Department of Health and Human Services
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Department of Health and Human Services
Maine People Living Safe, Healthy and Productive Lives
Paul R. LePage, Governor Ricker Hamilton, Acting Commissioner

TO: Maine Drug Utilization Review Board
DATE: 9/15/2017
RE: Maine DUR Board **Meeting** minutes from September 12, 2017

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		
Jeffrey S. Barkin MD, DFAPA Change Healthcare			X
Christopher Pezzullo, State Health Officer DHHS, DO	X		
Jill Kingsbury, MaineCare Pharmacy Director	X		

Guests of the Board: Ed Bosshart, PharmD, Change Healthcare

CALL TO ORDER: 5:30PM

Dr. Pezzullo called the meeting to order at 5:30 PM.

PUBLIC COMMENTS

Amy Tomaselle from Sunovion: Highlighted the attributes of Seebri Neohaler.
Patrick Cantael from Sanofi Genzyme: Highlighted the attributes of Kevzara
Jeff Olson from Gilead Sciences: Highlighted the attributes of Vosevi.
Franco Casagrande from Abbvie: Highlighted the attributes of Mavyret.
Shaffee Bacchus from Janssen: Highlighted the attributes of Tremfya.

OLD BUSINESS

DUR MINUTES

The June DUR meeting minutes were accepted as written.

MAINECARE UPDATE

No update at this time.

STIMULANTS IN COMBINATION WITH PSYCH MEDICATION SEPERARTED INTO AGE BANS

Long-acting stimulants have been used quite effectively to treat ADD and ADHD in children and adults. While they are not proven to be more effective than short-acting stimulants, their dosing frequency improves compliance and adherence to the treatment plan. Most people with ADD or ADHD are diagnosed in childhood, but up to two thirds of children will exhibit some symptoms into adulthood and approximately one half will exhibit enough symptoms to require medication. It is estimated that 2-6% of the adult population have ADHD/ADD. Many adults will not show symptoms of hyperactivity, but still require treatment for attention deficit issues. A number of adults are also on mood stabilizing medications along with stimulants as mood disorders frequently accompany ADD/ADHD. We used paid, non-reversed Medicaid pharmacy claims data from SFY2017. Partd and TPL claims were excluded. Identify members on long acting stimulants and percentages of total eligibles by age group. Further identify the number of members co-prescribed other psych medications by age band and the average concurrent drug per month at each age band.

Recommendation: Defer until next Retro DUR is discussed

Board Decision: N/A

NEW BUSINESS

ANNOUCE NEW DUR CHAIR

Kenneth McCall, PharmD has been appointed the new Maine DUR chairperson.

RETRO-DUR DATA PRESENTATION: CO-PRESCRIBING OF OPIATE PAIN MEDICATIONS (INCLUDING COUGH SYRUPS), BENZODIAZEPINES AND "Z" DRUGS

The increased use and misuse of opioid pain medications and benzodiazepines is well documented and use of hypnotics (specifically "Z" drugs) for sleep is widespread. Polypharmacy with these drugs is not uncommon and there is increasing recognition of severe adverse effects when these drugs are combined, especially in those who take opioids on a daily basis. We looked at paid, non-reversed Medicaid pharmacy and medical claims data from CY2016. We identified members on opioids for greater than 30 days and

divide them into those taking more or less than 200 mg morphine equivalents. Then identified which of these members are on benzodiazepines or Z drugs (or both), not limiting our search to those who are on these medications chronically. We examined medical claims of these members to evaluate if medical care was required due to adverse effects from any combination of these drugs. Specifically, we will highlight ED visits and admissions, with particular attention to falls, overdoses and fractures.

Recommendation: Develop a general letter to be sent to prescribers to be sent out to prescribers and then a detailed letter sent to top prescribers of these combinations including a list of patients. Also, work with the Academic Detailing Program because they are going to continue to work on opioid for the next year. Pull another report in the next calendar year to see if we are trending downward.

Board Decision: The Board unanimously approved the above motion.

