Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

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TO: Maine Drug Utilization Review Board
DATE: 12/11/20
RE: Maine DUR Board **Meeting** minutes from December 8, 2020

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD			X
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR	X		
Mike Antoniello, MD			X
Kathleen Polonchek, MD	X		
Kenneth McCall, PharmD	X		
Erin Ackley, PharmD.			X
Corinn Martineau, PharmD.	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Jacquelyn Hedlund, MD, Change Healthcare	X		
Jan Wright, MaineCare Interim Pharmacy Director	X		
Fran Jensen, MaineCare Medical Director	X		

Guests of the Board: Ed Bosshart, PharmD

CALL TO ORDER: 6:30PM

Jan Wright called the meeting to order at 6:30 PM.

PUBLIC COMMENTS

Tom Arnhart from Ultragenyx Pharmaceuticals: Highlighted the attributes of Dojolvi.
Nikki Faulkner: Highlighted the attributes of Biqsimi.
Tom Algozzine from Novartis: Highlighted the attributes of Kesimpta.
Ken Smith from Genetech: Highlighted the attributes of Evrysdi, Enspryng and Polivy.
Benjamin Yungher from NS Pharma: Highlighted the attributes of Viltepso.
Brian Denger: Highlighted the attributes of Spravato.

OLD BUSINESS

DUR MINUTES

The October DUR meeting minutes were accepted.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE

On Emessage, 340B payment mythology was sent out on December 8, 2020

REVISED CLINICAL CRITERIA/PREFERRED REVIEW

None at this time.

2021 RETRODUR CALENDAR

- **March 10, 2021:**
  - Data presentation: Influenza Vaccination Rates
  - Introduce: Hydroxychloroquine use Pre and Post Covid-19
- **June 9, 2021**:
  - Data presentation: Hydroxychloroquine use Pre and Post Covid-19
  - Introduce: Long-acting Injectable Antipsychotics
- **September 8, 2021:**
  - Data presentation: Long-acting Injectable Antipsychotics
  - Introduce: Herpes Zoster vaccination rates
- **October 13, 2021:**
  - Data presentation: 2022 Potential RetroDUR Initiatives
  - Introduce: HPV vaccination rates
- **December 8, 2021:**
  - Data presentation: Herpes Zoster vaccination rates
  - Data presentation: HPV vaccination rates
  - Introduce: Codeine use in Pediatric Population
- **2022 Meeting #1:**
  - Data presentation: Codeine use in Pediatric Population

NEW BUSINESS

DATA PRESENTATION: CHANTIX USE

The benefits of smoking cessation are obvious. While some people quit on their own, either by tapering or going "cold turkey", many will require the aid of counseling, medications or both. It has been demonstrated that of those who use medication, long-term abstinence often requires counseling in addition to medication. Luckily, several medications have been used successfully, including nicotine replacement products (short- and long-acting), bupropion and varenicline (Chantix). While initially there was concern that Chantix was associated with neuropsychiatric side effects, including risk of suicide, a recent, large study (EAGLES trial of 8000 smokers randomized to NRT, bupropion or varenicline or placebo) showed that the risk was equal among treatments and a black box warning was removed. Many who take Chantix have already tried nicotine replacement products unsuccessfully. While Chantix is meant to be used alone, there has been some success in adding short-acting NRTs in those who continue to experience withdrawal symptoms. In those who have successfully quit at 12 weeks, some may benefit from an additional 12 weeks of therapy to prevent relapse. 2020 guidelines for tobacco cessation issued by the American Thoracic Society recommend Chantix as first line therapy over nicotine replacement products and bupropion and state that for many patients, longer duration of treatment (greater than 12 weeks) is necessary to ensure success with quitting. We used paid, non-reversed Medicaid pharmacy and medical claims date from calendar year 2019 excluding members with Part D, MaineRX and TPL. We looked at all members who were prescribed Chantix and evaluated the number of monthly prescriptions dispensed per member. Additionally, we analyzed which members were also simultaneously prescribed a short acting nicotine replacement product (gum, lozenges, inhaler, nasal spray). We also looked at members prescribed bupropion and how it was being prescribed with other

smoking cessation medications. There was a tremendous amount of variability in prescribing, with many members getting less than 12 weeks of treatment. Additionally, many members were prescribed 12 or 24 weeks (or more) of Chantix in the year, but not in consecutive fashion. In fact, most members did not complete 3 or 6 consecutive 28 day prescriptions.

Recommendation: Given the wide variation of use of Chantix, it is worth considering general education to providers in Maine about appropriate prescribing of Chantix, monitoring of use, and guidelines recommending using bupropion and short-term nicotine replacement products with Chantix may be warranted. With 75% of members not continuing treatment for the indicated treatment length per labeling, considerations should be made as to how we ensure that the product is being used appropriately, short of re-establishing PA requirements.

Board Decision: The Board unanimously approved the above recommendation.

