TO: Maine Drug Utilization Review Board  
DATE: 02/16/12  
RE: Maine DUR Annual Board meeting minutes from 02/14/12

<table>
<thead>
<tr>
<th>ATTENDANCE</th>
<th>PRESENT</th>
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<tr>
<td>Robert Weiss, M.D., Cardiologist, Chair</td>
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<td>Laurie Roscoe, R.Ph., Vice Chair</td>
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<td>Amy Enos, Pharm. D. Waltz LTC Pharmacy</td>
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<td>Laureen Biczak, D.O., Infectious Disease, GHS</td>
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<td>Lisa Wendler, Pharm. D., Clinical Pharmacy Specialist, Maine Medical CTR</td>
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<td>Lindsey Tweed, M.D., Psychiatrist</td>
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<td>Mark Braun, M.D., FACP, Internist/Geriatrician</td>
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<td>Mike Ouellette, R.Ph., GHS</td>
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<td>Rebecca M. St. Amand, R.Ph., Staff Pharmacist Community Pharmacy - Pittsfield</td>
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<td>Timothy Clifford, M.D., Family Practice, GHS</td>
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<td>Kevin Flanigan, M.D., Internist, Medical Director, OMS</td>
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<td><strong>Non – Voting</strong></td>
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<td>Jennifer Palow, Pharmacy Manager, OMS</td>
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**Guests of the board:** David Moltz M.D., Cassandra White Pharm D. Candidate  
Albany College of Pharmacy & Health Sciences

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**CALL TO ORDER: 6PM**

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**PUBLIC COMMENTS**

- Brian Denton from Pfizer spoke about Inlyta® (axitinib), a new oral tablet available for treatment of advanced renal cell carcinoma after failure of one prior systemic therapy. Inlyta® is a tyrosine kinase inhibitor with a recommended starting dose of 5 mg twice daily with or without food. Clinical data was presented, including the safety and efficacy of a phase 3 study. The single trial was a
randomized, open-label, multi-center clinical study of 723 patients whose disease had progressed on or after treatment with one prior systemic therapy. The study was designed to measure progression-free survival, the time a patient lived without the cancer progressing. Results showed a median progression-free survival of 6.7 months compared to 4.7 months with a standard treatment (sorafenib). No statistically significant difference was observed when comparing both arms in overall survival. Hypertension has been observed in patients taking Inlyta® (~20%); therefore blood pressure should be under control before initiation. Other warnings and precautions include arterial thromboembolic events, venous thromboembolic events, hemorrhage, gastrointestinal perforation and fistula formation, thyroid dysfunction, wound healing complications, reversible posterior leukoencephalopathy syndrome, proteinuria, elevation of liver enzymes, and hepatic impairment. It was recommended to avoid in pregnant patients due to potential fetal harm. The most common side effects are diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, palmar-plantar erythrodysesthesia (hand-foot) syndrome, weight decrease, vomiting, asthenia, and constipation. Lab abnormalities most often seen were increased creatinine, decreased bicarbonate, and hypocalcemia. There are no contraindications.

