Slide 1.

**Drug Formulary Commission**

Bureau of Health Care Safety and Quality

Department of Public Health

September 15, 2016

Slide 2.

**Presentation Agenda**

Review of July 14th meeting

Non-Opioid Pain Management List

Draft Formulary and Guidance

Interchangeable Abuse Deterrent Drug Products Evaluation

Xtampza ER®

Chemically Equivalent Substitutions

Xtampza ER®

Next Steps

Slide 3.

**Promulgation of Regulation and Formulary**

Present to the Drug Formulary Commission.

Propose the draft to Public Health Council as part of the proposal of a redrafted regulation, 105 CMR 720, List of Interchangeable Drug Products.

Present the draft regulation, including the draft Formulary of Chemically Equivalent Substitutions, for public hearing and comment.

Review comments and amend regulation as appropriate.

Present final draft regulation and draft formulary to PHC again for promulgation.

Review by Secretary of State.

Regulation becomes effective.

Issue guidance, including:

special substitution considerations as decided by the commission, and

the requirements and process of substitution.

Slide 4.

**Formulary Review and Evaluation**

Component 1: Opioids with a Heightened Public Health Risk

Component 2: Interchangeable Abuse Deterrent Opioids

Component 3: “Cross Walk” – Chemically Equivalent Substitutions

Draft Amended Formulary

Slide 5.

**Potential IAD Drug Product Evaluation
Xtampza ER**

Oxycodone extended-release

ADF Property

Physical/chemical barrier

Clinical abuse potential studies of the intranasal and oral routes

In vitro data indicates resistance to injection

FDA Approval April 2016 (final)

FDA ADF labeling approved April 2016 (final)

Available Strengths

9 mg, 13.5 mg, 18 mg, 27 mg, 36 mg

Equivalent to 10 mg, 15 mg, 20 mg, 30 mg, 40 mg oxycodone HCl, respectively

Slide 6.

**Potential IAD Drug Product Evaluation Xtampza ER®**

Xtampza ER® is formulated using DETERx® technology.2

DETERx® combines free active ingredient (oxycodone base) with myristic acid to produce a lipophilic compound. The compound is then suspended in wax microspheres and placed in capsules.2

In vitro data indicates the wax microspheres are resistant to particle size reduction and extraction via use of multiple solvents.2

In vitro data also indicates injection of the wax microspheres is relatively impossible using needles smaller than 18 gauge.2

An oral clinical abuse potential study indicates both intact and chewed/crushed Xtampza ER® is associated with less drug liking than crushed oxycodone immediate-release.2

An intranasal clinical abuse potential study indicates both intact oral and crushed intranasal Xtampza ER® is associated with less drug liking than crushed intranasal oxycodone immediate-release.2

Pharmacokinetic study data indicates that crushed Xtampza ER® microspheres are bioequivalent to intact Xtampza ER® capsules administered orally.2

Pharmacokinetic study data indicates that the peak plasma concentration (Cmax) is decreased when Xtampza ER® is crushed and insufflated compared to taken intact orally.2

Slide 7.

**Potential IAD Drug Product Evaluation Xtampza ER®Key Findings**

Initial dose (opioid naïve adults): 9 mg every 12 hours with food.1

Initial dose (converting from other opioids): 9 mg every 12 hours with food.1

Initial dose (converting from fentanyl patch): 9 mg every 12 hours with food for each 25 mcg/hr of fentanyl transdermal patch.1

Time to peak plasma concentration (Tmax) of intact Xtampza ER® capsules is approximately 4.5 hours.1

Tmax for crushed or chewed Xtampza ER® capsules approximately 4.0 to 4.5 hours.1

Xtampza ER® does not appear to dose dump in alcohol or other commonly ingestible solvents.1

Bioavailability of Xtampza ER® is dependent upon the food consumed and the fat and calorie content of the food consumed. High fat and high calorie meals increase the peak plasma concentration (Cmax) by 100 to 150% and extent of absorption (AUC) by 50 to 60% compared to fasted administration.1

Slide 8.

**Potential IAD Drug Product Evaluation Xtampza ER®**

Xtampza ER® is subject to the requirements of the Extended-Release and Long-Acting (ER/LA) Risk Evaluation and Mitigation Strategies (REMS) program.2

The FDA Advisory Committee voted unanimously to approve Xtampza ER® in September of 2015.\*

Final report submissions of formal observational studies intended to determine if the abuse-deterrent properties of Xtampza ER® reduce abuse in the community are due to the FDA in June of 2021.9

\* <http://www.innovativescience.net/fda-adcomm-blog/fda-advisory-committees-unanimously-recommend-approval-of-xtampza-er>

Slide 9

**Potential IAD Drug Product Evaluation Xtampza ER®**

Chemical name oxycodone extended-release

Dosage form Extended-release capsule

Formulation DETERx®

ADP\* Resistant to particle size reduction

 Resistant to dose dumping in solvents

 Resistant to passage through needle sizes under 18G

ADF studies Oral and intranasal studies performed

Slide 10

**Potential IAD Drug Products – Updates**

MorphaBond® (morphine extended-release)

FDA approved; however, not commercially available

Monograph to be completed when commercially available

Troxyca ER® (oxycodone extended-release/naltrexone)

FDA approved; however, launch planned for 1st Quarter 2017

Formulary Dossier to be available for review late 2016

Monograph to be completed when commercially available

Apadaz®(benzhydrocodone/acetaminophen)

FDA issued Complete Response Letter, indicating product is not approvable in its current form

SequestOx® (oxycodone IR/naltrexone)

FDA issued Complete Response Letter, indicating product is not approvable in its current form

Slide 11

**Potential IAD Drug Products – In Development**

Remoxy® (oxycodone ER)

PDUFA date 9/25/16

Arymo ER® (morphine ER)

PDUFA date 10/14/16

FDA advisory committee voted with recommendation to approve

Vantrela ER® (hydrocodone ER)

PDUFA date 11/11/15 (past date)

FDA advisory committee voted with recommendation to approve

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

Slide 12

**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** |
| Xtampza ER® | Collegium  | Oxycodone ER | Capsule | DETERx®Physical/chemical barrier | PENDING |
| MorphaBond® | Inspirion Delivery Technologies | Morphine ER | Tablet | Physical/chemical barrier | Not yet commercially available. |
| Troxyca ER®  | Pfizer | Oxycodone ER/Naltrexone | Capsule | Agonist/antagonist | Not yet commercially available.Launch planned for 1st Quarter 2017 |
| Apadaz® | KemPharm | Benzhydrocodone/Acetaminophen | Tablet | Prodrug | FDA Complete Response Letter indicates product is not approvable in its current form. |
| SequestOx® | Elite Pharmaceuticals | Oxycodone IR/ Naltrexone | Tablet | Agonist/antagonist | FDA Complete Response Letter indicates product is not approvable in its current form. |
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Slide 13
**“Cross Walk”**

Component 1: Opioids with a Heightened Public Health Risk

Component 2: Interchangeable Abuse Deterrent Opioids

Component 3: “Cross Walk” – Chemically Equivalent Substitutions

Draft Amended Formulary

Slide 14

**Meeting Schedule**

~~October 21, 2016~~

November 18, 2016

December 16, 2016

January 20, 2017

February 17, 2017

March 17, 2017

April 20, 2017

All meetings are from 9:00AM to 12:00PM at 250 Washington Street

Slide 15

**Meeting Summary**

Meeting Recap

Review of takeaways

Next steps

Next Meeting

November 18, 2016

9:00AM-12:00PM

250 Washington Street