**Abuse-Deterrent Opioids – Evidence Evaluation & Labeling**

Medication: Oxaydo® (oxycodone immediate-release tablet)

Evaluation Date: 06/02/2016 Evaluation History: [x]  Initial Version 1.0, or [ ]  Version \_\_\_\_\_\_\_\_\_

Current Product Labeling established: (select one) [[x]  Prior to] or [[ ]  After] publication of FDA Guidance to Industry Document (4/2015)

This is a: (Check all that apply)

[ ]  New product

[ ]  Existing product, new formulation

[ ]  Existing product with new/updated labeling

[x]  Other: Initial evaluation of existing product

**Product Abuse Deterrent Property Classification:** – Check all that apply

[x]  Physical / Chemical barrier

[ ]  Agonist / Antagonist combination

[x]  Aversion

[ ]  Delivery System

[ ]  New Molecular entity or Prodrug

[ ]  Combination (check combined items)

[ ]  Novel Approach

**Product Labeling:**

Does the product have FDA abuse deterrent labeling? [ ]  Yes or [x]  No Year obtained: \_\_\_\_\_\_\_\_

**Abuse Deterrent Evidence provided.** Summary of in-depth literature review and product evaluation based on FDA Guidance to Industry Document

[x]  Laboratory-based in vitro manipulation and extraction studies (Category 1)

Description of Research: Studies not readily available for review; however, NDA review summary concluded procedures and techniques were incomplete in assessing feasibility of preparing an injectable solution.

[ ]  Pharmacokinetic Studies (Category 2)

Description of Research:

[x]  Clinical Abuse potential studies (Category 3)

Description of Research: Single-center, single-dose, randomized, double-blind, active-controlled two-way crossover study. Intranasal clinical abuse potential with Roxicodone® as active control.

[ ]  Clinical Abuse potential studies (Category 3)

 Description of Research: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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[ ]  Clinical Abuse potential studies (Category 3)

 Description of Research: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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[ ]  Additional Studies / Post Market data which assessed the impact of abuse-deterrent formulation (Category 4)

[ ]  Post market

[ ]  Formal studies included recommended study design features (see page 19 FDA Guidance

document)

Description of Research: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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[ ]  Determination if use of product results in meaningful reductions in abuse, misuse, and related adverse clinical outcomes, including addiction, overdose, and death

Description of Research: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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[x]  Outcome Measures and Data Interpretation in Abuse Potential Studies

* + Standardized Instruments

[x]  Visual Analogue Scales (VAS)

Description of Research: Maximum effect (Emax) for Drug Liking, effect at 8 hours (E8h) post-dose for Take Drug Again, E8h for Overall Drug Liking. Nasal effects were also rated on a 6-point Subject Rated Scale.

[ ]  Profile of Mood States

Description of Research: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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* + Data Interpretation

[x]  Primary Analysis

Description of Research: Least squares mean Drug Liking Emax Oxecta®/Oxaydo® vs Roxicodone® (70.8 vs 93.5, respectively; P<0.0001).

[x]  Statistical Analysis

Description of Research: Linear mixed model with fixed

effects for sequence, period, and treatment and a random effect for subject nested in sequence. Least squares means for all endpoints analyzed. All reported as P<0.0001; however, FDA biometrics review found significant sequence effect. FDA halved sample size as a result of significant sequence effect and re-tested with Wilcoxon-Mann-Whitney, which revealed no significant differences for any endpoint.

[x]  Data and dropout for non-completers

Description of Research: One subject not evaluated due to vomiting after administration of study medication and active control and 21 subjects did not completely administer full dose of Oxaydo.

[ ]  None of the above

**Strength of Evidence of Abuse Deterrent Properties:**

[ ]  Evidence is based on physical/chemical property, theoretical assumptions or manufacturer’s claims and is not yet supported by scientifically sound outcome data which demonstrates a reduction in the abuse of the product in the community setting compared to levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available

[x]  Evidence is based on physical/chemical property, clinical abuse potential studies or laboratory manipulation studies and is not yet supported by scientifically sound outcome data which demonstrates a reduction in the abuse of the product in the community setting compared to levels of abuse, overdose, and death that occurred when only formulations of the same opioid without-abuse-deterrent properties were available

[ ]  There is evidence, supported by scientifically sound outcome data, which demonstrates a reduction in the abuse of the product in the community setting compared to levels of abuse, overdose, and death that occurred when only formulations of the same opioid without abuse-deterrent properties were available