



Department of Health and Human Services
 MaineCare Services
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TO: Maine Drug Utilization Review Board
 DATE: 10/13/11
 RE: Maine DUR Annual Board meeting minutes from 10/11/11

ATTENDANCE	PRESENT	ABSENT	EXCUSED
Robert Weiss, M.D., Cardiologist, Chair			X
Laurie Roscoe, R.Ph., Vice Chair	X		
Amy Enos, Pharm. D. Waltz LTC Pharmacy	X		
Laureen Biczak, D.O., Infectious Disease, GHS	X		
Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR,	X		
Lindsey Tweed, M.D., Psychiatrist	X		
Mark Braun, M.D., FACP, Internist/Geriatrician	X		
Mike Ouellette, R.Ph., GHS	X		
Rebecca M. St. Amand, R.Ph., Staff Pharmacist Community Pharmacy - Pittsfield	X		
Timothy Clifford, M.D., Family Practice, GHS	X		
Kevin Flanigan, M.D., Medical Director, OMS	X		
Non -Voting			
Jennifer Palow, Pharmacy Manager, OMS	X		

Guests of the board: Tanith Fales OMS, Erin Good Pharmacy Intern GHS, Sharon Treat Maine State Representative, Leila Rostamjad Pharm. D, Jon Bourque Pharm. D, Sara Howe R.Ph. GHS, Kim Curtis R.Ph. Clinical Coordinator GHS, Shelley Kelley GHS, Theresa Thompson GHS.

CALL TO ORDER: 1PM

PUBLIC COMMENTS

- Ray Pecin & Eric Sherr from Janssen, spoke about Edurant which is a new non-nucleoside recently approved by the FDA for treatment of HIV infection and treatment-naïve patients. Large Phase III clinical trials—ECHO and THRIVE— T cell increases were equivalent (192 with Edurant and 176 with Sustiva). There was stratification viral load, those patients who had less than 100,000 copies at baseline had 89% undetectable amounts of HIV in their blood after 48 weeks of treatment with Edurant vs. 83% with Sustiva. Side effects include dizziness, abnormal dreams, and rash. Edurant is pregnancy category E. Dr. Clifford asks what the

resistance issues are compared to Sustiva. The K103N mutation appears commonly associated with resistance to Sustiva. E138K resistance mutation has been seen with Edurant, which has not been seen frequently before.

- Laura Smith from Shire, spoke about Firazyr, which was recently approved for hereditary angiodema. Firazyr is a selective bradykinin 2 receptor antagonist. Supplied as 30mg 3ml prefilled single use syringe, stored at room temperature. There was a Phase 3 clinical trial approved by the FDA in August 2011 in which 43 patients were randomized to receive Firazyr 30mg single injection vs. placebo for 45 patients. Patients included in this trial were 18 or older who have had moderate to severe HAE attacks. 50% reduction was achieved with Firazyr by 2 hours vs. 19.8 hours with placebo. The resolution of the attack was 8 hours with Firazyr vs. 36 hours with placebo. 97% of patients have injection site reactions that are self limiting and resolve on their own without further medical intervention. Firazyr is approved for self administration for patients who recognize they are having an attack, and with training are able to treat themselves.
- Mary Cook from Purdue, spoke about Butrans. Butrans is a schedule III mu opioid partial agonist on the transdermal system, which delivers buprenorphine over 7 days and is indicated for the management of moderate to severe chronic pain in patients requiring a continuous, around-the-clock opioid analgesic for an extended period of time. Note that Butrans is not indicated for the treatment of addiction. Butrans label does include boxed warning describing the potential for abuse and proper patient selection. Butrans is available in 5,10, and 20 mcg/hour transdermal systems. The product has been studied in 5,415 subjects who were treated with Butrans in chronic pain clinical trials. Most common adverse events reported were consistent with what one would expect with opioid analgesic and transdermal delivery system. Respiratory depression is the most severe hazard for Butrans, other side effects include drowsiness, dizziness, alterations in judgment, and alterations in levels of consciousness including coma.
- Kristen Mar from Lilly, spoke about Cymbalta. Cymbalta has demonstrated efficacy as well as safety in patients with major depression and anxiety disorders. The clinical differentiation with Cymbalta (duloxetine) is that it is currently the only antidepressant that has been evaluated in large clinical trials for other chronic pain conditions such as diabetic neuropathic pain, fibromyalgia and recently for patients with chronic musculoskeletal pain, specifically lower back pain as well as chronic pain due to osteoarthritis. Supporting evidence has been shown thru 5 large randomized clinical trials, about 5-12 weeks in duration.
- Jeff Olson from Gilead, spoke about Complera, a new single tablet regimen that is composed of 3 antiretrovirals (rilpivirine tenofovir emtricitabine) for the treatment of HIV-1-infected adults. According to the CDC 56,000 Americans are newly infected each year with HIV. Although current combination therapy is highly effective, the results of many studies show that adherence is critical to suppress viral replication and prevent the emergence of drug resistant mutations, improve quality of life as well as increase survival. According to the Department of Health and Human Services guidelines, prescribing regimens that will facilitate adherence should have the following characteristics: simple to take, have a low pill burden, low frequency of dosing, have no food requirements, and have a low incidence and severity of adverse effects. There is a very strong need for regimens that meet these criteria. The simplest and least expensive antiretrovirals are single tablet regimens, or the combination of 3 antiretrovirals all in a single pill. Multiple studies show that single tablet regimens are associated with improved adherence, longer regimen persistence and improved clinical outcomes and

