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**Drug Formulary Commission**

Bureau of Health Care Safety and Quality

Department of Public Health

July 14, 2016

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**Presentation Agenda**

* Draft Formulary (105 CMR 720)
  + Schedule
  + Amendments
  + Comments
  + Guidance
* Interchangeable Abuse Deterrent Drug Products Evaluation
  + Pipeline
* CHIA Benefits Review
* Next Steps

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**Promulgation of Regulation and Formulary**

11/9/16 Public Health Council presentation of proposed redrafted regulation, 105 CMR 720, *List of Interchangeable Drug Products*

1/19/17 Next Drug Formulary Commission meeting (9:00AM)

Public hearing on proposed redrafted regulation (1:30PM)

1/24/17 Public comment period closes

Winter Review comments and amend regulation as appropriate.

Spring PHC presentation for promulgation of final regulation, 105 CMR 720, Drug Formulary Commission

Spring Regulation becomes effective upon review by Secretary of State.

Spring Issue guidance

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**Timeline**

8/6/14 Chapter 258 of the Acts of 2014 enacted reconstituted DFC

7/27/15 DFC members re-appointed by the Governor

8/6/15 First meeting of the reconstituted DFC

10/1/15 Informational Hearing

10/15/15 Component 1 completed: All Schedule II and III opioids placed on HPHR list

3/3/16 Component 2 completed: Five IAD drug products approved

6/2/16 Component 3 completed: Two IAD drug products found to be chemically equivalent substitutions for six HPHR opioids

9/15/16 Xtempza approved as additional IAD drug product

11/9/16 Draft Formulary and Regulation presented to PHC

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**Stages: Evaluation and Review Process Overview**

* Drug Formulary Commission Statutory Mission
* Schedule II and III Opioids
* Component 1: Opioids with a Heightened Public Health Risk
* Component 2: Interchangeable Abuse Deterrent Drug Products
* Component 3: “Cross Walk” Chemically Equivalent Substitutions
* Draft Formulary

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**Component 1: Generic Opioids with a Heightened Public Health Risk**

HPHR Opioids – Generic

Table listing Schedule 2 and 3 opioid products

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**Opioids with a Heightened Public Health Risk**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Product Name** | **Manufacturer** | **Ingredient(s)** | **Dose Form** | **Method of Abuse Deterrence** | **Date DFC Approved as Potential Substitute** |
| OxyContin® | Purdue | Oxycodone ER | Tablet | Crush-resistant Formulation | January 7, 2016 |
| Hysingla ER® | Purdue | Hydrocodone ER | Tablet | Crush-resistant Formulation | December 17, 2015 |
| Embeda® | Pfizer | Morphine ER and Naltrexone | Capsule | Antagonist | January 7, 2016 |
| Oxaydo® | Egalet | Oxycodone IR | Tablet | Aversion technology with assumed ADF properties | February 4, 2016 |
| Nucynta ER® | Jansen | Tapentadol | Tablet | Crush-resistant formulation | February 4, 2016 |
| Xtampza ER® | Collegium | Oxycodone ER | Capsule | DETERx®  Physical/chemical barrier | September 15, 2016 |

ER or Extended Release is a mechanism to prolong absorption of a drug to allow longer dosing intervals and minimize fluctuations in serum drug levels.

IR or Immediate Release indicates the release of the active ingredient within a small period of time, typically less than 30 minutes.

\*\*All decisions of the Drug Formulary Commission may be reconsidered upon receipt of new, relevant evidence.\*\*

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**Component 3: Chemically Equivalent Substitution**

In considering whether an IAD drug product is a chemically equivalent substitution**,** the Commission considered four statutorily mandated factors:

* + accessibility
  + cost prohibition
  + effectiveness for pain
  + effectiveness of abuse deterrent property

**“Chemically Equivalent Substitution”**, for the purpose of creating a formulary of drugs with abuse deterrent properties that the commission has determined may be appropriately substituted for opioids that have been determined to have a heightened public health risk due to the drugs’ potential for abuse and misuse, shall mean drug products which contain the same active ingredients, and are equivalent in strength or concentration, dosage form, and route of administration, and produce a comparable biologic effect. Prodrugs or ingredients without analgesic effect that are used solely for abuse deterrent formulations need not be equivalent.

