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**Drug Formulary Commission**

Bureau of Health Care Safety and Quality

Department of Public Health

March 20, 2017

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**Presentation Agenda**

* Interchangeable Abuse Deterrent Drug Products Evaluation
  + Troxeca ER®
* Chemically Equivalent Substitutions
  + Troxeca ER®
* Draft Formulary
  + 105 CMR 720
  + Prescriber Education
* CHIA Benefits Review
* Next Steps

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**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

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

* Oxycodone extended-release/naltrexone
* ADF Property
  + Agonist/antagonist
  + Clinical abuse potential studies of the intravenous (IV), intranasal and oral routes
* FDA Approval August 2016
* FDA ADF labeling approved August 2016
* Available Strengths
  + 10/1.2 mg, 20/2.4 mg, 30/3.6 mg, 40/4.8 mg, 60/7.2 mg, 80/9.6 mg

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

* Troxyca ER® is formulated as a capsule filled with extended-release beads of oxycodone with a sequestered naltrexone core.1
* Manipulation of these pellets could lead to a rapid release and absorption of a potentially fatal dose of oxycodone, as well as a sufficient quantity of naltrexone to precipitate withdrawal in opioid-dependent individuals.1
* An oral clinical abuse potential study indicates both intact and crushed Troxyca ER® is associated with less drug liking and drug high than crushed oxycodone immediate-release; however, the difference in willingness to take drug again scores were only statistically significant for the 40/4.8 mg dose (not statistically significant for 60/7.2 mg dose).6
* An intranasal clinical abuse potential study indicates crushed Troxyca ER® is associated with less drug liking and drug high than crushed oxycodone immediate-release.7
* An intravenous (IV) clinical abuse potential study indicates simulated crushed Troxyca ER® for injection is associated with less drug liking and drug high than oxycodone solution for injection. It is unknown whether these results using simulated crushed Troxyca ER® predict a reduction in abuse by the IV route until postmarketing data are available.1,2,8

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

* Initial dose (opioid naïve adults): 10/1.2 mg every 12 hours.1
* Initial dose (converting from other opioids):Manufacturer provides a table to guide conversion from other opioids (Table 7 in monograph)
* Initial dose (converting from fentanyl patch): 10/1.2 mg every 12 hours for each 25 mcg/hr of fentanyl transdermal patch.1
* Mean time to peak plasma concentration (Tmax) of intact Troxyca ER® capsules taken orally is approximately 12 hours (median Tmax 12.1 hours).1,6
* Median Tmax for crushed Troxyca ER® capsules taken orally approximately 0.6 hour; however, maximum drug liking scores were significantly lower for crushed Troxyca ER® capsules than equivalent doses of crushed oxycodone IR.1,6
* Administration of Troxyca ER® with 20% alcohol did not affect peak plasma concentration (Cmax) or exposure (AUC)1
* Administration of Troxyca ER® 20/2.4 mg with 40% alcohol increased Cmax by an average of 37% and AUC by 13% compared to administration with water.1

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

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

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Oral ADF** | **Intranasal ADF** | **Intravenous ADF** |
| FDA Advisory Committee\* | 9-6 vote against | 11-4 vote in favor | 9-6 vote in favor |
| FDA Labeling† | Yes | Yes | No |

* Final report submissions of formal observational studies, intended to determine if the abuse-deterrent properties of Troxyca ER® reduce abuse in the community, are due to the FDA in October of 2021.13

\*http://seekingalpha.com/news/3187924-ad-comm-backs-pfizers-long-acting-opioid-troxyca-9minus-6-vote

†http://www.pfizer.com/news/press-release/press-release-detail/fda\_approves\_troxyca\_er\_oxycodone\_hydrochloride\_and\_naltrexone\_hydrochloride\_extended\_release\_capsules\_cii\_with\_abuse\_deterrent\_properties\_for\_the\_management\_of\_pain

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**Troxyca ER® Summary**

* **Chemical name oxycodone extended- release/naltrexone**
* **Dosage form Extended-release capsule**
* **Formulation oxycodone extended-release beads with sequestered naltrexone core**
* **ADP\* Agonist/antagonist**
* **ADF studies Oral, intranasal and intravenous studies performed**
* **ADF labeling Oral and intranasal routes**

\*ADP = Abuse-deterrent properties

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**Potential IAD Drug Products – Updates**

* MorphaBond® (morphine extended-release)
  + FDA approved; however, not commercially available
  + Manufacturer has licensing agreement with Daiichi Sankyo to market
  + Monograph to be completed when commercially available
* Arymo ER® (morphine extended-release)
  + FDA approved, launch reportedly planned for 1st Quarter 2017
  + Formulary Dossier not yet available
  + Monograph to be completed when commercially available
* Vantrela ER®(hydrocodone extended-release)
  + FDA approved, launch reportedly planned for 1st Quarter 2017
  + Formulary Dossier not yet available
  + Monograph to be completed when commercially available
* Opana ER® (oxymorphone extended-release)
  + FDA advisory committee voted on 3/15/17 that potential benefits no longer outweigh risks associated with the product.
  + FDA must determine whether to take regulatory action.

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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** |
| Troxyca ER® | Pfizer | Oxycodone ER/  Naltrexone | Capsule | Agonist/antagonist | PENDING |
| MorphaBond® | Inspirion Delivery Technologies/ Daiichi Sankyo | Morphine ER | Tablet | Physical/chemical barrier | Not yet commercially available. |
| Arymo ER® | Egalet | Morphine ER | Tablet | Physical/chemical barrier | Not yet commercially available.  Launch planned for 1st Quarter 2017 |
| Vantrela ER® | Teva | Hydrocodone ER | Tablet | Physical/chemical barrier | Not yet commercially available.  Launch planned for 1st Quarter 2017 |
| Remoxy® | Pain Therapeutics/ DURECT | Oxycodone ER | Capsule | Physical/chemical barrier | FDA Complete Response Letter indicates product is not approvable in its current form. |

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**“Cross Walk”**

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**Promulgation of Regulation and Formulary**

History

* Proposed 105 CMR 720, *List of Interchangeable Drug Products,* including draft formulary, as redrafted, to the Public Health Council (11/9/2016)
* Public hearing held on proposed changes to regulation (1/19/2017)

Current

* DPH staff is reviewing comments and further amending as appropriate.

Pending

* DPH staff will present the final draft regulation to PHC for promulgation.
* Review by Secretary of State 🡪 Regulation becomes effective.

Next Step

* Issue guidance, including special substitution considerations, and the requirements and process of substitution.
* Conduct prescriber education on abuse deterrent substitutes.

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**Meeting Summary**

* + Meeting Recap
  + Review of takeaways
  + Next steps
  + Upcoming Meetings
    - April 20, 2017
    - May 18, 2017
    - June 20, 2017
      * 9:00AM-12:00PM
      * 250 Washington Street