reductions in the rates of hospitalization. Complera is a pregnancy category B. The most common side effects with Complera were insomnia and headache.

- Mr. Olson also spoke about Cayston (aztreonam), which is approved for Cystic Fibrosis and the treatment of patients who are infected with *Pseudomonas aeruginosa*. Cystic Fibrosis is a fatal, inheritable illness that afflicts approximately 30,000 Americans. Patients with chronic lung infections who received inhaled antibiotics have a lower risk of acute exacerbations, improved lung function and quality of life. Safety and effectiveness have not been established in pediatric patients below the age of 7 years, patients with FEV1 <25% or >75% predicted, or patients colonized with *Burkholderia*. Cayston is delivered via an Altera Nebulizer, which is portable, drug specific and allows the drug to be administered within 2-3 minutes. Common adverse reactions occurring more frequently in Cayston-treated patients were cough, nasal congestion, and wheezing. Cayston is in the monobactam antibiotic category and is pregnancy category B. Question was raised in regards to if there were any results in the comparable trial of Cayston vs. TOBI. A 24 head to head comparison between Cayston & TOBI showed that Cayston was superior from a statistical stand point.
- Jim Prodafikas from Astra Zeneca spoke about Brilinta. Brilinta is a P2Y12 platelet inhibitor indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS), including unstable angina, non-ST elevation myocardial infarction, or ST elevation myocardial infarction. When given with maintenance doses of less than 100mg of Aspirin, Brilinta has been shown to reduce the rate of a combined end point of cardiovascular deaths, myocardial infarction, or stroke compared to Plavix. In patients treated with percutaneous coronary intervention (PCI), it also reduces the rate of stent thrombosis. Brilinta is contraindicated in patients with active pathological bleeding, and those with history of intracranial hemorrhage as well as severe hepatic impairment. The PLATO trial compared Brilinta to Plavix, with a reduction of CV events in 18,624 patients. The study demonstrated that treatment with BRILINTA led to a greater reduction in the primary end point – a composite of CV death, MI, or stroke – compared to patients who received clopidogrel 16% relative risk reduction. Most common adverse reactions were bleeding and Dyspnea.
 - Dr. Clifford asks if there are any other ongoing studies. Mr. Prodafikas confirmed the other ongoing studies are associated with long term usage.
- Arlene Price from Janssen spoke about Xarelto and Nucynta ER. Xarelto is the first oral direct factor Xa inhibitor on the market and is indicated for the prophylaxis of deep vein thrombosis (DVT) for 35 days after hip replacement and 12 days after knee replacement. Given orally, once a day dosing, and does not require routine monitoring. Boxed warning on Spinal/Epidural hematomas. Major bleeding rates were low and comparable for patients treated with Xarelto compared to Enoxaparin. Xarelto should not be used in patients with renal impairment or moderate to severe hepatic impairment.
 - A member of the board asks if Xarelto is looked at differently in the geriatric population. Ms. Price confirmed that a subgroup analysis showed that age was not a factor in terms in efficacy or bleed rates for Xarelto however a patient seeing decreasing renal or hepatic function may need dosing adjustments.
- Ms. Price spoke briefly on Nucynta ER, which is a mu-opioid agonist and norepinephrine reuptake inhibitor combined in a single molecule. Indicated for treatment of chronic moderate to severe pain, BID dosing, and long term studies have shown no development of tolerance. Nucynta ER has a better safety and tolerability profile and comparable efficacy to oxycodone, and comes in a tamper resistant formulation to deter abuse.

