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Massachusetts Department of Public Health
Minutes of the Drug Formulary Commission
Meeting of Thursday, February 4, 2016

Henry I. Bowditch Public Health Council Room, 2nd Floor
250 Washington Street, Boston, MA

Date of Meeting: Thursday, February 4, 2016
Beginning Time: 2:03 PM
Ending Time: 4:00 PM

Advisory Council Members Present: The following eleven (11) appointed members of the Drug Formulary Commission attended on February 4, 2016, establishing the required simple majority quorum (9) pursuant to Massachusetts Open Meeting Law (OML): DPH Interim Director Bureau Health Care Safety and Quality Eric Sheehan (Chair); Dr. Douglas Brandoff; Cheryl Campbell; Ray Campbell; Daniel Carr; Dr. Joanne Doyle-Petrongolo; Stephen Feldman; Dr. Paul Jeffrey; Cindy Steinberg; Dr. Jeffrey Supko; Tammy Thomas; and Dr. Alexander Walker.

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1. Welcome and Introductions

Department of Public Health (DPH) Interim Director Bureau of Health Care Safety and Quality, and Advisory Council, Chair Eric Sheehan called the meeting to order at 2:03PM and provided brief introductory remarks.

Mr. Sheehan reminded the attendees that this is a recorded, public hearing, and confirmed that no one in audience was recording.

Mr. Sheehan summarized the January 7, 2016 meeting. He reminded the attendees that written testimony and minutes are available online. He noted that the Commission at their last meeting began their work evaluating the individual drug products for placement on the formulary as a potential therapeutically equivalent substitute. The Commission approved both of the FDA approved ADF labeled drugs products discussed at the last meeting, OxyContin HR and Embeda. At the December 17, 2015 meeting, you also approved Hysingla HR to be considered in Component 3 of the process, and denied consideration of Targiniq and any other drug products that are not marketed on the United States.

Mr. Sheehan also noted that the work achieved at the last meeting enabled the Commission to make substantial progress towards completing Component 2 of the Evaluation and Review process. Referring to the overview slide for today's presentation, Mr. Sheehan noted that Component 1 (determining which groups of drugs should be designated as having a heightened public health risk), was complete. Moving on to Component 2 (determining which drugs should be identified as a potential therapeutically equivalent substitute to the drugs that have a heightened public health risk), Mr. Sheehan noted that at November 5, 2015, the Commission approved the monograph and at the December 17, 2015 meeting evaluation of drug products according to the criteria began and would continue today and in one or more meetings to come..

Moving onto Component 3, Mr. Sheehan again noted that following completion of components 1 and 2, that the Commission will then move onto completing a crosswalk and develop a formulary of therapeutically equivalent substitutes for drugs determined to have a heightened public health risk. Following completion of these components, the Commission will have a draft Formulary.

Mr. Sheehan reminded the Commission that the formulary is guidance for prescribers and is not mandatory. It will be another tool that prescribers can use but it will not be mandated to substitute drugs just because the formulary recommends that action.

Mr. Sheehan set forth the goals of today's meeting

- To continue to work on Component 2 and evaluate the three drugs having claims of ADF technology according to the monograph criteria. This work will include: a presentation of each drug product through the approved monograph with a vote to be taken after each presentation to place the drug product on the formulary as a potential therapeutically equivalent substitute.

2. Approval of Minutes

Mr. Sheehan called for approval of the minutes from the January 7, 2016 meeting.

- Typos on pages 2, 3 and 4 were noted by members
- Motion to approve: Cindy Steinberg
- Second: Stephen Feldman
- All in favor: Motion carried unanimously

3. Cost Assessment

Mr. Sheehan informed the Commission that at the last meeting, the Commission voted to request an Insurance benefit Review by the Center for Health Information and Analysis (CHIA). While this review may assist the Commission to begin our discussion of cost impact, and the benefit and payment implications of placing drug products on the formulary while eliminating cost barriers to safe prescribing, we have more information to give you a better understand of the process. To conduct its review, CHIA will use monograph information we have received from our vendor and information from votes that you have already taken.

CHIA expects this review to take some time, with a report available in about 6 months, meaning evaluation and crosswalking may be complete already, but the results of the review, should appear in the Commission's report and be referenced in the final draft formulary document. To avoid any delay, CHIA will look to have the three FDA approved labeled drugs you have approved and the five remaining drugs products with ADF claims, and compare each drug product to each of the 28 Heightened Public Health Risk drugs to determine the cost to commercial insurance of potential substitutions.

