Abuse-Deterrent Opioids – Evidence Evaluation & Labeling

Medication: Xtampza ER® (oxycodone extended-release)

Evaluation Date: 09/15/2016 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: _____

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: 2016

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 the greatest amount of particle size reduction of microspheres achieved was 17.8% and 12.8% using two tools out of ten tested. One solvent out of seven tested was able to extract 77% of the oxycodone in manipulated Xtampza ER® (oxycodone extended-release) microspheres after eight hours; however, all other solvents extracted less than 40%. Passage of a suspension of microspheres through needles smaller than 18 gauge was not possible, and attempts to draw molten microspheres into a needle resulted in solidification of the wax.

☒ Pharmacokinetic Studies (Category 2)

Description of Research: Pharmacokinetic studies indicated manipulated Xtampza ER® was bioequivalent to intact Xtampza ER® when administered orally. Peak plasma concentration of oxycodone was lower when microspheres were crushed and insufflated than when taken orally.

☒ Clinical Abuse potential studies (Category 3)

Description of Research: Oral clinical abuse potential study assessed peak Drug Liking score as primary endpoint after oral administration of chewed Xtampza ER® (fed and fasted states), intact Xtampza ER® (fed and fasted states), oxycodone IR (fasted state) and placebo. Peak drug liking was significantly lower for both chewed and intact Xtampza ER® compared to oxycodone IR ($P<0.0001$).

☒ Clinical Abuse potential studies (Category 3)

Description of Research: Intranasal clinical abuse potential study assessed Drug Liking scores as the primary endpoint after administration of crushed Xtampza ER® intranasal, crushed oxycodone IR intranasal, intact Xtampza ER® oral and placebo. The least squares mean difference (LSMD) between crushed oxycodone IR intranasal and crushed Xtampza ER® intranasal indicated that crushed Xtampza ER® intranasal was liked significantly less ($P\leq0.0001$).

☐ 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: Peak "Drug Liking" (E_{max}), "Take Drug Again", "Good Effects", "Feeling High", "Bad Effects", "Sick", "Nausea", "Sleepy", "Any Effects", Addiction Research Center Inventory/Morphine Benzedrine Group (ARCI/MBG) questionnaire scores, and "Overall Drug Liking" from the Drug Effects Questionnaire-Visual Analogue Scale (DEQ-VAS).

☐ Profile of Mood States
Description of Research: _____
_____

- Data Interpretation

☒ Primary Analysis
Description of Research: Comparison of least squares means (LSM) of peak Drug Liking (E_{max}) (Study 1); LSMD between E_{max} values (Study 2)

☒ Statistical Analysis
Description of Research: Details unavailable (Study 1); Analyses of variance (ANOVA) included calculation of LSM, differences between treatment LSM, and standard errors associated with differences. LSM (marginal means) are arithmetic means adjusted by using a linear mixed model with fixed effects for sequence, period, and treatment, and random effects for patients nested in sequence. (Study 2)

☒ Data and dropout for non-completers
Description of Research: Data regarding dropout and non-completers was not provided, and study is not yet published in a peer-reviewed journal (Study 1); Data regarding dropout and non-completers was provided (Study 2).

☐ 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)