- John Mastrianni from Geneotech spoke about Zelboraf, a kinase inhibitor indicated for the treatment of patients with unresectable or metastatic melanoma with BRAFV600E mutation as detected by an FDA-approved test. Zelboraf is not recommended for use in patients with wild-type BRAF melanoma. Zelboraf is thought to work by targeting and suppressing cells with the mutated BRAF protein and preventing the cells from growing. Dose is 960 mg orally twice daily, approximately 12 hours apart with or without a meal. Management of symptomatic adverse drug reactions may require dose reduction, treatment interruption, or treatment discontinuation of Zelboraf. Dose reductions resulting in a dose below 480 mg twice daily are not recommended. Most common side effects include rash, hair loss, and sun sensitivity. Other serious reactions include Cutaneous squamous cell carcinoma, hypersensitivity reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, and QT prolongation.
- Judy Kando from Sunovion spoke about Latuda, an Atypical Antipsychotic agent that was approved in October 2010 by the FDA for the treatment of adults with schizophrenia. Efficacy and safety was established in four double blind placebo controlled fixed dose trials that were 6 weeks in duration. In these trials, the primary outcome measure was the Positive and Negative Syndrome Scale (PANSS) and secondary measurement scale was Clinical Global Impression severity scale (CGI-S). FDA has approved Latuda in the dosage range of 40-80mg tablets. 40mg is recommended starting dose, does not need to be titrated, can be taken once daily, needs to be taken with a food containing 350 calories or more. Latuda is contraindicated with strong CYP3A4 inhibitors and strong CYP3A4 inducers. The most commonly reported adverse events were somnolence, akathisia, nausea, parkinsonism and agitation. Average weight gain during the 6 week trial was .75 kg for Latuda and .26 kg for placebo. Latuda is a Pregnancy Category B drug.
- John Renna from Shire spoke about Intuniv, which is a selective alpha2A-adrenergic receptor agonist approved in September 2009 for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) monotherapy and as adjunctive therapy to stimulant medications. Intuniv is an extended release dosage, available in 1 mg, 2 mg, 3 mg and 4 mg tablets and should not be crushed, chewed or broken before swallowing. Once tablet is released in GI tract, it is rapidly and completely absorbed in approximately 2.5 hours. The intent of developing Intuniv was to optimize clinical effects in the treatment of ADHD. This was accomplished by slowing the rate of absorption. Intuniv has a delayed Tmax, reduced Cmax and lower bioavailability compared to those of the same dose of immediate-release guanfacine. Most common adverse reactions include Somnolence, Fatigue, Nausea, Lethargy, and Hypotension.
- Kevin Langlois from Daiichi Sankyo spoke about Welchol, and would like to ask the Board to consider adding Welchol to the PDL as an oral anti-diabetic agent. Currently Welchol is listed only as a anti-lipid agent. Welchol is the first FDA approved drug to reduce both LDL and A1C. In patients with type 2 diabetes, Welchol has been proven to get a 1% reduction in A1C on metformin, metformin combination therapy, sulfonylurea or insulin with a A1C of 8.5. In patients with A1C of 8.1 Welchol has been proven .6% reduction in patients on metformin, metformin combination therapy, sulfonylurea or insulin. Welchol has been proven 22% reduction in LDL-C when added to metformin. Welchol has been proven 42% reduction in LDL-C when added to low-dose simvastatin, and 48% reduction in LDL-C when added to low-dose Atorvastatin. Welchol is a Pregnancy Category B drug.

