Janet T. Mills
Governor

Jeanne M. Lambrew, Ph.D.
Commissioner

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

TO: Maine Drug Utilization Review Board
DATE: 06/15/2019
RE: Maine DUR Board **Meeting** minutes from June 11, 2019

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		
Steve Diaz, MD	X		
Erin Ackley, PharmD.			X
Corinn Martineau, PharmD.			X
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Jacquelyn Hedlund, MD, Change Healthcare	X		
Jill Kingsbury, MaineCare Pharmacy Director	X		

Guests of the Board: Laureen Biczak, DO

CALL TO ORDER: 5:30PM

Jill Kingsbury called the meeting to order at 5:30 PM.

PUBLIC COMMENTS

Karen Phillips from Amgen: Highlighted the attributes of Evenity.
Eric Sherr from VIIV: Highlighted the attributes of Dovato.
Katherine Miller from Sobi: Highlighted the attributes of Gamifant.
Shaffee Bacchus from J&J: Highlighted the attributes of Spravato.
Sarah Hnath from Abbvie: Highlighted the attributes of Skyrizi.
Joel Brown from Novartis: Highlighted the attributes of Mayzent.
Colleen Moffitt from Alnylam: Highlighted the attributes of Onpattro.

OLD BUSINESS

DUR MINUTES

The March DUR meeting minutes with correction: Gordon Smith, Esq were accepted as written.

Board Decision: The Board unanimously approved the above recommendation.

MAINECARE UPDATE

No update at this time.

HEPATITIS C PA FORM FOLLOW UP

Change Healthcare presented data from various states of the provider specialty requirement on the Hepatitis C treatment.

Dr. Biczak, Medical Director with Change Healthcare presented a clinically updated Hepatitis C prior authorization (PA) form.

Board Decision: Approved clinically updated Hepatitis PA form with no change to the specialty consult.

NEW BUSINESS

DATA PRESENTATION: CONTINUOUS USE OF ANTIDEPRESSANTS AT 3, 6 AND 12 MONTHS AFTER INITIATION

The use of antidepressants is common in MaineCare members and they are used to treat both unipolar and bipolar depression as well as anxiety disorders. The lifetime prevalence of major depressive disorder is 16 %. %. The World Health Organization has determined that depression is the 11th greatest cause of disability and mortality in the world. In the US population it is 2nd among all diseases and injuries for disability and is highly recurrent, with rates upwards of 40% at 2 years and 75% in patients at 5 years who have had two or more previous depressive episodes. Clinical trials and meta-analysis have been conducted comparing the various antidepressants, but there is general agreement that there is not one preferred class of medication, or within a class, one preferred drug. Additionally, adherence tends to be poor in patients treated by primary care providers. It is generally advised that patients also receive behavioral therapy and with certain diagnoses, such as bipolar depression, patients will need to be on other mood stabilizing drugs to prevent escalation into mania. Initiation of antidepressant therapy typically involves a gradual increase in the dose of antidepressant, sometimes switching to an alternative agent based on the side effects of the initial drug. The continuation phase of treatment generally lasts from 9-12 months, with many patients progressing on to maintenance therapy.

Identified members with at least one prescription for an antidepressant (SSRIs, SNRIs, TCAs, MAOIs, atypical antidepressants, serotonin modulators). For each, looked at duration of therapy at time points 3,6 and 12 months, switches to other antidepressants, co-administration of other antidepressants and diagnosis. For those with bipolar depression, identified if members are on other recommended mood stabilizing drugs concomitantly.

Our observations of the data are that few members are started on a tricyclic antidepressant, despite their effectiveness, tolerability and low cost, and that there is no more frequent switching to other class of antidepressant from TCIs due to their side-effects. There is a high incidence of discontinuation of drugs of all classes before 3 months. This could be due to delayed effectiveness and impatience, side-effects or failure. A significant percentage of members are on more than one antidepressant.

Additionally, a small minority of patients with a diagnosis of bipolar disorder are on mood stabilizing drugs, despite the fact that use of antidepressants alone can exacerbate the bipolar symptoms and patients become tolerized and refractory to the antidepressant effects.

Recommendation: Given the morbidity associated with bipolar disorder, targeted education to the psychiatric community about mood stabilizing drug benefits might be warranted. General education to the medical community at large about the cost-effectiveness and clinical benefit of TCAs also may be worthwhile.

Board Decision: The Board unanimously approved the above recommendation. Further data will be gathered on age of patients and a sample of providers will be pulled to look at their specialty.

INTRODUCATION: APPROPRIATE USE OF ASTHMA CONTROLLER MEDICATIONS

The National Heart, Lung and Blood Institute has published Guidelines for the Diagnosis and Management of Asthma. The treatment of asthma is done in a step-wise manner, and depending on disease severity, a combination of several agents may be needed. For anyone who requires use of a short acting agent ≥ 2 days/week, a controller medication daily is recommended. The Guidelines state that the frequency of short acting beta-adrenergic inhaler (SABA) use can be clinically useful as a measure of disease activity since increased use of a SABA has been associated with increased risk for death or near death in patients who have asthma. Use of more than one SABA canister every one to two months is also associated with an increased risk of an acute exacerbation. Therefore, the use of more than one SABA canister (e.g., albuterol 200 puffs per canister) during a one-month period most likely indicates over reliance on this drug and suggests inadequate control of asthma. Additionally, inhaled corticosteroids (ICS) are the preferred long-term control therapy in asthma for all ages, although leukotriene receptor antagonists (LTRA) are listed as an alternative. Long-acting beta-adrenergic inhalers (LABAs) should never be used without first using ICS inhalers due to the increased risk of asthma exacerbations and death.

