Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

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TO: Maine Drug Utilization Review Board
DATE: 12/14/2024
RE: Maine DUR Board Meeting minutes from December 12, 2023

ATTENDANCE	EXCUSED	IN-PERSON	REMOTELY
Linda Glass, MD			X
Kathleen Polonchek, MD			X
Erin Ackley, PharmD.			X
John Deason, PharmD.			X
Charmaine Patel, MD			X
Caitlin Morrow, PharmD.			X
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare		X	
Jacquelyn Hedlund, MD, Change Healthcare		X	
Anne-Marie Toderico, PharmD MaineCare Pharmacy Director		X	

Guests of the Board:

CALL TO ORDER: 6:30PM

Erin Ackley called the meeting to order at 6:30 PM.

PUBLIC COMMENTS

Christine Dube from Astrazeneca: Highlighted the attributes of Airsupra.
Anita Gulmiri from Tarsus: Highlighted the attributes of Xdemvy.
Chad Sanders from Ipsen: Highlighted the attributes of Sohonos.
Dr. Cecila Brain from Axsome: Highlighted the attributes of Auvelity.
Candace Andersson from Axsome: Highlighted the attributes of Auvelity.
Andrea Jeknavorian from Pfizer: Highlighted the attributes of Ngenla.

MAINECARE UPDATE- ANNE-MARIE TODERICO

No updates at this time.

OLD BUSINESS

DUR MINUTES

Approval of November 2023, DUR meeting minutes

Board Decision: The Board unanimously approved the above recommendation.

FOLLOW UP ON 1/1/2024 PDL CHANGES

Updates/correction on PDL placement for January 1, 2024, PDL.

Recommendation:

- Dyanavel XR SUS remains preferred.
- Xeljanz XR Sol move to preferred to meet the contract requirements.
- Veozah update clinical criteria: Veozah for use of moderate to severe vasomotor symptoms (VMS) associated with menopause AND documentation has been provided detailing the frequency and severity of these symptoms AND the patient has had a documented side effect, allergy, contraindication, or treatment failure, defined by at least 4 weeks of therapy, to one preferred Hormone Replacement Therapy (HRT) and two preferred non-hormonal therapies (i.e., SSRIs, SNRIs, gabapentin, pregabalin, clonidine

Board Decision: The Board unanimously approved the above recommendation.

UPDATED DUR MEETING DATES

The DUR Committee will meet from 5:30pm to 8:30pm on:

March 19, 2024
June 11, 2024
September 10, 2024
November 5, 2024(1:00pm to 2:30pm Closed Session, 2:30pm to 5:30pm Public Session)
December 10, 2024

Recommendation: To move the March meeting to March 19, 2024.

Board Decision: The Board unanimously approved the above recommendation.

NEW BUSINESS

PRESENTATION: CO-PRESCRIBING OF OPIOIDS, BENZODIAZEPINES, AND MUSCLE RELAXANTS

The co-prescribing of opioids, benzodiazepines, and muscle relaxants is known to cause significant morbidity and has been shown to increase the likelihood of hospital admissions. A retrospective cohort study was published in 2019 examining data from the Medical Expenditure Panel Survey longitudinal data set and the affiliated Prescribed Medicines Files from 2013-2014,1 weighted to reflect the actual US population. The results showed that 0.53% of the population took all three classes of medications simultaneously and compared with non-users, the odds ratio of hospitalization was 8.52 in 2013.1 Respiratory and CNS depression are the primary reasons for hospitalizations and Deaths associated with concurrent use.2 A study done in Washington State found that opioid users had a 12-fold increased rate of death when also taking a benzodiazepine and muscle relaxant. While the FDA has issued warnings about the combined use of benzodiazepines and opioids, adding a muscle relaxant contributes to the risk of hospitalization and poor outcomes. Short-term use of an opioid and benzodiazepine has been deemed reasonable in specific situations, although the use of triple drug therapy with opioids, benzodiazepines, and muscle relaxants, even in the short-term, is not considered appropriate patient care. FDA Warnings about the co-prescribing of benzodiazepines and opioids has brought attention to the risks, however, short-term overlapping prescriptions are sometimes seen, although less frequently over the last few years. It is expected that there will be very little overlapping use of these 3 classes of medications in Maine.

We used non-reversed Medicaid medical claims from Calendar Year 2022, excluding members with Part D, MaineRX and TPL. We identified members who had been prescribed an opioid, benzodiazepine, and muscle relaxant with overlapping dates of service and determined if the members had the same or different prescribers. This combination presents a dangerous risk, and we will identify all cases where there is overlap, even if short-term. We also looked at the pharmacies filling these prescriptions, to see if the members were getting drugs from all three overlapping drug classes filled at the same pharmacy or different ones.

Recommendation: Under 1% of patients prescribed a drug from at least one of these drug classes were prescribed one from each drug class in overlapping fashion. 42% had at least 2 prescribers, 58% had the same prescriber. The concern is that medical reconciliation is not being done appropriately at office visits and that pharmacies are not checking with prescribers when members are being prescribed drugs from all 3 classes in overlapping fashion, ignoring the safety issues, given 96% of prescriptions are coming from the same pharmacies. Possible interventions include doing a sample chart check to see why members are on drugs from all three classes simultaneously, sending targeted educational information to the prescribers and pharmacies that dispensed the drugs, or doing general educational mailings to all providers and pharmacies. It is good to see that children and the very elderly, who are most vulnerable to the side effects, are not being prescribed this combination of medications.