INTRODUCE: INFLUENZA VACCINATION RATES

Influenza vaccination rates are routinely significantly lower than recommended by the CDC. Influenza is responsible for many thousands of deaths annually, including among children and those with chronic illnesses. It is somewhat surprising that more people are not immunized, given the many avenues available for immunization, including pharmacies, work sites, sponsored clinics and PCP/medical specialty offices. While children are often the highest group affected by flu every year, immunization rates are dismal, at around 20% annually. This year especially will be critical given COVID -19 illness, which continues to rage throughout the US. Immunization guidelines are that all people above the age of 6 months receive influenza vaccinations yearly, unless there is a history of severe reactions to previous flu shots. Even those with egg allergies are eligible to get the vaccinations, contrary to popular belief. We will use paid, non-reversed Medicaid pharmacy and medical claims date from calendar year 2019 excluding members with Part D, MaineRX and TPL. We will look at all members who were eligible for vaccination in 2019 and determine the rate of vaccination for the 2019-20 flu season. Additionally, we will look at those who were prescribe Tamiflu in 2018-2019 flu season, to see if previous infection had any effect on improving vaccination rates compared with the general public. We will also look at high risk group, those with COPD, to see if there was a better vaccination rate than that of the general public overall, given higher likelihood of severe infection and death.

Board Decision: After board discussion it was asked to add into the results a break down by county and date adjustment may be made in order to have a complete flu season. No other action needed at this time.

NEW DRUG REVIEW

Airduo® Digihaler (fluticasone propionate & salmeterol); **PDL category-** Anti-asthmatic- Adrenergic Combinations

AirDuo® Digihaler is a combination product containing fluticasone (a synthetic corticosteroid with anti-inflammatory activity) and salmeterol (a beta2-adrenergic bronchodilator, causing relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells). It is indicated for the treatment of asthma in patients aged 12 years and older. It should be used for patients not adequately controlled on a long-term asthma control medication such as an inhaled corticosteroid or whose disease warrants initiation of treatment with both an inhaled corticosteroid and long acting beta2-adrenergic agonist (LABA). AirDuo® Digihaler is not

indicated for the relief of acute bronchospasm. AirDuo® Digihaler should be used for patients not adequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid or whose disease warrants initiation of treatment with both an inhaled corticosteroid and long acting beta2-adrenergic agonist (LABA). AirDuo® Digihaler is not indicated for the relief of acute bronchospasm. Its efficacy and safety were based on primarily on data from AirDuo® Respiclick. AirDuo® Digihaler includes a QR code (on the top of the inhaler) and contains a built-in electronic module which automatically detects, records, and stores data on inhaler events, including peak inspiratory flow rate (L/min). AirDuo® Digihaler may pair with and transmit data to the mobile app where inhaler events are categorized. There is no evidence the use of the app leads to improved clinical outcomes, including safety and effectiveness. Use of the app is not required for administration of fluticasone propionate and salmeterol to the patient.

Recommendation: AirDuo® Digihaler to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Alkindi® Sprinkle (hydrocortisone granule); **PDL category-** Glucocorticoids/Mineralocorticoids

Hydrocortisone, the active ingredient of Alkindi® Sprinkle, is a corticosteroid, also known as cortisol. Hydrocortisone is a glucocorticoid, which cause varied metabolic effects. In addition, it modifies the body's immune responses to diverse stimuli. Naturally occurring glucocorticoids, such as hydrocortisone and cortisone, which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. It is indicated as a replacement therapy in pediatric patients with adrenocortical insufficiency. There are no clinical trials included in the prescribing information for this product. Following oral administration, a dose of four Alkindi® Sprinkle 5mg capsules was about 87% bioavailable when compared to IV hydrocortisone in dexamethasone-suppressed healthy adult male volunteers. In an open-label, single-dose study in 24 pediatric patients with adrenocortical insufficiency, Alkindi® Sprinkle (1-4mg based on body surface area) increased cortisol levels from baseline to median cortisol level 19.4mcg/dl (range 12.5-52.4mcg/dL) at Cmax (60 minutes post-dose). It is the first and only FDA-approved granular hydrocortisone formulation intended for children for adrenocortical insufficiency. Generic oral hydrocortisone tablets are available. There is no evidence to suggest that Alkindi® Sprinkle is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Alkindi® Sprinkle to non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Armonair® Digihaler (fluticasone propionate); **PDL category**- Anti-asthmatic- Steroid Inhalants

Fluticasone propionate, the active ingredient of Armonair® Digihaler, is a synthetic trifluorinated corticosteroid with anti-inflammatory activity. Inflammation is an important component in the pathogenesis of asthma. Corticosteroids have been shown to have a wide range of actions on multiple cell types (e.g. mast cells, eosinophils) and mediators (e.g. histamine, eicosanoids, leukotrienes, and cytokines) involved in inflammation. It is indicated for the maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older. Armonair® Digihaler is not indicated for the relief of acute bronchospasm. The safety and efficacy of fluticasone propionate (Armonair® Respiclick) were assessed in 2130 patients with asthma. The development program included 2 confirmatory trials of 12 weeks in duration, a 26-week safety trial, and 2 dose-ranging trials of 12 weeks duration. The efficacy of Armonair® Digihaler is based primarily

on the dose-ranging trials and the confirmatory trials of Armonair® Respiclick. Armonair® Respiclick has been available for numerous years and was found to be a safe and effective product; however, it was withdrawn from the market by the manufacturer. Its efficacy and safety were based primarily on data from Armonair® Respiclick. There is no evidence to suggest that Armonair® Digihaler is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Armonair® Digihaler to non-preferred.