We will use paid, non-reversed Medicaid pharmacy claims from January 2018 through December 2018, excluding members with Part D, MaineRX and TPL. Change Healthcare will review paid non-reversed pharmacy and medical claims with dates of service from 1/1/2018 through 12/31/2018, excluding members who had a diagnosis of cystic fibrosis, COPD or emphysema. Members will be stratified by age and the number of short acting inhalers used per year. In addition, the number of members in each group who had an ER visit or hospitalization associated with an asthma diagnosis during the study period will be reported. We will compare the rates of ER visits and hospitalizations to the rates seen in the 2015 analysis, examining whether the educational interventions provided by the Board had an impact in reducing rates of asthma exacerbations, understanding that the populations are not identical. Additional analysis will be done on those using more than 12 short acting inhalers/year and sorted geographically. The prescribers for these members will be identified to look at providers who are possibly practicing outside of guideline recommendations, perhaps identifying those who would be appropriate for more targeted education.

Board Decision: No action needed at this time.

ANTI- OBESITY MEDICATIONS

Dr. Pezzullo worked with obesity specialist from EMMC and MaineGeneral on proposed anti- obesity medication coverage.

Criteria for approval:

a) Patient must be at least 12 years of age (Xenical only) at least 16 years of age (Apidex, Phentermine, Lomaira) or at least 18 years of age (Belviq, Contrave, Qsymia, Saxenda), **And;**
b) Less than 5% weight loss over a 3month period, after documented attempts at lifestyle changes initiated and followed by PCP monthly. Instruction for lifestyle changes must include behavioral modification, dietary change instruction and instruction for increased physical activity. If such lifestyle change instruction is not able to be provided or directed by the PCP, patient should be referred to an Obesity Medicine Specialist before medication is considered.
    - For pediatric population-involvement in a comprehensive multi-disciplinary team of ILT for 3 months without improvement in BMI % and ≥ 95% BMI
c) C. Baseline body mass index (BMI) must be:
    - ≥ to 30kg/m^2 with no risk factors, **OR**
    - ≥ to 27kg/m^2 with at least 1 very high risk factor **OR** at least 2 other risk factors (See Table 1), **OR**
    - Waist circumference must be:
        - 102 cm for men and .88cm for women with at least 1 very high- risk factor or at least 2 other risk factors (See Table 1)
    - Pediatric Patients: BMI >/= 95th%
d) No contraindications (disease state or current therapy) should exist, unless prescriber documents that benefits outweigh risks. (See Table 2)
e) Postop regain after bariatric surgery
f) Medication induced weight gain of 5% or greater
g) Binge Eating Disorder Independent of weight gain or BMI

Criteria for Renewal:

a) On-going prescriber documentation in regards to lifestyle change.
b) Renewal at 6 month intervals will be considered if patient has achieved or maintained weight loss of 5% or BMI improvement of at least 5%. For Pediatric population, a stabilization or decrease in BMI % above the 95th%.
c) No contraindications (disease state or current therapy) should exist; unless prescriber documents that benefits outweigh risks.
d) Xenical may not be approved for therapy beyond four (4) years of therapy.

Criteria for Denial:

a) Prior approval will be denied if approval criteria are not met.

Exceptions to Approval and Renewal Criteria:

a) Prescribers working in a High Intensity Multidisciplinary setting as Obesity Medicine Specialists, ABOM providers.

Recommendation: Approve the above criteria with the change that the exception to approval and renewal criteria be removed and that all providers be subject to PA requirements.

Board Decision: The Board unanimously approved the above recommendation.

NEW DRUG REVIEW

Apadaz® (benzhydrocodone & acetaminophen (APAP)); **PDL category-** Narcotics, Misc.

Apadaz® is an immediate-release, fixed-dose combination of benzhydrocodone (an opioid agonist) and acetaminophen. Benzhydrocodone is a pro-drug of hydrocodone, a full opioid agonist with relative selectivity for the mu-opioid receptor. The main therapeutic action of hydrocodone is analgesia. Like all full opioid agonists, there is no ceiling effect for analgesia with hydrocodone. Acetaminophen is a non-opioid, non-salicylate analgesic. The mechanism of action has not been determined but it is thought to primarily involve central actions. Apadaz® contains benzhydrocodone, a Schedule II controlled substance. It is indicated for the short-term (no more than 14 days) management of acute pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz® for use in patients for whom alternative treatment options (e.g. non-opioid analgesics):

- have not been tolerated, or are not expected to be tolerated
- have not provided adequate analgesia, or are not expected to provide adequate analgesia

There were no clinical trials listed in the prescribing information for Apadaz®. Apadaz® met the bioequivalence criteria for hydrocodone AUC and Cmax to other immediate-release hydrocodone combination products. Benzhydrocodone was not detectable in plasma after oral administration in clinical studies, indicating that exposure to benzhydrocodone was minimal and transient. Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve Apadaz® for use in patients for whom alternative treatment options (e.g. non-opioid analgesics) have not been tolerated or are not expected to be tolerated OR have not provided adequate analgesia or are not expected to provide adequate analgesia. Benzhydrocodone is a prodrug of hydrocodone. Apadaz® is not expected to deter abuse by the oral or nasal routes of administration. Apadaz® should be non-preferred and authorized only after trial of every preferred opioid analgesic-APAP combination.