Board Decision: The Board unanimously approved the above recommendation.

INTRODUCE: THE EFFECT OF HEMLIBRA ON THE COST OF CARE IN HEMOPHILIA A PATIENTS

Hemlibra (emicizumab), a bispecific - and factor X -directed antibody is used to treat factor VIII deficient patients (hemophilia A), with or without inhibitors. It activates the coagulation cascade downstream of the factor VIII activating pathway, thereby negating the need for factor VIII for normal coagulation. It was initially developed for patients with inhibitors to factor VIII1, which usually develop after only a few exposures to factor products, to reduce the need for immune tolerance with very high doses of factor and to avoid the used of bypassing agents, such as NovoSeven. However, it is now routinely used as the initial prophylactic treatment in children born with hemophilia, due to the ease of subcutaneous administration and only rare incidences of inhibitor development2. If bleeding occurs, traditional factor replacement is used. Hemlibra may be given weekly, every other week or monthly. In children, it prevents the need for central line placement with the risks of infection and prevents in all patients the need for IV prophylaxis several times a week. The medical and scientific advisory council (MASAC) of the National Bleeding Disorders Foundation recommends Hemlibra as one possible prophylactic agent for the treatment of patients with factor VIII deficiency. While Hemlibra is more costly per month than traditional factor infusions, it is possible that patient quality of life improvement and the overall cost of care for patients is decreased, due to better compliance with prophylaxis (no IV required), less development of inhibitors, which are more costly to treat, and less use of medical care, such as hospitalizations for infections from central lines, bleeds, and trauma-related care.

We will use paid, non-reversed Medicaid pharmacy and medical claims from SFY 2022, excluding members with Part D, TPL and Maine RX coverage. For members taking Hemlibra during SFY 22, we will analyze medical claims, looking at number and cost of hospitalizations, ER visits, factor use and provider visits for the year prior to starting Hemlibra and 1 year after starting the medication in those who had been on traditional factor prophylaxis prior to starting Hemlibra, to see if the increased cost of Hemlibra is offset by decreased utilization of medical care, including factor use. Possible secondary analysis,

compare kids who start Hemlibra with those who initially started factor or look at those who started Hemlibra after developing an inhibitor to look at pre and post costs.

Recommendation: None at this time.

Board Decision: None needed.

NEW DRUG REVIEW

Airsupra® (albuterol & budesonide inhalation aerosol); **PDL category- Antiasthmatic- Adrenergic Combinations**

Airsupra® Inhalation Aerosol contains a combination of micronized albuterol sulfate (a relatively selective, short-acting beta2-adrenergic agonist) and micronized budesonide (a corticosteroid) for oral inhalation. It is indicated for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients with asthma 18 years of age and older. The efficacy of Airsupra® was assessed in the MANDALA and DENALI studies, which will be described below. While patients 12 to 17 years of age were included in these trials, Airsupra® is not approved in this age group; thus, efficacy results are presented for adults only. The primary efficacy endpoint of the MANDALA study was the time to first severe asthma exacerbation, and treatment with Airsupra® as compared with albuterol MDI 180mcg demonstrated statistically significant reductions in the risk of severe asthma exacerbations among adult patients, as assessed by the time to first severe asthma exacerbation. Compared with albuterol, patients receiving Airsupra® experienced a statistically significant 28% reduction in the risk of a severe asthma exacerbation. While there is some evidence to suggest that Airsupra® may be more effective than albuterol 180mcg regarding the primary endpoint of time to first severe asthma exacerbation in a phase 3 study, there is no evidence at this time to support that Airsupra® is safer or more effective than the other currently preferred, more cost-effective medications, including using the combination of budesonide and albuterol or the combination of any cost effective inhaled corticosteroid and SABA.

Recommendation: Airsupra® to non-preferred

Akeega® (niraparib tosylate and abiraterone acetate); **PDL category-** Cancer

Akeega® is a combination tablet that contains niraparib tosylate (a poly (ADP-ribose) polymerase (PARP) inhibitor) and abiraterone acetate (an inhibitor of CYP17). Niraparib is an inhibitor of PARP enzymes, including PARP-1 and PARP-2, that play a role in DNA repair. In vitro studies have shown that niraparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. Niraparib decreased tumor growth in mouse xenograft models of human cancer cell lines with deficiencies in BRCA1/2 and in human patient-derived xenograft tumor models with homologous recombination deficiency (HRD) that had either mutated or wild-type BRCA1/2. Abiraterone acetate is converted in vitro to abiraterone, an androgen biosynthesis inhibitor, that inhibits CYP17. This enzyme is expressed in testicular, adrenal, and prostatic tumor tissues and is required for androgen biosynthesis. CYP17 catalyzes two sequential reactions, including the conversion of pregnenolone and progesterone to their 17α-hydroxy derivatives by 17α-hydroxylase activity, as well as the subsequent formation of dehydroepiandrosterone (DHEA) and androstenedione, respectively. DHEA and androstenedione are androgens and are precursors of testosterone. Inhibition of CYP17 by abiraterone can also result in increased mineralocorticoid production by the adrenals. Androgen sensitive prostatic carcinoma responds to treatment that

