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: February 9, 2016
RE: Maine DUR Board **Meeting** minutes from February 9, 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		
Mike Ouellette, R.Ph., GHS	X		
Jeffrey S. Barkin MD, DFAPA	X		
Kathleen Polonchek, MD	X		
Non –Voting			
Jan Yorks-Wright, Pharmacy Supervisor, OMS			X
Roger Bondeson, Director of Operations, OMS	X		

Guests of the Board: Jacquelyn Hedlund,MD, Ed Bosshart Pham.D, Jennifer Allen

CALL TO ORDER: 6:10PM

PUBLIC COMMENTS

Ken Skidmore and **Alexandrea Malinowski** from Alexion Pharmaceuticals presented on Strensiq®. In the United States a rare disease is defined as a disease that affects no more than 200,000 people at any given time. In regard to severity, for those patients with signs and symptoms consistent with HPP at birth or first 6 months of life, classified as perinatal/infantile onset, hypophosphatasia can be life threatening and is generally fatal. Natural history studies on hypophosphatasia have described a 6 month survival rate of 42% for patients presenting in the early perinatal/infantile periods. The patients that go on to survive this initial period or those that present 6 months after life, classic juvenile onset patients, themselves suffer from skeletal disfigurations, growth complications, chronic and debilitating pain, significant limitations in ambulation, myopathy, weakness, inability to participate in social activities and over all increased poor quality of life. These children typically do not lead a normal childhood. In regards to asfotase alfa, Strensiq® for HPP, it was approved in October 2015 and it is the first and only

approved therapy indicated for HPP. It is an enzyme replacement therapy developed for addressing the underlying cause of the disease. HPP is a genetic disorder that results in the deficiency of tissue non-specific to alkaline phosphatase. This disorder will lead to accumulation in the substrates that are responsible for poor bone mineralization and muscle weakness that is characteristic to these patients with HPP. Our clinical trial experience, involves 71 patients and safety data from over 200 patients years of life. In the perinatal/infantile treatment group, asfotase alfa treated patients showed significant improvement in survival with 97% survival rate at 6 months, versus the 42% survival rate mentioned earlier. In general, asfotase alfa treated patient's demonstrated improvements in bone mineralization, respiratory status, height, weight, strength and mobility. Of the 8 patients that we able to perform a 6 minute walk test, zero percent at baseline fell within their age and height adjusted normative ranges whereas after 48 months of treatment, 100% of subject achieved normalcy with the median improvement of 240 meters. Overall as part of the clinical trial program, asfotase alfa treatment was safe and well tolerated. Most common adverse reactions occurring in greater than 10% of the study population were injection site reactions, lipodystrophy, ectopic calcifications and hypersensitivity reactions.

Cathy Mullooly from Novo Nordisk presented on Tresiba®. Tresiba® is a once a day, long acting basal insulin analog and it is indicated to improve glycemic control in adults with diabetes. What makes this first new insulin molecule approved by the FDA in 10 years different from other basal insulins currently on the market? Minor changes made to the human insulin molecule in the formulation. Tresiba® slowly but steadily enters the circulation from the subcutaneous depo. This results in a 25 hour half-life and at least a 42 hour duration of action. Another difference in Tresiba® is that half-life and duration of action is independent of dose. What this means is, once daily administration at any time of day in all patients with type 1 and type 2 diabetes. There are nine studies in the package insert; two of those studies investigate any time of day timing in what was investigated into worst-case scenarios. This was performed in both a type 1 population and a type 2 population. The subjects were instructed to take their prescribed Tresiba dose on Monday, Wednesday, Friday mornings and Tuesday, Thursday, Saturday, Sunday evenings. While this is not a recommended dosing regimen to be using in clinical practice, the reality is that patients often miss or delay injections. Weekends are different than weekdays, work and travel interrupt plans and caregivers are not always timely. But even in these trials, the worst case scenario arm using Tresiba® was not inferior to A1C, and did not demonstrate any clinically relevant differences in hypoglycemia compared to the same time of day dosing arm using Tresiba® and Lantus. Per the label, while the dose can be given at any time, patients do need to ensure a minimum of 8 hours between dosing. Another difference is that Tresiba® is available in the flex touch pen in two different formulations. U-100 flex touch pen contains 300 units of insulin and can be administered in one dose increments up to 80 units. The U-200 flex touch pen contains 600 units of insulin and can be delivered in two unit increments up to a dose of 160 units per injection. That is twice the amount of insulin in most insulin pens and of course the limit with the syringe is 100 units. Each pen shows the number of insulin units to be delivered and no conversion is needed between pen devices. It goes without saying that flex touch pens should not be shared between patients. The final differences is that Tresiba® can be stored in the refrigerator until its expiration date, but once it is removed, it has the longest in-use time of any insulin of 56 days. When Tresiba® is prescribed, it can be can started on type 2 patients at 10 units dose and then can be titrated up based on blood sugar goals. If the patient is already on basal insulin, then it is a 1:1 conversion ratio from the total daily dose and that is the starting dose that can be started. The most common adverse reaction with this insulin is of course, hypoglycemia. In summary, Tresiba® is new to market; it's a once daily injectable basal insulin.