Recommendation: Apadaz® be 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. Please refer to General Criteria category E.

Board Decision: The Board unanimously approved the above recommendation.

Balversa® (erdafitinib); **PDL category**- Cancer

Erdafitinib, the active ingredient of Balversa®, is a kinase inhibitor that binds to and inhibits enzymatic activity of fibroblast growth factor receptor 1 (FGFR1), FGFR2, FGFR3, and FGFR4 based on in vitro data. Erdafitinib inhibited FGFR phosphorylation and signaling and decreased cell viability in cell lines

expressing FGFR genetic alterations, including point mutations, amplifications, and fusion. It is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma that has:

- Susceptible FGFR3 or FGFR2 genetic alterations, and
- Progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy

Select patients for therapy based on an FDA-approved companion diagnostic for Balversa®. This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. The safety and efficacy of Balversa® were assessed in a multicenter, open-label, single-arm study that included patients with locally advanced or metastatic urothelial carcinoma (mUC). In a single-arm phase 3 study, the overall response rate for Balversa® was 32.2% and a duration of response of 5.4 months.

Recommendation: Balversa® be non-preferred.

Clinical Criteria: Balversa will be considered for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma that has: Susceptible FGFR3 or FGFR2 genetic alterations, and Progressed during or following at least one line of prior platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy

Board Decision: The Board unanimously approved the above recommendation.

Cablivi® (caplacizumab-yhdp); **PDL category**- Hematologic Disorder Treatment Agents

Caplacizumab-yhdp, the active ingredient of Cablivi®, is a von Willebrand factor (vWF)-directed antibody fragment that consists of 2 identical humanized building blocks. Caplacizumab-yhdp targets the A1-domain of vWF, and inhibits the interaction between vWF and platelets, thereby reducing both vWF-mediated platelet adhesion and platelet consumption. It is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy. The efficacy of Cablivi® for the treatment of adults with acquired thrombotic thrombocytopenic purpura (aTTP) in combination with plasma exchange and immunosuppressive therapy was established in a multicenter, randomized, double-blind, placebo-controlled study (HERCULES). In a clinical trial, its efficacy was based on time to normalization of platelet count as compared with placebo, as well as reduction of composite events of TTP-related death, recurrence of TTP, or major thromboembolic events.

Recommendation: Cablivi® be non-preferred.

Clinical Criteria:

- Cablivi is recommended for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.

Board Decision: The Board unanimously approved the above recommendation.

Diacomit® (stiripentol); **PDL category**- Anticonvulsants

Stiripentol, the active ingredient of Diacomit®, is an anticonvulsant. The exact mechanism of action is not known, but possible mechanisms of action include direct effects mediated through the gamma-aminobutyric acid $(GABA)_A$ receptor and indirect effects involving inhibition of CYP450 activity with resulting increase in blood levels of clobazam and its active metabolite. It is indicated for the treatment of seizures associated with Dravet syndrome (DS) in patients 2 years of age and older taking clobazam. There are no clinical data to support the use of Diacomit® as monotherapy in DS. The safety and efficacy of Diacomit® were assessed in 2 multicenter, placebo-controlled, double-blind, randomized studies that included patients 3 years of age to less than 18 years of age with Dravet syndrome and inadequately controlled on clobazam and valproate. Patients had at least 4 generalized clonic or tonic-clonic seizures per month despite optimized therapy. There are no clinical data to support the use of Diacomit® as monotherapy in Dravet syndrome. In clinical trials as add-on to clobazam and valproate, Diacomit® significantly improved response rates and the changes in seizure frequency as compared to placebo. These were small randomized studies that included pediatric patients uncontrolled on their current regimen. There is no evidence that Diacomit® is safer or more effective than the currently available, less costly treatment options.

Recommendation: Diacomit® be non-preferred.

Clinical Criteria:

- Clinical PA required for appropriate diagnosis.
- Diacomit is for the treatment of seizures associated with Dravet syndrome (DS) in patients 2 years of age and older taking clobazam. There are no clinical data to support the use of Diacomit® as monotherapy in DS.
- DDI: Concomitant use of Diacomit® with other CNS depressants, including alcohol, may increase the risk of sedation and somnolence. Concomitant use of strong inducers (CYP1A2, CYP3A4, or CYP2C19 inducers, such as rifampin, phenytoin, phenobarbital, and carbamazepine) should be avoided, or dosage adjustments should be made.

Board Decision: The Board unanimously approved the above recommendation.