decreases androgen levels. Androgen deprivation therapies, such as treatment with gonadotropin-releasing hormone (GnRH) agonists or orchiectomy, decrease androgen production in the testes but do not affect androgen production by the adrenals or in the tumor. Abiraterone decreased serum testosterone and other androgens in patients in the placebo-controlled trials. It is not necessary to monitor the effect of abiraterone on serum testosterone levels. Changes in serum prostate specific antigen (PSA) levels may be observed but have not been shown to correlate with clinical benefit in individual patients. In mouse xenograft models of prostate cancer, the combination of niraparib and abiraterone acetate increased anti-tumor activity when compared to either drug alone. It is indicated with prednisone, for the treatment of adult patients with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC). Select patients for therapy based on an FDA-approved test for Akeega®.The efficacy of Akeega® was assessed in Cohort 1 of MAGNITUDE, a randomized, double-blind, placebo-controlled, multicohort, multicenter study in which patients with homologous recombination repair (HRR) gene-mutated (HRRm) mCRPC (N=423) were randomized to receive niraparib 200mg and abiraterone 1000mg (N=212) or placebo and abiraterone (N=211) until unacceptable toxicity or progression. All patients received prednisone 10mg daily and a GnRH analog or had prior bilateral orchiectomy. The major efficacy outcome was radiographic progression free survival (rPFS), and results suggested that a statistically significant improvement in rPFS for niraparib plus abiraterone compared to placebo plus abiraterone was observed in BRCAm patients, and the Cohort 1 intention to treat (ITT) population. In an exploratory analysis in the subgroup of 198 patients with non-BRCA mutations, the rPFS hazard ratio was 0.99 and the overall survival hazard ratio was 1.13, indicating that improvement in the ITT population was mainly due to the results seen in the subgroup of patients with BRCAm. Akeega® is the first and only dual action oral tablet with this indication.

Recommendation: Akeega® to non-preferred.

Elrexfio (elranatamab); **PDL category**- Cancer

Elranatamab-bcmm, the active ingredient of Elrexfio®, is a bispecific B-cell maturation antigen (BCMA)-directed T-cell engaging antibody that binds BCMA on plasma cells, plasmablasts, and multiple myeloma cells and CD3 on T-cells leading to cytolysis of the BCMA-expressing cells. Elranatamab-bcmm activated T-cells, caused proinflammatory cytokine release, and resulted in multiple myeloma cell lysis. Elrexfio® is a BCMA-directed CD3 T-cell engager that is a bispecific, humanized immunoglobulin 2-alanine kappa antibody derived from two monoclonal antibodies. It is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The efficacy of Elrexfio® monotherapy was assessed in patients with relapsed or refractory multiple myeloma in an open-label, single-arm, multicenter study, which included patients who were refractory to at least one proteasome inhibitor (PI), one immunomodulatory agent (IMiD), and one anti-CD38 monoclonal antibody. This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial(s). Elrexfio® has a box warning regarding CRS and neurologic toxicity, including ICANS. Because of the risk of CRS and neurologic toxicity, including ICANS, Elrexfio® is available only through a restricted program under a REMS called the Elrexfio® REMS.

Recommendation: Elrexfio® to non-preferred.

Eylea® HD (aflibercept) **PDL category-** Op. of Interest

Aflibercept, the active ingredient of Eylea® HD, is a recombinant fusion protein consisting of portions of human vascular endothelial growth factor (VEGF) receptors 1 and 2 extracellular domains fused to the Fc portion of human IgG1. It is indicated for : For the treatment of: Neovascular (wet) age-related macular degeneration (nAMD), Diabetic macular edema (DME), Diabetic retinopathy (DR). The safety and efficacy of Eylea® HD were assessed in a randomized, multicenter, double-masked, active-controlled study (PULSAR) in treatment-naïve patients with nAMD (N=1009). Both Eylea® HDq12 and Eylea® HDq16 treatments were shown to be non-inferior and clinically equivalent to Eylea® 2mg Q8W treatment with respect to the primary endpoint of change in BCVA score at week 48. Efficacy data for Eylea® HD in DR are derived from the PHOTON study. The proportion of patients who achieved a ≥2-step improvement from baseline in the ETDRS-DRSS score at week 48 was assessed. The Eylea® HDq16 group did not meet the non-inferiority criteria for the proportion of patients with a ≥2-step improvement on ETDRS-DRSS and is not considered clinically equivalent to Eylea® administered every 8 weeks. Eylea® HD at a higher dose and given at a longer interval has been found to be non-inferior to Eylea® 2mg given every 8 weeks, with the exception of Eylea® HD administered every 16 weeks for DR. There is no evidence at this time to support that Eylea® HD is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Eylea® HD to non-preferred.

Clinical criteria:

- PA required to confirm appropriate diagnosis and clinical parameters for use.

Iyuzeh® (latanoprost ophthalmic solution 0.005%); **PDL category**- OP. Prostaglandins

Latanoprost, the active ingredient of Iyuzeh®, is a prostaglandin F-2α analogue that is believed to reduce the intraocular pressure (IOP) by increasing the outflow of aqueous humor. Studies in animals and man suggest that the main mechanism of action is increased uveoscleral outflow. Elevated IOP represents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the chance of optic nerve damage and visual field loss. Reduction of the IOP in man starts about 3-4 hours after administration and the maximum effect is reached after 8-12 hours. IOP reduction is present for at least 24 hours. It is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. In randomized, controlled clinical trials of patients with open angle glaucoma or ocular hypertension with mean baseline IOP of 19-24mmHg, Iyuzeh® lowered IOP by 3-8mmHg versus 4-8mmHg by latanoprost ophthalmic solution preserved with benzalkonium chloride. In clinical trials, Iyuzeh® lowered IOP by 3-8mmHg versus 4-8mmHg by latanoprost ophthalmic solution preserved with benzalkonium chloride. Iyuzeh® is the first and only preservative-free latanoprost with this indication for patients with open-angle glaucoma or ocular hypertension.

