Nonmedical Use of Xtampza® ER and Other Oxycodone Medications in Adults Evaluated for Substance Abuse Treatment: Real-World Data from the Addiction Severity Index-Multimedia Version (ASI-MV®)

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Purpose: The purpose of this study was to evaluate real-world data related to past 30-day nonmedical use (NMU) and routes of administration of Xtampza® ER and comparator oxycodone medications in the US as captured within the Addiction Severity Index-Multimedia Version® (ASI-MV®).

Methods: Data were collected from July 2016 through December 2019 from 647 centers located in 44 states using the ASI-MV, a clinical instrument used to evaluate substance use and treatment planning. Demographic characteristics were assessed using Pearson’s chi-square test for categorical data and quarterly NMU rates were calculated. Distribution of route of administration was studied using a proportional reporting ratio (PRR) analysis.

Results: Of 192,810 assessments, 42,279 (21.9%) indicated past 30-day NMU of at least one prescription opioid, including Xtampza ER (N=73, 0.2%), other oxycodone ER (n=3802, 9.0%) and oxycodone IR (n=14,579, 34.5%). All quarterly Xtampza ER NMU rates per 100 ASI-MV assessments were significantly lower than those for other oxycodone ER and oxycodone IR. Overall, quarterly Xtampza ER NMU drug utilization adjusted rates were significantly lower than quarterly rates observed for other oxycodone ER NMU but not consistently significantly lower than oxycodone IR NMU. Although not all statistically significant, all ratios from the PRR analysis were less than 1.0, indicating that rates of use of any alternate route, any non-oral route, snorting, and injecting were higher for other oxycodone ER and oxycodone IR than for Xtampza ER.

Conclusion: Xtampza ER had significantly lower rates of NMU than other oxycodone ER products and oxycodone IR products, as well as significantly lower rates of non-oral NMU than oxycodone IR products, in a population of individuals seeking substance abuse treatment. Understanding risks associated with different opioid medications is important for prescribers as they manage risks of opioid misuse and abuse with effective pain therapy.

Keywords: pain management, analgesic, opioid, drug abuse, substance abuse treatment, real-world data

Introduction

Opioid therapy for chronic pain remains a challenge as providers weigh the medical need for therapy with the risks of opioid-related misuse, abuse, diversion, and overdose. A systematic review and meta-analysis evaluated the efficacy of opioid
therapy in chronic pain. Based upon 15 studies that met the inclusion criteria, opioids appear to be efficacious for treatment of non-cancer chronic pain for up to 3 months. Published studies evaluating the risks of prescription opioid therapy suggest that rates of opioid misuse range from 21% to 29% and rates of opioid addiction range from 8% to 12%. Prescription opioid medications with abuse-deterrent properties (also known as abuse-deterrent formulations [ADF]) are opioid medications designated by the US Food and Drug Administration (FDA) as products that may meaningfully deter abuse, even if they do not fully prevent abuse. Currently marketed ADF opioid products are intended to deter manipulation for the purpose of snorting, smoking or injecting of the active ingredient. Almost all ADF opioid products are extended-release (ER) formulations. Compared with immediate-release (IR) formulations, ER products contain higher amounts of the active ingredient. When an ER mechanism can be defeated so that most or all of the active ingredients become immediately available (for example, by crushing, grinding or dissolving), the product becomes particularly attractive for abuse by nonoral routes (eg, snorting, smoking or injecting). Prescription opioid abuse via nonoral routes of administration has been associated with a significantly higher risk (2.5 times higher) of life-threatening effects or death than abuse via oral routes as demonstrated by a study of cases managed by poison centers.

Xtampza® ER (Collegium Pharmaceutical, Inc, Stoughton, MA, USA) is a Schedule II, abuse-deterrent, ER oral formulation of oxycodone indicated for the management of pain severe enough to require daily, around-the-clock long-term management for which alternative treatment options are inadequate. Xtampza ER is available in capsule form and is intended to be ingested orally. Xtampza ER was approved by the FDA in April 2016, with ADF labeling, specifically that the formulation was expected to make abuse via injection difficult, and to reduce abuse by the oral and intranasal routes. Xtampza ER became available to patients in Q3 2016.