Dovato® (dolutegravir sodium and lamivudine); **PDL category**- Antiretrovirals

Dovato® is a fixed-dose combination tablet containing dolutegravir (an integrase strand transfer inhibitor or INSTI) and lamivudine (a nucleoside analogue reverse transcriptase inhibitor or NRTI). Dolutegravir inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral DNA integration, which is essential for the HIV replication cycle. Lamivudine inhibits reverse transcriptase via DNA chain termination after incorporation of the nucleotide analogue. It is indicated as a complete regimen for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in adults with no antiretroviral treatment history and with no known substitutions associated with resistance to the individual components of Dovato®. The safety and efficacy of Dovato® is supported by data from 2 randomized, double-blind, controlled trials that included HIV-1 infected adults with no antiretroviral treatment history. The components of Dovato® are available as two individual tablets at a significantly lower net cost and should be used when this combination therapy is appropriate

Recommendation: Dovato® be non-preferred.

Clinical Criteria:

- Request will require use of the individual components.

Board Decision: The Board unanimously approved the above recommendation.

Evenity® (romosozumab-aqqg); **PDL category**- Osteoporosis

Romosozumab-aqqg, the active ingredient of Evenity®, is a humanized monoclonal antibody (IgG2) produced in a mammalian cell line (Chinese Hamster Ovary) by recombinant DNA technology that binds to and inhibits the action of sclerostin. Sclerostin is a regulatory factor in bone metabolism. Evenity® increases bone formation, and to a lesser extent, decreases bone resorption. It is indicated for the treatment of osteoporosis in postmenopausal women at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. The anabolic effect of Evenity® wanes after 12 monthly doses of therapy. Therefore, the duration of Evenity® should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.

Recommendation: Evenity® be 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.
- Quantity limits apply, please see dosage consolidation list.
- Evenity® should be limited to 12 monthly doses

Board Decision: The Board unanimously approved the above recommendation.

Firdapse® (amifampridine); **PDL category**- Neurologics, Miscellaneous

Amifampridine phosphate, the active ingredient of Firdapse®, is a voltage-gated potassium channel blocker. The mechanism by which it exerts its therapeutic effects for its indication has not been fully established. Amifampridine is a broad-spectrum potassium channel blocker. It is indicated for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults. The safety and efficacy of Firdapse® for the treatment of LEMS were assessed in 2 randomized, double-blind, placebo-controlled discontinuation studies that included adults with a confirmed diagnosis of LEMS based on either neurophysiology studies or a positive anti-P/Q type voltage-gated calcium channel antibody test (N=64). Compared with placebo, it was found to be associated with significantly higher muscle strength scores and patient satisfaction scores. It is recommended that Firdapse® should be non-preferred in order to confirm the appropriate diagnosis and clinical parameters for its use.

Recommendation: Firdapse® be non-preferred.

Clinical Criteria:

- Firdapse is recommended for the treatment of Lambert-Eaton myasthenic syndrome (LEMS) in adults.

Board Decision: The Board unanimously approved the above recommendation.

Gamifant® (emapalumab- lzsg); **PDL category**- Monoclonal Antibody

Emapalumab-lzsg, the active ingredient of Gamifant®, is an interferon gamma blocking antibody produced in Chinese Hamster Ovary cells by recombinant DNA technology. It is a monoclonal antibody that binds to and neutralizes interferon gamma. Nonclinical data suggest that interferon gamma plays a pivotal role in the pathogenesis of hemophagocytic lymphohistiocytosis (HLH) by being hypersecreted. It is indicated for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent, or progressive disease or intolerance with conventional HLH therapy. The safety and efficacy of Gamifant® were assessed in a multicenter, open-label, single-arm study that included pediatric patients (N=27) with suspected or confirmed HLH with either refractory, recurrent, or progressive disease during conventional HLH therapy or who were intolerant of conventional HLH therapy. The efficacy of Gamifant® was based on overall response rate (ORR) at the end of treatment, defined as achievement of either a complete or partial response or HLH improvement.

Recommendation: Gamifant® be non-preferred.

Clinical Criteria:

- Gamifant is recommended for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent, or progressive disease or intolerance with conventional HLH therapy.

Board Decision: The Board unanimously approved the above recommendation.

Inbrija® (levodopa); **PDL category**- Parkinson's- Dopaminergics/Carbidopa/Levodopa

Levodopa, the active ingredient of Inbrija®, is the metabolic precursor of dopamine. It crosses the blood-brain barrier and presumably is converted to dopamine in the brain. This is thought to be the mechanism where levodopa relieves symptoms of Parkinson's disease. It is indicated for the intermittent treatment of OFF episodes in patients with Parkinson's disease treated with carbidopa/levodopa. The safety and efficacy of Inbrija® for the treatment of OFF episodes in patients with Parkinson's disease treated with carbidopa/levodopa were assessed in a randomized, placebo-controlled, double-blind study (N=226) of 12 weeks in duration. In a clinical trial compared with placebo, Inbrija® was found to have a significant change in the UPDRS Part III motor score. In addition, significantly more in the Inbrija® group returned to an ON state and sustained that ON state through 60 minutes post-dose as compared with placebo (NNT 5).

Recommendation: Inbrija® be non-preferred.