4. Evaluation of Drug Products with ADF Claims

Mr. Sheehan informed the Commission that at the January 7, 2016 meeting, the Commission applied the criteria that were determined should be utilized to evaluate if a drug product should be placed on the formulary as a potential therapeutically equivalent substitute. Upon application of the criteria, the Commission determined that OxyContin ER and Embeda should proceed to the next phase of evaluation. In December, the Commission also determined that Hysingla HR should proceed to the next phase of the evaluation and that Targiniq should not procced, nor should other drugs that are not available on the US market.

Mr. Sheehan continued by informing the Commission that the department was ready to present information, through the amended monographs, to assist them in the evaluation of Nucynta ER, Oxaydo and Opana ER for potential placement on the formulary as substitutes for drug products having a heightened public health risk.

Mr. Sheehan noted that we will use the evaluation guide to record your evaluation process. An amended version that includes the remaining five drugs with ADF claims is in your packets.
Mr. Sheehan continued; our intention is to use this guide to mark your consideration of each part of the monograph. Additionally, it is to tool to help us track whether the monograph has meet the Commission's expectations for the data requested and needed to make a determination whether the drug products should be placed on the formulary as

a potential therapeutically equivalent substitute. Throughout our discussion, Jon Mundy will note the consensus of the group as to each factor under discussion.

The three drug products that we will consider today have claims of ADF technology, but no FDA approved labelling.

Monographs for these three drugs are also in your packets. Studies associated with these monographs have been sent to you and are available for your perusal in the notebooks by the door.

The fact that these drug products do not have FDA approved ADF labelling should not prevent you from determining that they may provide a prescriber a viable treatment option, and therefore considering them for inclusion in Component 3.

Furthermore, once approved for the crosswalk, if it turns out that no drug product on the heightened public health risk list is appropriate for substitution, a new drug product may come to market at a later date that will be appropriate for substitution. Also, the approved potential substitute may still be useful as an initial therapy.

Please remember that we still have to crosswalk these drug products in Component 3 to determine if any of the drug products we approve in Component 2 may be appropriately substituted for any other drug products determined to have a Heightened Public Health Risk.

It also bears noting, as you discussed at the last meeting, that the drug products being evaluated for potential substitution have many of the same side effects, contraindications, and overdose risks as many other similar drugs.

This commission is being asked to evaluate these abuse deterrent alternatives, while trusting that safe prescribing practices and robust prescriber-patient relationships will allow for substitution of drug products with Heightened Public Health Risks by drug products with FDA Approved ADF labelling and ADF claims in appropriate cases.

To get us started, I'd like to invite David Dunn to facilitate this conversation. But first, I want to make an announcement. This will be Mr. Dunn's last meeting of the Drug Formulary Commission. He is pursuing other opportunities outside of state government. Mr. Sheehan noted that he will be missed and thanked him for his dedication to this commission and to the Department of Public Health.

Mr. Dunn then made some remarks, expressing to the commission that it has been his pleasure to serve such a dedicated, thoughtful group of individuals that are championing this important process forward.

You will notice that we have an addition to our staff at the table. Tyson Thompson, a pharmacist who has been intimately involved with this effort since the beginning, will be assisting the commission going forward. I'd like to welcome Mr. Thompson, who may be answering some of your questions today and going forward.

Mr. Sheehan then invited Mr. Dunn to facilitate this conversation.

Mr. Dunn presented the monograph for **Oxaydo**.

Discussion:
Mr. Feldman commented that there is evidence of ADF properties in other drugs and that Oxaydo does not necessarily have this evidence. He suggested putting a new category on the formulary, differentiating drugs with ADF properties from drugs that only seemed to have ADF claims. A level of evidence grading system was suggested. Mr. Feldman felt Oxaydo only had claims, at this point.

Mr. Sheehan stated that the monograph was approved by commission members, so a revised monograph would require approval by the commission members. He stated that this could not be voted on today, but thoughts could be gathered on amending the process today.

Dr. Carr stated that he agreed with Mr. Feldman that the level of evidence demonstrating ADF properties of Oxaydo seems weaker than some of the other drugs. He inquired whether any other drugs were intended to replace immediate-release formulations. If this is the only IR drug available, he would want more scrutiny of the evidence of ADF properties rather than less. Does Oxaydo meet the FDA guidance criteria for ADF labelling?