Premarket in vitro and in vivo testing of Xtampza ER is well documented and demonstrates the difficulties in manipulating the product as well as the product’s pharmacokinetic profile and human abuse potential. Published postmarket data is limited to a recent publication comparing Xtampza ER to IR oxycodone, other ADF ER opioids, and non-ADF ER opioids which suggested that Xtampza ER has low relative abuse rates and low relative likelihood of non-oral use. While these results were consistent across several data sources, additional real-world data are needed to further understand the relative risk of abuse of currently available opioid medications.

The goal of this study was to evaluate real-world data from the Addiction Severity Index-Multimedia Version® (ASI-MV®; Inflexxion, Irvine, CA, USA), a clinical tool used to evaluate substance abuse and treatment planning. Past 30-day nonmedical use (NMU) and route of administration of Xtampza ER were compared to other oxycodone products currently available in the United States (US).

Methods
A cross-sectional surveillance study design was used to examine past 30-day NMU and routes of administration for Xtampza ER and comparator prescription oxycodone products among adults aged 18 years or older evaluated for substance abuse problems and treatment planning using the ASI-MV assessment tool. The comparator prescription oxycodone product groups included: 1) other oxycodone ER and 2) oxycodone IR (Table 1). The comparator groups are not mutually exclusive as one assessment could have included reported NMU of multiple products; hence, one assessment could be included in more than one study group.

ASI-MV Data Collection
This study included ASI-MV assessments completed from 01 July 2016 (Q3 2016) through 31 December 2019 (Q4 2019), representing a 3.5-year time period. Xtampza ER was launched in Q3 2016 and added to the ASI-MV in Q3 2017, allowing for a 1-year transition period as the product was introduced to the US market. The ASI-MV is a clinical tool used in standard workflow to gather biopsychosocial data of individuals evaluated for substance use for the purpose of triage and treatment planning. This validated self-administered standardized tool is based on the Addiction Severity Index (ASI), a standard clinical assessment tool with well-established reliability and validity designed for use on admission to drug and alcohol treatment.

In addition to patient characteristics, substance use and treatment history, and biopsychosocial domain assessments, the ASI-MV gathers self-reported NMU of specific prescription opioid medications. Respondents who report prescription opioid NMU are asked to identify the specific prescription opioid products used in the past 30 days from
Table 1 Utilization of Xampza ER and Comparator Oxycodone Groups Within the ASI-MV Network

| Group             | Description                                                                 | Prescriptions Dispensed | % of All Opioids Dispensed | % of All Oxycodone Dispensed | % of All Oxycodone ER Dispensed |
|-------------------|-----------------------------------------------------------------------------|-------------------------|----------------------------|-----------------------------|---------------------------------|
| Xampza ER         | Xampza ER (entered market in Q3 2016; added to ASI-MV Q3 2017)              | 831,552                 | 0.1                        | 0.5                         | 7.8                             |
| Other oxycodone ER* | Other oxycodone ER products excluding Xampza ER (solid oral dosage forms) | 9,891,591               | 1.5                        | 6.1                         | 92.2                            |
| Oxycodone IR      | Oxycodone IR products (solid oral dosage forms), including single-entity and combination products | 150,629,158             | 23.0                       | 93.4                        | N/A                             |

Note: “During the study period, the prescriptions dispensed within the other oxycodone ER product grouping were almost solely comprised of OxyContin and authorized generics (>99%).

Abbreviations: ER, extended-release; IR, immediate-release; ASI-MV, Addiction Severity Index-Multimedia Version.

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a list of brand and generic products. Product photos are presented to assist with product identification. Routes of administration ever used for each product are also collected.

Secondary analysis of ASI-MV data for research purposes has been determined to be exempt from institutional review board review by the New England Institutional Review Board. All data accessed complied with relevant data protection and privacy regulations.

