebo-controlled, parallel-group clinical trial. The trial included patients (N=323) with PAH (WHO Group 1 FC II or III) who were randomized to Winrevair® (target dose 0.7mg/kg) or placebo administered SC once every 3 weeks. There is some evidence at this time to suggest that Winrevair® plus background therapy is more effective than background therapy alone for the primary endpoint of improved exercise capacity; however, there is no evidence at this time to support that Winrevair® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Winrevair® to non-preferred.

Criteria:

- Add Require WHO Group 1 diagnosis of primary PAH (Primary Pulmonary Hypertension) and NYHA (WHO) functional class 2 or 3.

Board Decision: The Board unanimously approved all the above recommendations.

Xphozah® (tenapanor); **PDL category-** Phosphate Binders

Tenapanor, the active ingredient of Xphozah®, is a locally acting inhibitor that targets the sodium/hydrogen exchanger 3 (NHE3), an antiporter expressed on the apical surface of the epithelium of the small intestine and colon. Inhibition of NHE3 by tenapanor results in reduced sodium absorption and decreased phosphate absorption by reducing phosphate permeability through the paracellular pathway. It is indicated to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who

are intolerant of any dose of phosphate binder therapy. The efficacy of Xphozah® for the ability to lower serum phosphorus in adults with CKD on dialysis was assessed in 3 trials, including TEN-02-201, TEN-02-301, and TEN-02-202. Data from the two phase 3 monotherapy studies suggested that during the randomized withdrawal period, phosphorus levels significantly rose in the placebo group relative to patients who remained on Xphozah®. There is some evidence in a phase 3 study to suggest that Xphozah® in combination with phosphate binder may be more effective for lowering serum phosphorus compared to placebo plus phosphate binder; however, there is no evidence at this time to support that Xphozah® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Xphozah® 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: Xphozah® to non-preferred.

Criteria:

- Add Xphozah to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

Board Decision: The Board unanimously approved all the above recommendations.

Zilbrysq® (zilucoplan); **PDL category-** Neurologics, Misc.

Zilucoplan, the active ingredient of Zilbrysq®, is a complement inhibitor. It binds to the complement protein C5 and inhibits its cleavage to C5a and C5b, preventing the generation of the terminal complement complex, C5b-9. The exact mechanism of action of zilucoplan for its approved indication is not known but it is presumed to involve reduction of C5b-9 deposition at the neuromuscular junction. It is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive. The efficacy of Zilbrysq® for the treatment of gMG in adults who are anti-AChR antibody positive was established in a 12-week, multicenter, randomized, double-blind, placebo-controlled study. At week 12, treatment with Zilbrysq® demonstrated a statistically significant improvement from baseline compared to placebo for MG-ADL total score (primary endpoint) and QMG total score. Zilbrysq® is the first FDA-approved treatment for adults with anti-AChR antibody-positive gMG that may be self-administered.

Recommendation: Zilbrysq® to non-preferred. Remove Prostigmin tabs from the PDL.

Criteria:

- Add new sub-category Myasthenia Gravis.
- Add For the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AChR) antibody positive.
- Add Zilbrysq recommended to vaccinate patients for meningococcal infection per current Advisory Committee on Immunization Practices (ACIP) recommendations at least 2 weeks prior to administering the first dose.

Board Decision: The Board unanimously approved all the above recommendations.

Zituvio® (sitagliptin); **PDL category-** Diabetic- DPP-4 Enzyme Inhibitors

Sitagliptin free base, the active ingredient of Zituvio®, is a dipeptidyl peptidase-4 (DPP-4) inhibitor, which

is thought to exert its actions in patients with type 2 DM by slowing the inactivation of incretin hormones. Concentrations of the active intact hormones are increased by sitagliptin, thus increasing and prolonging the action of these hormones. Incretin hormones (including glucagon-like peptide-1 [GLP-1] and glucose-dependent insulinotropic polypeptide [GIP]) are released by the intestine and levels are increased in response to a meal. These hormones are rapidly inactivated by the enzyme, DPP-4. It is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (DM). There were about 5200 patients with type 2 DM randomized in 9 double-blind, placebo-controlled clinical safety and efficacy trials conducted to evaluate the effectiveness of sitagliptin on glycemic control. In patients with type 2 DM, treatment with sitagliptin produced clinically significant improvements in A1c, fasting plasma glucose (FPG), and 2-hour post-prandial glucose (PPG) compared to placebo. The studies found in the Zituvio® prescribing information were the same as those found in the Januvia® prescribing information, which is a brand name for sitagliptin that has been available for several years.

Recommendation: Zituvio® to non-preferred.