Clinical Criteria:

- Inbrija is recommended for the intermittent treatment of OFF episodes in patients with Parkinson's disease treated with carbidopa/levodopa.

Board Decision: The Board unanimously approved the above recommendation.

Krintafel® (tafenoquine succinate); **PDL category-** Antimalarial Agents

Tafenoquine succinate, the active ingredient of Krintafel®, is an 8-aminoquinoline antimalarial drug. It is active against the liver stages, including the hypnozoite (dormant stage) of *P. vivax*. It is active against pre-erythrocytic (liver) and erythrocytic (asexual) forms as well as gametocytes of *P. vivax*. The activity of tafenoquine against the pre-erythrocytic liver stages of the parasite prevents the development of the erythrocytic forms of the parasite, which are responsible for relapses in *P. vivax* malaria. In addition to its effect on the parasite, tafenoquine causes red blood cell shrinkage in vitro. The molecular target of tafenoquine is not known. A potential for development of resistance of *Plasmodium* species to tafenoquine was not evaluated. It is indicated for the radical cure (prevention of relapse) of Plasmodium vivax malaria in patients 16 years of age and older who are receiving appropriate antimalarial therapy for acute P. vivax infection. Krintafel® is not indicated for the treatment of acute P. vivax malaria. The safety and efficacy of Krintafel® were assessed in a double-blind, controlled trial that included adults (N=522) positive for P.vivax across 3 regions (Asia, Africa, and Latin America). All patients received chloroquine to treat the acute infection in addition to either a one-time dose of Krintafel® on day 1 or day 2 (N=260), an active control (N=129), or placebo (N=133). Compared with placebo plus chloroquine, Krintafel® plus chloroquine demonstrated a statistically significantly higher rate of recurrence-free efficacy.

Recommendation: Krintafel® be preferred.

Clinical criteria:
- Krintafel is preferred for ≥ 16 years of age.
- DDI: Krintafel® with Organic Cation Transporter 2 (OCT2) and Multidrug and Toxin Extrusion (MATE) substrates (e.g. dofetilide, metformin).

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

Mavenclad® (cladribine); **PDL category-** Multiple Sclerosis- Non-Interferons

Cladribine, the active ingredient of Mavenclad®, is a nucleoside metabolic inhibitor. The mechanism by which it exerts its therapeutic effects in patients with MS has not been fully elucidated but is thought to involve cytotoxic effects on B and T lymphocytes through impairment of DNA synthesis, resulting in depletion of lymphocytes. It is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Because of its safety profile, use of Mavenclad® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. Mavenclad® is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile. **:** The efficacy of Mavenclad® was demonstrated in a 96-week randomized, double-blind, placebo-controlled clinical study in patients with relapsing forms of MS. Compared to placebo in a phase 3 study, Mavenclad® significantly lowered the annualized relapse rate. Because of its safety profile, use of Mavenclad® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate drug indicated for the treatment of MS. Mavenclad® is not recommended

for use in patients with clinically isolated syndrome (CIS) because of its safety profile. There is no evidence at this time that Mavenclad® is safer than the currently preferred, more cost-effective medications. Furthermore, Mavenclad® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternative drug indicated for the treatment of MS due to its safety profile.

Recommendation: Mavenclad® be non-preferred.

Clinical Criteria:

- Preferred drugs must be tried and failed due to lack of efficacy or intolerable side effects before non-preferred drugs will be approved (in step order), unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.
- Multiple trials of preferred MS agents including Mayzent for secondary progressive disease

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

Mayzent® (siponimod); **PDL category-** Multiple Sclerosis- Non-Interferons

Siponimod, the active ingredient of Mayzent®, is a sphingosine-1-phosphate (S1P) receptor modulator. It binds with high affinity to S1P receptors 1 and 5 and blocks the capacity of lymphocytes to egress from lymph nodes, reducing the number of lymphocytes in peripheral blood. While the mechanism by which siponimod exerts its effect in multiple sclerosis is not known, it may involve reduction of lymphocyte migration in the CNS. 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 Mayzent® was demonstrated in a randomized, double-blind, parallel-group, placebo-controlled, time-to-event study in patients with secondary progressive MS (SPMS) who had evidence of disability progression in the prior 2 years, no evidence of relapse in 3 months prior to the study, and an Expanded Disability Status Scale (EDSS) score of 3.0-6.5 at study entry (N=1651). In a clinical trial, it significantly decreased the proportion of patients with confirmed disability progression at 3 months as compared with placebo; however, it did not demonstrate a significant effect on the timed 25-foot walk test. Comparator studies with other active agents indicated for MS were not found. It is recommended to test patients for CYP2C9 variants to determine CYP2C9 genotype before starting treatment. An FDA-cleared or FDA-approved test for the detection of CYP2C9 variants to direct the use of siponimod is not currently available. Dosing is based on CYP2C9 genotypes.

Recommendation: Mayzent® be non-preferred.

Clinical Criteria:

- DDI: Due to significant increases in exposure to siponimod, concomitant use of Mayzent® and drugs that cause moderate CYP2C9 and moderate or strong CYP3A4 inhibition is not recommended.
- Relapsing forms of MS – multiple trials of preferred agents, including an intravenous MS product.
- Active secondary progressive disease- prior trials of two preferred agents

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

Motegrity® (prucalopride); **PDL category-** GI- Misc.