Mr. Feldman suggested creation of a key to identify if a drug is an ADF.

Dr. Jeffrey voiced support for the concept of an evidence level grading system to determine if evidence of particular claims is sufficient. He stated that it would be possible to grandfather the other drugs already approved. In addition, he recommended that each drug have a review from a website like www.bluelight.org or similar source to see how easily a particular ADF could be abused.

Mr. Dunn responded to Dr. Carr that Oxaydo was approved before there was FDA guidance to industry on ADF labeling, and that only the one clinical abuse potential study was available for it. He noted that he researched www.bluelight.org for each and every drug product being considered. Mr. Dunn reiterated the abuse potential findings from the literature, and suggested that the evidence showed a pretty successful ADF property.

Mr. Feldman raised questions about the design of the study, and inquired whether information on study design could be obtained from the manufacturer. He expressed concern that the commission would not want to be fooled by faulty study design.

Dr. Thompson explained that the study was available in a peer-reviewed journal, so the study design could be evaluated appropriately. It was explained that the study was similar to that of all of the ADF products in that a relatively small amount of recreational opioid users were recruited, and the crushed tablets of Oxaydo were compared to crushed non-ADF oxycodone IR in terms of drug liking reported by the opioid users.

Ms. Steinberg inquired whether Oxaydo could temporarily be considered an adequate substitute, since it is the only IR drug being considered as a substitute for a highly abused medication. If so, she raised the question of if the view of the DFC could be changed in the future if a new drug with better ADF properties became available.

Mr. Sheehan responded that this is a living, breathing commission that is able to adapt as time goes on. Mr. Sheehan emphasized that we may not be able to find perfect products, but should be thinking about products that have ADF claims, especially when they may be the only substitute available for a highly abused product.

Ms. Steinberg suggested a system of assigning a "strength of decision" score on each drug as a caveat, which would allow for the drug to be revisited down the line.

Mr. Feldman commented that eventually data will start to present, and that the DFC needed a place to put the data.

Dr. Carr suggested that the DFC could adopt the GRADE process as a model to rate the strength of evidence associated with each ADF. He commented that this would allow the DFC to balance risks and benefits and provide a rating for "strength of opinion" from the DFC on a particular drug. He stated that the model was available on www.gradeworkinggroup.org.

Mr. Sheehan asked for clarification as to what the members were requesting. He restated that the members were asking for rating approach when there was not enough evidence for a drug product that had claims but no labelling.

Dr. Carr agreed but clarified that he was looking for a way to capture the nature of the evidence, rather than quantifying the evidence.

Dr. Thompson reiterated that the study was in the package insert, just like drug products with labelling. The only difference in the labeling for Oxaydo compared to other FDA-labeled ADFs is that it was approved prior to the FDA issuing any guidance to industry on ADFs.

Mr. Sheehan clarified his previous comments on categorical changes. He stated that the monograph would require a vote to be changed, but the evaluation guide would not require a vote to change it, as it is just a guideline and was not created by a vote. If members thought more evidence categories were required in the monograph, we could vote on that, but if they believe the monograph categories were correct, but that they wanted to note their consideration of those factors more specifically

Dr. Carr commented that the GRADE process is easily transferable to analgesic trials.

Dr. Walker suggested that the grading piece could be added to the crosswalk. He commented that the crosswalk would be an appropriate place for this information, since the question as to whether it should be a substitute was clearly answered by the studies and the monograph. He indicated the graphic that showed what happens to the drug when water is added.

The DFC members were asked to vote on whether or not the monograph for Oxaydo met the needs of the commission on all of the following parameters as Mr. Dunn presented the highlights of each section of the monograph.

A consensus was reached that each section of the monograph met the needs of the commission

Dr. Brandoff commented, on the section about dosage form, that it is important for those monitoring prescribers to be aware that since the product is only available in 5 and 7.5 mg tablets that it may appear that prescribers are prescribing more units.

Mr. Sheehan opened up Oxaydo for discussion once more.

Dr. Carr inquired as to whether the ADF mechanism could be bypassed by extraction using alcohol. He commented that this was not addressed.