INTRODUCE: COMPLIANCE WITH GLP-1 AGONISTS IN TYPE II DIABETES MELLITUS

GLP-1 (glucagon-like peptide 1 receptor) agonists are incretin mimetics which have several benefits for diabetes management. They suppress post-prandial glucagon release, delay stomach emptying, and increase insulin sensitivity. Significantly lower rates of hypoglycemia accompany GLP-1 therapy than many alternative hypoglycemics including insulin and sulfonylureas. This class also has the side effect of modest weight reduction and reduction of systolic blood pressure. Although they improve glycemic control, there are few long-term studies of GLP-1 agonists to assess clinically important health outcomes (cardiovascular events, mortality), durability of weight loss, or safety. Many questions remain unanswered regarding clinical use in type 2 diabetes, including long-term benefits and risks and their role in combination with other diabetes medications.

Although the standard has been to add insulin or sulfonylurea as the second step for patients who fail initial therapy with lifestyle intervention and metformin, the addition of a GLP-1 receptor agonist is an alternative, although expensive, option listed in both the ADA and ACE guidelines, especially if avoidance of hypoglycemia is a high priority. GLP-1 receptor agonists are more often prescribed in combination with metformin (and/or another oral agent) for patients who fail initial therapy with one or two oral agents, particularly when weight loss or avoidance of hypoglycemia is a primary consideration, the A1C level is close to target (within 1 to 1.5 percentage points), and cost or injection therapy are not major barriers. Because the GLP-1 drugs are all injectable, compliance is an issue that must be addressed. In addition, 5% of patients in clinical trials discontinued the drugs due to the GI side effects of nausea, vomiting and diarrhea. In clinical practice, it is estimated that 5-10% of patients discontinue the medications due to GI intolerance.

Recommendation: We will use paid, non-reversed MaineCare pharmacy and medical claims data from SFY 2015 and 2016, excluding members with MaineRX, TPL and Part D. We will look for members who are prescribed a GLP-1 medication (exenatide, liraglutide, albiglutide, dulaglutide) with a diagnosis of type II DM, assessing rates of discontinuation by drug and/or poor adherence to a prescribed regimen. We will examine this data using standard measures of compliance including the medication possession ratio (MPR). We will also assess the number and type of additional diabetic medications that a patient is on while on the GLP-1 therapy.

Board Decision: The Board would like to add combination GLP-1 medication in a separate column within the analyst.

Imfinzi® (durvalumab); **PDL category**- Cancer

Durvalumab, the active ingredient of Imfinzi®, is a human immunoglobulin G1 kappa (IgG1k) monoclonal antibody that blocks the interaction of programmed cell death ligand 1 (PD-L1) with the PD-1 and CD80 (B7.1) molecules. By binding to its receptors, PD-L1 reduces cytotoxic T-cell activity, proliferation, and cytokine production. Blockade of PD-L1/PD-1 and PD-L1/CD80 interactions releases the inhibition of immune responses, without inducing antibody dependent cell-mediated cytotoxicity. Imfinzi® is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Recommendation: Imfinzi ® be non-preferred.

Clinical Criteria: Imfinzi will be considered for patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

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

Kevzara ® (sarilumab); **PDL category**- Rheumatoid Arthritis

Sarilumab, the active ingredient of Kevzara®, is a human recombinant monoclonal antibody of the IgG1 subclass that binds to the IL-6 receptor. It has been shown to inhibit IL-6 mediated signaling through these receptors. Il-6 has been shown to be involved in diverse physiological processes, such as T-cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis, and simulation of hematopoietic precursor cell proliferation and differentiation. Kevzara® is a subcutaneous injection indicated for the treatment of adults with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more DMARDs. Kevzara® was found to be more effective as compared to placebo in clinical trials for various endpoints, including ACR20, ACR50, and ACR70.