Prucalopride succinate, the active ingredient of Motegrity®, is a serotonin type 4 (5-HT4) receptor agonist. It is a gastrointestinal (GI) prokinetic agent that stimulates colonic peristalsis (high-amplitude propagating contractions [HAPCs]), which increases bowel motility. In isolated GI tissues from various animal species, prucalopride facilitated acetylcholine release to enhance the amplitude of contractions and stimulate peristalsis. It is indicated for the treatment of chronic idiopathic constipation (CIC) in adults. The safety and efficacy of Motegrity® were assessed in 6 double-blind, placebo-controlled, randomized multicenter studies that included adults with CIC (N=2484). It was found in clinical trials to have a significantly higher responder rate in 5 of the 6 studies, with a responder being defined as a patient with an average of ≥3 CSBMs per week, over the 12-week treatment period. A 2018 systematic review and meta-analysis by Nee et al[2] included 27 placebo-controlled trials to assess the safety and efficacy approved treatments for OIC. The most common primary outcome was 3 or more complete SBMs a week over the trial period. Results suggested that overall, the mu-opioid receptor antagonists, lubiprostone, and prucalopride were superior to placebo for the treatment of OIC.

Recommendation: Motegrity® be 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.

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

Onpattro® (patisiran injection, lipid complex); **PDL category**- hATTR Agents

Patisiran, the active ingredient of Onpattro®, is a double-stranded small interfering ribonucleic acid (siRNA) formulated as a lipid complex for delivery to hepatocytes. Patisiran causes degradation of mutant and wild-type transthyretin (TTR) messenger RNA (mRNA) through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. It is indicated for the treatment of polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. The safety and efficacy of Onpattro® were assessed in a randomized, double-blind, placebo-controlled, multicenter study that included adults with polyneuropathy caused by hATTR amyloidosis. It has been shown to provide some benefit to patients with this disease but is extremely costly (more than ten times the cost required to meet the ICER cost-effectiveness threshold).

Recommendation: Onpattro® be non-preferred.

Clinical Criteria:

- PA required for appropriate diagnosis.
- 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. As listed in MaineCare Policy, certain drugs require specific diagnoses for approval.

Board Decision: The Board unanimously approved the above recommendation.

Qmiiz® ODT (meloxicam); **PDL category-** COX-2 Inhibitors Selective/Highly Selective

Meloxicam, the active ingredient of Qmiiz® ODT, is a nonsteroidal anti-inflammatory drug. It has analgesic, anti-inflammatory, and antipyretic properties. The mechanism of action, like that of other NSAIDs, is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2). Meloxicam is a potent inhibitor of prostaglandin synthesis in vitro. It is indicated for the relief of the signs and symptoms of osteoarthritis (OA) in adults, the relief of the signs and symptoms of rheumatoid arthritis (RA) in adults, the relief of the signs and symptoms of pauciarticular or polyarticular course juvenile rheumatoid arthritis (JRA) in pediatric patients who weigh ≥60kg. The clinical trials section for Qmiiz® ODT included the same trials that are included in the prescribing information for Mobic® (meloxicam tablets). Mobic® and its generic equivalent have been available for numerous years and have been found to be safe and effective for its approved indications, which are the same as Qmiiz® ODT. Qmiiz® ODT has been shown to meet bioequivalence criteria for both Cmax and AUC as compared to Mobic® tablets, but the Tmax was delayed with food. Qmiiz® ODT is not interchangeable with other formulations of oral meloxicam product even if the total mg strength is the same, as Qmiiz® ODT has not shown equivalent systemic exposure with a comparable pharmacokinetic profile to other approved formulations of oral meloxicam.

Recommendation: Qmiiz® ODT be non-preferred.

Board Decision: The Board unanimously approved the above recommendation.

Rocklatan® (netarsudil and latanoprost); **PDL category**- Op-Rho Kinase Inhibitors/Prostaglandin Combinations

Rocklatan® is a fixed-dose combination ophthalmic product containing a Rho kinase inhibitor (netarsudil) and a prostaglandin F2α analogue (latanoprost). Both active ingredients decrease elevated IOP. Rocklatan® is believed to reduce IOP by increasing the outflow of aqueous humor. Elevated IOP represents a major risk factor for glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and glaucomatous visual field loss. It is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension. The safety and efficacy of Rocklatan® were assessed in 2 randomized and controlled trials (study 301 and study 302) that included patients with open-angle glaucoma and ocular hypertension with an IOP <36mmHg. There is some evidence to suggest that Rocklatan® is more effective as compared with either of its individual ingredients; however, there is no evidence at this time to suggest that Rocklatan® is safer or more effective than the currently preferred, more cost-effective medications, including other monotherapy or combination therapies.

Recommendation: Rocklatan® be non-preferred.

Clinical Criteria: Preferred drugs must be tried and failed, in step-order, due to lack of efficacy (failure to reach target IOP reduction) or intolerable side effects before non-preferred drugs will be approved, unless an acceptable clinical exception is offered on the Prior Authorization form, such as the presence of a condition

that prevents usage of the preferred drug or a significant potential drug interaction between another drug and the preferred drug(s) exists.

