MaineCare Services
An Office of the Department of Health and Human Services
Paul R. LePage, Governor Mary C. Mayhew, Commissioner

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TO: Maine Drug Utilization Review Board
DATE: September 20, 2016
RE: Maine DUR Board **Meeting** minutes from September 13, 2016

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Linda Glass, MD			X
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR	X		
Mark Braun, M.D., FACP, Internist/Geriatrician			X
Mike Antoniello, MD			X
Kathleen Polonchek, MD	X		
Kenneth McCall, PharmD	X		
Steve Diaz, MD	X		
Non –Voting			
Mike Ouellette, R.Ph., Change Healthcare	X		
Jeffrey S. Barkin MD, DFAPA	X		
Jan Yorks-Wright, Pharmacy Supervisor, OMS	X		
Roger Bondeson, Director of Operations, OMS	X		
Christopher Pezzullo, State Health Officer DHHS, DO	X		

Guests of the Board: Jacquelyn Hedlund, MD

CALL TO ORDER: 5:30PM

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

PUBLIC COMMENTS

Paula Pierce from Biogen: Highlighted the attributes of Tecfidera®.
Karen Debusk from AbbVie: Highlighted the attributes of Zinbryta®.

OLD BUSINESS

DUR MINUTES

The committee reviewed the minutes and Dr. Hedlund noted that Darzalex was incorrectly assigned a preferred recommendation. The committee accepted the recommendation that the drug be non-preferred and that clinical prior authorization be required to ensure appropriate indication. Correction was accepted. No other changes made and the corrected minutes were accepted by the committee.

MAINECARE UPDATE

Roger Bondeson updated the board that Dr. Mark Braun has resigned after eight years of service on the DUR. The state will start to recruit to fill the open physician and pharmacy slots.

NEW BUSINESS

RETRO-DUR SCHEDULE 2017

Dr. Hedlund presented possible DUR topics for 2017. There are 4 meetings scheduled in 2017, so the committee needs to choose 4 topics. Suggested topics:

Co-prescribing of stimulants and benzodiazepines. Dr. McCall requested adding the "Z" drugs to the list too, given the similar adverse effects to the benzodiazepines.

Co-prescribing of opiate pain medications (including cough syrups) and benzodiazepines. Again the recommendation was put forward to add the "Z" drugs

Assessing the pattern of usage of long-acting stimulants, specifically looking at more than once a day dosing patterns and use among different age groups, including pediatrics.

Assessing the use and adherence of GLP1 receptor agonists looking at frequency of administration, compliance and persistent usage for members.

With new CDC guidelines for use of fluoroquinolone use, assess recent usage patterns for specific diagnoses (first line, second line treatment). Diagnoses of interest include sinusitis, pneumonia/bronchitis and UTI.

A discussion ensued about the use of antipsychotics. Dr. Pezzullo requested a report on the use of antipsychotics by age, number of different anti-psychotics prescribed per patients and geographic distribution to be discussed at the October meeting. Not a request for a formal retroDUR report. Dr Pezzullo also questioned why we have such low utilization of naltrexone in Maine. Dr. Barkin suggested looking at the number of members on Naltrexone (and other abuse deterrent formulations) divided by the number of members on non-methadone opiate medications, to quantify the percentage of potential patients that could be shifted to safer medications.

Dr. Wendler would like to see data on noncompliance with Hepatitis C drugs. Would like to know better what member characteristics put one at risk for poor compliance with medications.

No new retro DUR was presented in detail for the next meeting.

Board Decision: No action required

PRESENT RESULTS - DIABETES – APPROPRIATE UTILIZATION OF ANGIOTENSIN MODULATORS IN PATIENTS WITH DIABETES AND HYPERTENSION

Mike Ouellette requested an extension for delivering the report. Data received from analysts seemed incorrect and Change Healthcare needs more time to do data verification. Mike explained the complexity of merging pharmacy data with medical claims data and the results looked incorrect, with many members with the diagnosis of hypertension not having any pharmacy claims for antihypertensive medications. Mike and the physicians at Change Healthcare would like to QC the data and work more intensively with the data analysts to ensure the data is valid. The committee agreed to postpone the presentation until the October meeting.

Board Decision: No formal action required, but the Board concurred with moving forward with this RetroDUR evaluation.