Definition of NMU

NMU was defined with the use of an algorithm of responses to several questions (Figure 1). Using this algorithm, any deviation from legitimate medical use as prescribed was considered NMU. For purposes of this study, legitimate medical use is use of one’s own prescription medication from a healthcare provider only in the manner in which it was prescribed (frequency, dose and route of administration). While the ASI-MV captures NMU, abuse (a subtype of NMU) was not specifically collected. The FDA defines abuse as “the nonmedical use of a drug, repeatedly, or even sporadically, for the positive psychoactive effects it produces”. The ASI-MV does not query the intention or reason for reported NMU of opioid medications; hence, rates of any NMU were reported rather than “abuse” or “misuse”.

Data Analyses

Demographic characteristics were assessed using Pearson’s chi-square test (or Fisher’s exact test for comparisons with small cell size) for categorical data and Wilcoxon rank sum tests for ordinal data. Statistical significance was determined for tests where p<0.05. Quarterly NMU was assessed during the study period using the following approaches: 1) rate (95% confidence interval) adjusted for volume of ASI-MV assessments completed during the study period, 2) rate (95% confidence interval) adjusted by the number of prescriptions dispensed, and 3) rate adjusted by the number of solid oral dosage units (eg, tablets, capsules, caplets) dispensed. Prescriptions and units dispensed data were obtained from the National Prescription Audit™ (NPA; IQVIA, Danbury, CT, USA), an industry standard source of national prescription activity for all pharmaceutical products. NPA includes prescriptions and units dispensed from the universe of retail, standard mail service, specialty mail service, and long-term care pharmacies. The database produces projected total prescriptions dispensed (counts) and projected total number of units dispensed (counts) at various levels of aggregation including state and 3-digit ZIP code for all opioid products by individual manufacturer and available dosage strengths. For the purposes of this analysis, only solid oral dosage formulations were included (tablets or capsules) and only states with sites that contributed at least one assessment to the ASI-MV dataset during a specific quarter during the study period were included in the prescription-adjusted analyses for that quarter. The prescriptions dispensed- and units dispensed-adjusted rates account for the variability in drug utilization of Xampza ER and the comparator groups. 95% confidence intervals (CIs) for NMU rates were calculated using a binomial distribution or Poisson distribution (ie, in instances in which the number of cases is less than 30). Units dispensed was included as an adjuster for drug availability because each tablet represents an individual opportunity for abuse.21

The proportional reporting ratio (PRR) is a commonly used method to assess disproportionality in pharmacovigilance surveillance data and has been deemed a validated...
Medical Questions

Do you have a pain problem? That is, physical pain that is more than the usual aches and pains?

In the past 30 days, have you taken any prescribed opiate medicine for your pain?

Product-Specific Prescription Opioid Panel Questions

The following questions are presented for each product endorsed for the past 30-day use.

On how many of these days did you use <Opioid> in a way not prescribed by your doctor? That is, using it for how it made you feel and not to help with pain.

How have you usually used <Opioid>? Please select all that apply.

Response Options (select all that apply): Swallowed it whole; Chewed it, and then swallowed it;

Dissolved it in my mouth like a cough drop; Drank it after it dissolved in liquid; Dissolved it on my tongue; Dissolved it on the inside of my cheek (buccal); Snorted it; Smoked it; Injected it with a needle into my skin or muscle; Injected it with a needle into my vein; Other

Where did you get the <Opioid>? Please select all that apply.

Response Options (select all that apply): My own prescription from one doctor; My own prescriptions from several doctors; Bought it online without a doctor’s visit; Bought it from family or friend; Stole it from family or friend; Given to me by family or friend; Bought it from a dealer (a known seller); Wrote or bought a fake prescription; Stole them; Traded for it; Other

Figure 1 Items used in algorithm to define past 30-day nonmedical use (NMU) of prescription opioid products.

Note: Italics represent verbatim question as presented in the ASI-MV.

method in drug safety research and surveillance for signal detection.\textsuperscript{22,23} The PRR was calculated for specific routes of administration reported for Xtampza ER NMU versus routes of administration reported for comparator NMU. An individual assessment may include reported NMU of more than one oxycodone product by more than one route of administration. Each mention of a product and route was used to calculate the ratios. These ratios indicate if different routes of administration were more or less likely to be used for Xtampza ER NMU versus the comparators. Routes of administration included Any Oral (swallow whole, chew then swallow, dissolve like a cough drop, dissolved in liquid then drank) and Any Non-Oral (snort, smoke, inject). Multiple routes could be reported for each product; hence, routes are not mutually exclusive. All analyses were carried out using SAS Enterprise Guide version 7.1 (Cary, NC).