Recommendation: Iyuzeh® to non-preferred.

Izervay® (avacincaptad); **PDL category**- Op. of Interest

Avacincaptad pegol, the active ingredient of Izervay®, is a complement C5 inhibitor. It is a ribonucleic acid (RNA) aptamer, covalently bound to an approximately 43-kiloDalton (kDa) branched polyethylene glycol (PEG) molecule. Avacincaptad pegol is an RNA aptamer, a PEGylated oligonucleotide that binds to and inhibits complement protein C5. By inhibiting C5, avacincaptad pegol may prevent its cleavage to C5a and C5b, thus decreasing membrane attack complex (MAC) formation. It is indicated for the treatment of

geographic atrophy (GA) secondary to age-related macular degeneration (AMD). : The safety and efficacy of Izervay® were demonstrated in two randomized, multicenter, double-masked, sham-controlled, 18- and 12- month studies (GATHER1 and GATHER2, respectively) that included patients with GA due to AMD. Patient ages ranged from 51 to 97 years, with a mean of 77 years. In total, 292 patients were treated with avacincaptad pegol 2mg and 332 patients received sham. . In each study, over a 12-month period, there was a statistically significant reduction of the rate of GA growth in patients treated with Izervay® compared to sham. Up to 35% slower progression was seen with Izervay® over sham.

Recommendation: Izervay® to non-preferred.

Clinical criteria:

- PA required to confirm appropriate diagnosis and clinical parameters for use.

Motpoly® XR (lacosamide cap extended- release); **PDL category**- Anticonvulsants

Lacosamide, the active ingredient of Motpoly® XR, is a functionalized amino acid. The exact mechanism of action for its approved indication in humans remains to be fully elucidated. In vitro electrophysiological studies have shown that lacosamide selectively enhances slow inactivation of voltage-gated sodium channels, resulting in stabilization of hyperexcitable neuronal membranes and inhibition of repetitive neuronal firing. Motpoly® XR is a Schedule V controlled substance. It is indicated for the treatment of partial-onset seizures in adults and pediatric patients weighing at least 50kg. The efficacy of Motpoly® XR is based on the relative bioavailability of Motpoly® XR compared to immediate release lacosamide in healthy adults. Immediate release lacosamide is under the brand name Vimpat®, which is available as both a brand and generic. Motpoly® XR offers prescribers another treatment option.

Clinical Criteria:

- Motpoly XR must be weighing at least 50kg pediatric patients. Requires multiple preferred medication tried and failed including generic lacosamide.

Ngenla® (somatrogon-ghla); **PDL category**- Growth Hormone

Somatrogon-ghla, the active ingredient of Ngenla®, is a human growth hormone analog. It is a fusion protein produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology. It is comprised of the amino acid sequence of human growth hormone (hGH) with one copy of the C-terminal peptide (CTP) from the beta chain of human chorionic gonadotropin at the N-terminus and 2 copies of CTP (in tandem) at the C-terminus. Somatrogon-ghla binds to the GH receptor and initiates a signal transduction cascade culminating in changes in growth and metabolism. Its binding leads to activation of the STAT5b signaling pathway and increases the serum concentration of Insulin-like Growth Factor (IGF-1). GH and IGF-1 stimulate metabolic changes, linear growth, and enhance growth velocity in pediatric patients with growth hormone deficiency. It is indicated for the treatment of pediatric patients aged 3 years and older who have growth failure due to an inadequate secretion of endogenous growth hormone. A multicenter, randomized, open-label, active-controlled, parallel-group, phase 3 study was conducted in treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency. The primary efficacy endpoint was annualized height velocity at week 52, and results suggested that treatment with once-weekly Ngenla® for 52 weeks resulted in an annualized height velocity of 10.1 cm/year while treatment with daily somatropin achieved an annualized height velocity of 9.8 cm/year after 52 weeks of treatment.

Recommendation: Ngenla® 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.

Odactra® (dermatophagoides pteronyssinus & dermatophagoides farinae); **PDL category**- Allergen Immunotherapy

Odactra® tablets contain house dust mite allergen extract from Dermatophagoides farinae and Dermatophagoides pteronyssinus. The precise mechanisms of action of allergen immunotherapy have not been fully established. It is indicated that an allergen extract indicated as immunotherapy for the treatment of house dust mite (HDM)-induced allergic rhinitis, with or without conjunctivitis, confirmed by positive in vitro testing for IgE antibodies to Dermatophagoides farinae or Dermatophagoides pteronyssinus house dust mites, or by positive skin testing to licensed house dust mite allergen extracts. Odactra® is approved for use in persons 12 through 65 years of age. Note that Odactra® is not indicated for the immediate relief of allergic symptoms. The efficacy of Odactra® for the treatment of HDM-induced allergic rhinitis was investigated in two double-blind, placebo-controlled, randomized, clinical field efficacy studies (Studies 1 and 2) and one environmental exposure chamber (EEC) study. . The primary efficacy endpoint for Study 1 and 2 was the difference between treatment and placebo groups in the average TCRS during about the last 8 weeks of treatment. The difference relative to placebo (estimate) was -17.2% in Study 1 and -16.1% in Study 2.The primary endpoint in Study 3 was the difference relative to placebo in the average TNSS at week 24; the difference relative to placebo (estimate) in this study was -48.6%. Per the full-text of study 1 by Nolte et al2, there was a significantly lower average TCRS with 12 SQ-HDM as compared to placebo ($p<0.001$). There is no evidence at this time to support that Odactra® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Odactra® to non-preferred.

