Abuse-Deterrent Opioids – Evidence Evaluation & Labeling

Medication: Hysingla ER®

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

Current Product Labeling established: ☒ 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: 2014

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: Study data indicates that Hysingla ER ® tablets are resistant to crushing, breaking and dissolution using different solvents.

☒ Pharmacokinetic Studies (Category 2)

Description of Research: Study data indicates that Hysingla ER® retain some extended-release properties when the tablets are crushed or chewed. Finely milled tablets and chewed tablets had longer times to peak concentration than hydrocodone solution.

☒ Clinical Abuse potential studies (Category 3)

Description of Research: Intranasal clinical abuse potential study assessed Maximum Scores (Emax) on Drug Liking and Take Drug Again as primary endpoints after intranasal administration of finely crushed Hysingla ER®, coarsely crushed Hysingla ER® and hydrocodone powder. In addition, pharmacokinetic (PK) profile (Cmax, Tmax and AUC) were performed for the intranasally administered Hysingla ER® (fine and coarsely crushed) compared to hydrocodone powder.

☐ Clinical Abuse potential studies (Category 3)

Description of Research: Oral abuse potential study assessed Maximum Scores (Emax) on Drug Liking and Take Drug Again as primary endpoints following oral administration of intact Hysingla® ER 60 mg tablet, milled Hysingla ER®, and chewed Hysingla ER® compared to hydrocodone 60 mg oral solution and placebo. In addition, PK profile (Cmax, Tmax and AUC) were performed for the orally administered intact, milled and chewed Hysingla ER® compared to hydrocodone oral solution and placebo.

☐ 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: Primary pharmacodynamic (PD) measures included VAS for "At the Moment Drug Liking" and "High". Secondary measures included VAS for "Overall Drug Liking" and "Take Drug Again".

☐ Profile of Mood States
Description of Research: _____
_____

- Data Interpretation

☒ Primary Analysis
Description of Research: Primary PD and PK measurements were done up to 36 hours postdose and difference of mean Emax Drug Liking and Take Drug Again as well as assessments of intranasal irritation (Study 1) and pupillometry were performed in both studies.

☒ Statistical Analysis
Description of Research: Primary PD endpoints analyzed using mixed-effect model for crossover studies.

☐ Data and dropout for non-completers
Description of Research: Data regarding dropout and non-completers was provided in all clinical abuse potential studies.

☐ 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 (Category III)

☒ 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 (Category II)

☐ 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 (Category I)