Slide 1

**Drug Formulary Commission**

Bureau of Health Care Safety and Quality

Department of Public Health

February 4, 2016

Slide 2  
**Opening Remarks**

* Drug Formulary Commission Statutory Mission
* Schedule II and III Opioid Universe
* Component 1: Drugs of Heightened Public Health Risk
* Component 2: Drug Formulary Therapeutic Substitutes With Abuse Deterrent Properties
* Component 3: “Cross Walk”
* Draft Amended Formulary

Slide 3  
**Presentation Agenda**

## Review of January 7thmeeting

### Voted to request a cost assessment from the Center for Health Information and Analysis (CHIA)

### Voted to approve Oxycontin CR

### Voted to approve Embeda

## Continued evaluation and discussion of the drug products with manufacturer claims of ADF technology as potential therapeutic equivalent substitutes

### Oxaydo

### Opana ER

### Nucynta ER

# Slide 4

**Monograph Review  
Schedule II Opioids**

Slide 5  
**Therapeutically Equivalent Substitutes FDA Approved ADF Labeling**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **List of Medications with Abuse-Deterrent Claims in FDA-Approved Labeling** | | | | | |
| **Product Name** | **Manufacturer** | **Ingredient(s)** | **Dose Form** | **Method of Abuse Deterrence** | **DFC Action** |
| Targiniq ER | Purdue | Oxycodone ER and Naloxone | Tablet | Antagonist | Voted NOT to approve for Crosswalk consideration at  December 17, 2015 meeting |
| OxyContin | Purdue | Oxycodone ER | Tablet | Crush-resistant Formulation | Voted to approve for Crosswalk consideration at  January 7, 2016 meeting |
| Hysingla ER | Purdue | Hydrocodone ER | Tablet | Crush-resistant Formulation | Voted to approve for Crosswalk consideration at  December 17, 2015 meeting |
| Embeda | Pfizer | Morphine ER and Naltrexone | Capsule | Antagonist | Voted to approve for Crosswalk consideration at  January 7, 2016 meeting |

Slide 6  
**Therapeutically Equivalent Substitutes Abuse-Deterrent Claims no FDA-Approved Labeling**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **List of Medications with Abuse-Deterrent Claims in FDA-Approved Labeling** | | | | | |
| **Product Name** | **Manufacturer** | **Ingredient(s)** | **Dose Form** | **Method of Abuse Deterrence** | **DFC Action** |
| Opana ER | Endo | Oxymorphone | Tablet | Crush-resistant formulation | For review at  February 4, 2016  Meeting |
| Oxaydo | Egalet | Oxycodone ER | Tablet | Aversion technology with assumed ADF properties | For review at  February 4, 2016  Meeting |
| Nucynta ER | Jansen | Tapentadol | Tablet | Crush-resistant formulation | For review at  February 4, 2016  Meeting |
| Zohydro ER | Pernix Therapeutics | Hydrocodone ER | Capsule | BeadTek Technology | To be considered at  February 18, 2016  Meeting |
| Zubsolv | Orexo | Buprenorphine and Naloxone | Sublingual Tablet | Antagonist | To be considered at  February 18, 2016  Meeting |

Slide 7  
**Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Oxaydo®**

## **Oxaydo® IR Monograph Review**

## Chemical name oxycodone HCL

## FDA approval June 2011

## Available Strength 5mg & 7.5mg

## ADF Product Classification Aversion

## FDA ADF Labeling No

# Slide 8 **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Oxaydo®**

## Oxaydo® is and immediate-release oxycodone tablet formulated using AVERSION® technology, which includes an inactive ingredient designed to cause irritation to nasal passages upon insufflation.3

## AVERISON® technology is also reported by the manufacturer to cause a viscous, gelatinous mixture that prevents injection upon attempts to dissolve crushed tablet; however, the manufacturer has not made *in vitro* manipulation study data readily available.