Dr. Thompson said that this factor was not required, but was typical. It is an unknown for this drug product,

Dr. Feldman responded that this type of information is in the product labeling. He noted that if the factor is not discussed during the approval process, a manufacturer would not put in in the literature.

Mr. Sheehan called for a motion to approve **Oxaydo** for consideration in Component 3.

- Motion to approve: Ray Campbell
- Second: Alec Walker
- All in favor: Motion carried unanimously
- Dr. Carr wished to bring to the evaluative process some indication that there may be some gaps in the evidence based on the timing of FDA approval.
- Mr. Sheehan expressed that this information would be captured during the crosswalk phase.

Mr. Sheehan then asked Mr. Dunn to continue the meeting by presenting the next drug product for consideration.

Mr. Dunn presented the monograph for **Opana ER**.

Discussion:
Dr. Carr inquired whether the HIV outbreak and IV Opana ER abuse occurred with the INTAC technology. He also inquired if the reports described how the formulation was prepared for IV injection.

Dr. Thompson answered that the CDC report didn't mention the method in which the individuals used for preparation of Opana ER for IV injection, but that it was the Opana ER with INTAC that was abused.

Mr. Dunn stated that all reports of dissolving and injecting the product involved shaking.

Dr. Carr suggested that the abuse deterrent properties did not appear very strong.

Dr. Brandoff commented that he disagrees with the manufacturer putting out recommendations for dosing in opioid naïve patients. He also commented that Opana ER is difficult to use in his patients because it must be given around mealtimes. Dr. Brandoff stated that sometimes in cancer patients, there are appetite issues and they have to take every opportunity to get certain patients to eat if whenever their appetite presents. He noted that a Time magazine story highlighted this drug as one that was fueling the opioid epidemic in Appalachia. He voiced that there appears to be no evidence of abuse-deterrent properties for Opana ER, and the FDA agrees. He believes this drug should not be approved as a potential substitute on the formulary.

Ms. Steinberg asked if there was some FDA petition issue with this medication.

Mr. Dunn believed there was some sort of petition related to the patent; he speculated that it had to do with generic formulations.

Dr. Thompson stated that after Opana ER was reformulated with INTAC, the manufacturer put out a citizen's petition to keep generics with the original formulation off the market, citing safety concerns with the original formulation.

Dr. Supko voiced his agreement with Dr. Brandoff's statements.

Mr. Sheehan called for a motion to reject **Opana ER** for consideration for Component 3.

- Motion to reject: Douglas Brandoff
- Second: Alec Walker
- All in favor: Motion carried unanimously
- Dr. Walker made a further motion to vote that the monograph met all criteria, satisfying the needs of the commission.
- There was a consensus among commission members that the monograph met the needs of the commission in all areas for consideration.

Break 3:17- 3:27 PM

Mr. Sheehan welcomed everyone back from the break and invited Mr. Dunn to continue the meeting by presenting the next drug product.

Mr. Dunn presented the monograph for **Nucynta ER**.

Discussion:
Dr. Carr inquired what the specific technology is constituting a potential abuse-deterrent property of the Nucynta ER formulation was.

Mr. Dunn commented that tablet hardness is the abuse-deterrent property.

Dr. Carr asked whether this is replacing a non-abuse deterrent drug product. Is there an earlier formulation of ER tapentadol?

Dr. Thompson stated that the only previous formulation of Nucynta or tapentadol was an immediate-release formulation, and that the extended-release formulation itself has not been reformulated.

Dr. Carr inquired why oxycodone was selected as a comparator in clinical abuse potential studies. He stated that tapentadol and oxycodone are not equivalent. It is a different molecule and should not be considered as an equivalent product.

Dr. Thompson answered that he cannot be sure why oxycodone was chosen as a comparator, but theorized that it could have been selected as a comparator simply because it is a known drug of abuse. This study was on willingness to abuse and how much drug could be extracted only.

Mr. Sheehan, in response to Dr. Carr, asked if it may be possible that Nucynta ER could be a potential substitute for something in the future.

Dr. Jeffrey commented that the only suitable substitute at this time would seem to be Nucynta immediate-release, which is rarely utilized, and may not even be on the market anymore. He also suggested that the ER formulation of this drug may not be a suitable substitute since it is rarely utilized.

Dr. Brandoff stated that one of the reasons Nucynta is rarely used could be related to the fact that it is rarely covered by insurance. He also asked how Nucynta ER fits in, and posed the question of if there is less drug liking for Nucynta ER simply because tapentadol is weaker than other opioids. He also asked whether the serotonin piece makes this more complicated.