Chris Danes from Takeda Oncology presented on Ninlaro®. Multiple myeloma is where Ninlaro® received its indication, which is cancer of the plasma cells. 27,000 new cases of multiple myeloma will be diagnosed in the United States in 2015, making up about 1.6 % of all cancers diagnosed in the United States in 2015. Multiple myeloma is a disease of the elderly, with an average age of onset being 69 years of age. In terms of multiple myeloma, it is an incurable disease and patients will go through several relapses and upon each relapse the disease becomes more and more aggressive. The clinical presentation of this disease includes anemia, lytic bone lesions, and renal impairment. As in most cancers, multiple myeloma varies from patient to patient. There are risk stratifications that need to be considered. Some of these things that go into the risk stratification include tumor burden, plasma cytomas, renal impairment and molecular markers like cytogenic risks. Going into therapy decisions for clinicians for patients with relapse multiple myeloma, there are several factors that need to be considered. Disease related factors that related to the aggressiveness of the disease. In the relapse setting, previous therapies should also be considered and how they responded to such. As this is a disease of the elderly, comorbidities must also be considered. The health status of the patient should be considered to determine what therapy the patient can tolerate. In the past few years, there has been an emerging approach to multiple myeloma, where continuous therapy has been a new approach. Studies have been done showing progression free survival and overall survival benefits as compared to fixed duration. This is a challenge because in the clinic, administering something over a continuous therapy can be a challenge due to logistics and additive toxicities. New therapies that can have a minimal toxicity and are simple to give can give a clinician a better option for that continuous therapy. Ninlaro® was approved by the FDA November 20, 2015. It is indicated in combination with lenalidomide and dexathasone for patients with multiple myeloma who have received at least one prior therapy. The clinical trial that resulted for the approval was the TOURMALINE MM1 study. This was an international, randomized, double blinded, placebo controlled study conducted in 722 patients. Ninlaro® is given at 4mg once a week for three weeks, with one week off for a total of a 28 day cycle. The regimen was given until progression. The primary endpoint for this study was progression free survival. At the first interim analysis, it was determined that the Ninlaro® regimen resulted in a statistically significant improvement in progression free survival of 6 months compared to the placebo regimen. In addition to that, the overall response rate was superior in the Ninlaro® regimen, 78% compared to 71%. Patients with high risk cytogenetics were looked at, and it was found that the patients in this population, Ninlaro® regimen resulted in an 11 month progression free survival benefit compared to the placebo regimen. In terms of safety, the addition of Ninlaro® to lenalidomide and dexamethasone resulted in slight increase in toxicities. There was a slightly higher rate of GI toxicities, peripheral neuropathies, rash and thrombocytopenia. This regimen is an all oral regimen, which allows more flexibility for clinicians to administer to patients.

Christian Lesuisse from Taiho Oncology presented on Lonsurf®. Lonsurf® is indicated for patients with metastatic colorectal cancer who have previously been treated with fluoropyrimidine-, oxalipatin and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy. Phase III trial has been done, RECOURSE trial. The trial was organized into two arms, first arm included Lonsurf® and the second arm was the placebo arm. The overall survival, which was the primary endpoint, was 7.1 months in the Lonsurf® arm versus 5.3 months in the placebo arm. The hazard ratio was 0.68. There was continuation of the study with the 39 surviving patients. 37 were still on Lonsurf® and 2 were on placebo. In terms of safety, Lonsurf® can cause severe adverse events. One patient in the trial died due to neutropenia. The most common adverse reactions are fatigue, nausea, decreased appetite, diarrhea, vomiting and pyrexia. Based on the data, the NCCN guidelines added the regimen of Lonsurf® as a second line therapy. Lonsurf® is a combination of trifluridine & tipiracil. Trifluridine is a thymidine-based nucleoside analog and tipiracil is a thymidine phosphorylase inhibitor. In summary,