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**Component 3: Cross Walk**

* The Commission reviewed the IAD drug products to determine if any of them were chemically equivalent substitutes for HPHR opioids.
* The following potential substitutions were proposed for evaluation ‡:

|  |  |
| --- | --- |
| **HPHR Opioid** | **IAD Drug Product** |
| Kadian® (morphine ER capsules) | Embeda® (morphine sulfate ER/naltrexone capsule) |
| Morphine ER 12 or 24 hour capsules (generic Kadian®) |
| Morphine ER 24 hour capsules (generic Avinza®) |
| Morphine ER tablet (generic MS Contin®) |
| MS Contin® (morphine ER tablet) |
| Zohydro ER® (hydrocodone ER capsule) | Hysingla ER® (hydrocodone ER tablet) |
| Oxycodone IR capsules | Oxaydo® (oxycodone IR tablet)  (rejected as a chemically equivalent substitution) |
| Roxicodone® tablets |
| Oxycodone IR, tablets (generic Roxicodone) |

‡ There are no U.S. marketed HPHR opioids available for substitution by these IAD drug products. Note that one chemical (e.g. morphine) or dosing mechanism (ER/IR) may not be substituted for another (e.g. hydrocodone):

* Nucynta ER® (tapentadol ER tablet)
* OxyContin® (oxycodone ER tablet)
* Oxycodone ER tablet
* Xtampza ER capsule (Oxycodone ER)

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**Formulary – Substitutions**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **HPHR Opioid** | **Interchangeable Abuse Deterrent Drug Product** | **Commercially Available Strengths** | **Dosing Frequency** | **ADP Efficacy Category** |
| Kadian® (morphine ER capsules) | Embeda® (morphine sulfate extended-release/naltrexone capsule) | 20 mg/0.8 mg | Q24H or Q12H | Category II |
| Morphine ER 12 or 24 hour capsules (generic Kadian®) | 30 mg/1.2 mg |
| Morphine ER 24 hour capsules (generic Avinza®) | 50 mg/2 mg |
| Morphine ER tablet (generic MS Contin®)† | 60 mg/2.4 mg |
| MS Contin® (morphine ER tablet)† | 80 mg/3.2 mg |
| Zohydro ER® (hydrocodone ER capsule)† | Hysingla ER® (hydrocodone extended-release tablet) | 20 mg | Q24H | Category II |
| 30 mg |
| 40 mg |
| 60 mg |
| 80 mg |
| 100 mg |
| 120 mg |

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**Formulary – No Substitutions**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No equivalent HPHR opioid identified | Nucynta ER® (tapentadol extended-release tablet) | 50 mg | Q12H | Category II |
| 100 mg |
| 150 mg |
| 200 mg |
| 250 mg |
| No equivalent HPHR opioid identified | Oxaydo® (oxycodone immediate-release tablet) | 5 mg | Q4-6H | Category III |
| 7.5 mg |
| No equivalent HPHR opioid identified | Oxycodone extended-release tablet‡ | 10 mg | Q12H or Q8H | Category II |
| 15 mg |
| 20 mg |
| 30 mg |
| 40 mg |
| 60 mg |
| 80 mg |
| No equivalent HPHR opioid identified | OxyContin® (oxycodone extended-release tablet) | 10 mg | Q12H or Q8H | Category II |
| 15 mg |
| 20 mg |
| 30 mg |
| 40 mg |
| 60 mg |
| 80 mg |
| No equivalent HPHR opioid identified | Xtampza ER® (oxycodone ER capsule) | 9 mg | Every 12 hours with food | Category II |
| 13.5 mg |
| 18 mg |
| 27 mg |
| 36 mg |

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**Thank You**

The Department would like to acknowledge all the members of the Drug Formulary Commission for their dedication and hard work in developing the nation’s first Formulary of Chemically Equivalent Substitutions and their substantial contribution to the fight against opioid abuse and misuse in the commonwealth.

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**Background**

* + The amendments to this regulation, 105 CMR 720.000,  *List of Interchangeable Drug Products,* are proposed as part of the regulatory review process, mandated by Executive Order 562, which requires all state agencies to undertake a review of each regulation under its jurisdiction currently published in the Code of Massachusetts Regulations.
  + Significant changes also reflect the changes to the mission of the Drug Formulary Commission, as set forth in M.G.L. c. 17 §13.

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**Proposed Amendment**

**The proposed amendments will achieve the following:**

* Changing the title of the regulation from “List of Interchangeable Drug Products” to “Drug Formulary Commission”.
* Update the references to interchangeable drug products;
* Remove the outdated list of generic drugs; and
* Include the drug formulary of chemically equivalent substitutions for opioids with a heightened public health risk.

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**Proposed Amendment Highlights: Formulary of Interchangeable Drug Products**Meeting Recap

**Current Regulation:**

* Contains outdated means of determining which generic drugs can be substituted for brand name drugs.

**Proposed Amendment:**

* Deletes unnecessary sections related to the process of placing a drug on the Formulary of Interchangeable Drug Products to reflect the current practice whereby Massachusetts defers to the FDA’s list of approved generic drugs, as identified in the publication “Approved Drug Products with Therapeutic Equivalence Evaluations” (known as “the Orange Book”).
* Deletes Appendix A of the regulation which contains the list of interchangeable drugs and references to the FDA’s process for approving interchangeable drugs.