Recommendation: Kevzara ® be non-preferred

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

Mavyret (glecaprevir & pibrentasvir); **PDL category**- Hepatitis C

Mavyret® is a fixed-dose combination tablet containing glecaprevir (a HCV NS3/4A protease inhibitor) and pibrentasvir (a HCV NS5A inhibitor). Both are direct-acting antiviral agents active against the hepatitis C virus. Mavyret® is a fixed-dose combination tablet indicated for the treatment of adults with chronic HCV

genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) and for the treatment of adults with HCV genotype 1 infection who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both. All patients should be tested for evidence of current or prior hepatitis B virus (HBV) infection by measuring hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc). It was found to be safe and effective in subjects with severe renal impairment, with no need for dose adjustments.

Recommendation: Mavyret® be preferred with conditions.

Clinical Criteria: Approvals will require clinical PA. Please see the Hepatitis PA form for criteria

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

Radicava® (edaravone); **PDL category**- Neurologics- ALS

The exact mechanism of action of edaravone, the active ingredient of Radicava®, for use in amyotrophic lateral sclerosis (ALS) is not known. Radicava® is IV infusion for the treatment of amyotrophic lateral sclerosis (ALS). Compared to placebo in clinical trials, the ALSFRS-R scores with Radicava® worsened to a significantly lesser degree than compared with placebo.

Recommendation: Radicava® be non-preferred in a new category Neurologics-ALS.

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

Seebri® Neohaler (glycopyrrolate inhalation powder); **PDL category**- Antiasthmatic- Anticholinergics-Inhaler

Glycopyrrolate, the active ingredient of the Seebri® capsules, is a long-acting muscarinic antagonist, also known as an anticholinergic. In the airways, glycopyrrolate exerts its effect through inhibition of muscarinic receptor M3 at the smooth muscle, which leads to bronchodilation. The 2017 GOLD COPD guidelines suggest the use of a long-acting antimuscarinic (LAMA) OR long-acting beta2-agonist (LABA) for patients with a GOLD Grade B.[2] Numerous single products are available for the treatment of COPD. Seebri® Neohaler is an FDA approved long-acting anticholinergic indicated for the long-term, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. It was found to be effective as compared with placebo.

Recommendation: Seebri ® Neohaler be non-preferred.

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

Siliq ® (brodalumab); **PDL category**- Psoriasis Biologicals

Brodalumab, the active ingredient of Siliq®, is a human monoclonal IgG2k antibody that selectively binds to human interleukin-17 receptor A (IL-17RA) and inhibits its interactions with cytokines IL-17A, IL-17F, IL-17C, IL-17A/F, and IL-25. Blocking IL-17RA inhibits IL-17 cytokine-induced responses, including the release of pro-inflammatory cytokines and chemokines. Siliq® is a subcutaneous injection indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies. It

was found to be more effective as compared to placebo in clinical trials with various endpoints, including PASI 75, PASI 100, sPGA success of clear or almost clear. It was also found in these studies to be more effective as compared to ustekinumab for these same outcomes. Siliq® does, however, have a box warning regarding the increased risk for suicidal ideation and behavior with use. In addition, Siliq® is contraindicated for use in Crohn's disease.

Recommendation: Siliq ® be non-preferred.

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

Syndros® (dronabinol solution); **PDL category**- Antiemetic- 5HT3 Receptor Antagonists/Substance P Neurokinin

Dronabinol, the active ingredient of Syndros®, is an orally active cannabinoid which has complex effects on the CNS, including central sympathomimetic activity. Dronabinol is the main psychoactive component in marijuana. Syndros® is a Schedule II controlled substance indicated for nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments and for anorexia associated with weight loss in patients with AIDS. Its efficacy was established based on studies of dronabinol capsules. While it does not have any box warnings, it is associated with numerous adverse reactions and should be used with caution in those with a history of substance abuse.

Recommendation: Syndros ® be non-preferred.

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

Tremfya ® (guselkumab); **PDL category**- Psoriasis Biologicals

Guselkumab, the active ingredient of Tremfya®, is a human immunoglobulin G1 lambda monoclonal antibody produced using recombinant DNA technology. It selectively binds to the p19 subunit of interleukin 23 (IL-23) and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of pro-inflammatory cytokines and chemokines. Tremfya® is a human monoclonal antibody indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. In phase 3 clinical trials, it was found to be more effective as compared to placebo, and more effective as compared to adalimumab with secondary endpoints of PASI 90 and PASI75 response, as well as IGA score of 0 or 1. In addition, it was found to be more effective as compared with ustekinumab in subjects with an inadequate response with ustekinumab for achieving an IGA score of 0 or 1.