Lonsurf® provides managed care organizations and patients with a tolerable and effective regimen for metastatic colorectal cancer who have failed previous therapies. Lonsurf® is administered orally and available in two dosage strengths. 15mg and 20mg. The drug is given twice daily, once in the morning within an hour after breakfast and then again an hour after dinner.

Ray Mastriani from Acetelion Pharmaceuticals asked if anyone had any questions on Uptravi®

OLD BUSINESS

DUR MINUTES

The November 2015 minutes were approved with one change on page 4; typo third paragraph down. Should read: Dr. Mark Braun states specific lab testing to show intolerance to a statin may be too *rigid.* Instead of …may be too *ridged*.

MAINECARE UPDATE

No updates at this time.

NEW BUSINESS

UPDATE: PCSK 9-CRITERIA REGARDING LAB TESTING FEEDBACK

Dr. Hedlund presented the PA and criteria form for PCSK 9 inhibitors. She has talk to two lipidologists in the Portland area, and they seem to think this is reasonable set of criteria

What is required is that patients if they are teenagers, we need to know that they have Homozygous Familial Hypercholesterolemia, that there is documented adherence to prescribed lipid lowering medications in the past 3 months, that there is no tobacco use in the last 3 months and that it is a recommended treatment by a lipidologist or cardiologist (this doesn't mean that they have to be the one prescribing, but they should have at least been consulted)

Member must be in one of these categories:

- Diagnosis of Heterozygous Familial Hypercholesterolemia
    - Total cholesterol >290 mg/dL or LDL-C > 190 mg/dL **AND**
    - Presence of tendon xanthomas OR in 1st or 2nd degree relative – documented tendon xanthomas, MI at age ≤60 years of age or TC > 290mg/dL **OR** confirmation of diagnosis by gene or receptor testing **AND**
    - Unable to reach goal LDL-C with maximally tolerated dose of statin + ezetimibe (Zetia®) 10 mg daily + another concurrently administered lipid lowering agent
        - A trial of 2 or more statins, at least ONE must be either atorvastatin or rosuvastatin, is required

- Diagnosis of Clinical Atherosclerotic Cardiovascular Disease
    - History of MI, angina, coronary or other arterial revascularization, stroke, TIA or PVD of atherosclerotic origin **AND**
    - Unable to reach goal LDL-C with maximally tolerated dose of statin + ezetimibe (Zetia®) 10 mg daily + another concurrently administered lipid lowering agent
        - A trial of 2 or more statins, at least ONE must be either atorvastatin or rosuvastatin, is required
- Diagnosis of Homozygous Familial Hypercholesterolemia
    - Total Cholesterol and LDL-C > 600mg/dL and TG within reference range **OR**
    - Confirmation of diagnosis by gene or receptor testing **AND**
    - Unable to reach goal LDL-C with maximally tolerated dose of statin + ezetimibe (Zetia®) 10 mg daily + at least 1 other concurrently administered lipid lowering agent **AND**
    - Age ≥ 13 years old

It was decided that the prescriber needed to attest to the fact that the patient was not smoking.

Dr. Wendler asked if we knew how many MaineCare members have Homozygous Familial Hypercholesterolemia and while it is unknown, Dr. Hedlund stated that one of the lipidologist she talked to thinks that it will be a narrow spectrum of patients requiring these drugs. He feels that trials of different statins should be able to help lower lipids that they can tolerate.

Board Decision: No action required

UPDATE: APPROPRIATE TESTOSTERONE USE – CHART REVIEWS

Mr. Ouellette presented on appropriate testosterone use findings from chart review. It was thought that there might be misuse of testosterone within MaineCare members. GHS took a sample of patients who had testosterone prescriptions without a medical billing code seen in the year preceding treatment for testosterone levels, CBC. lipid panel, etc.

GHS excluded those under the age of 21 (8 members) as past chart reviews show that these members or of the transgender population or males with delayed puberty, because testosterone is not being used to treat a deficiency.