Board Decision: The Board unanimously approved the above recommendation.

Skyrizi® (risankizumab-rzaa); **PDL category**- Psoriasis Biologicals

Risankizumab-rzaa, the active ingredient of Skyrizi®, is a humanized immunoglobulin G1 (IgG1) monoclonal antibody produced using recombinant DNA technology. It selectively binds to the p19 subunit of human interleukin 23 (IL-23) cytokine and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Risankizumab-rzaa inhibits the release of pro-inflammatory cytokines and chemokines. It is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. The safety and efficacy of Skyrizi® were assessed in 4 multicenter, randomized, double-blind studies (ULTIMMA-1, ULTIMMA-2, IMMHANCE, and IMMVENT) that included adult subjects ≥18 years of age with moderate to severe plaque psoriasis who had a body surface area (BSA) involvement of ≥10%, a static Physician's Global Assessment (sPGA) score of ≥3 (moderate) in the overall assessment (plaque thickness/induration, erythema, and scaling) of psoriasis on a severity scale of 0 to 4, and a Psoriasis Area and Severity Index (PASI) score ≥12. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$ vs placebo and ustekinumab). In addition, 63 (63%) receiving ustekinumab achieved sPGA 0 or 1. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$ vs placebo and ustekinumab). In the ULTIMMA-2 study, 47 (47.5%) of the ustekinumab group achieved PASI 90. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$ vs placebo and ustekinumab). In addition, 61 (61.6%) receiving ustekinumab achieved sPGA 0 or 1. Skyrizi® was significantly more effective than placebo and ustekinumab for this endpoint ($p<0.0001$).

Recommendation: Skyrizi® be 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.

Board Decision: The Board unanimously approved the above recommendation.

Spravato® (esketamine); **PDL category**- Antidepressants- Selected SSRIs

Esketamine, the active ingredient of Spravato®, is a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist. The mechanism by which it exerts its antidepressant effect is not known. Esketamine is the S-enantiomer of racemic ketamine. It is indicated in conjunction with an oral antidepressant, for the treatment of treatment-resistant depression (TRD) in adults. It is not approved as an anesthetic agent. The safety and effectiveness of Spravato® as an anesthetic agent have not been established. The safety and efficacy of Spravato® were assessed in a randomized, placebo-controlled, double-blind, multicenter short-term phase 3 study of 4 weeks duration that included adults 18 to <65 years of age with treatment

resistant depression. It is not approved as an anesthetic agent as the safety and efficacy of use as an anesthetic agent have not been established. Patients in the short-term study met DSM-5 criteria for MDD and in the current depressive episode had not responded adequately to at least 2 different antidepressants of adequate dose and duration. Spravato® plus a newly initiated oral antidepressant demonstrated statistical superiority for the change from baseline in the MADRS total score at the end of 4 weeks as compared with placebo nasal spray and a newly initiated oral antidepressant. Because of serious adverse outcomes from sedation, dissociation, and abuse and misuse, Spravato® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Spravato® REMS.

Recommendation: Spravato® be non-preferred.

Clinical Criteria:

Antidepressants- Selected SSRI's

- Remove criteria for new starters <18 years of age: Must have had fluoxetine trial for at least 30 days before accessing other preferred antidepressants without PA.
- Remove requirement of anxiety diagnosis on prescriptions
- Paroxetine: Continue to have Strong caution with pediatric population.
- Spravato- Administered in an equipped and accredited conscious sedation facility or department. Psychiatry recommended.

Board Decision: The Board unanimously approved the above recommendation.

Tegsedi® (inotersen); **PDL category**- hATTR Agents

Inotersen, the active ingredient of Tegsedi®, is an antisense oligonucleotide (ASO) inhibitor of human transthyretin (TTR) protein synthesis. It causes degradation of mutant and wild-type TTR mRNA through binding to the TTR mRNA, which results in a reduction of serum TTR protein and TTR protein deposits in tissues. Serum TTR is a carrier of retinol binding protein, which is involved in the transport of vitamin A in the blood. Mean reductions in serum retinol binding of 71%, and serum vitamin A of 63%, were seen at week 65. It is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults. The efficacy of Tegsedi® was assessed in a randomized, double-blind, placebo-controlled, multicenter study that included adults with polyneuropathy caused by hATTR amyloidosis. In a clinical trial compared with placebo, changes from baseline to week 66 on co-primary endpoints significantly favored Tegsedi®. Tegsedi® is the second RNA interference (RNAi) therapy, after Onpattro® (patisiran), to be approved for the treatment of hATTR amyloidosis with familial amyloidotic polyneuropathy. Both drugs have been shown to provide some benefit to patients with this disease, but both are extremely costly (more than ten times the cost required to meet the ICER cost-effectiveness threshold). Unlike Onpattro® (patisiran), Tegsedi® (the costlier of the two) has a box warning (for thrombocytopenia and renal toxicity) that requires additional monitoring. It is available through a REMS program and limited pharmacy network.

