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

Medication: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Troxyca ER® (oxycodone extended-release/naltrexone) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Evaluation Date: \_\_\_3/20/2017\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ 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

[ ]  Physical / Chemical barrier

[x]  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: \_\_\_\_*In vitro* data indicates crushing pellets results in the simultaneous release of oxycodone and naltrexone.\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  Pharmacokinetic Studies (Category 2)

 Description of Research: \_\_\_Pharmacokinetic studies indicate crushed Troxyca ER® resulted in similar oxycodone plasma exposures to equivalent doses of oxycodone IR. Crushed Troxyca ER® had similar oxycodone peak plasma concentration (Cmax) to crushed oxycodone IR; however, Cmax for crushed Troxyca ER® was approximately 4-fold higher than intact Troxyca ER® . Time to peak plasma concentration (Tmax) was shorter for crushed Troxyca ER® (0.6 hour) compared to intact Troxyca ER® (12.1 hours).\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  Clinical Abuse potential studies (Category 3)

 Description of Research: Oral clinical abuse potential study assessed peak drug liking and peak drug high scores as co-primary endpoints after oral administration of intact and crushed Troxyca ER®, crushed oxycodone IR and placebo. Peak drug liking and drug high for both intact and crushed Troxyca ER® at all doses was significantly lower compared to equivalent doses of crushed oxycodone IR\_(P<0.0001).\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  Clinical Abuse potential studies (Category 3)

 Description of Research: Intranasal clinical abuse potential study assessed peak drug liking and peak drug high scores as co-primary endpoints after intranasal administration of crushed Troxyca ER®, crushed oxycodone IR and weight matched placebos. Peak drug liking and drug high scores were significantly lower for crushed Troxyca ER® compared to an equivalent dose of oxycodone IR (P<0.0001).\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  Clinical Abuse potential studies (Category 3)

 Description of Research: Simulated intravenous (IV) clinical abuse potential study assessed peak drug liking and peak drug high scores as co-primary endpoints after IV administration of simulated crushed Troxyca ER®, IV oxycodone solution and IV placebo. Peak drug liking and drug high scores were significantly lower for simulated crushed Troxyca ER® IV solution compared to an equivalent dose of oxycodone IR IV solution (P<0.001).\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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

* + Standardized Instruments

[x]  Visual Analogue Scales (VAS)

Description of Research: Drug liking, drug high, take drug again, any drug effects, bad drug effects, good drug effects, feel sick, nausea, sleepy and dizzy.\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[ ]  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 and Drug High VAS scores (Emax and AUE0-2) (oral and IV studies); comparison of mean (95% CI) values of peak Drug Liking and Drug High VAS scores (Emax and AUE0-2) (intranasal study);

[x]  Statistical Analysis

Description of Research: Data analyzed using mixed-effect model with treatment, period, and sequence as fixed effects, and participant nested within sequence as random effect (all studies).\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

[x]  Data and dropout for non-completers

Description of Research: Data regarding dropout and non-completers accounted for (all 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)

[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)