NEW DRUG REVIEWS

Bevespi® (glycopyrrolate/formoterol**; PDL category**- Antiasthmatic- Adrenergic Anticholinergic

Bevespi® is 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 is not indicated for the relief of acute bronchospasm or for the treatment of asthma. Bevespi® Aerosphere is a metered-dose inhaler that contains the combination of micronized glycopyrrolate (an anticholinergic) and micronized formoterol fumarate (a long-acting beta2-adrenergic agonist or LABA). Glycopyrrolate is a long-acting antimuscarinic (often referred to as an anticholinergic) that works through inhibition of the M3 receptor at the smooth muscle, leading to bronchodilation. Formoterol is a LABA with a rapid onset of action that acts locally in the lungs as a bronchodilator.

Recommendation: Bevespi® be non-preferred
Criteria: 1.) Dosing limits apply, please see dosing consolidation list. 2.) The safety and efficacy of use in children under the age of 18 years have not been established. 3.) DDI: Avoid concomitant use of Bevespi with other anticholinergic-containing drugs, due to an increased risk of anticholinergic adverse events. Bevespi® should be used with extreme caution in patients being treated with MAO inhibitors, TCAs, or other drugs known to prolong the QTc interval.

Briviact® (brivaracetam); **PDL category**- Anticonvulsants

Briviact® is indicated as adjunctive therapy in the treatment of partial-onset seizures in patient's ≥16 years of age with epilepsy. Brivaracetam, the active ingredient of Briviact®, has a high and selective affinity for synaptic vesicle protein 2A (SV2A) in the brain. While the exact mechanism of action by which Briviact® exerts its anticonvulsant activity is not known, it is thought its affinity for SV2A may contribute to its anticonvulsant effect.

Recommendation: Briviact® be non-preferred
Criteria: 1.) Adjunctive therapy in the treatment of partial-onset seizures in patient's ≥16 years of age with epilepsy.

Epclusa® (sofosbuvir/velpatasvir); **PDL category**- Hepatitis C Agents

Epclusa® is indicated the treatment of adult patients with chronic HCV genotype 1, 2, 3, 4, 5, or 6 infections: without cirrhosis or with compensated cirrhosis AND with decompensated cirrhosis for use in combination with ribavirin. Epclusa® is a fixed-dose combination tablet containing velpatasvir (an NS5A inhibitor) and sofosbuvir (a nucleotide analog hepatitis C virus (HCV) NS5B polymerase inhibitor). These are both direct-acting antiviral agents against the hepatitis C virus. Sofosbuvir is an inhibitor of the HCV NS5B RNA-dependent RNA polymerase, which is required for viral replication. Velpatasvir is an inhibitor of the HCV NS5A protein, which is also required for viral replication.

Recommendation: Epclusa® be preferred with conditions.
Criteria: 1.) Approvals will require clinical PA. Please see the Hepatitis PA form for criteria.

Viekira® XR (dasabuvir, ombitasvir, paritaprevir, & ritonavir tabs); **PDL category** -Hepatitis C Agents

Viekira® XR is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV): genotype 1b infection without cirrhosis or with compensated cirrhosis, genotype 1a infection without cirrhosis or with compensated cirrhosis for use in combination with ribavirin. Viekira® XR is a fixed-dose combination tablet that includes a hepatitis C virus (HCV) non-nucleoside NS5B palm polymerase inhibitor (dasabuvir), a HCV NS5A inhibitor (ombitasvir), a HCV NS3/4A protease inhibitor (paritaprevir), and a CYP3A inhibitor (ritonavir) that inhibits CYP3A mediated metabolism of paritaprevir to provide increased plasma levels of paritaprevir. Dasabuvir, ombitasvir, and paritaprevir are directing-acting HCV antiviral agents with distinct mechanisms of action, while ritonavir is not active against HCV.

Recommendation: Viekira® XR be preferred with conditions
Criteria: 1.) Approvals will require clinical PA. Please see the Hepatitis PA form for criteria.

