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**Massachusetts Department of Public Health
Minutes of the Drug Formulary Commission
Meeting of Thursday, September 15, 2016**
Henry I. Bowditch Public Health Council Room, 2nd Floor
250 Washington Street
Boston, MA 02114

Date of Meeting:	Thursday, September 15, 2016
Beginning Time:	10:10 AM
Ending Time:	11:04 AM

Advisory Council Members Present: The following (10) appointed members of the Drug Formulary Commission attended on July 14, 2016, establishing the required simple majority quorum (9) pursuant to Massachusetts Open Meeting Law (OML): DPH Bureau Health Care Safety and Quality, Policy Director, Lauren B. Nelson, for Director Eric Sheehan (Chair); Dr. Douglas Brandoff; Cheryl Campbell, Dr. Daniel Carr; Dr. Joanne Doyle-Petrongolo; Stephen Feldman, Dr. Kenneth Freeman, Dr. Paul Jeffrey; Dr. Virginia Lemay; Tammy Thomas and Dr. Alexander Walker.

1. Welcome and Introductions

Lauren B. Nelson called the meeting to order at 10:10AM

Ms. Nelson informed the members that she would be chairing the meeting today in place of BHCSQ Director, Eric Sheehan for today's meeting, but that she would not vote or count toward quorum.

Ms. Nelson thanked everyone for being here today, and reminded everyone that the meeting was being recorded. She then asked if anyone was recording, receiving no affirmative response.

Ms. Nelson informed the members that Will de Groot had resigned due to a job out of state and reminded the members that there are now two vacancies on the DFC, one pain management physician and one member of the public.

Ms. Nelson recapped the last meeting on July 14, 2016, noting the DFC's approval of the Non-Opioid Pain Management list and the need to update the list each year by September 1st; and the presentation by staff of the first draft Formulary of Chemically Equivalent Substitutions.

2. July 14, 2016 Minutes

Ms. Nelson asked if there are any changes to the July 14th meeting minutes. After noting member changes, Ms. Nelson asked for a motion to approve the minutes as changed.

- Motion to Approve: Mr. Feldman
- Second: Dr. Doyle
- All in favor: 8; Opposed: 0; Abstentions: Dr. Freedman; Ms. Campbell

3. Formulary Review and Evaluation

Ms. Nelson congratulated DFC members on the completion of the first Draft Formulary and reminded them that the work of the commission would be ongoing in order to update the formulary with potential Interchangeable Abuse Deterrent (IAD) Drug Products to include as List A drugs for Formulary 2.0. Ms. Nelson stated that the DFC vote on October 15, 2015, to include all Schedule II and III opioids on the Heightened Public Health Risk (HPRH) list, allows all new opioids to automatically be placed on the HPRH opioid list upon FDA approval, until approved as IAD drug products by the DFC, thereby allowing Component 1 to be skipped.

To begin work on Component 2, Ms. Nelson introduced Dr. Tyson Thompson to present evidence that was sent to members a few days earlier. Ms. Nelson noted that evidence exhibits were available on the table by the door for member and audience reference.

Dr. Thompson presented evidence of abuse deterrence on Xtampza ER, oxycodone ER capsule, noting a chemical barrier to abuse, clinical abuse studies indicating that the product is resistant to IV injection, and that it received final approval from FDA this past April. Dr. Thompson informed the members that Xtampza ER is formulated using DETERx technology, and includes an oxycodone base with myristic acid to produce a liquid compound, which is suspended in wax microspheres and placed in capsules. These microspheres are resistant to particle size reduction and extraction via use of multiple solvents, making injection of the wax microspheres relatively impossible using needles smaller than 18 gauge.

Dr. Thompson stated that crushed/chewed Xtampza ER is associated with less "drug liking" than with oxycodone IR in the same manner, and that crushed Xtampza ER is bioequivalent to intact Xtampza ER.

Dr. Carr stated that 18 gauge would be a typical gauge to provide fluid going into an operating room patient. While it is a big gauge, it is not exclusive to horses.

Dr. Thompson stated that there was only 30% of drug availability when injected through 18 gauge needle.

Dr. Thompson went over initial dosing and pharmacokinetics. He noted an important counseling point that bioavailability was dependent on the presence and type of food. Evidence showed increased peak plasma concentration with high fat food.

Dr. Brandoff stated that patients should not be on this medication if they are opioid naïve so opioid naïve dosing is fundamentally flawed.

Dr. Thompson stated that Xtampza ER is subject to REMS program as are all other ER/LA opioids, and that we will not see data from community until 2021.

Dr. Jeffrey asked about absorption with food and how peak plasma concentration is significantly higher with high fat food. Dr. Thompson stated this was in comparison to fasting state.

Seeing no further questions, Ms. Nelson asked for motion to approve Xtampza ER as an IAD drug product on formulary.

Dr. Lemay asked if DETERx is exclusive to this product.

Dr. Thompson stated this was their proprietary technology.

Ms. Nelson noted that this was a manufacturer based out of Canton, MA.