- Dr. Jane Ruby presented on behalf of the medical affairs department of Reckitt Benckiser, owner and manufacturer of Suboxone® products. She expressed concerns regarding the legal, regulatory, and safety implications associated with repackaging Suboxone® tablets in Maine. She stated that blister packaging is not FDA approved for Suboxone® in the United States (compliance policy guidelines section 430.100). This practice also raises other issues regarding safety, such as abnormal stability and purity profiles due to repackaging in multiple pharmacies. The compatibility of the packaging material with Suboxone® is unknown. Blister packaging of these tablets affects the integrity of the drug because the formulation is not designed to withstand dispensing in this manner. These are not conventional tablets, but rapidly dissolvable tablets formed by loose compression methods in which tablets are compressed at a much lower force to allow them to disintegrate in the mouth. [Picture shown comparing Suboxone® to a tightly compressed conventional tablet]. Suboxone® is highly fragile to extensive handling and puncture through a blister pack. As the repackaging of Suboxone® tablets falls outside of the chain of RBP operations and custody, RBP will not assume responsibility for complaints regarding issues related to repackaged product. There are serious questions about loss of child resistant packaging per Consumer Safety Division Protocol. The foil seal on blister packaging totally eliminates any child protection as this is soft and easy to puncture. A child who gets access may get access to multiple tablets at one time and increases the risk of multiple-dose exposure. Information from the global safety database, with reports from the 61 U.S. poison control centers, indicates that from 2006-2011 there were 40 confirmed exposures to tablets in children under 6 with 4 fatalities. Comparing the films and tablets from the time of the film’s 2010 entry into the market until the end of 2011, there were 14 exposures to the tablets with 3 fatalities. There were 3 exposures to the film with no fatalities. Autopsy results from each of the tablet-related fatalities revealed that each child death involved multiple-tablet exposures. The Suboxone®SL film provides a single unit dosing system with a highly child resistant packet, second highest U.S. rating score of F2, that significantly reduces the potential for multi-dose exposure. If I were to give you each of you this packet right now, you would instinctively try to open it like a mustard packet and would likely fail. That is because it requires a multi-step process to read through and follow through to open it. It is also important to note from the last meeting minutes we realized that some patients are being charged at least $1 for the external packaging process. We are concerned that this may
violate copayment restrictions set forth in the MaineCare benefits manual chapter 1 section 1.09. Lastly, Suboxone® film is designed to reduce or eliminate diversion, abuse, and unintended pediatric exposure while continuing to provide an effective and safe treatment for patients. We hope this information discourages any consideration of repackaging Suboxone® into blister packs and further serves to protect the children of Maine as well as the public health in general. [Document provided regarding federal regulations and concerns about good manufacturing processes].

Question: Is the film able to be divided so that it can be used in a different strength?

Answer: At the present time, it is only available in the 2 and 8 mg strengths. As a pharmacist would understand, if something is not scored we cannot guarantee that the product is equally distributed throughout the entire tablet or film. Without scoring, no drug has that guarantee. We are in the process of developing other dosages for the film which have to go through FDA approval as a subsequent NDA.

Question (Dr. Barkin): Do you have any data regarding superiority data on the film over the tablet in regards to safety and overdose?

Answer: In terms of safety and child poisoning, the information I provided tonight could be developed into writing for you.

Retort: But that was multi-year data...

Answer: The film only came out in September of 2010 so our comparison data is limited. The trend is that exposures to the film are trending downward in terms of safety issues. We need statistical significance and a larger period of time in order to compare. We have 10 years of experience with the tablet and only a year and a half with the film. Safety breaks down into a lot of different sub-categories, but in regards to aggregate toxicity there is no difference between the two products. For approval of the film the FDA did not require efficacy because it is the same drug. They did require equivalency and safety of the film, of which there was no difference.

OLD BUSINESS

DUR MINUTES

- January minutes were approved, with a motion to approve initiated by Dr. Mark Braun.

PSYCH WORK GROUP MONTHLY UPDATE

- Dr. David Moltz, Chief of Outpatient Behavioral Health Sciences at Mid Coast Hospital in Brunswick, Maine served as representative for the Psych Work Group monthly update. He works for the Addiction Resource Center which treats around 150 patients with Suboxone® at any given time. They are concerned that because it is a small community, a portion of the Suboxone® available on the street is coming from their Center. The Center has been working over the past one to two years on ways to prevent diversion. They started using bubble packing as one way of ensuring accurate pill counts. Urine testing can show whether someone is taking other drugs but not how much of the Suboxone® dose they are taking. The only way to show that someone is not diverting their
medication is through pill counts. But there is a major flaw with pill counts when they are packaged in a bottle: the patient can borrow or buy pills from others to make up the count. The advantage to bubble packing is that once the pill is out of the bubble it can’t be replaced. [Hands out article about blister packaging in Europe]. Each card has the patient’s name on it and they bring in the card for a more accurate pill count. When they started a year ago, there were two main concerns with the blister packing. One was that the pharmacies wouldn’t want to do it. In fact, many already had the capacity and only two in the area, the two independents, charge $1 per card. All the others only ask that the Center give them 24 hours notice. The other concern was child-proofing. They talked to the head of the Maine Poison Control outlining the benefits and risks of bubble packing. The children deaths from pills occurred not from blister packs, but from child-proof pill bottles. People can leave the containers open, put them in a different place, drop them on the floor. Plus when pills are diverted, they aren’t usually in the original containers. So anything we are doing to prevent diversion in protecting children and people from misuse. The results from their study showed that when they used blister packaging for twenty people, pill counts improved 133% compared to before bubble packs were instituted. Another thing that has happened is that a large number of people have been excluded from the program because they no longer come to the pill count. The safety and cost savings from these exclusions is hard to measure but is there.