Recommendation: Tremfya ® be non-preferred.

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

Tymlos® (abaloparatide); **PDL category**- Osteoporosis

Abaloparatide, the active ingredient of Tymlos®, is a synthetic 34 amino acid peptide. It is an analog of human parathyroid hormone related peptide (PTHrP) that acts as an agonist at the PTH1 receptor. This results in activation of the cAMP signaling pathway in target cells. In animals, abaloparatide had an anabolic effect on bone, with increases in bone mineral density (BMD) and bone mineral content that

correlated with increases in bone strength at vertebral and/or nonvertebral sites. Tymlos® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Tymlos® reduces the risk of vertebral fractures and nonvertebral fractures. Due to the unknown relevance of the rodent osteosarcoma findings to humans, cumulative use of Tymlos® and parathyroid hormone analogs (e.g. teriparatide) for more than 2 years during a patient's lifetime is not recommended. Tymlos® was found to be significantly effective as compared to placebo for various endpoints assessed in adults with osteoporosis. In addition, once treatment was completed and patients were switched to alendronate, the Tymlos®→alendronate group resulted in significant improvements as compared with the placebo→alendronate group for the same endpoints assessed as in the original study.

Recommendation: Tymlos ® be non-preferred.

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

Vosevi® (sofosbuvir, velpatasvir, & voxilaprevir); **PDL category**- Hepatitis C

Vosevi® is a fixed-dose combination tablet containing sofosbuvir (a nucleotide analog HCV NS5B polymerase inhibitor), velpatasvir (an NS5A inhibitor), and voxilaprevir (a NS3/4A protease inhibitor). These are all direct-acting antiviral agents active against the hepatitis C virus. Vosevi® is a fixed-dose combination tablet indicated for the treatment of adults with chronic HCV infection without cirrhosis or with compensated cirrhosis who have: genotype 1, 2, 3, 4, 5, or 6 infection and have previously been treated with an HCV regimen containing an NS5A inhibitor OR genotype 1a or 3 infection and have previously been treated with an HCV regimen containing sofosbuvir without an NS5A inhibitor. Additional benefit of Vosevi® over sofosbuvir/velpatasvir was not shown in adults with genotype 1b, 2, 4, 5, or 6 infection previously treated with sofosbuvir without an NS5A inhibitor. All patients should be tested for evidence of current or prior hepatitis B virus (HBV) infection by measuring hepatitis B surface antigen (HBsAg) and hepatitis B core antibody (anti-HBc). While it is recommended that amiodarone be avoided during Vosevi® use, if no other treatment options are available, specific cardiac monitoring is recommended. The evidence-based IDSA/AASLD guidelines[2] are frequently updated and include several recommended regimens for the various genotype infections, but have not yet been updated to include this drug. Hepatitis C treatment is a rapidly changing therapeutic area and the recommendation for treatment for specific genotypes and clinical situations are continuing to evolve.

Recommendation: Vosevi ® be non-preferred.

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

FDA SAFETY ALERTS

Brilinta (ticagrelor) 90 mg tablets, 8-count Physician Sample Bottles: Recall of Lot # JB5047 - Due to Report of Another Medicine in One Bottle
https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm560786.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Mibela 24 Fe Chewable Tablets by Lupin Pharmaceuticals Inc.: Recall - Out of Sequence Tablets and Missing Expiry/Lot Information
https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm560908.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Novopen Echo Insulin Delivery Device by Novo Nordisk: Recall - May Crack or Break If Exposed To Certain Chemicals
https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm565955.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA requests removal of Opana ER for risks related to abuse
https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm562401.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Board Decision: No formal action required

ADJOURNMENT: 8:30PM

The next meeting will be held on **October 10, 2017** 1:00pm –4:30pm at the Augusta Armory.