Clinical Criteria:

- Remove Armonair Respiclick and criteria from the PDL as it is no longer available.

Board Decision: The Board unanimously approved the above recommendation.

Bafiertam® (monomethyl fumarate) **PDL category-** Multiple Sclerosis- Non Interferons

Monomethyl fumarate (MMF), the active ingredient of Bafiertam® has been shown to activate the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway in vitro and in vivo. The Nrf2 pathway is involved in the cellular response to oxidative stress. MMF has been identified as a nicotinic acid receptor agonist in vitro. However, the mechanism by which MMF exerts its therapeutic effect in multiple sclerosis is not known. It is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. The efficacy of Bafiertam® is based upon bioavailability studies in healthy subjects comparing oral dimethyl fumarate delayed-release capsules to Bafiertam® delayed-release capsules. The clinical studies included in the prescribing information for Bafiertam® were conducted using dimethyl fumarate. The efficacy of Bafiertam® is based upon bioavailability studies in healthy subjects comparing oral dimethyl fumarate delayed-release capsules to Bafiertam® delayed-release capsules. There is no evidence at this time to suggest that Bafiertam® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Bafiertam® be non-preferred. In reviewing the category Dimethyl Fumarate will be added to preferred.

Board Decision: The Board unanimously approved the above recommendation.

Blenrep® (belantamab mafodotin-blmfl); **PDL category**- Cancer

Belantamab mafodotin-blmf, the active ingredient of Blenrep®, is a B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate. The antibody is produced in a mammalian cell line using recombinant DNA technology. Belantamab mafodotin-blmf is an antibody-drug conjugate (ADC) composed of 3 components, including

1. an afucosylated, humanized immunoglobulin G1 monoclonal antibody covalently linked to
2. the microtubule inhibitor MMAF via
3. a protease-resistant maleimidocaproyl linker

The antibody component is an afucosylated IgG1 directed against BCMA, a protein expressed on normal B lymphocytes and multiple myeloma cells. The small molecule component is MMAF, a microtubule inhibitor. Upon binding to BCMA, belantamab mafodotin-blmf is internalized followed by release of MMAF via proteolytic cleavage. The released MMAF intracellularly disrupts the microtubule network, leading to cell cycle arrest and apoptosis. It is indicated for the treatment of adults with relapsed or

refractory multiple myeloma who have received at least 4 prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). The safety and efficacy of Blenrep® were assessed in an open-label, multicenter study (DREAMM-2) that included patients with relapsed or refractory multiple myeloma, had previously received 3 or more therapies including an anti-CD38 monoclonal antibody, and were refractory to an immunomodulatory agent and a proteasome inhibitor. Patients had measurable disease by International Myeloma Working Group (IMWG) criteria. Patients with corneal epithelial disease, except mild punctate keratopathy, at baseline were excluded from the study. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). In an open-label study that included 97 patients who received Blenrep® at a dose of 2.5mg/kg the overall response rate was 31%.

Recommendation: Blenrep® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Breztri® Aerosphere (budesonide, glycopyrrolate, formoterol fumarate); **PDL category**- Antiasthmatic Adrenergic Combinations

Breztri® Aerosphere is a metered dose inhaler that delivers a combination of three active ingredients, including budesonide (an anti-inflammatory corticosteroid), glycopyrrolate (a long-acting antimuscarinic agent, or anticholinergic, that exhibits pharmacological effects through inhibition of the M3 receptor at the smooth muscle leading to bronchodilation), and formoterol fumarate (a long-acting selective beta2-adrenergic agonist, or beta2-agonist, with a rapid onset and that cause relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from the cell, especially mast cells). It is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). It is not indicated for the relief of acute bronchospasm or for the treatment of asthma. The safety and efficacy of Breztri® Aerosphere were assessed in two randomized, double-blind, multicenter, parallel-group studies that included subjects with moderate to very severe COPD who remained symptomatic while receiving 2 or more inhaled maintenance treatments for COPD for at least 6 weeks prior to screening. Breztri® Aerosphere was more effective than either of the dual active comparators of budesonide plus formoterol fumarate or glycopyrrolate plus formoterol fumarate for various endpoints in two phase 3 studies that included moderate to severe symptomatic COPD patients, including significantly improving the rate of on-treatment moderate or severe exacerbations over 52 weeks (the primary endpoint in Trial 1). However, at 24 weeks, there was a non-significant improvement in the change from baseline in morning pre-dose trough FEV1 at week 24 as compared with glycopyrrolate plus formoterol fumarate (in Trial 2). There is some evidence at this time to suggest that Breztri® Aerosphere may be more effective than the dual ingredient comparators that were composed of its components (budesonide plus formoterol fumarate or glycopyrrolate plus formoterol fumarate) for certain endpoints assessed in two phase 3 studies, including the rate of on-treatment moderate or severe COPD exacerbations over 52 weeks and an increase in on-treatment FEV1 AUC0-4 at week 24 relative to a budesonide/formoterol fumarate MDI only (the change from baseline in morning pre-dose trough FEV1 at week 24 with Breztri® Aerosphere as compared with glycopyrrolate plus formoterol fumarate was not significant.). However, there is no evidence to suggest that Breztri® Aerosphere is safer or more effective than the other currently preferred, more cost-effective medications including the three ingredients taken separately.