Clinical criteria:

- Odactra® is approved for use in persons 12 through 65 years of age. Note that Odactra® is not indicated for the immediate relief of allergic symptoms.

Ojjaara® (momelotinib) **PDL category**- Cancer

Momelotinib, the active ingredient of Ojjaara®, is a kinase inhibitor. It is an inhibitor of wild type Janus Kinase 1 and 2 (JAK1/JAK2) and mutant JAK2V617F, which contribute to signaling of a number of cytokines and growth factors that are important for hematopoiesis and immune function. Momelotinib and its major human circulating metabolite, M21, have higher inhibitory activity for JAK2 compared to JAK3 and tyrosine kinase 2 (TYK2). Momelotinib and M21 additionally inhibit activin A receptor type 1 (ACVR1), also known as activin receptor like kinase 2 (ALK2), which produces subsequent inhibition of liver hepcidin expression and increased iron availability resulting in increased red blood cell production. It is indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF (post-polycythemia vera [PV] and post-essential thrombocythemia [ET]), in adults with anemia. The efficacy of Ojjaara® in the treatment of adults with intermediate 1, intermediate 2, or high-risk MF (including primary MF, post-PV MF, or post-ET MF, as defined by the Dynamic International Prognostic

Scoring System (DIPSS) or International Prognostic Scoring System (IPSS) for MF) was established in the MOMENTUM trial and in a subpopulation of adults with anemia in the SIMPLIFY-1 trial. In the MOMENTUM trial, a randomized, double-blind, active-controlled study, the efficacy of Ojjaara® was established based on a significantly higher percentage of patients treated with Ojjaara® compared to danazol achieving a MFSAF v4.0 Total Symptom Score reduction of 50% or more at week 24 compared with their own baseline score. Other endpoints, including transfusion independence, spleen volume reduction, MFSAF v4.0 Total Symptom Score change from baseline, and patients with no transfusions, were significantly in favor of Ojjaara® compared with danazol.

Recommendation: Ojjaara® to non-preferred.

Olpruva® (sodium phenylbutyrate); **PDL category**- Urea Cycle Disorder

Sodium phenylbutyrate, the active ingredient of Olpruva®, is a nitrogen binding agent. It is a pro-drug and is metabolized to phenylacetate. Phenylacetate is a metabolically active compound that conjugates with glutamine via acetylation to form phenylacetylglutamine. Phenylacetylglutamine is excreted by the kidneys, hence providing an alternate vehicle for waste nitrogen excretion. In patients with urea cycle disorders, sodium phenylbutyrate decreased elevated plasma ammonia and glutamine levels. It is indicated as an adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients weighing 20kg or greater and with a body surface area (BSA) of 1.2m2 or greater, with urea cycle disorders (UCDs) involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). Limitations of use include that episodes of acute hyperammonemia may occur in patients while on Olpruva®. Olpruva® is not indicated for the treatment of acute hyperammonemia, which can be a life-threatening medical emergency that requires rapid acting interventions to reduce plasma ammonia levels. There were no clinical trials provided in the prescribing information of Olpruva®. Sodium phenylbutyrate is available in other dosage forms, including tablets and bottles of powder (brand Buphenyl®), that have been available and approved for urea cycle disorders. Olpruva® treatment should be supervised by a healthcare provider experienced in the treatment of urea cycle disorders and is available as pellets in packets for reconstitution. This provides patients with another dosage formulation option.

Recommendation: Olpruva® to non-preferred.

Clinical Criteria:

- Olpruva: As adjunctive therapy to standard of care, which includes dietary management, for the chronic management of adult and pediatric patients weighing 20kg or greater and with a body surface area (BSA) of 1.2m2 or greater, with urea cycle disorders (UCDs) involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS).

Omisirge® (omidubicel-onlv kit); **PDL category**- Cancer

Omisirge® (omidubicel-onlv) is a cryopreserved nicotinamide modified allogeneic hematopoietic progenitor cell therapy derived from cord blood consisting of 2 cell fractions, including a Cultured Fraction (CF) and a Non-cultured Fraction (NF) which are both derived from the same patient-specific cord blood unit (CBU). It was indicated for the use in adults and pediatric patients 12 years and older with hematologic malignancies who are planned for umbilical cord blood transplantation following myeloablative

conditioning to reduce the time to neutrophil recovery and the incidence of infection. Omisirge® was assessed in an open-label, multicenter, randomized study of Omisirge® transplantation or umbilical cord blood (UCB) transplantation following myeloablative conditioning in patients with hematologic malignancies. The efficacy of Omisirge® was established based on time to neutrophil recovery following transplantation and the incidence of BMT CTN Grade 2/3 bacterial or Grade 3 fungal infections through day 100 following transplantation. The median time to neutrophil recovery was 12 days with Omisirge® and 22 days with UCB. The incidence of Grade 2/3 bacterial or Grade 3 fungal infections through 100 days following transplantation was 39% with Omisirge® vs 60% with UCB. Per the full-text study by Horwitz, statistically significant differences in favor of Omisirge® were observed for median time to neutrophil recovery. It is recommended that Omisirge® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for use.