GHS chose a random sample of 20 from the original 100 to do a chart review:

- 3 members were also being treated for HIV (commonly presents a need for testosterone supplementation but only after determining that levels are low)
- About half of members were being treated for depression/psychiatric issues
- 3 members with diabetes
- No major themes seen in the members sampled. No obvious indications for testosterone supplementation that would not first require testosterone levels to be drawn.

Of the 20 providers sampled:

- 10 practice general family medicine
- 4 are endocrinologists
- 2 are HIV specialist
- 1 urologist
- 1 orthopedist

- 1 critical care/pulmonologist
- No trends seen in prescribers (1 member of the sample had 2 separate prescribers for their testosterone but were located at the same practice)

The second page of the presented document showed provider, any other concomitant treatments patients received, feedback from the provider and more importantly the pre-treatment lab verification of the 9 that we got back, 6 had labs verified by the providers.

It is common to see the medical claims lag behind the pharmacy data.

Dr. Barkin wanted to know if the providers also did CBCs, because testosterone can cause polycythemia.

GHS is still reaching out to these providers and will continue to gather the information and present updated information at the next meeting

Board Decision: No action required

UPDATE: ATYPICAL MONITORING

Dr. Barkin presented on antipsychotic use and metabolic monitoring. Atypical antipsychotics are associated with weight gain and diabetes. Some years ago, this committee was looking at how good the prescribers in the state of Maine were at monitoring their patients.

Using medical and pharmacy claims of people that are new users to antipsychotics, what percent of them are actually being monitored for glucose and lipid profiles?

There are 4 graphs. The first graph with the blue hash bars shows the total number of MaineCare members that started an antipsychotic. The lower bars shows a 6 month period to capture the labs whereas the taller bars show from a one year period.

What is seen, especially in the one-year time frame, there is a really nice increase in monitoring rates that go back to 2011.

Because these are being obtained from medical claims, they are an underestimate. This means that of all MaineCare members that started an antipsychotic, more than 40% are being monitored within a year of starting.

The second graph shows only atypical antipsychotics with the same motif, the lower bars show after 6 months after starting and the taller bars are a year after starting. Again, there is a nice trend that shows over time, more and more people are being monitored.

The third graph shows non-atypical antipsychotics for patients under the age of 18, it shows less monitoring because metabolic monitoring is not required for use with this class of drugs.

The fourth graph is looking at people under the age of 18 who started on an atypical antipsychotic where monitoring is needed. What is seen, particularly in this group (≤18 years old), when put on an

atypical antipsychotic, there is a 13-fold increase in risk for diabetes. This graph shows that close to half of these kids are being monitored, which is really good.

The last graph, shown in red, is an underestimate because it is quite likely that we are not capturing every lab.

Mr. Ouellette stated that 4 years ago, this would have shown less than 20%

Dr. Barkin stated that from the best he could tell, this was some of the highest monitoring rates in the country

This will be continued to be looked at, the information has been brought to the psych work group.

While we are able to obtain large sample sizes, at some point we may want to drill down to specific counties or other geographically area.

Mr. Ouellette stated that as part of the work done by the committee and the awareness, we also implemented PA requirements for monitoring submission.

Board Decision: No action required

POTENTIAL RETRODUR INITIATIVES FOR 2016

Mr. Ouellette presented the one page document of potential retroDUR initiatives for 2016.

- Diabetes – appropriate utilization of angiotensin modulators in patients with diabetes and hypertension*
- PPI use – potential inappropriate continuation after d/c from hospital*
- Use of Alzheimer medications off label*
- Chronic use of transdermal scopolamine
- Use of “not recommended” regimens for HIV*
- Use of Naltrexone in Children
- Diabetes – GLP1 receptor agonist

Recommendations: The recommendation is to work with analysis at GHS and present one of the stared DUR initiates above every other month.

NEW DRUG REVIEWS

Alecensa® the common name alectinib is in the PDL category Cancer. Alecensa® is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC).

Recommendation: The recommendation is for Alecensa® to be non-preferred

Belbuca® the common name buprenorphine is in the PDL category Narcotics, long-acting. Belbuca® 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.

Recommendation: The recommendation is for Belbuca® to be non-preferred

Cotellic® the common name cobimetinib is in the PDL category Cancer. Cotellic® is indicated for the treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, in combination with vemurafenib.