Results

During the study period, 647 sites located in 44 states contributed 192,810 assessments to the ASI-MV network. A total of 42,279 assessments (21.9\%) reported past 30-day NMU of at least one prescription opioid. Less than 1\% of those reporting prescription opioid NMU specified past 30-day Xtampza ER NMU (n=73; 0.2\%). Past 30-day NMU of other oxycodone ER was reported by 9.0\% (n=3,802) and over one-third reported past 30-day oxycodone IR NMU (n=14,579, 34.5\%) (Table 2). Those who reported Xtampza ER NMU were more likely to be female (54.8\% versus 48.6\% of those reporting other oxycodone
Table 2 Patient Demographics and Characteristics

| Response                  | Past 30-Day | Past 30-Day | Past 30-Day | Xtampza ER versus | Xtampza ER versus |
|---------------------------|-------------|-------------|-------------|-------------------|-------------------|
|                           | Xtampza ER  | Other Oxycodeine ER | Oxycodeine IR | Other Oxycodeine ER | Oxycodeine IR |
|                           | ER NMU      | ER NMU      | IR NMU      | ER NMU            | IR NMU            |
|                           | (n = 73; 0.2%) | (n = 3802; 9.0%) | (n = 14,579; 34.5%) |                   |                   |
| **Gender**                |             |             |             |                   |                   |
| Male                      | 33          | 1955        | 7380        | 0.29              | 0.36              |
| Female                    | 40          | 1847        | 7197        |                   |                   |
| Unknown/no response       | 0           | 0           | 2           |                   |                   |
| **Age**                   |             |             |             |                   |                   |
| 18–24 years               | 8           | 605         | 2152        | 0.09              | 0.05              |
| 25–34 years               | 28          | 1599        | 6519        |                   |                   |
| 35–44 years               | 19          | 990         | 3693        |                   |                   |
| 45–54 years               | 16          | 421         | 1525        |                   |                   |
| 55 + years                | 2           | 187         | 690         |                   |                   |
| **Race**                  |             |             |             |                   |                   |
| Caucasian                 | 57          | 2886        | 10,907      | 0.63              | 0.41              |
| African American          | 4           | 381         | 1695        |                   |                   |
| American Indian/Alaskan Native | 3         | 92          | 319         |                   |                   |
| Asian                     | 0           | 0           | 27          |                   |                   |
| Pacific Islander/Native Hawaiian | 0       | 0           | 0           |                   |                   |
| Hispanic/Latino           | 6           | 283         | 1065        |                   |                   |
| Other Race                | 3           | 152         | 566         |                   |                   |
| Unknown/no response       | 0           | 0           | 0           |                   |                   |
| **Marital status**        |             |             |             |                   |                   |
| Married                   | 14          | 824         | 3329        | 0.82              | 0.72              |
| Separated, divorced, widowed | 19       | 907         | 3418        |                   |                   |
| Never married             | 37          | 2049        | 7741        |                   |                   |
| Unknown/no response       | 3           | 22          | 91          |                   |                   |
| **Employment**            |             |             |             |                   |                   |
| Professional              | 5           | 225         | 881         | 0.93              | 0.94              |
| Administrative, clerical, sales | 9        | 444         | 1736        |                   |                   |
| Skilled or semi-skilled   | 23          | 1523        | 5814        |                   |                   |
| Student                   | 2           | 57          | 248         |                   |                   |
| Homemaker                 | 7           | 312         | 1228        |                   |                   |
| Other manual/unskilled    | 10          | 441         | 1661        |                   |                   |
| Did not work for pay last 3 years | 3       | 202         | 735         |                   |                   |
| Disabled                  | 7           | 277         | 1070        |                   |                   |
| No occupation             | 6           | 299         | 1120        |                   |                   |
| Unknown/no response       | 1           | 22          | 86          |                   |                   |
| **Treatment Modality**    |             |             |             |                   |                   |
| Residential/Inpatient     | 46          | 2208        | 8041        | 0.25              | 0.15              |
| Outpatient/Non-Methadone  | 18          | 844         | 3664        |                   |                   |
| Methadone                 | 7           | 268         | 888         |                   |                   |
| Drug Court                | 0           | 0           | 255         |                   |                   |
| Probation/Parole          | 0           | 0           | 185         |                   |                   |
| DUI/DWI                   | 0           | 0           | 201         |                   |                   |
| Other Corrections         | 0           | 0           | 95          |                   |                   |
| Temporary Assistance for Needy Families (Welfare) | 0 | 0 | 90 |                   |                   |
| Other                     | 2           | 272         | 1160        |                   |                   |
| **Current pain problem**  |             |             |             |                   |                   |
| Yes                       | 52          | 2289        | 8123        | 0.04              | 0.005             |
| No                        | 20          | 1509        | 6432        |                   |                   |
| Unknown/no response       | 1           | 4           | 24          |                   |                   |
| **Criminal justice**      |             |             |             |                   |                   |
| Yes                       | 23          | 888         | 3557        | 0.07              | 0.11              |
| No                        | 47          | 2894        | 10,949      |                   |                   |
| Unknown/no response       | 3           | 20          | 73          |                   |                   |