Recommendation: Breztri® Aerosphere be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Cystadrops® (cysteamine opthalmic); **PDL category**- OP- Of Interest

Cysteamine, the active ingredient of Cystadrops®, acts as a cystine-depleting agent by converting cystine to cysteine and cysteine-cysteamine mixed disulfides and reduces corneal cystine crystal accumulation. It is indicated for the treatment of corneal cystine crystal deposits in adults and children with cystinosis. The safety and efficacy of Cystadrops® were assessed in 2 studies, including a single-arm study conducted for 5 years (OCT-1 study) and a randomized controlled study conducted for 90 days (CHOC study). In a small clinical trial, Cystadrops® was associated with a greater reduction from baseline to 90 days in the IVCM total score across all corneal layers compared with control. It is the only eye drop FDA approved for this indication for four times a day use.

Recommendation: Cystadrops® be non-preferred.

Clinical Criteria:

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

Board Decision: The Board unanimously approved the above recommendation.

Cystaran® (cysteamine ophthalmic); **PDL category**- Op- Of Interest

Cysteamine, the active ingredient of Cystaran®, acts as a cystine-depleting agent by converting cystine to cysteine and cysteine-cysteamine mixed disulfides and reduces corneal cystine crystal accumulation. It is indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis. The safety and efficacy of Cystaran® were assessed in controlled trials in approximately 300 patients. The primary endpoint was the response rate defined as a reduction of at least 1 unit in the photo-rated Corneal Cystine Crystal Score (CCCS) at some time point during the study when baseline CCCS ≥1, or a lack of an increase of more than 1 unit in CCCS throughout the study when baseline CCCS <1. In 2 small trials, Cystaran® was associated with a response rate of 33% to 67%. Corneal crystals accumulate if Cystaran® is discontinued.

Recommendation: Cystaran® be non-preferred.

Clinical Criteria:

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

Board Decision: The Board unanimously approved the above recommendation.

Dojolvi® (triheptanoin liquid); **PDL category**- Electrolytes/Nutritionals

Triheptanoin, the active ingredient of Dojolvi®, is a synthetic medium odd-chain (C7) triglyceride; it is a medium-chain triglyceride consisting of three odd-chain 7-carbon length fatty acids (heptanoate) that provide a source of calories and fatty acids to bypass the long-chain fatty acid oxidation disorder enzyme deficiencies for energy production and replacement. Long-chain fatty acid oxidation disorders (LA-FAOD) are a group of rare life-threatening disorders where the body is not able to convert long-chain fatty acids

to energy. Dojolvi® circumvents the enzyme deficiencies that cause LC-FAOD and provide a source of calories and fatty acids that can be converted to energy. It is indicated as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD). The efficacy of triheptanoin as a source of calories and fatty acids was assessed in a one study (Study 3), which was a 4-month double-blind, randomized controlled study that compared triheptanoin (7-carbon chain fatty acid) with trioctanoin (8-carbon chain fatty acid) that included 32 adult and pediatric patients with a confirmed diagnosis of LC-FAOD and evidence of at least one significantly episode of rhabdomyolysis and at least 2 of the following diagnostic criteria: disease specific elevation of acylcarnitine on a new born blood spot or in plasma, low enzyme activity in cultured fibroblasts, or one or more known pathogenic mutations in CPT2, ACADVL, HADHA, or HADHB. In one study, 4 months of triheptanoin (Dojolvi®) resulted in similar mean changes from baseline as trioctanoin in left ventricular ejection fraction and wall mass on resting echocardiogram, as well as similar maximal heart rates on treadmill ergometry in a population with LC FAOD.

Recommendation: Dojolvi® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Enspryng® (satralizumab); **PDL category**- Monoclonal Antibody

Satralizumab-mwge, the active ingredient of Enspryng®, is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody based on a human IgG2 framework. It is produced by recombinant DNA technology in Chinese hamster ovary cells. Its exact mechanism of action is not known but it is presumed to involve inhibition if IL-6 mediated signaling through binding to soluble and membrane-bound IL-6 receptors. It is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults who are anti-aquaporin-4 (AQP4) antibody positive. The safety and efficacy of Enspryng® for the treatment of NMOSD were established in 2 studies. In two placebo-controlled trials, the time to the first Clinical Endpoint Committee (CEC)-confirmed relapse was significantly longer with the Enspryng® group compared to placebo. In addition, significantly more in the Enspryng® group than placebo group were relapse-free at 96 weeks. While there are 3 treatments available for NMOSD, Enspryng® is the only product that can be self-administered by the patient.