- Sarah Marshall from Boehringer spoke about Pradaxa, indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. In the RE-LY study Pradaxa was paired with open-label warfarin in more than 18,000 patients. The outcomes of that trial Pradaxa 150mg, twice a day, significantly reduced the risk of ischemic stroke, hemorrhagic stroke and systemic embolism by 35%. The rate of intracranial hemorrhage was 59% lower with Pradaxa. Major bleeding was similar with Pradaxa and Warfarin however the rates of total major gastrointestinal bleeding were higher with Pradaxa. In regards to Drug Interactions, the concomitant use of Pradaxa with P-gp inducers reduces exposure to dabigatran and should generally be avoided. P-gp inhibitors ketoconazole, verapamil, amiodarone, quinidine, and clarithromycin do not require dose adjustments. These results should not be extrapolated to other Pgp inhibitors. The most common adverse reactions reported were dyspepsia and gastritis like symptoms.
- Carla McSpadden from Forest spoke about Viibryd and Daliresp. Daliresp is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations. Recommended dosage is one 500 mcg tablet per day, orally with or without food. Daliresp and its active metabolite are selective inhibitors of phosphodiesterase 4 (PDE4) which is a major metabolizer of cyclic AMP, this activity leads to accumulation of intracellular cyclic AMP and reduce activation of the cells in the lung tissue. The efficacy and safety of Daliresp in COPD was evaluated in 8 randomized double-blind, controlled, parallel group clinical trials in 9394 adult patients with COPD. Most common adverse reactions reported were diarrhea, weight loss, nausea, headache. Contraindication in patients with moderate to severe liver impairment.
 - Dr. Clifford asks if there is any proven efficacy in less severe forms COPD. Ms. McSpadden confirmed that Daliresp was evaluated in patients with more moderate forms of COPD and they did have some positive results but that did not end up being where the most benefit was seen. Therefore indication approved by FDA is in severe to very severe cases.
- Ms. McSpadden spoke briefly on Viibryd, indicated for the treatment of major depressive disorder (MDD). Viibryd binds with high affinity and selectively to the serotonin transporter, inhibiting serotonin reuptake. Also binds selectively with high affinity to the serotonin 1A receptors, and is thought to be a receptor partial agonist. Viibryd's antidepressant effect is thought to be related to its enhancement of serotonergic activity in the Central Nervous System, although the relative impact or contribution of each of those mechanisms are unknown. The efficacy of Viibryd was established in two 8-week, phase III double blind placebo-controlled trials in 800 adult patients with MDD. The most common adverse reactions were: diarrhea, nausea, vomiting, and insomnia. Not indicated for children or adolescence. Viibryd is Pregnancy Category C.
 - Mr. Ouellette asks if there is a starter pack available due to the specific titrating dosage. Ms. McSpadden confirms there will be starter packs available at the pharmacy soon if not available already.
 - Dr. Clifford asks if Ms. McSpadden would be willing to assert that Viibryd produces fewer sexual side-effects than any specific SSRI's or the SSRI's as a class. Ms. McSpadden declines saying that every study is different and it is difficult to compare adverse events being pulled from different studies. But she will say that the numbers that they saw in the clinical trials look fairly positive in regards to sexual function. She has not been told that any further studies are being conducted.