Recommendation: The recommendation is for Cotellic® to be non-preferred

Empliciti® the common name elotuzumab is in the PDL category Cancer. Empliciti® is indicated for the treatment of patients with multiple myeloma who have received one to three prior therapies, to be used in combination with lenalidomide and dexamethasone.

Recommendation: The recommendation is for Empliciti® to be non-preferred

Genvoya® the common name elvitegravir, cobicistat, emtricitabine and tenofovir alafenamide is in the PDL category Antiretrovirals. Genvoya® is a fixed-dose combination of antiretroviral drugs and a boosting agent. It is indicated as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients ≥ 12 years of age who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 <50 copies/ml).

Recommendation: The recommendation is for Genvoya to be preferred

Criteria: Genvoya is available to those for whom there is a clinical need for the improved renal safety profile provided by tenofovir alafenamide that cannot be met with other more cost-effective combination regimens and also to document that the patient is either treatment naïve or virologically-suppressed (HIV-1 RNA < 50 copies/ml) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya. Preferred for the treatment of HIV-1 infection in adults and pediatric patients ≥ 12 years of age.

Imlygic® the common name talimogene laherparepvec is in the PDL category Cancer. Imlygic® is indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

Recommendation: The recommendation is for Imlygic® to be non-preferred

Lonsurf® the common name trifluridine & tipiracil is in the PDL category Cancer. Lonsurf® was presented by Christian Lesuisse from Taiho Oncology earlier in the meeting.

Recommendation: The recommendation is for Lonsurf® to be non-preferred

Ninlaro® the common name ixazomib is in the PDL category Cancer. Ninlaro® was presented by Chris Danes from Takeda Oncology earlier in the meeting.

Recommendation: The recommendation is for Ninlaro® to be non-preferred

Nucala® the common name mepolizumab is in the PDL category Antiasthmatic-Antiinflammatory Agents. Nucala® is indicated as an add-on maintenance treatment for patients with severe asthma aged 12 years and older, and with eosinophilic phenotype.

Recommendation: The recommendation is for Nucala® to be non-preferred

Strensiq® the common name asfotase alfa solution is in the PDL category Osteoporosis/Bone agents. Strensiq® was presented by Alexandrea Malinowski from Alexion Pharmaceuticals earlier in the meeting.

Recommendation: The recommendation is for Strensiq® to be non-preferred

Tagrisso® the common name osimertinib is in the PDL category Cancer. Tagrisso® is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, woh have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy.

Recommendation: The recommendation is for Tagrisso® to be non-preferred

Tresiba® the common name insulin degludec injection is in the PDL category Diabetic –Penfills. Tresiba® was presented by Cathy Mullooly from Novo Nordisk earlier in the meeting.

Recommendation: The recommendation is for Tresiba® to be non-preferred

Uptravi® the common name selexipag is in the PDL category Pulmonary Antihypertensives. Uptravi® is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group 1) to delay disease progression and reduce the risk of hospitalization for PAH.

Recommendation: The recommendation is for Uptravi® to be non-preferred

Varubi® the common name rolapitant is in the PDL category Antiemetics-5HT3 Receptor Antagonists/Substance P Neurokinin. Varubi® is indicated in adults for the prevention of delayed nausea and vomiting associated with initial and repeat course of emetogenic cancer chemotherapy

Recommendation: The recommendation is for Varubi® to be non-preferred

Vivlodex® the common name meloxicam is in the PDL category Cox 2 Inhibitors – Selective/Highly Selective. Vivlodex® is indicated for the management of osteoarthritis pain.

Recommendation: The recommendation is for Vivlodex® to be non-preferred

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

FDA SAFETY ALERTS

Children's Guaifenesin Grape Liquid and Guaifenesin DM Cherry Liquid by Perrigo Company: Recall – Potential Defect with Dosage Cup

FDA Drug Safety Communication: FDA cautions about dosing errors when switching between different formulations of antifungal Noxafil (posaconazole); label changes approved

FDA Drug Safety Communication: FDA eliminates the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone – containing diabetes medicines

Board Decision: No action required

ADJOURNMENT: 8:25PM

The next meeting will be held on **May 10, 2016** 6:00p.m. – 8:00p.m at the Augusta Armory.