Recommendation: Enspryng® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Evrysdi® (risdiplam) allergen powder-dnfp); **PDL category**- Neurologics- SMA

Risdiplam, the active ingredient of Evrysdi®, is a survival of motor neuron 2 (SMN2) splicing modifier designed to treat patients with spinal muscular atrophy (SMA) caused by mutations in chromosome 5q that lead to SMN protein deficiency. Risdiplam was demonstrated to increase exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts and production of full-length SMN protein in the brain. It is indicated for the treatment of spinal muscular atrophy (SMA) in patients 2 months of age and older. The efficacy of Evrysdi® for the treatment of patients with infantile-onset and later-onset spinal muscular atrophy (SMA) was assessed in 2 clinical studies. The overall findings of these studies support the effectiveness of Evrysdi® in SMA patients 2 months of age and older and appear to support the early initiation of treatment with Evrysdi®. In addition, 41% treated with Evrysdi® were able to sit independently for ≥5 seconds after 12 months of treatment. These results are superior to the natural history of the

disease. In the later-onset SMA study, the change from baseline in MFM32 total score at month 12 demonstrated a clinically meaningful and statistically significant difference between patients treated with Evrysdi® and placebo, favoring Evrysdi®.

Recommendation: Evrysdi® be non-preferred.

Clinical Criteria:

- Clinical PA is required to establish diagnosis and medical necessity.
- For patients 2 months of age and older.

Board Decision: The Board unanimously approved the above recommendation.

Gavreto® (pralsetinib); **PDL category**- Cancer

Pralsetinib, the active ingredient of Gavreto®, is an oral receptor tyrosine kinase inhibitor. It is a kinase inhibitor of wild-type RET and oncogenic RET fusions. It is indicated for the treatment of adults with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). The efficacy of Gavreto® was assessed in patients with RET fusion-positive NSCLC in a multicenter, non-randomized, open-label, multi-cohort study. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). In a single-arm, open-label study of patients taking Gavreto®, the overall response rate for RET fusion-positive NSCLC patients who received prior platinum-based chemotherapy was 57%, while for treatment-naïve RET fusion-positive NSCLC patients the overall response rate was 70%.

Recommendation: Gavreto® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Hemady® (dexamethasone); **PDL category**- Glucocorticoids/Mineralocorticoids

Dexamethasone, the active ingredient of Hemady®, is a corticosteroid with anti-inflammatory effects and low mineralocorticoid activity. The exact mechanism of action for its approved indication is not known. Dexamethasone induces apoptosis of multiple myeloma cells. It is indicated in combination with other anti-myeloma products for the treatment of adults with multiple myeloma (MM). There were no clinical trials listed in the Hemady® prescribing information. Following oral administration of a single dose of dexamethasone tablet to healthy subjects, the decrease in mean baseline cortisol concentration was maximal by 12 hours post-dose, with mean cortisol concentrations returning to near baseline about 3 days after drug administration. There is no evidence to suggest that Hemady® is safer or more effective than the other currently preferred, more cost-effective medications.

Recommendation: Hemady® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Inqovi® (cedazuridine and decitabine); **PDL category**- Cancer

Inqovi® is a combination tablet containing both decitabine (a nucleoside metabolic inhibitor) and cedazuridine (a cytidine deaminase inhibitor). It is believed that decitabine exerts its effects after phosphorylation and direct incorporation into DNA and inhibition of DNA methyltransferase, causing hypomethylation of DNA and cellular differentiation and/or apoptosis. Decitabine inhibits DNA methylation in vitro, which is achieved at concentrations that do not cause major suppression of DNA synthesis. Decitabine-induced hypomethylation in cancer cells may restore normal function to genes that are critical for the control of cellular differentiation and proliferation. It is indicated for the treatment of adults with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS with the following French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML]) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups. Inqovi® was assessed in an open-label, randomized, 2-cycle, 2-sequence crossover study that included adults with MDS (International Prognostic Scoring System [IPSS] Intermediate-1, Intermediate-2, or high-risk) or chronic myelomonocytic leukemia (CMML).

Recommendation: Inqovi® be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Kesimpta® (ofatumumab); **PDL category**- Multiple Sclerosis- Non Interferons

Ofatumumab, the active ingredient of Kesimpta®, is a recombinant human monoclonal immunoglobulin G1 (IgG1) antibody that binds to human CD20 expressed on B-cells. The exact mechanism of action by which ofatumumab exerts its therapeutic effects for its approved indication is not known, but is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, ofatumumab results in antibody-dependent cellular cytolysis and complement-mediated lysis. It is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. The safety and efficacy of Kesimpta® were assessed in 2 randomized, double-blind, double-dummy, active comparator-controlled trials of identical design that included patients with relapsing forms of MS. In two phase 3 clinical trials, Kesimpta® was found to be significantly more effective than teriflunomide for the primary endpoint of ARR, with Kesimpta® being associated with lower annualized relapse rates than teriflunomide. Kesimpta® was significantly more effective than teriflunomide for other secondary endpoints assessed. There is some evidence to suggest that Kesimpta® is more effective than oral teriflunomide in two phase 3 studies for the primary endpoint of annualized relapse rate, as well as some secondary endpoints assessed. However, there is no evidence to suggest that Kesimpta® is safer or more effective than other currently preferred, more cost-effective medications.