## The results of a clinical abuse potential study in nondependent recreational opioid users (n=40) demonstrated significantly lower “Drug Liking” and “Take Drug Again” scores for Oxaydo® compared to Roxicodone® via insufflation.4

Slide 9  
**Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Oxaydo®**

****

# Slide 10

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Oxaydo®**

## Oxaydo ® ADF Claims

## Oxaydo® is not currently subject to a Risk Evaluation and Mitigation Strategies (REMS) program.6

## There is currently no data available regarding clinical abuse potential of Oxaydo® via IV injection.

## The FDA will require an epidemiological study to address whether or not Oxaydo® results in a decrease in misuse and abuse in the community.5

# Slide 11 **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Oxaydo®**

## Oxaydo® was approved for the US Market in September 2015.

## The first epidemiological post-marketing study data to assess abuse in the community is not due to the FDA until June 2016.5

## The timetable for submission of post-marketing data to the FDA may no longer be valid due to sale of Oxaydo® to a different manufacturer. June 2016 was agreed upon with the original manufacturer of Oxecta® (original name for Oxaydo®), not Egalet.5

# Slide 12

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Oxaydo®**

## Initial Dose (opioid naïve): 5 to 15 mg every 4 to 6 hours as needed for pain.1

## Initial Dose (converting from other opioids): The manufacturer does not provide specific conversion factors for patients converting from other opioids.1

## Time to peak plasma concentration (Tmax) for intact Oxaydo®1:

### Fasted Tmax: 1.2 to 1.4 hours

### Fed Tmax: 1.25 to 3.00 hours

### Food effects on Tmax are not considered clinically relevant.1,2

## The Tmax of crushed or otherwise tampered with Oxaydo® tablets has not been published

# Slide 13

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Oxaydo®**

## Oxaydo® Summary

## Chemical name oxycodone HCL

## Dosage form immediate release tablet

## ADF classification Aversion® technology

## ADF claims snorting & injection

## ADF studies expected June 2016

## Studies significantly lower “Drug liking” & “Take drug again”

# Slide 14

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Opana ER®**

## **OPANA ER Monograph Review**

## Chemical name oxymorphone ER

## FDA approval June, 2006 re-introduction

## December, 2011 new Formulation

## Available strengths 5mg, 7.5mg, 10mg, 20mg, 30mg,40mg

## ADF product classification physicochemical barrier

## FDA ADF labeling No

## 

# Slide 15

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Opana ER®**

## Reformulated in 2012 with INTAC® technology in order to impart crush-resistant properties.10

## Opana ER® with INTAC® is more difficult to crush than the original Opana ER® formulation.10

## Despite increased resistance to crushing, the FDA determined10:

### Extended-release properties of Opana ER® with INTAC® can be bypassed when manipulated by cutting, grinding and chewing for oral misuse and abuse.

### Opana ER® with INTAC® is readily prepared for injection, despite the manufacturer’s claims of “poor syringeability.”

### Opana ER® with INTAC® can also be prepared for insufflation using commonly available tools and methods.

### Opana ER® with INTAC® postmarketing investigations are inconclusive, and one investigation suggests that a higher percentage of Opana ER® with INTAC® abuse is via injection than with the original Opana ER®.

# Slide 16

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Opana ER®**

## The CDC found needle sharing and IV abuse of Opana ER® with INTAC® to be responsible for an HIV outbreak in Indiana from 2014 to 2015.11

## The FDA stated that the abuse potential and warning section of Opana ER® with INTAC® is “virtually identical” to the previous version; therefore, ADF labeling was not granted by the FDA.12

# Slide 17

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Opana ER®**

## Initial dose (opioid naïve adults): 5 mg every 12 hours.1

## Initial dose (converting from other opioids): The manufacturer provides a table of conversion factors to calculate initial doses for patients converting from other opioids (Table 5 in monograph).1

## Time to peak plasma concentration (Tmax) of intact Opana ER® tablets1:

### Fasted Tmax: 1 hour

### Fed Tmax: 2 hours

### Fasted peak plasma concentration (Cmax): 2.8 ng/mL

### Fed Cmax: 4.25 ng/mL

### Food effects: Manufacturer recommends dosing at least 1 hour prior to a meal or 2 hours after a meal.

## Tmax for crushed or otherwise tampered with Opana ER® tablets has not been published.

# Slide 18

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Opana ER®**

## Opana ER® is subject to the requirements of the Extended-Release and Long-Acting (ER/LA) Risk Evaluation and Mitigation Strategies (REMS) program.13

## Information regarding the FDA advisory committee voting on Opana ER® is not readily available

## Information regarding FDA requirements of the manufacturer related to post-marketing epidemiological studies is not available. This is likely due to the lack of ADF labeling.