Dr. Doyle-Petrongolo inquired what the relevance of Nucynta ER was. She also commented that it is not necessarily a clear switch from tramadol.

Dr. Jeffrey commented that the drug liking study comparing Nucynta ER to oxycodone was not a clear comparison. He noted that Nucynta immediate-release to Nucynta ER may have been a better comparison. Dr. Jeffrey posed the question of whether or not the serotonin-related activity of Nucynta ER is more likely to solve or create problems. In addition, he noted that there are multiple less costly alternatives.

Dr. Carr stated that tramadol was not really sought after, similar to Nucynta. He wonders why Nucynta was scheduled so much higher than tramadol.

Dr. Jeffrey noted that tramadol use has increased in the last two years.

Dr. Brandoff questioned whether Nucynta ER was a potential substitute for tramadol, and that prescribing may be going in the direction of these light opioid.

Dr. Walker noted that Nucynta ER could be a great substitute if a tramadol ER comes out in the future. He also commented that the issue currently at hand is assessing whether or not Nucynta ER seems to be abuse-deterrent. He stated that it appears to have abuse-deterrent properties, and commented that he felt these properties were sufficient to proceed to Component 3.

The DFC members were asked to vote on whether or not the monograph for Nucynta ER met the needs of the commission on all of the following parameters as Mr. Dunn presented the highlights of each section of the monograph.

A consensus was reached that each section of the monograph met the needs of the commission

Mr. Sheehan opened the floor for further discussion of Nucynta ER.

Dr. Carr thanked staff for putting together the monographs.

Mr. Sheehan called for a motion to approve **Nucynta ER**.

- Motion to approve: Stephen Feldman
- Second: Daniel Carr
- All in favor: Motion carried unanimously

5. Closing Remarks; Adjournment

Mr. Sheehan thanked the Commission members for their participation today and the progress that was made and reminded Commission members that the next schedule meeting is February 18, 2016 and that the meeting is scheduled for 9:00 AM to 12:00 PM.

Mr. Sheehan also noted that in addition to the materials for their meeting today, Commission members were also sent a schedule of meetings through May, 2016. Mr. Sheehan highlighted the Commission that there is a change of location for the March 3rd meeting. This meeting will be held at the Health Professions Licensure Board Room at 239 Causeway Street, Room 417. This location is directly across from North Station.

Mr. Sheehan reminded the Commission that meetings cannot be held if there is no quorum and asked if there were a change to your schedule that would prevent you from attending to contact Lauren Nelson.

As was evidenced by the January 21st meeting cancellation, please remember that we cannot hold a meeting if we do not have quorum. If your schedule has changed for future meetings, please let Lauren know.

Mr. Sheehan reminded the members that the next meeting was being held during school vacation week, so the staff would like to hear as soon as possible if it looks like this meeting time will not work.

Please add any documents you received today to your binders and take them with you when you leave here. These binders will be helpful at home and in future meetings, so we encourage you to being them with you each time, as you will be provided with more materials to add.

Mr. Sheehan also addressed one final item about parking before the Commission adjourned.

At our first meeting, staff provided documents for you to fill out if you were seeking reimbursement for parking while attending a DFC meeting. On October 7, 2015, Suzanne Cray, on my behalf, reminded you of this process and re-sent the forms. Unfortunately, this action was taken in error, and we will be unable to reimburse members for parking or any other incidental cost you may incur while attending DFC meetings. This practice of similar boards and commissions is based on explicit statutory authority that does not exist for the DFC.

We truly apologize for any confusion or inconvenience this may cause.

Being no further business before the commission, Mr. Sheehan asked for a motion to adjourn.

- Motion: Dr. Paul Jeffrey
- Second: Dr. Joanne Doyle-Petrongolo
- All in favor: unanimous

The Drug Formulary Commission meeting concluded at 4:00 PM.

Documents Presented to DFC at the *February 4, 2016* Meeting

- DFC Minutes from January 7, 2016
- DFC PowerPoint presentation
- Monographs for Oxaydo, Opana ER and Nucynta ER plus associated studies.

Documents can be found at: http://www.mass.gov/eohhs/gov/departments/dph/programs/hcq/drug-control/drug-formulary-commission.html