Board Decision: The Board unanimously approved all the above recommendations.

Zoryve® Foam (roflumilast topical foam); **PDL category-** Topical- Antiseborrheics

Roflumilast, the active ingredient of Zoryve®, and its active metabolite (roflumilast N-oxide) are inhibitors of phosphodiesterase 4 (PDE4). Roflumilast and roflumilast N-oxide inhibition of PDE4 (a major cyclic 3'5'-adenosine monophosphate [cyclic AMP] metabolizing enzyme) activity leads to accumulation of intracellular cyclic AMP. The specific mechanism(s) by which roflumilast exerts its therapeutic action is not well defined. It is indicated for the treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older. The efficacy of Zoryve® foam was assessed in two randomized, double-blind, vehicle-controlled trials that included adult and pediatric subjects (N=683 total) with seborrheic dermatitis involving the scalp, face, and/or body with an Investigator Global Assessment (IGA) of moderate or severe (IGA of 3 or 4 on a 5-point scale from 0-4). In each trial, subjects were randomized to receive Zoryve® foam or vehicle foam applied once daily for 8 weeks. The primary endpoint was the proportion of subjects who achieved IGA treatment success at week 8, with success being defined as a score of 'clear' (0) or 'almost clear' (1), plus a 2-grade improvement from baseline. More in the Zoryve® foam group achieved IGA success as compared with the vehicle foam. Per the full-text study (STRATUM) by Blauvelt et al[2], the results for IGA success were statistically significantly in favor of Zoryve® foam ($p<0.001$). Head-to-head studies with other active ingredients were not found.

Recommendation: Zoryve® Foam to non-preferred.

Criteria:

- Add Zoryve Foam: For the treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older.

Board Decision: The Board unanimously approved all the above recommendations.

Zurzuvae® (zuranolone); **PDL category-** Antidepressants- Selected SSRIs and Others

Zuranolone, the active ingredient of Zurzuvae®, is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator. The mechanism of action of zuranolone in the treatment of

postpartum depression is not fully understood but is thought to be related to its positive allosteric modulation of GABA-A receptors. It is indicated for the treatment of postpartum depression (PPD) in adults. The efficacy of Zurzuvae® for the treatment of PPD in adults was demonstrated in two randomized, placebo-controlled, double-blind, multicenter studies (Study 1 and Study 2) that included women with PPD who met the DSM-5 criteria for a major depressive episode with onset of symptoms in the third trimester or within 4 weeks of delivery. The primary endpoint for both studies was the change from baseline in depressive symptoms as measured by the HAMD-17 total score at day 15. In these studies, patients in the Zurzuvae® groups experienced statistically significantly greater improvement on the primary endpoint compared to patients in the placebo group.

Recommendation: Zurzuvae® to non-preferred.

Criteria:

- Add Approval will be limited to a 14-day treatment course.
- Add DDI: Reduce the Zurzuvae® dosage when used with a strong CYP3A4 inhibitor.

Board Decision: The Board unanimously approved all the above recommendations.

Zymfentra® (infliximab-dyyb injetion); **PDL category-** Rheumatoid Arthritis

Infliximab-dyyb, the active ingredient of Zymfentra®, is a tumor necrosis factor (TNF) blocker. It is a chimeric IgG1κ monoclonal antibody. Infliximab-dyyb neutralizes the biological activity of TNFα by binding with high affinity to the soluble and transmembrane forms of TNFα and inhibit binding of TNFα with its receptors. It is indicated in adults for maintenance treatment of: Moderately to severely active ulcerative colitis following treatment with an infliximab product administered intravenously. Moderately to severely active Crohn's disease following treatment with an infliximab product administered intravenously. The safety and efficacy of Zymfentra® were assessed in a randomized, double-blind, placebo-controlled clinical trial (*UC Trial I*) that included adult subjects with moderately to severely active UC (defined as a modified Mayo score [mMS] between 5 to 9 with endoscopic subscore [ES] of 2 or 3). This product does have a box warning regarding serious infections and malignancy. Statistically significant differences were observed with Zymfentra® as compared with placebo for the primary endpoints in both studies.

Recommendation: Zymfentra® to non-preferred.

Criteria:

- Add Zymfentra: In adults for maintenance treatment of: Moderately to severely active ulcerative colitis following treatment with an infliximab product administered intravenously. Moderately to severely active Crohn's disease following treatment with an infliximab product administered intravenously.

Board Decision: The Board unanimously approved all the above recommendations.

FDA SAFETY ALERTS

None at this time.

Board Decision: No action.

ADJOURNMENT: 8:30PM

The next meeting will be held on September 2024 6:00pm-8:30pm hybrid.