# Slide 19

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Opana ER®**

## **Opana ER® Summary**

## Chemical name oxymorphone ER

## Dosage form extended release tablet

## ADF classification Intact®

## ADF claim poor syringability

## ADF studies Info not available

## Studies inconclusive.

## higher percentage of iv abuse with Intact FDA denied ADF labeling

Slide 20  
**Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Nucynta®**

## **Nucynta® Monograph Review**

## Chemical name tapentadol ER

## FDA approvals November 2008

## August 2011

## Available strengths 50mg, 100mg, 150mg, 200mg, 250mg,

## ADF product classification physicochemical barrier, crush resistant

## FDA approved ADF labeling No

# Slide 21

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Nucynta®**

## *In vitro* laboratory manipulation extraction study data indicates13:

### Attempts to crush or break Nucynta ER® tablets using a variety of tools results in minimal deformation, with the exception of use of a hammer.

### Nucynta ER® tablets can be flattened using a hammer.

### Flattened Nucynta ER® tablets may be susceptible to releasing over 50% of the tapentadol in the tablet when placed in solution and vigorously shaken over extended periods of time.

### Flattened Nucynta ER® tablets release tapentadol faster than intact tablets, with 30% released over 30 minutes.

# Slide 22

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Nucynta®**

## Clinical abuse potential study data indicates14:

### Recreational opioid users were significantly less willing to insufflate particles made from Nucynta ER® tablets compared to a non-ADF oxycodone ER tablet

#### Nucynta ER® 50 mg 24% willing, Nucynta ER® 250 mg 16% willing compared to non-ADF oxycodone ER 40 mg 100% willing; P<0.001

### Recreational opioid users were able to extract significantly less drug from Nucynta ER® tablets compared to non-ADF oxycodone ER tablets.

#### Nucynta ER® 50 mg 🡪 3.5% extracted compared to non-ADF oxycodone ER 40 mg 🡪 37% extracted; P=0.008

# Slide 23

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Nucynta®**

## A postmarketing survey study indicated that abuse of Nucynta ER® was reported significantly less frequently than all other long-acting comparator opioids with the exception of hydromorphone extended-release.15

### Of note, the study surveyed the period of time from January 2011 to September 2012. Nucynta ER® became available in the US in August 2011.15

# Slide 24

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Nucynta®**

## Nucynta ER® (tapentadol extended-release) is subject to requirements of the shared system Extended-Release and Long-Acting (ER/LA) Risk Evaluation and Mitigation Strategies (REMS) program.16

## Initial Dose (opioid naïve): 50 mg every 12 hours.1

## Initial Dose (converting from other opioids): The manufacturer does not provide specific conversion factors or initial dosing for patient converting to Nucynta ER® from other opioids.

## Information related to FDA advisory committee voting for approval of Nucynta ER® is not readily available.

# Slide 25

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Nucynta®**

## Information regarding FDA requirements of the manufacturer related to postmarketing epidemiological studies is not available. This is likely due to the lack of ADF labeling.

## Time to peak serum concentration (Tmax) of intact Nucynta ER® is 3 to 6 hours.

## *In vivo* data for flattened Nucynta ER® tablets is not available; however, *in vitro* data indicates that 30% of tapentadol is released after 30 minutes.13

# Slide 26

# **Therapeutically Equivalent Substitutes Abuse-Deterrent Claims Nucynta®**

## **Nucynta® Summary**

## Chemical name tapentadol

## Dosage form immediate release tablet

## extended release tablet

## ADF classification physiochemical barrier

## ADF claims snorting injection

## ADF studies Info not available

## Studies users less willing to snort particles

## User able to extract less drug compared to oxycodone ER

Slide 27  
**Meeting Schedule**

## February 18, 2016 9:00AM-12:00PM

## March 3, 2016 2:00PM-5:00PM

### 239 Causeway Street, 4th Floor, Boston, MA

## March 17, 2016 9:00AM-12:00PM

## April 7, 2016 2:00PM-5:00PM

## April 21, 2016 9:00AM-12:00PM

## May 5, 2016 2:00PM-5:00PM

## May 19, 2016 9:00AM-12:00PM

Slide 28  
**Meeting Summary**

## Meeting Recap

## Review of takeaways

## Next steps

## Next Meeting

### February 18, 2016 9:00AM-12:00PM