Recommendation: Omisirge® to non-preferred.

Opfolda® (miglustat capsules); **PDL category**- Pompe Disease Agents

Miglustat, the active ingredient of Opfolda®, is an N-alkylated iminosugar, a synthetic analog of D-glucose. The pharmacologic class is enzyme stabilizer. Miglustat binds with, stabilizes, and reduces inactivation of cipaglucosidase alfa-atga (Pombiliti®) in the blood after infusion. The bound miglustat is dissociated from cipaglucosidase alfa-atga after it is internalized and transported into lysosomes. Miglustat alone has no pharmacologic activity in cleaving glycogen. It is in combination with Pombiliti®, for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40kg and who are not improving on their current enzyme replacement therapy (ERT). : Trial 1 was a randomized, double-blind, active-controlled, international, multicenter study that included adults ≥18 years of age diagnosed with LOPD (late-onset Pompe Disease) to assess the safety and efficacy of Opfolda® in combination with Pombiliti® as compared with a non-U.S.-approved alglucosidase alfa product with placebo every other week for 52 weeks. Results suggested that patients treated with Opfolda® in combination with Pombiliti® demonstrated a mean change in sitting FVC from baseline at week 52 of -1.1% as compared with patients treated with a non-U.S.-approved alglucosidase alfa product with placebo of -3.3% (estimated treatment difference of 2.3%). There is no evidence at this time to support that Opfolda® in combination with Pombiliti® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Opfolda® to non-preferred.

Clinical Criteria:

- Opfolda are for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40kg and who are not improving on their current enzyme replacement therapy (ERT).

Opvee® (nalmefene HCl); **PDL category**- Narcotic- Antagonists

Nalmefene, the active ingredient of Opvee®, is an opioid antagonist, a 6-methylene analogue of naltrexone. It is an antagonist at opioid receptors and it reverses the effects of natural and synthetic opioids, including respiratory depression, sedation, and hypotension. Pharmacodynamic studies have shown that nalmefene injection has a longer duration of action than naloxone injection at fully reversing doses. Nalmefene has no opioid agonist activity. It is indicated for the emergency treatment of known or suspected overdose induced by natural or synthetic opioids in adults and pediatric patients aged 12 years

and older, as manifested by respiratory and/or central nervous system depression. Opvee® is intended for immediate administration as emergency therapy in settings where opioids may be present. It is not a substitute for emergency medical care. There were no clinical efficacy trials identified in the prescribing information for Opvee®. In a pharmacokinetic study that included healthy adults, the relative bioavailability of one 2.7mg Opvee® nasal spray in one nostril was compared to a single dose of nalmefene 1.0mg administered as an IM injection. It is not a substitute for emergency medical care. The nasal device does not need to be primed or assembled, as it is ready for use. Deliver one spray by intranasal administration and seek emergency medical assistance as soon as possible after administration of the first dose. Additional doses may be required. Head-to-head comparator efficacy trials with other agents were not identified. There is no evidence at this time to support that Opvee® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Opvee® to non-preferred.

Clinical criteria:

- For the treatment of adult and pediatric patients 12 years of age and older

Pombiliti® (cipaglucosidase alfa-atga for injection); **PDL category**- Pompe Disease Agents

Cipaglucosidase alfa-atga, the active ingredient of Pombiliti®, is a hydrolytic lysosomal glycogen-specific recombinant human α-glucosidase (rhGAA) enzyme derived from a Chinese Hamster Ovary (CHO) cell line using perfusion methodology, resulting in cellularly (CHO)-derived N-glycans. Cipaglucosidase alfa-atga is a glycoprotein with 1.3 mols of bis-mannose-6-phosphate (bis-M6P) per mol of enzyme. It is indicated in combination with Opfolda®, for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40kg and who are not improving on their current enzyme replacement therapy (ERT). Trial 1 was a randomized, double-blind, active-controlled, international, multicenter study that included adults ≥18 years of age diagnosed with LOPD (late-onset Pompe Disease) to assess the safety and efficacy of Pombiliti® in combination with Opfolda® as compared with a non-U.S.-approved alglucosidase alfa product with placebo every other week for 52 weeks. Results suggested that patients treated with Pombiliti® in combination with Opfolda® demonstrated a mean change in sitting FVC from baseline at week 52 of -1.1% as compared with patients treated with a non-U.S.-approved alglucosidase alfa product with placebo of -3.3% (estimated treatment difference of 2.3%). There is no evidence at this time to support that Pombiliti® in combination with Opfolda® is safer or more effective than the other currently preferred, more cost-effective medications. It is therefore recommended that Pombiliti® (in combination with Opfolda®) 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: Pombiliti® to non-preferred.

Clinical criteria:

- Pombiliti are for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40kg and who are not improving on their current enzyme replacement therapy (ERT).