Recommendation: Kesimpta® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Lampit® (nifurtimox); **PDL category**- Antiprotozoals

Nifurtimox, the active ingredient of Lampit®, is an antiprotozoal. While the mechanism of action is not fully understood, studies suggest that nifurtimox is metabolized/activated by Type I (oxygen insensitive) and Type II (oxygen sensitive) nitro reductases (NTR) leading to production of toxic intermediate

metabolites and/or reactive oxygen species that induce DNA damage and cell death of both intracellular and extracellular forms of T. cruzi. It is indicated in pediatric patients (birth to less than 18 years of age and weighing at least 2.5kg) for the treatment of Chagas disease (American Trypanosomiasis) caused by Trypanosoma cruzi. This indication is approved under accelerated approval based on the number of treated patients who became immunoglobulin G (IgG) antibody negative or who showed an at least 20% decrease in optical density on two different IgG antibody tests against antigens of T. cruzi. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). The safety and efficacy of Lampit® for the treatment of Chagas disease in pediatric patients' birth to less than 18 years of age and weighing at least 2.5kg were demonstrated in one prospective, randomized, double-blind study conducted in Argentina, Bolivia, and Columbia. Pediatric patients (N=330) with serologic evidence of T. cruzi infection and without Chagas disease-related cardiac or gastrointestinal symptoms were randomly assigned to a 60-day or 30-day treatment regimen with nifurtimox. Patients were followed up for one year. Continued approval for this indication may be contingent upon verification and description of clinical benefits in a confirmatory trial. Lampit® tablets should not be split mechanically with a table splitting device, but rather should be broken by hand. In a randomized, double-blind trial, serologic response was superior in the 60-day arm compared with the 30-day arm treatment groups. Note that the 30-day regimen is not an approved dosing regimen.

Recommendation: Lampit® to be preferred.

Clinical Criteria:

- Clinical PA required for appropriate diagnosis.

Board Decision: The Board unanimously approved the above recommendation.

Licart® (diclofenac epolamine); **PDL category**- NSAIDs

Diclofenac epolamine, the active ingredient of Licart®, is a nonsteroidal anti-inflammatory drug with analgesic, anti-inflammatory, and antipyretic properties. The exact mechanism is not completely understood but involves inhibition of cyclooxygenase. Diclofenac is a potent inhibitor of prostaglandin synthesis. It is indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions. f Licart® begins to peel-off, the edges of the topical system may be taped down. If problems with adhesion persist, patients may overlap the topical system with a mesh netting sleeve, where appropriate. The mesh netting sleeve must allow air to pass through and not be occlusive (i.e. non-breathable). Do not apply Licart® to non-intact or damaged skin resulting from any etiology. In addition, do not wear Licart® when bathing or showering. The safety and efficacy of Licart® for the treatment of patients with minor sprains, strains, and/or contusions were assessed in two randomized, double-blind, parallel-arm, placebo- and active-controlled studies. In a study with healthy human volunteers, activated partial thromboplastin time (aPTT), a measure of coagulation, was unchanged following multiple Licart® applications. Flector® has the same active ingredient and indication as Licart® but Flector® is indicated to be used twice daily; it does not contain heparin as an inactive ingredient. In addition, Flector® is available generically.

Recommendation: Licart® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Mycapssa® (octreotide); **PDL category**- Somatostatic Agents

Octreotide, the active ingredient of Mycapssa®, is a somatostatin analog. Octreotide exerts pharmacologic actions similar to the natural hormone somatostatin, but is a more potent inhibitor of growth hormone, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses luteinizing hormone (LH) response to gonadotropin-releasing hormone (GnRH), decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide. It is indicated for the long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide. The efficacy of Mycapssa® was established in a 9-month, randomized, double blind, placebo-controlled study that included patients with acromegaly. The primary endpoint was somatostatin dose-adjusted proportion of patients who maintain their biochemical response, defined as an IGF-1 level ≤ ULN at the end of 9 months of treatment. Results suggested that 58% in the Mycapssa® group vs 19% treated with placebo maintained their biochemical response. There is no evidence to suggest that Mycapssa® is safer or more effective than the other currently preferred, more cost-effective medications. Furthermore, the indication does specifically state use is for patients who have responded to and tolerated treatment with octreotide or lanreotide.

Recommendation: Mycapssa® to be non-preferred.

Clinical Criteria:

- Non-preferred products must be used in specified step order.

Board Decision: The Board unanimously approved the above recommendation.

Ongentys® (opicapone); **PDL category**- Parkinson's- COMT Inhibitors

Opicapone, the active ingredient of Ongentys®, is a peripheral, selective, and reversible catechol-O-methyltransferase (COMT) inhibitor. COMT catalyzes the transfer of the methyl group of S-adenosyl-L-methionine to the phenolic group of substrates that contain a catechol structure. Physiological substrates of COMT include catecholamines (dopamine, norepinephrine, and epinephrine) and their hydroxylated metabolites. When decarboxylation of levodopa is prevented by carbidopa, COMT becomes the major metabolizing enzyme for levodopa, catalyzing its metabolism to 3-methoxy-4-hydroxy-L-phenylalanine (3-OMD). It is indicated as an adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease (PD) experiencing 'off' episodes. The efficacy of Ongentys® for the adjunctive treatment to levodopa/carbidopa in patients with PD experiencing 'off' episodes was assessed in two double-blind, randomized, parallel-group studies of 14 to 15 weeks in duration, with study 1 being placebo- and active-controlled and study 2 being placebo-controlled. The primary endpoint of the least-squares mean change from baseline in absolute time in the off state was -1.605 in the entacapone group. Opicapone 50mg was superior to placebo and non-inferior to entacapone. Entacapone was also superior to placebo. In addition, the % of patients with a reduction of ≥1 hour in time in the off state was 70% with Ongentys® 50mg and 58% with entacapone 200mg, which was not significantly different (p=0.063). For the placebo group, the % of patients was 48%. Opicapone was significantly different from placebo (p=0.001) but entacapone was not significantly different from placebo (p=0.094). There is no evidence to suggest that Ongentys® is safer or more effective than the other currently preferred, more cost-effective medications.
Recommendation: Ongentys® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Onureg® (azacitidine); **PDL category**- Cancer

