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

Medication: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Xtampza ER® (oxycodone extended-release)\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Evaluation Date: \_\_\_\_09/15/2016\_\_\_\_\_\_ Evaluation History: [x]  Initial Version 1.0, or [ ]  Version \_\_\_\_\_\_\_\_\_

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

This is a: (Check all that apply)

[x]  New product

[ ]  Existing product, new formulation

[ ]  Existing product with new/updated labeling

[ ]  Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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

[x]  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? [x]  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

[x]  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.\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  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.\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  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). \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  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≤0.0001). \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[ ]  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: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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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: Peak “Drug Liking” (Emax), “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: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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* + Data Interpretation

[x]  Primary Analysis

Description of Research: Comparison of least squares means (LSM) of peak Drug Liking (Emax) (Study 1); LSMD between Emax values (Study 2)\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  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)\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  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)

[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 (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)