Rykindo® (risperidone injection, extended-release microspheres); **PDL category**- Antipsychotics- Atypicals

Risperidone, the active ingredient of Rykindo®, is an atypical antipsychotic. The mechanism of action of risperidone in schizophrenia is unclear. The drug's therapeutic activity could be mediated through a combination of dopamine Type 2 (D2) and serotonin Type 2 (5HT2) receptor antagonism. The clinical effect from risperidone results from the combined concentrations of risperidone and its major metabolite, 9-hydroxyrisperidone (paliperidone). Antagonism at receptors other than D2 and 5HT2 may explain some of the other effects of risperidone. It is indicated for treatment of schizophrenia in adults and as monotherapy or as adjunctive therapy to lithium or valproate for the maintenance treatment of bipolar I disorder in adults. The efficacy of Rykindo® in the treatment of schizophrenia is based on an adequate and well-controlled study with risperidone long-acting injection (intramuscular). The effectiveness of risperidone long-acting injection (intramuscular) was established, in part, on the basis of the established effectiveness of the oral formulation of risperidone as well as in a 12-week, placebo-controlled trial in adult inpatients and outpatients who met the DSM-IV criteria for schizophrenia. The efficacy of Rykindo® for schizophrenia, for maintenance treatment of bipolar I disorder as monotherapy, and as an adjunct to treatment with lithium or valproate for the maintenance treatment of bipolar I disorder, is based on an adequate and well-controlled study of risperidone long-acting injection (intramuscular). There is no evidence at this time to support that Rykindo® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Rykindo® to non-preferred.

Sohonos® (palovarotene); **PDL category**- Osteoporosis/Bone Agents: FOP Agents

Palovarotene, the active ingredient of Sohonos®, is an orally bioavailable retinoid that acts as a retinoic acid receptor (RAR) agonist with particular selectivity at the gamma subtype of RAR. It is indicated for reduction in volume of new heterotopic ossification in adults and pediatric patients aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP). Sohonos® is a retinoic acid receptor agonist indicated for the reduction in volume of new heterotopic ossification in adults and pediatric patients 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP). It carries a box warning regarding embryo-fetal toxicity and premature epiphyseal closure in growing pediatric patients. Dosing for Sohonos® includes both daily dosing and flare-up dosing. Its efficacy was assessed in a single arm study that included subjects with FOP (N=97) and utilized the Natural History Study (NHS, N=101) as an external control. The primary efficacy endpoint was annualized volume of new HO. Results suggested that the mean annualized new HO was 9.4 cm3/year in subjects receiving the chronic/flare-up Sohonos® treatment and 20.3 cm3/year in untreated subjects in the NHS based on a linear mixed effect model (treatment effect was about 10.9 cm3/year).

Recommendation: Sohonos® to non-preferred.

Clinical criteria:

- Clinical PA for indicated required.
- Sohonos: For the reduction in volume of new heterotopic ossification in adults and pediatric patients aged 8 years and older for females and 10 years and older for males with fibrodysplasia ossificans progressiva (FOP).

Talvey® (talquetamab); **PDL category-** Cancer

Talquetamab-tgvs, the active ingredient of Talvey®, is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T-cells and G protein-coupled receptor class C group 5 member D (GPRC5D) expressed on the surface of multiple myeloma cells and non-malignant plasma cells, as well as healthy tissues such as epithelial cells in keratinized tissues of the skin and tongue. In vitro, talquetamab-tgvs activated T-cells caused the release of proinflammatory cytokines and resulted in the lysis of multiple myeloma cells. Talquetamab-tgvs had anti-tumor activity in mouse models of multiple myeloma. Talquetamab-tgvs is a bispecific GPRC5D-directed CD3 T-cell engager. It is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. : The efficacy of Talvey® monotherapy was assessed in patients with relapsed or refractory multiple myeloma in an open-label, single-arm, multicenter study, which included patients who had previously received at least 3 prior systemic therapies, including a proteasome inhibitor (PI), an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The efficacy of Talvey® monotherapy was assessed in patients with relapsed or refractory multiple myeloma in a single-arm, open-label, multicenter study with efficacy results that included patients who had received at least 4 prior lines of therapy. Efficacy was based on ORR. The ORR was 73% for the 0.4mg/kg weekly dose group and 73.6% for the 0.8mg/kg biweekly (every 2 weeks) dose group.

Recommendation: Talvey® to non-preferred.

Vanflyta® (quizartinib); **PDL category-** Cancer

Quizartinib, the active ingredient of Vanflyta®, is a kinase inhibitor. It is a small molecule inhibitor of the receptor tyrosine kinase FLT3. Quizartinib, and its major active metabolite AC886, bind to the adenosine triphosphate (ATP) binding domain of FLT3 with comparable affinity, and both had 10-fold lower affinity towards FLT3-ITD mutation compared to FLT3 in a binding assay. Quizartinib and AC886 inhibited FLT3 kinase activity, preventing autophosphorylation of the receptor, thus inhibiting downstream FLT3 receptor signaling and blocking FLT3-ITD-dependent cell proliferation. It is indicated in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test. A limitation of use includes that Vanflyta® is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with Vanflyta® in this setting has not been demonstrated. The efficacy of Vanflyta® in combination with chemotherapy was assessed in a randomized, double-blind, placebo-controlled study (QuANTUM-First Study) that included patients (N=539) with newly diagnosed FLT3-ITD positive AML. Patients were randomized to Vanflyta® or placebo in combination with induction and consolidation therapy and as maintenance monotherapy per the initial assignment. Vanflyta® is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation; improvement in overall survival with Vanflyta® in this setting has not been demonstrated. Vanflyta® has a box warning regarding QT prolongation, Torsades de Pointes, and cardiac arrest. Because of the risk of QT prolongation, Torsades De Pointes, and cardiac arrest, Vanflyta® is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) called the Vanflyta® REMS. The efficacy of Vanflyta® was assessed in a randomized double-blind, placebo-controlled study, where efficacy was established on the basis of overall survival. The study demonstrated a statistically significant improvement in overall survival for the Vanflyta® arm.