(Continued)
ER product NMU and 49.4% of those reporting oxycodone IR NMU). Approximately 25% of those who reported Xtampza ER NMU were aged 45 years or older compared to 16.0% of those reporting NMU of other oxycodone ER products and 15.2% of those reporting NMU of oxycodone IR products. Those reporting Xtampza ER NMU were more likely than those endorsing comparator opioid drug NMU to self-report a current pain problem (71.2% versus 60.2% of other oxycodone ER product nonmedical users and 55.7% of oxycodone IR nonmedical users). Patients with moderate to extreme drug severity scores were similar across the study groups.

Quarterly past 30-day NMU rates of Xtampza ER per 100 ASI-MV assessments ranged from 0.01 (Q3 2017) to

### Table 2 (Continued).

| Response                              | Past 30-Day | Past 30-Day | Past 30-Day | Xaptiona ER versus | Xaptiona ER versus |
|---------------------------------------|-------------|-------------|-------------|--------------------|--------------------|
| Past 30-day marijuana use             |             |             |             |                    |                    |
| Yes                                   | 37          | 50.7%       | 1901        | 50.0%              | 6915               | 47.4%              | 0.86               | 0.54               |
| No                                    | 36          | 49.3%       | 1901        | 50.0%              | 7664               | 52.6%              |                    |                    |
| Past 30-day illicit drug use (other than marijuana)** |             |             |             |                    |                    |
| Yes                                   | 58          | 79.5%       | 2631        | 69.2%              | 9199               | 63.1%              | 0.06               | 0.004              |
| No                                    | 15          | 20.6%       | 1171        | 30.8%              | 5380               | 36.9%              |                    |                    |
| Past 30-day heroin use                |             |             |             |                    |                    |
| Yes                                   | 28          | 38.4%       | 1604        | 42.2%              | 5174               | 35.5%              | 0.50               | 0.62               |
| No                                    | 45          | 61.6%       | 2189        | 57.6%              | 9405               | 64.3%              |                    |                    |
| Lifetime heroin use                   |             |             |             |                    |                    |
| Yes                                   | 44          | 60.3%       | 2324        | 61.1%              | 7824               | 53.7%              | 0.87               | 0.27               |
| No                                    | 29          | 39.7%       | 1471        | 38.7%              | 6728               | 46.2%              |                    |                    |
| Unknown/no response                   | 0           | 0.0%        | 7           | 0.2%               | 27                 | 0.2%               |                    |                    |
| Lifetime injection of any drug        |             |             |             |                    |                    |
| Yes                                   | 34          | 46.6%       | 1886        | 52.2%              | 6620               | 45.4%              | 0.34               | 0.84               |
| No                                    | 39          | 53.4%       | 1816        | 47.8%              | 7959               | 54.4%              |                    |                    |
| Drug severity score                   |             |             |             |                    |                    |
| No real problem/slight problem        | 2           | 2.7%        | 216         | 5.7%               | 1210               | 8.3%               | 0.55               | 0.38               |
| Moderate/considerable problem         | 28          | 38.4%       | 1352        | 35.6%              | 5896               | 40.4%              |                    |                    |
| Extreme problem                       | 32          | 43.8%       | 1998        | 52.6%              | 6637               | 45.5%              |                    |                    |
| Unknown/no response                   | 11          | 15.1%       | 236         | 6.2%               | 836                | 5.7%               |                    |                    |
| Medical severity score                |             |             |             |                    |                    |
| No real problem/slight problem        | 19          | 26.0%       | 1478        | 38.9%              | 6362               | 43.6%              | 0.02               | 0.002              |
| Moderate/considerable problem         | 51          | 69.9%       | 2123        | 55.8%              | 7522               | 51.6%              |                    |                    |
| Extreme problem                       | 0           | 0.0%        | 105         | 2.8%               | 349                | 2.4%               |                    |                    |
| Unknown/no response                   | 3           | 4.1%        | 96          | 2.5%               | 346                | 2.4%               |                    |                    |
| Family severity score                 |             |             |             |                    |                    |
| No real problem/slight problem        | 31          | 42.5%       | 1717        | 45.2%              | 7214               | 49.5%              | 0.14               | 0.02               |
| Moderate/considerable problem         | 22          | 30.1%       | 1578        | 41.5%              | 5724               | 39.3%              |                    |                    |
| Extreme problem                       | 14          | 19.2%       | 139         | 3.6%               | 1106               | 7.6%               |                    |                    |
| Unknown/no response                   | 6           | 8.2%        | 143         | 3.8%               | 535                | 3.7%               |                    |                    |
| Employment severity score             |             |             |             |                    |                    |
| No real problem/slight problem        | 26          | 35.6%       | 1712        | 45.0%              | 7331               | 50.3%              | 0.03               | 0.001              |
| Moderate/considerable problem         | 33          | 45.2%       | 1654        | 43.5%              | 5785               | 39.7%              |                    |                    |
| Extreme problem                       | 11          | 15.1%       | 296         | 7.8%               | 936                | 6.4%               |                    |                    |
| Unknown/no response                   | 3           | 4.1%        | 140         | 3.7%               | 527                | 3.6%               |                    |                    |