- Joanna Huang from Novo Nordisk spoke about Victoza is a (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes. 5 clinical trials were conducted to determine efficacy. Comparing reduction in A1c end level baseline to baseline 22-52 weeks is between .8-1.5. Demonstrating greater A1c reduction compared to monotherapy. There has been added benefit in terms of weight loss, of 2-6 lbs following treatment with Victoza. In terms of hyperglycemia, in all phase 3 trials there were 7 reported major hyperglycemia in Victoza related in patients. Victoza is contraindicated in Multiple Endocrine Neoplasia syndrome type 2. In the clinical trials, there have been reported cases of thyroid C-cell hyperplasia. Most commonly reported adverse reaction was nausea.
- Ms. Huang spoke briefly on Levemir, would like the board to consider adding Levemir to the preferred side of the PDL.
 - Dr. Clifford advises that Levemir has been on the preferred side for some time now, but Novo Nordisk is no longer willing to contract with the State to keep the product preferred.
 - Julia Hoff from Novo Nordisk spoke up and addressed that Novo Nordisks main focus is on Diabetes and to bring new products to the market that would provide the best care. Health Care Reform has created numerous challenges along with mandated federal rebates in addition what is going on with the donut hole.
- Tom Algozzine from Pfizer spoke on Lyrica, indicated for neuropathic pain associated with diabetic peripheral neuropathy, epilepsy as well. New Guidelines announce Lyrica as the only "Level A" treatment recommended for painful diabetic peripheral neuropathy.
- Ann Woloson representing Prescription Policy Choices, which is a nonprofit, nonpartisan public policy organization with the goal of improving access to effective, safe, and affordable prescriptions in Maine as well as the U.S. Most of their funding comes in the form of grants or contracts with public or private health foundations, not drug companies. They work with consumers, healthcare providers, and payors to promote evidence based prescribing, specifically to promote the unbiased, objective information about the effectiveness, safety and cost effectiveness of prescription drugs. She wanted to say that she believes that the DUR committee has improved patient safety and health patients with a personal or family history of medullary thyroid carcinoma or in patients with outcomes, thru the use of the PDL. However there seems to be more room for cost savings and she thinks the State Medicaid Program needs to take a look at how medications are being prescribed and make sure that there is program monitoring going on and that baseline data is being gathered.

CLOSED SESSION TO DISCUSS FINANCIALS

OLD BUSINESS

RE-OPEN SESSION

DUR MINUTES

September minutes were approved with no corrections.

Caring..Responsive..Well-Managed..We are DHHS.

NEW BUSINESS

DRUG REVIEWS

Board looked over New Drug Reviews:

Complera- recommended to be added to the PDL as Non-Preferred
Cuvposa- recommended to be added to the PDL as Non-Preferred
Edurant- recommended to be added to the PDL as Non-Preferred
Firazyr- recommended to be added to the PDL as Non-Preferred
Sylatron- recommended to be added to the PDL as Non-Preferred
Teflaro- recommended to be added to the PDL as Non-Preferred
Yervoy- recommended to be added to the PDL as Non-Preferred
Zelboraf- recommended to be added to the PDL as Non-Preferred
Zytiga- recommended to be added to the PDL as Non-Preferred

The Board voted all in favor with one not in favor for the above recommendations.

PDL REVIEW

- A motion was made to nonprefer Clarithromycin Tabs.
 - A motion was made by a board member to table this recommendation til the November meeting in order to look at DDI's and prescribers.
 - All in favor.
- A motion was made to nonprefer Avelox, allowing patients starting Avelox in hospital to finish the course of therapy.
 - Dr. Clifford motioned to make this non-preferred and also remind pharmacies via newsletter of the 4-day override, and address in PA criteria allowing finishing course of therapies that already started in hospital.
 - Motion was passed with one abstention.
- A motion was made to nonprefer generic Colistimethate and prefer brand Coly-Mycin-M.
 - All in favor.
- A motion was made to prefer Incivek and Victrelis, as well as PegIntron. Approvals of Incivek and Victrelis will require clinical PA to establish genotype, baseline viral loads and will require periodic SVR's. Must have concurrent peg-a or peg-l and ribavirin therapies.
 - All in favor of preferring Incivek and Victrelis with Clinical PA requirement, and preferring PegIntron.
- A motion was made to nonprefer Budesonide EC.
 - All in favor.
- A motion was made to prefer Plan B One Step as step 1, also prefer Ella and Levonorgestrel as step 2's.