Mr. Feldman questioned the lack of data to understand how strong evidence is to determine if this is abuse deterrent. He stated that he did not see any result for outcome measures and data interpretation. Dr. Thompson stated that the results were in monograph, using a sheet (included in evidence) as reference for industry.

Mr. Feldman noted that the purpose of the monograph is to state that this is what the evidence is, and that he was suggesting that for the first section under outcome measures and data, as well as the two that follow it, it should refer back to the results, because this is what we're going to look at. There should be a sentence stating that the results indicated on other side of the form.

Dr. Thompson stated on the other side of the form are the results.

Ms. Nelson suggested that the information was present, and that we would address the structure of that information at upcoming meetings if members were interested.

Dr. Lemay asked about an earlier product that was not approved, and asked to be reminded why.

Dr. Thompson reminded the members that the drug's issues with food effects were too significant because it had to be given on empty stomach. Dr. Lemay asked if there was a greater difference in AUC than this drug. Dr. Thompson stated that he would have to look back at the evidence specifically.

Dr. Doyle-Perongolo stated that we had concerns about dose dumping with other agents, and asked why not with this one and dose dumping. Dr. Thompson noted that dose dumping was mainly concerned with alcohol.

Ms. Nelson reminded members of the steps in the approval process and suggested that a drug should be approved as an IAD if abuse deterrent affects were significant enough. Then, once we

get to crosswalk section, members can consider it for substitution. Thus far, the only drugs proposed by staff and not approved as IADs were based on unavailability in the market or lack of evidence for abuse deterrence.

Ms. Nelson asked if there was any further discussion on this.

Dr. Lemay noted that it only goes up to equivalence of 40mg of oxycodone, not 80mg.
Dr. Thompson agreed and stated that a patient would have to take two instead of one tablet.

Ms. Nelson requested a motion.

- Motion to Approve: Dr. Walker
- Second: Mr. Feldman
- All in favor: 10; Opposed: 0; Abstentions: 0

4. Drug Products for Future Consideration

Dr. Thompson noted that while Xtampza was the only newly approved drug product to be presented at this meeting, there are several others that may be ready for presentation in the coming months, including the following:

- MorphaBond: not commercially available, monograph to be completed when it is.
- Remoxy (Oxycodone ER): PDUFA date of 9/25/16, not likely to go through an advisory committee so decision should come soon.
- Arymo ER (Morphine ER): PDUFA date 10/14/16, recommended for approval by advisory committee.

Dr. Carr asked if approval means approval as an abuse deterrent.

Dr. Thompson stated that it meant approval as a new drug generally and as an abuse deterrent.

5. Cross-Walk: Chemically Equivalent Substitutions

Ms. Nelson stated that, since there was only one drug to present today, in the interest of time, we would present ADP efficacy evidence on Xtampza ER at this meeting. Ms. Nelson noted that there would be no crosswalk because there are no therapeutic equivalents, bringing us to five drugs on list A with no pairings on list B.

Dr. Thompson presented evidence of ADP efficacy for Xtampza ER, noting that there was not enough data to prove abuse deterrence in the community.

Ms. Nelson asked for questions or comments.

Dr. Carr stated that under product labeling it says category I, and then II or III. He asked if there was a key to what the categories mean in the front or back of the document.

Dr. Thompson noted that categories I-III on the front referred to studies, and was taken from draft formulary. On the back, is our evidence grading system based on recommendations by the

commission. Dr. Carr stated that the front of the page categories referred to type, not strength of evidence, and that the back of the page referred to strength of evidence. He stated that it may be worth emphasizing that some of these portions of these forms are laid out where category means one thing in the front, and another in the back, for clarity.

Mr. Feldman agreed with Dr. Carr's observation. He noted that when we designed this form, we wanted to align that form with requirements as FDA stated it, and that these guidelines the FDA came out with were for the pharmaceutical industry. Dr. Carr agreed and asked for more clarity. S. Feldman agreed and asked for similar nomenclature.

Dr. Thompson noted that, other than the members of this commission, people would only see the strength of evidence category, not type of evidence category.

Ms. Nelson asked if there was any more discussion. She noted that this issue was not going for a vote, but would be used in further discussions.

6. Meeting Schedule

Ms. Nelson presented the schedule of DFC meetings for upcoming months.

Dr. Doyle pointed out that the dates listed were all Fridays. Ms. Nelson apologized for the error and noted that the dates should be the third Thursdays of each month.

Ms. Nelson stated that there would be no October meeting, because there are no new drugs ready to present. Ms. Nelson informed members that they should expect communication around rescheduling of February and April meetings, which are currently scheduled during February and April school vacation weeks, which have historically been difficult for members.

Ms. Nelson asked members to hold the dates on the slide (as corrected), and assume that we will have meetings. She assured members that staff would make efforts to notify well in advance of cancellations.

Ms. Nelson asked for any final discussion or questions, then called for a motion to adjourn.

- Motion to Adjourn: Dr. Jeffrey
- Second: Dr. Doyle-Petrongolo
- All in favor: 10; Opposed: 0; Abstentions: 0