- Question (Dr. Weiss): How do you know that being in these bubble packs doesn’t affect the quality of the medicine?
  - Answer: Nobody has complained. Sometimes they complain about the 2 mg pills being crumbly, but that’s whether or not they were in the bubble pack. There have been a number of complaints since we switched to the film as far as effectiveness, but nobody has complained about the bubble packs. The bubble packs are actually quite popular among the patients because it helps them stay organized and see if somebody is stealing from them.

- There have been multiple reports from patients coming in to the program that Suboxone® is now harder to get on the street. The film is plentiful by the way. The price of the pill is up and it is harder to get. Finally, law enforcement, including the Maine DEA, has said on several occasions that they have yet to find diverted Suboxone® in blister packs. We can’t bubble pack strips, so as a result of the new MaineCare’s preferred drug list, this year’s program is finished. We can still do the bubble packing but only for those who are self-paid or have private insurance. For some unknown reason, the numbers on the strips are not sequential. This leaves no way for us to do the same type of rigorous pill count. What we are proposing is that we get an exemption for our three prescribing physicians and one back-up physician. If the four of us could be exempted from the requirement for the strips and continue doing the pills, we could continue to work on diversion.
  - Question: Is there any other national data on blister packing other than your personal experience?
    - Answer: The only data I know is mentioned in this article pointing out that one of the virtues of blister packing is it prevents tampering. There is also evidence that it is cost-effective, certainly in nursing homes, since the pills in blister packs can be reused. I feel they can prevent diversion.
  - Question (Dr. Wendler): Do you always prescribe under a 30-day supply?
    - Answer: We do a maximum of 28 days (4 weeks).
  - More discussion followed regarding:
- Hard copies of results and conversations from study by Dr. Moltz requested.
- Dr. Ruby brought up the fact that she hopes certain requirements are being met such as: providing the package insert and safety warnings, providing the lot numbers from which the drug came, the name and address of the manufacturer on the blister pack to trace it back, and other requirements needed to take something out of the chain of command from a manufacturer and repackaging it. Especially since this concerns a schedule III drug which is highly regulated.
- Are pharmacies using the proper procedure and materials when handling this medication and putting the Suboxone® in blister packs?
- Films: numbered but not consecutively. Bar code is only on the box but not the individual strips themselves. This leads to difficulty in counts and verifying which specific strips were supplied to which patients.
  - One solution is to Xerox copy the films being dispensed in order to log specific film strip numbers. This is not supposed to alter the integrity of the medication. Film counts can be done in this way.

**NEW BUSINESS**

**STATIN/LIPID UPDATE**

- Deferred to next meeting.

**ANTIPSYCHOTIC METABOLIC MONITORING**

- Report showing data from 2010 and 2011 on MaineCare atypical antipsychotics
  - Page 1 contained users numerical data, Page 2 was equivalent percentages
    - Categories included:
      - First 6 Months of 2010 (more complete/accurate)
      - First 6 Months of 2011
      - In 2011 and 2010
      - New to 2011
    - Groups Included:
      - Lipid Test
      - Lipid RX
      - Blood Sugar
        - Did not include values from CMP/BMPs
      - DM RX
      - BP RX
        - Clonidine and Guanfacine excluded for 0-18 age group (ADHD)
    - Sorted by Age (years)
      - 0-18
      - 19-44
- 45-64
- 65+
- Will require routine monitoring for patients receiving atypical antipsychotic medication.
  - In accordance with the American Diabetes Association Screening Guidelines for Patients on Second-Generation (atypical) antipsychotics
  - Doctors must submit baseline (measured within 6 months prior to initiation) and repeat monitoring after 12 weeks for:
    - Family history of diabetes
    - Fasting glucose
    - Fasting lipid profile
    - Weight
    - Blood pressure
  - If information is not received by week 20, ongoing prescribing of atypical antipsychotics will require Prior Authorization

