Abuse-Deterrent Opioids – Evidence Evaluation & Labeling

Medication: Oxaydo® (oxycodone immediate-release tablet)

Evaluation Date: 06/02/2016 Evaluation History: ☒ Initial Version 1.0, or ☐ Version _____

Current Product Labeling established: (select one) [☒ 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
☒ Other: Initial evaluation of existing product

Product Abuse Deterrent Property Classification: – Check all that apply

☒ Physical / Chemical barrier
☐ Agonist / Antagonist combination
☒ 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 ☒ No Year obtained: _____

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

☒ 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: _____

☒ 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: _____

☐ Clinical Abuse potential studies (Category 3)
Description of Research: _____

☐ 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: _____

☐ 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: _____

☒ Outcome Measures and Data Interpretation in Abuse Potential Studies

- Standardized Instruments
  - ☒ Visual Analogue Scales (VAS)
    Description of Research: Maximum effect (E_{max}) for Drug Liking, effect at 8 hours (E_{8h}) post-dose for Take Drug Again, E_{8h} for Overall Drug Liking. Nasal effects were also rated on a 6-point Subject Rated Scale.

    ☐ Profile of Mood States
    Description of Research: _____
- Data Interpretation
  - ☒ Primary Analysis
    Description of Research: Least squares mean Drug Liking E_{max} Oxecta®/Oxaydo® vs Roxicodone® (70.8 vs 93.5, respectively; P<0.0001).

    ☒ 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.

    ☒ 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

☒ 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