Recommendation: Tegsedi® be 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. As listed in MaineCare Policy, certain drugs require specific diagnoses for approval.
- Tegsedi® should be non-preferred and approved for patients for whom other treatments, including Onpattro®, have been ineffective.
- PA required for appropriate diagnosis.

Board Decision: The Board unanimously approved the above recommendation.

Xyosted® (testosterone enanthate); **PDL category**- Androgens/Anabolic

Testosterone enanthate, the active ingredient of Xyosted®, is an ester derivative of the endogenous androgen testosterone. Endogenous androgens, including testosterone, are responsible for the normal growth and development of the male sex organs and for maintenance of secondary sex characteristics. Xyosted® is a Schedule III controlled substance. It is indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.

- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter's syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

The safety and efficacy of Xyosted® in adult males with 'age-related hypogonadism' (also referred to as 'late-onset hypogonadism') have not been established. The safety and efficacy of Xyosted® in males less than 18 years of age have not been established. Xyosted® has a box warning regarding blood pressure increases. Xyosted® can cause blood pressure increases that can increase the risk for major adverse cardiovascular events (MACE), including non-fatal MI, non-fatal stroke, and cardiovascular death, with greater risk for MACE in patients with cardiovascular risk factors or established cardiovascular disease. The safety and efficacy of Xyosted® were assessed in a 52-week, open-label study that included adult males with hypogonadism. In clinical studies, Xyosted® was found to deliver physiologic amounts of testosterone, producing circulating testosterone levels that approximate normal concentrations (of 300-1100ng/dL) in healthy men.

Recommendation: Xyosted® be 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. Additionally, laboratory evidence of a testosterone deficiency must be supplied. One of each dosage form should be tried (tablet, injection, and topical).

Board Decision: The Board unanimously approved the above recommendation.

Yupelri® (revefenacin); **PDL category**-

Revefenacin, the active ingredient of Yupelri®, is a long-acting muscarinic antagonist, which is often referred to as an anticholinergic. It has similar affinity to the subtypes of muscarinic receptors M1 to M5. In the airways, it exhibits its pharmacological effects through inhibition of the M3 receptors at the smooth muscle, leading to bronchodilation. It is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). The safety and efficacy of Yupelri® were assessed in 2 dose-ranging studies, 2 replicate 12-week, phase 3 confirmatory studies, and a 52-week safety trial. The efficacy of Yupelri® is mainly based on the two replicate, phase 3 placebo-controlled confirmatory trials. Yupelri® is the first and only once-daily inhaled bronchodilator FDA approved for COPD. Lonhala® Magnair is an inhaled long-acting bronchodilator indicated for COPD and it is the first nebulized long-acting antimuscarinic approved but is to be used twice daily. Yupelri® has been found to be effective for COPD treatment as compared with placebo; however, no comparator trials with other active ingredients have been found.

Recommendation: Yupelri® be 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.

Board Decision: The Board unanimously approved the above recommendation.

Zemdri® (plazomicin); **PDL category**- Aminoglycosides

Plazomicin, the active ingredient of Zemdri®, is a semi-synthetic aminoglycoside antibacterial derived from sisomicin. It acts by binding to bacterial 30S ribosomal subunit, thus inhibiting protein synthesis. It is indicated for the the treatment of complicated urinary tract infections (cUTI), including pyelonephritis caused by the following susceptible microorganism(s): *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis*, and *Enterobacter cloacae*. As only limited clinical safety and efficacy data for Zemdri® are currently available, reserve Zemdri® for use in cUTI patients who have limited or no alternative treatment options. The safety and efficacy of Zemdri® were assessed in a multicenter, double-blind, non-inferiority study that included adults hospitalized with cUTI, including pyelonephritis (N=609) who were randomized to Zemdri® or meropenem (1g IV Q8H as a 30-minute infusion). As only limited clinical safety and efficacy date for Zemdri are currently available, reserve Zemdri for use in cUTI patients who have limited or no alternative treatment options. In a clinical trial comparing Zemdri with meropenem, Zemdri® was found to demonstrate efficacy and be as effective as meropenem for composite cure at day 5 and test of cure.

Recommendation: Zemdri® be non-preferred.

Clinical Criteria:

- Zemdri will be reserved for patients with limited or no alternative treatment of care.

Board Decision: The Board unanimously approved the above recommendation.

FDA SAFETY ALERTS

The U.S. Food and Drug Administration today approved Mavyret (glecaprevir and pibrentasvir) tablets to treat all six genotypes of hepatitis C virus (HCV) in children ages 12 to 17. Mavyret was previously approved to treat HCV in adults in 2017.
http://s2027422842.t.en25.com/e/es?s=2027422842&e=210380&elqTrackId=78D8A052C380BCBFF284D754BEBE9730&elq=380e0dc31c3f4cd2b39485cf0d6eb7b6&elqaid=7835&elqat=1

FDA Hepatitis Update: VIREAD Pregnancy Label Updates
http://s2027422842.t.en25.com/e/es?s=2027422842&e=208411&elqTrackId=78D8A052C380BCBFF284D754BEBE9730&elq=ce5ca0323e0f457cba72a3050f17ff99&elqaid=7752&elqat=1

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **September 10, 2019** 5:30pm –8:30pm at the Augusta Armory.