Keveyis® (dichlorphenamide); **PDL category** -Diuretics

Keveyis® is indicated for the treatment of primary hyperkalemic periodic paralysis, primary hypokalemic periodic paralysis, and related variants. Dichlorphenamide, the active ingredient of Keveyis®, is an oral carbonic anhydrase inhibitor. However, the exact mechanism of action by which it exerts its therapeutic effects in patients with periodic paralysis is not known. Results of the hypokalemic sub-study demonstrated that acute intolerable worsening was seen in 2 patients in the Keveyis® group as compared with 11 in the placebo group. This difference was statistically significant (p=0.02). Results of the hyperkalemic sub-study demonstrated that there were 2.3 fewer attacks per week in the Keveyis® group than with placebo. This was a statistically significant difference.

Recommendation: Keveyis® be non-preferred
Criteria: 1.) DDI: The concomitant use of Keveyis® with high dose aspirin is contraindicated.

Kyprolis® (carfilzomib); **PDL category** -Cancer

Kyprolis® is indicated for relapsed or refractory multiple myeloma: In combination with dexamethasone or with lenalidomide plus dexamethasone for treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy. As a single agent for treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy. Carfilzomib, the active ingredient of Kyprolis®, is a tetrapeptide epoxyketone proteasome inhibitor that irreversibly binds to the N-terminal threonine-containing active sites of the 20S proteasome. In vitro it had antiproliferative and proapoptotic activities in solid and hematologic tumor cells.

Recommendation: Kyprolis® be non-preferred
Criteria: 1.) PA required to confirm FDA approved indication

Tecentriq® (atezolizumab); **PDL category** -Cancer

Tecentriq® is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who: have disease progression during or following platinum-containing chemotherapy. 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 durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Atezolizumab, the active ingredient of Tecentriq®, is an Fc-engineered, humanized, monoclonal antibody that binds to PD-L1 and blocks interactions with the PD-1 and B7.1 receptor. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T-cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production. Atezolizumab is an IgG1 kappa immunoglobulin that binds to PD-L1 and blocks its interactions with both receptors, which prevents the PD-L1/PD-1 mediated inhibition of the immune response.

Recommendation: Tecentriq® be non-preferred
Criteria: PA required to confirm FDA approved indication

Nuplazid® (pimavanserin); **PDL category** -Antipsychotics, Atypical

Nuplazid® is indicated for the treatment of hallucinations and delusions associated with Parkinson's disease psychosis. Pimavanserin, the active ingredient of Nuplazid®, is an atypical antipsychotic. The mechanism of action for its approved indication is not known; however, it is thought to be mediated through a combination of inverse agonist and antagonist activity at serotonin 5-HT2A receptors and to a lesser extent at serotonin 5-HT2C receptors.

Recommendation: Nuplazid® to be non-preferred
Criteria: 1.) DDI: The concomitant use of Nuplazid with other drugs known to prolong the QT interval (e.g. Class IA antiarrhythmics, Class 3 antiarrhythmics, antipsychotics, and antibiotics such as gatifloxacin and moxifloxacin).

Ocaliva® (obeticholic aid); **PDL category** -GI-Misc

Ocaliva® is indicated for the treatment of primary biliary cholangitis (PBC; formerly called primary biliary cirrhosis), in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as monotherapy in adults unable to tolerate UDCA. This indication is approved under accelerated approval based on a reduction in alkaline phosphatase

(ALP). An improvement in survival or disease-related symptoms has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. Obeticholic acid, the active ingredient of Ocaliva®, is a farnesoid X receptor (FXR) agonist. FXR is a nuclear receptor expressed in the liver and intestine and is a main regulator of bile acid, inflammatory, fibrotic, and metabolic pathways. FXR activation decreases the intracellular hepatocyte concentrations of bile acids. The overall size of the circulating bile acid pool becomes limited while promoting choleresis (bile acid secretion from the liver), thus reducing hepatic exposure to bile acids.

Recommendation: Ocaliva® be non-preferred
Criteria: 1.) PA required to confirm FDA approved indication.

