**Assessment of an ADF product's route of administration profile

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**Background**

Over the past several years, a number of opioid analgesics have been formulated with technologies intended to reduce abuse of these products via alternative routes of administration (ROA) such as snorting and injection. Assessing the impact of abuse-deterrent opioid formulations (ADFs) on patterns of abuse has focused, in part, on comparisons of the ADF’s ROA profile with its baseline prior to ADF introduction. Recent guidance from the U.S. Food and Drug Administration (FDA) for evaluating potential ADFs recommends direct comparison of abuse levels for an ADF product to historical abuse baselines of non-ADF competitor1. However, ROAs that deter abuse may be influenced by several factors, including continued availability of the original formulation and availability of non-ADF ADFs which may provide alternate routes for abuse. A simple pre-post comparison of ROA profiles assumes that abuse of the original product would remain unchanged in the time period following introduction of the ADF. To examine this assumption, we reviewed ROA profiles for both original and reformulated extended-release (ER) opioids, and generics after introduction of reformulated crush-resistant ER oxymorphone.

A reformulated version of oxymorphone ER designed to be crush-resistant (OPANAL ER — oxymorphone hydrochloride extended-release tablets, Endo Pharmaceuticals Inc., Malvern, PA) became commercially available in February 2012, concurrent with the cessation of production and diminishing supply of the original (non-ADF) brand formulation of the product. Existence of the original brand and generic ER oxymorphone formulations currently offer potential non-ADF alternatives for abuse of original oxymorphone ER.

**Methods**

**Sample**

Data were collected from a large convenience sample of adults assessed for substance abuse problems and treatment planning at centers located across the U.S. using the NAVIPRO Addiction Severity Index Multimedia Version (ASI-MMV) system during the period October 1, 2012 through March 31, 2014. Evaluation of past 30-day abuse via specific ROA categories including oral (swallowed whole), snorting, and injection were conducted for reformulated oxymorphone ER and non-ADF oxymorphone formulations in two separate analyses:

1. Comparison of ROAs for reformulated oxymorphone ER from October 2012 through March 2014 to original oxymorphone ER during a three-year historical baseline period January 2009 through December 2011.


For the two analyses, assessments from a subset of sites within the ASI-MMV network that contributed data across the respective time periods of interest were used as follows:


2. Comparison of ROAs during October 2012 through March 2014 for reformulated oxymorphone ER and non-ADF oxymorphone formulations: N=77,175 for 44 sites from 37 states.

**ASI-MMV Assessment**

The ASI-MMV is a standard clinical interview and intake assessment designed for use in admission to drug and alcohol treatment that has demonstrated validity and reliability. The ASI-MMV contains questions about past 30-day abuse of illegal substances and prescription medications with product-specific questions about ROA and abuse of drugs; identification of abuse behavior is determined by presenting images with audio of individual medications including medication names, slang names, and street names.

**Estimation of Abuse via Specific ROA**

Abuse via specific ROA was measured as the percentage of individuals who reported abuse via a ROA among only those individuals who reported past 30-day abuse of the product or compound of interest (i.e., reformulated oxymorphone ER, original oxymorphone ER, generic oxymorphone ER).

**Results**

**Comparison of ROA for OxyContin ER Pre- and Post-Reformulation**

**Comparison of ROA for Reformulated Oxymorphone ER and non-ADF Oxymorphone ER Formulations**

- Among abusers of the product, historical abuse of original oxymorphone ER during the three-year baseline period was mostly via snorting (77%), with 23% of abusers reporting oral (swallowed whole) abuse of the product and 17% reporting injection (Figure 1).

- During the past 18 months (October 2012 through March 2014), a low level of snorting was observed for reformulated oxymorphone ER compared to observed historically for original oxymorphone ER (21% versus 77%). During the same period, a higher percentage of abusers reported injection of reformulated oxymorphone ER than historically for original oxymorphone ER (95% versus 7%) and similar percentages were reported for oral abuse (28% and 25%) (Figure 1).

- Currently, while abusers of original oxymorphone ER continue to indicate abuse via snorting (57%), a higher percentage report injection (38%) compared to observed historically during the three-year baseline period (17%) (Figure 1).

- Over time, the quarterly percentage of individuals who reported abuse of original oxymorphone ER via snorting decreased (ranging from 61% in Q1 2009 to 43% in Q1 2014) while the percentage of individuals who reported abuse of the product via injection increased on a quarterly basis (ranging from a low of 6% in Q2 2009 to 55% in Q1 2014) (Figure 2).

- During the past 18 months (October 2012 through March 2014) quarterly abuse of reformulated oxymorphone ER via snorting was consistent over time (ranging between 17% and 27%) and lower than the percentage of snorting for original oxymorphone ER and non-ADF oxymorphone ER products (Figure 4).

- Quarterly, the percentage of abusers of reformulated oxymorphone ER reporting injection during the past 18 months (range 55% to 75%) was greater than the percentage of injection observed for non-ADF oxymorphone ER products (Figure 5).

- The RDA profile for reformulated oxymorphone ER (over the past 18 months) suggests lower abuse of this product via snorting compared to other non-ADF oxymorphone ER products (including original brand and generic formulations). The percentage of snorting for reformulated oxymorphone ER was also lower than observed historically for original oxymorphone ER prior to the reformulation.

- ROA patterns for oxymorphone ER products indicate some change over time where a higher percentage of injection has been observed for original oxymorphone ER in the past 18 months compared to historical baseline levels. Higher reported percentages of abuse via injection for reformulated oxymorphone ER compared to other non-ADF oxymorphone ER products also continues to be observed in this population of adults assessed for substance abuse treatment.

- Understanding the public health impact of ADFs should take into account the current market environment and volume and availability, the ROA profiles (particularly injection) for ADF and non-ADF oxymorphone ER formulations may change.

- Given the significant market changes over time for oxymorphone products, comparison of patterns of abuse of reformulated oxymorphone ER to historical baseline levels of abuse of original oxymorphone ER alone does not provide the most meaningful evaluation of abuse of this product.

- These data provide an early impression of the pattern of ROA of a reformulated oxymorphone ER among this sample of adults assessed for substance abuse treatment after transition from the original formulation oxymorphone ER and during a period after significant market change for oxymorphone products. As such, these data continue to be monitored to determine if current observed patterns of abuse are sustained and further evaluations via formally designed epidemiologic studies are conducted.

**References**