Azacitidine, the active ingredient of Onureg®, is a nucleoside metabolic inhibitor; it is a pyrimidine nucleoside analog of cytidine that inhibits DNA/RNA methyltransferases. Azacitidine is incorporated into DNA and RNA after cellular uptake and enzymatic biotransformation to nucleotide triphosphates. Incorporation of azacitidine into the DNA of cancer cells in vitro, including acute myeloid leukemia cells, inhibited DNA methyltransferases, reduced DNA methylation and altered gene expression, including re-expression of genes regulating tumor suppression and cell differentiation. Incorporation of azacitidine into the RNA of cancer cells, including leukemic cells, inhibited RNA methyltransferases, reduced RNA methylation, decreased RNA stability and decreased protein synthesis. It is indicated for continued treatment of adults with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy. The safety and efficacy of Onureg® were assessed in a multicenter, randomized, double-blind, placebo-controlled study (QUAZAR) that included adults 55 years of age or older who had AML and were within 4 months of achieving first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) with intensive induction chemotherapy. Due to substantial differences in pharmacokinetic parameters, the recommended dose and schedule for Onureg® are different from those for the IV or SC azacitidine products. Treatment of patients using IV or SC azacitidine at the recommended dosage of Onureg® may result in a fatal adverse reaction. Do not substitute Onureg® for IV or SC azacitidine as the indications and dosage regimen for Onureg® differ from that of IV or SC azacitidine. In a phase 3, placebo-controlled trial, a statistically significant improvement in overall survival was established for patients randomized to Onureg® as compared with placebo.

Recommendation: Onureg® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Polivy® (polatuzumab); **PDL category**- Cancer

Polatuzumab vedotin-piiq, the active ingredient of Polivy®, is a CD79b-directed antibody-drug conjugate (ADC) consisting of 3 components, including the humanized immunoglobulin G1 (IgG1) monoclonal antibody specific for human CD79b; the small molecule anti-mitotic agent MMAE; and a protease-cleavable linker (maleimidocaproyl-valine-citrulline-p-aminobenzyloxycarbonyl or mc-vc-PAB) that covalently attaches MMAE to the polatuzumab antibody. Polatuzumab vedotin-piiq is a CD79b-directed ADC with activity against dividing B cells. The small molecule, MMAE, is an anti-mitotic agent covalently attached to the antibody via a cleavable linker. The monoclonal antibody binds to CD79b, a B-cell specific surface protein, which is a component of the B-cell receptor. Upon binding CD79b, polatuzumab vedotin-piiq is internalized, and the linker is cleaved by lysosomal proteases to enable intracellular delivery of MMAE. MMAE binds to microtubules and kills dividing cells by inhibiting cell division and inducing apoptosis. It is indicated in combination with bendamustine and a rituximab product for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, after at least 2 prior therapies. Accelerated approval was granted for this indication based on complete response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. The efficacy of Polivy® was assessed in an open-label, multicenter study that included a cohort of 80 patients with relapsed or refractory DLBCL after at least one prior regimen. Patients were randomized to receive either Polivy® in combination with bendamustine and a rituximab product (BR) or BR alone for six 21-day cycles. Eligible patients were not candidates for autologous HSCT at study entry. Premedication with an antihistamine and antipyretic was given.

Accelerated approval was granted for this indication based on complete response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. In a clinical trial, the objective response rate at the end of treatment in patients with relapsed or refractory DLBCL was 45% for patients treated with the Polivy® combination as compared with 18% with patients treated with only bendamustine and a rituximab product.

Recommendation: Polivy® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Tecartus® (brexucabtagene autoleucel suspen); **PDL category**- Cancer

Tecartus® is a CD19-directed genetically modified autologous T cell immunotherapy. To prepare Tecartus®, a patient's own T cells are harvested and genetically modified ex vivo by retroviral transduction to express a chimeric antigen receptor (CAR) comprising a murine anti-CD19 single-chain variable fragment (scFv) linked to CD28 and CD3-zeta co-stimulatory domains. The anti-CD19 CAR T cells are expanded and infused back into the patient, where they can recognize and eliminate CD19-expressing target cells. It is indicated for the treatment of adults with relapsed or refractory mantle cell lymphoma (MCL). This indication is approved under accelerated approval based on overall 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. A single-arm, open-label, multicenter study (ZUMA-2) assessed the safety and efficacy of a single infusion of Tecartus® in adults with relapsed or refractory mantle cell lymphoma (MCL) who had previously received anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody, and a Bruton tyrosine kinase inhibitor (BTKi; ibrutinib or acalabrutinib). Eligible patients also had disease progression after their last regimen or refractory disease to their most recent therapy.