Xiidra® (ophthalmics); **PDL category**- Ophthalmics- Of Interest

Xiidra® is indicated for the treatment of signs and symptoms of dry eye disease. Lifitegrast, the active ingredient of Xiidra®, is a lymphocyte function-associated antigen-1 (LFA-1) antagonist. Lifitegrast binds to the integrin LFA-1, a cell surface protein found on leukocytes, and blocks the interaction of LFA-1 with its cognate ligand intercellular adhesion molecule-1 (ICAM-1). ICAM-1 may be overexpressed in corneal and conjunctival tissues in dry eye disease. LFA-1 and ICAM-1 interaction can contribute to the formation of an immunological synapse resulting in T-cell activation and migration to target tissues. The exact mechanism of action in dry eye disease is not known.

Recommendation: Xiidra® be non-preferred

Xtampza® ER (oxycodone extended-release); **PDL category**- Narcotics, Long Acting

Xtampza® ER is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. Due to the risk of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, Xtampza® ER should be reserved for use in patients for whom alternative treatment options (e.g. non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Xtampza® ER is not indicated as an as-needed (prn) analgesic. Xtampza® ER, as it contains oxycodone, is a Schedule II controlled substance. While Xtampza® ER can be abused and is subject to misuse, addiction, and criminal diversion, it is considered an abuse-deterrent formulation. An enriched-enrollment, randomized-withdrawal, double-blind, placebo-controlled, parallel-group study was performed to assess the safety and efficacy of Xtampza® ER in patients (N=740) with persistent, moderate-to-severe chronic lower back pain, with inadequate pain control from prior treatment. Patients were titrated to a stable and tolerated dose between 18mg and 72mg BID in an open-label design during the first six weeks of the trial. After the titration phase, 53% (N=389) met the randomization criteria of adequate analgesia and acceptable tolerability of Xtampza® ER and then entered into the randomized, double-blind maintenance phase.

Recommendation: Xtampza® ER to be non-preferred

Zinbryta® ER (daclizumab); **PDL category**- Multiple Sclerosis Agents-Misc

Zinbryta® ER is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (MS). Due to its safety profile, the use of Zinbryta® should generally be reserved for patients who have had an inadequate response to two or more drugs indicated for the treatment of MS. Daclizumab, the active ingredient of Zinbryta®, is a humanized monoclonal antibody that binds to the alpha sub-unit of the interleukin-2 receptor (IL-2Rα, CD25). While the exact mechanism of action for use in MS is not known, it is thought to involve modulation of IL-2 mediated activation of lymphocytes through binding to CD25, a subunit of the high-affinity IL-2 receptor. Zinbryta® has a box warning regarding the increased risk of hepatic injury, including autoimmune hepatitis and other immune-mediated disorders. Zinbryta® can cause severe liver injury, including life-threatening events, liver failure and autoimmune hepatitis. It is therefore recommended to obtain serum transaminases (ALT and AST) and total bilirubin levels prior to starting treatment, and then monthly for 6 months after the last dose of Zinbryta®.

Recommendation: Xtampza® to be non-preferred
Criteria: 1.) The safety and efficacy of use in children under the age of 17 years have not been established. 2.) 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 recommendation.

FDA SAFETY ALERTS

Multistate Outbreak of Burkholderia cepacia Infections
http://www.cdc.gov/hai/outbreaks/b-cepacia/index.html?source=govdelivery&utm_medium=email&utm_source=govdelivery

Zecuity (sumatriptan) Migraine Patch: Drug Safety Communication - FDA Evaluating Risk of Burns and Scars
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm504736.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA Drug Safety Communication: FDA warns about serious heart problems with high doses of the antidiarrheal medicine loperamide (Imodium), including from abuse and misuse
http://www.fda.gov/Drugs/DrugSafety/ucm504617.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA Drug Safety Communication: FDA strengthens kidney warnings for diabetes medicines canagliflozin (Invokana, Invokamet) and dapagliflozin (Farxiga, Xigduo XR)
http://www.fda.gov/Drugs/DrugSafety/ucm505860.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA Drug Safety Communication: FDA warns about serious bleeding risk with over-the-counter antacid products containing aspirin

http://www.fda.gov/Drugs/DrugSafety/ucm504328.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

FDA Drug Safety Communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects
http://www.fda.gov/Drugs/DrugSafety/ucm511530.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Board Decision: The board would like to look into the claims of fluoroquinolone due to the above FDA alert and have the information brought back to the October meeting.

ADJOURNMENT: 8:30PM

The next meeting will be held on **October 11, 2016** 12pm –4pm at the Augusta Armory.