HEPATITIS C UPDATE

- January data updated for adherence to Incivek™ and Victrelis™
- Continue to gain new patients
- Still apparent premature discontinuations of therapy
- Suggestion made to consider calling patient to remind them to pick up their drugs and ensure they are taking the supplementary medication
  - Make certain they are taking the medications in the proper sequence and combination
- Could consider specialty pharmacy for more effective monitoring

PDL NEW DRUG REVIEW

- Not voting on these drugs yet, awaiting financial data
  - Information provided ahead of time for review at next month’s meeting
    - Picato® (ingenol mebutate topical gel)
    - Inlyta® (axitinib)
    - Bydureon® (exenatide ER for injectable suspension)
      - PDL Placement for All = interim Non-Preferred until financials reviewed at next meeting and formal voting occurs

DRUG-DRUG INTERACTIONS & DOSING LIMITATIONS

- **Victrelis™ (boceprevir):** New FDA drug warning (2/6/12) regarding Victrelis™ and co-administration with ritonavir-boosted HIV protease inhibitors.
  - Reduced exposures of the HIV medicines and Victrelis™
  - Concerns Victrelis™ with Norvir® in combination with Reyataz® or Prezista®, or with Kaletra®
- **Pradaxa® (dabigatran):** New dosing restrictions in those with severe CrCl (15-30 mL/min), recommended dose is 75 mg BID.
Those with moderate renal impairment (CrCl 30-50) AND using the P-gp inhibitors dronedarone or systemic ketoconazole, recommended to consider reducing dose to 75 mg BID.

- **Tradjenta™ (linagliptin):** Dosing limits of one tablet daily.
  - DDI with Rifampin (decreases linagliptin exposure). Package insert strongly recommends alternative treatment when linagliptin is administered with a P-gp or CYP3A4 inducer.

- **Brilinta™ (ticagrelor):** Dosing limit of 2 tablets per day. It is a non-preferred drug but is available with a special PA with diagnosis.
  - Verify that patient is on ASA (100mg max) when allowing for override (either by profile or with the pharmacist giving the override). A DDI exists for using maintenance ASA dose >100mg, as it reduces the effectiveness of Brilinta™.
  - Concomitant use with strong CYP3A4 inhibitors should be avoided (including ketoconazole, itraconazole, voriconazole, clarithromycin, nefazodone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir, and telithromycin).
  - Doses of simvastatin and lovastatin >40mg should be avoided.

- **Arcapta™ (indacaterol inhalation powder):** Non-preferred, dosing limit of one capsule/inhalation per day.

- **Juvisync™ (sitagliptin + simvastatin):** Dosing limits of one tablet per day.
  - DDI with simvastatin total daily doses >40mg.
  - DDI with verapamil or diltiazem: max dose should not exceed 100/10mg Juvisync™.
  - DDI with amiodarone, amlodipine, or ranolazine: max dose should not exceed 100/20mg per day of Juvisync™.
  - DDI with strong CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, posaconazole, HIV protease inhibitors, erythromycin, clarithromycin, telithromycin, and nefazodone). These combinations are contraindicated.
  - DDI with gemfibrozil, cyclosporine, and danazol. These combinations are contraindicated.

- **Zocor® (simvastatin):** Revised dosing limitations. See [http://www.fda.gov/drugs/drugsafety/ucm283137.htm](http://www.fda.gov/drugs/drugsafety/ucm283137.htm) for more information.

The board voted all in favor except for one person not in favor of the Pradaxa® recommendation.

  - Disagreement based on lack of human evidence with the 75 mg dose. The recommendation is based on pharmacokinetic studies as opposed to clinical trial data.

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**CLOSED SESSION**

Topic CMS clarifications concerning line extensions and potential fiscal impact to state

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**ADJOURNMENT: 8PM**

- The next meeting will be held on March 13, 2012.