Recommendation: Tecartus® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Uplizna® (inebilizumab-cdon); **PDL category**- Monoclonal Antibody

Inebilizumab-cdon, the active ingredient of Uplizna®, is a CD19-directed humanized afucosylated IgG1 monoclonal antibody produced by recombinant DNA technology in Chinese hamster ovary (CHO) cell suspension culture. Its exact mechanism of action is not known but is presumed to involve binding to CD19, a cell surface antigen present on pre-B and mature B lymphocytes. After cell surface binding to B lymphocytes, inebilizumab-cdon results in antibody-dependent cellular cytolysis. It is indicated for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adult patients who are anti-aquaporin-4 (AQP4) antibody positive. The safety and efficacy of Uplizna® for the treatment of NMOSD were assessed in a randomized, double-blind, placebo-controlled study that included adults with NMOSD where 213 adults were anti-AQP4 antibody positive and 17 were anti-AQP4 antibody negative. In clinical trials compared to placebo, the time to the first adjudicated relapse was significantly longer in patients treated with Uplizna® as compared with placebo. Uplizna® use is contraindicated in patients with active hepatitis B infection and with active or untreated latent tuberculosis.

Recommendation: Uplizna® to be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Viltepso® (viltolarsen); **PDL category**- Muscular Dystrophy Agents

Viltolarsen, the active ingredient of Viltepso®, is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. It is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping. It is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Viltepso®. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. The effect of Viltepso® on dystrophin production was assessed in one study that included DMD patients with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. atients treated with Viltepso® 80mg/kg once weekly in a clinical trial (N=8) had mean dystrophin levels increase from 0.6% of normal at baseline to 5.9% of normal by week 25, with a mean change in dystrophin of 5.3% of normal levels (p=0.01). The clinical significance of the increase in dystrophin level – a proxy marker - is unknown at present.

Recommendation: Viltepso® to be non-preferred.

Clinical Criteria:

- Clinical prior authorization to verify diagnosis and use of stable dose of corticosteroid for at least 3 months

Board Decision: The Board unanimously approved the above recommendation.

Xywav® (calcium, magnesium, potassium, & sodium oxybates solution); **PDL category**- Stimulant-Stimulants Like

Xywav® is a CNS depressant that contains a mixture of calcium oxybate, magnesium oxybate, potassium oxybate, and sodium oxybate. The chemical name of oxybate is gamma-hydroxybutyrate (GHB), which is an endogenous compound and metabolite of the neurotransmitter GABA. The exact mechanism of action for its approved indication is not known, but it is hypothesized that the therapeutic effects of Xywav® are mediated through GABAB actions during sleep on noradrenergic and dopaminergic neurons, as well as at thalamocortical neurons. It is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy. It is a Schedule III controlled substance. The efficacy of Xywav® for the treatment of cataplexy and excessive daytime sleepiness in adults with narcolepsy was established in a double-blind, placebo-controlled, randomized-withdrawal study. Results of a clinical trial in adults indicated that patients taking stable doses of Xywav® who discontinued Xywav® treatment and were randomized to placebo during the double-blind, randomized-withdrawal period experienced a significant worsening in the average weekly number of cataplexy attacks and in ESS score as compared with patients randomized to continue treatment with Xywav®. The efficacy of Xywav® in pediatric patients is based upon a clinical study in patients treated with Xyrem®.

Recommendation: Xywav® to be non-preferred. In reviewing the category Xyrem Sol will be moved to the STIMULANT - STIMULANT LIKE category as non-preferred.

Clinical Criteria:

- For patients 7 years of age and older with narcolepsy.
- Xywav: Diagnosis of cataplexy associated with narcolepsy OR excessive daytime sleepiness associated with narcolepsy. Diagnosis must be confirmed by submission of supporting documentation to include the specialist's interpretation of the Polysomnography (PSG) and Multiple Sleep Latency Test (MSLT) results
- FDA reminded healthcare professionals and patients that the combined use of Xyrem (sodium oxybate) with alcohol or central nervous system (CNS) depressant drugs can markedly impair consciousness and may lead to severe breathing problems (respiratory depression

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

CDER proposes withdrawal of approval for Makena
https://www.fda.gov/drugs/drug-safety-and-availability/cder-proposes-withdrawal-approval-makena?utm_medium=email&utm_source=govdelivery

FDA advises health care professionals and patients about insulin pen packaging and dispensing
https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-health-care-professionals-and-patients-about-insulin-pen-packaging-and-dispensing?utm_medium=email&utm_source=govdelivery

FDA Warns that Using a Type of Pain and Fever Medication in Second Half of Pregnancy Could Lead to Complications
https://www.fda.gov/news-events/press-announcements/fda-warns-using-type-pain-and-fever-medication-second-half-pregnancy-could-lead-complications?utm_medium=email&utm_source=govdelivery

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **March 9, 2021** 5:30pm –8:30pm at the Augusta Armory.