**Rationale:**

* Makes the regulation consistent with federal law.
* Reflects the current practice whereby pharmacists consult with the First DataBank, which is updated based on regular FDA notices.

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**Proposed Amendment Highlights: Statutory Changes to Drug Formulary Commission**

* Chapter 258 of the Acts of 2014 changed the mandate of the Drug Formulary Commission to expand its responsibilities and tasked it with preparing a drug formulary of substitutions for Schedule II or III opioids that have a heightened level of public health risk due to the drugs’ potential for abuse and misuse.
* Once the formulary is adopted by regulation:
  + Prescribers may choose to prescribe the abuse-deterrent opioids in place of other opioids;
  + Pursuant to statute, where an opioid with a heightened level of public health risk has been prescribed without a notation of “dispense as written”, pharmacists must dispense an interchangeable abuse-deterrent product if one exists;
  + DPH will issue guidance and engage in outreach and education to convey these changes.

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**Proposed Amendment Highlights: Statutory Changes to Drug Formulary Commission**

To reflect the statutory changes to the Drug Formulary Commission, the proposed regulations make the following changes:

* Adds definitions for terms necessary to implement a formulary of abuse-deterrent drug products that can be substituted for opioids with a heightened public health risk;
* Describes the information the Drug Formulary Commission considers in determining which drugs to place on the new formulary, including analysis by leading experts and interagency collaboration;
* Includes the new formulary of chemically equivalent substitutions for opioids with a heightened public risk; and
* Specifies the procedures for amending the new formulary as new abuse-deterrent opioids are approved by the FDA.

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**Next Steps**

* The Department will conduct a public hearing to solicit comments on the proposed amendment.
* Following the public comment period, the Department will return to the Public Health Council to report on testimony and any recommended changes to this amendment, and seek final promulgation.

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**Potential IAD Drug Products – Updates**

* MorphaBond® (morphine extended-release)
  + FDA approved; however, not commercially available
  + Monograph to be completed when commercially available
  + Manufacturer reached licensing agreement with Daiichi Sankyo, Inc. to commercialize MorphaBond
  + Awaiting response from Daiichi Sankyo on availability of Formulary Dossier and planned launch date.
* Troxyca ER® (oxycodone extended-release/naltrexone)
  + FDA approved; however, launch planned for 1st Quarter 2017
  + Formulary Dossier was requested by DFC staff on 12/5/16
  + Monograph to be completed when commercially available
* Remoxy® (oxycodone ER)
  + FDA issued Complete Response Letter on 9/26/16
  + Manufacturer has plans for further discussion with FDA on addressing additional actions specified in Complete Response Letter.

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**Medication with ADF Claims or FDA Approved ADF Labeling**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **List of Medications with Abuse-Deterrent Claims or FDA-Approved Labeling** | | | | | |
| **Product Name** | **Manufacturer** | **Ingredient(s)** | **Dose Form** | **Method of Abuse Deterrence** | **DFC Action** |
| MorphaBond® | Inspirion Delivery Technologies | Morphine ER | Tablet | Physical/chemical barrier | Not yet commercially available. Manufacturer has partnered with Daiichi Sankyo for commercialization. |
| Troxyca ER® | Pfizer | Oxycodone ER/  Naltrexone | Capsule | Agonist/antagonist | Not yet commercially available.  Launch planned for 1st Quarter 2017 |
| Remoxy® | Pain Therapeutics | Oxycodone ER | Capsule | Physical/chemical barrier | FDA Complete Response Letter indicates product is not approvable in its current form. |

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**Potential IAD Drug Products – In Development**

* Arymo ER® (morphine ER)
  + PDUFA date 10/14/16 (past date)
  + FDA advisory committee voted with recommendation to approve
  + FDA has communicated with manufacturer to inform them more time is needed for evaluation
* Vantrela ER® (hydrocodone ER)
  + PDUFA date 11/11/15 (past date)
  + FDA advisory committee voted with recommendation to approve
  + No update on FDA activity as of 12/5/16
* Oxaydo® (oxycodone IR)
  + DFC previously voted down as substitute for oxycodone IR due to inadequate data regarding ADP and prohibitive cost
  + Manufacturer submitted sNDA to FDA seeking ADF labeling on 12/1/16, reportedly with *in vitro* data that manufacturer suggests shows deterrence of IV abuse
  + May need to discuss re-evaluation if new data is available

\*PDUFA – Prescription Drug User Fee Act (anticipated date of FDA decision)

sNDA – Supplemental New Drug Application

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**Meeting Schedule**

* January 19, 2017
* *February 16, 2017*
* March 16, 2017
* *April 20, 2017*

All meetings are from 9:00AM to 12:00PM

at 250 Washington Street

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**Meeting Summary**

* Meeting Recap
* Review of takeaways
* Next steps
* Next Meeting
  + January 19, 2016
  + Public Hearing to follow