- All in favor.
- A motion was made to prefer Yaz, Seasonale, and Tri-norinyl and non-prefer Loseasonique.
 - A motion was made to non-prefer Loseasonique and grandfather current users.
 - A motion was made to approve as is, current users of Loseasonique grandfathered, and discuss clinical issues of Yaz at November meeting.
- A motion was made to nonprefer Levemir with 3 month transition.
 - Motion was passed with one abstention.
- A motion was made to prefer Tradjenta.
 - Motion was passed with one abstention.
- A motion was made to prefer Byetta over Victoza making Byetta step 8 and Victoza step 9.
 - All in favor.
- A motion was made to nonprefer Calcitonin NS, Prolia, Xgeva, and Zometa.
 - All in favor.
- A motion was made to nonprefer Nutropin and prefer Nutropin AQ Nuspin.
 - All in favor.
- A motion was made to nonprefer Sanctura.
 - All in favor.
- A motion was made to prefer Tiazac.
 - All in favor.
- A motion was made to nonprefer Azor, Caduet, and Advicor.
 - All in favor.
- A motion was made to nonprefer Revatio and prefer Adcirca.
 - All in favor.
- A motion was made to nonprefer Arcapta, Aralast and Zemaira as step 8's, and nonprefer Triamcinolone NS, Glassia, and Prolastin as step 9's.
 - All in favor.
- A motion was made to nonprefer nitrofurantoin macr susp, Phoslyra, calcium acetate and metronidazole. Also prefer Eliphos, Renagel, and Metrogel.
 - All in favor with one abstention on nitrofurantoin.
- A motion was made to prefer Intuniv; nonprefer alfuzosin, Viibryd, Adderall XR and methylphenidate ER as step 8's, and nonprefer dextroamphetamine ER as step 9.
 - All in favor.
- A motion was made to nonprefer Nudexta and discuss PA criteria at November meeting. Prefer donepezil, nonprefer Aricept tabs & ODT as step 5's, nonprefer Nicoderm CQ & Gum, Trexix as step 8, Conzip and Nucynta ER as step 9's.
 - All in favor.
- A motion was made to prefer Suboxone Film, nonprefer Suboxone Tabs.
 - Motion was made to table this vote til the November meeting in order to speak with Dr. Publicker and Dr. Moltz and see which form of Suboxone they prefer when prescribing.
 - All in favor of tabling vote.
- A motion was made to nonprefer Sprix, Cimzia and nonprefer Horizant, Gralise, Amrix as step 8's, cyclobenzaprine ER as step 9. Prefer Enbrel as step 2 and prefer Maxalt.
 - Before discussing grandfather on Cimzia at November meeting, Dr. Clifford will check to see how many patients who are on Cimzia have been thru one of the other preferred medications, meeting criteria.
 - All in favor.

- A motion was made to nonprefer Xarelto, enoxaparin, fondaparinux, and Pradaxa. Also nonprefer Brilinta as step 8, would have store override available for members scheduled for stent placement or have had placement in the last 12 months.
 - All in favor.
- A motion was made to prefer Moxeza and latanoprost sol, nonprefer Lotemax Susp, Vexol, Lumigan Soln, and Optivar as step 8's and nonprefer bromfenac and epinastine as step 9's.
 - All in favor.
- A motion was made to prefer Tazorac, tretinoin gel, amifostine, and letrozole. Nonprefer Retina A gel, Zyclara, Ethyol, and Femera.
 - All in favor.

CLOSED SESSION TO DISCUSS CONTRACTS

ADJOURNMENT: 7PM

The next DUR meeting will be held November 8th 2011 6:00-8:00pm