Recommendation: Vanflyta® to non-preferred.

Vyjuvek® (beremagene geperpavec-svdt); **PDL category-** Topical- Wound/Decubitus Care

Vyjuvek® (beremagene geperpavec-svdt) is a suspension of a herpes-simplex virus type 1 (HSV-1) vector-based gene therapy, mixed with the supplied sterile excipient gel for topical application on wounds. It is a live, replication defective HSV-1 based vector that has been genetically modified to express the human type VII collagen (COL7) protein. It is indicated for the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene. The efficacy of Vyjuvek® gel in subjects one year of age and older with DEB with mutation(s) in the COL7A1 gene was assessed in a randomized, double-blind, intra-subject placebo-controlled trial. Efficacy was established based on improved wound healing defined as the difference in the proportion of complete (100%) wound closure at 24 weeks confirmed at two consecutive study visits two weeks apart, assessed at weeks 22 and 24 or at weeks 24 and 26, between the Vyjuvek® gel-treated and the placebo gel-treated wounds. Efficacy was supported by the difference in the proportion of complete wound closure assessed at weeks 8 and 10 or at weeks 10 and 12 between the Vyjuvek® gel-treated and the placebo gel-treated wounds. Significantly more complete wound closure occurred in the Vyjuvek® gel group as compared with the placebo gel group. Vyjuvek® is the first and only treatment that focuses on the genetic cause of DEB as a gel formulation for wound healing.

Recommendation: Vyjuvek® to non-preferred.

Clinical criteria:

- For the treatment of wounds in patients 6 months of age and older with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene.

Xdemvy® (lotilaner ophthalmic solution); **PDL category-** OP: Anti-parasitic

Lotilaner, the active ingredient of Xdemvy®, is a member of the isoxazoline family of compounds. It is a gamma-aminobutyric acid (GABA)-gated chloride channel inhibitor selective for mites. Inhibition of these GABA chloride channels causes a paralytic action in the target organism leading to its death. It is indicated for the treatment of Demodex blepharitis. The safety and efficacy of Xdemvy® for the treatment of Demodex blepharitis were assessed in two randomized, multicenter, double-masked, vehicle-controlled studies (Saturn-1 and Saturn-2) that were of 6 weeks in duration. Patients (N=833) were randomized to either Xdemvy® or vehicle dosed twice daily in each eye. . In both studies, Xdemvy® was significantly more effective than vehicle for the primary endpoint. In addition, Xdemvy® was significantly more effective than vehicle for mite eradication and erythema cure in both studies. It is currently the only FDA-approved agent that targets and eradicates the Demodex mites that cause Demodex blepharitis.

Recommendation: Xdemvy® to non-preferred.

Clinical criteria:

- For the treatment of Demodex blepharitis.

Yargesa® (miglustat); **PDL category-** Gaucher Disease

Miglustat, the active ingredient of Yargesa®, is an inhibitor of the enzyme glucosylceramide synthase, which is a glucosyl transferase enzyme responsible for the first step in the synthesis of most glycosphingolipids. It is indicated as a monotherapy for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g., due to allergy, hypersensitivity, or poor venous access). The efficacy of miglustat capsules in type 1 Gaucher disease has been investigated in two open-label uncontrolled trials and one randomized, open-label, active-controlled trial with enzyme replacement therapy (imiglucerase). The clinical trials in the Yargesa® prescribing information were the same as in the Zavesca® prescribing information. Yargesa® offers providers a different generic option.

Recommendation: Yargesa® to non-preferred.

Clinical criteria:

- Clinical PA for indication required.
- Yargesa: As monotherapy for the treatment of adult patients with mild to moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (e.g., due to allergy, hypersensitivity, or poor venous access).

Ycanth® (cantharidin); **PDL category-** Topical- Molluscum Contagiosum

Cantharidin, the active ingredient of Ycanth®, is a vesicant for topical administration. The mechanism of action for its approved indication is not known. It is indicated for the topical treatment of molluscum contagiosum in adult and pediatric patients 2 years of age and older. In two double-blind, randomized, placebo-controlled trials (Trial 1 and Trial 2), subjects aged 2 years and older with molluscum contagiosum were randomized by household to treatment with either Ycanth® or vehicle. The safety and efficacy of Ycanth® were assessed in two double-blind, placebo-controlled trials. The primary efficacy endpoint was the proportion of patients achieving complete clearance of all treated molluscum contagiosum lesions by day 84. Results suggest that more in the Ycanth® group as compared with placebo achieved complete clearance (46% vs 18%, respectively, in Trial 1; 54% vs 13%, respectively, in Trial 2). Per the full-text study by Eichenfield et al3, the differences between Ycanth® and vehicle in both trials were statistically significantly different, in favor of Ycanth®. There is no evidence at this time to support that Ycanth® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Ycanth® to non-preferred.

Clinical criteria:

- For the topical treatment of molluscum contagiosum in adult and pediatric patients 2 years of age and older.

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

FDA SAFETY ALERTS

- None at this time.

ADJOURNMENT: 8:00PM

The next meeting will be held on March 19, 2024 530pm-8pm hybrid.