**Notes:** Admission to substance abuse treatment was required or encouraged of the respondent by a judge, probation or parole officer, or other criminal justice official. Illicit drugs include heroin, cocaine, illicit amphetamines/methamphetamines, hallucinogens, inhalants, ecstasy, GHB, ketamine, K2, rohypnol, bath salts, and street fentanyl. Unknown/no responses categories (ie, missing data) were excluded from statistical testing. Due to low cell size (n<5), the Fisher’s exact test was run in place of the chi-square test for age, race, and treatment modality. The categories for employment and treatment modality were collapsed prior to running statistical testing. Employment categories included professional/administrative, clerical or sales; skilled, semi-skilled, other manual; homemaker; disabled; no occupation; and other (includes the remaining categories with cell counts of n=5). Treatment modality categories included residential/inpatient, outpatient/non-methadone, corrections (drug court, probation/parole, DUI/DWI, other corrections); and other (methadone, Temporary Assistance for Needy Families, and other).

**Abbreviations:** ER, extended-release; IR, immediate-release; NMU, nonmedical use.
0.10 (Q1 2018), other oxycodone ER NMU rates ranged from 1.25 (Q4 2019) to 2.97 (Q4 2016), and oxycodone IR NMU rates ranged from 10.87 (Q4 2019) to 23.37 (Q3 2016) (Figure 2A). All quarterly Xtampza ER NMU rates per 100 ASI-MV assessments were significantly lower than those for other oxycodone ER and oxycodone IR, as determined by discrete confidence intervals. Past 30-day oxycodone IR NMU quarterly rates per 100 ASI-MV assessments were significantly higher than all other groups.

When adjusting for the volume of prescriptions dispensed during the study period, past 30-day Xtampza ER NMU was reported at rates between 4.46 (Q4 2018) and 31.10 (Q4 2017), other oxycodone ER NMU rates ranged from 38.65 (Q4 2019) to 59.94 (Q3 2016), oxycodone IR NMU rates ranged from 16.35 (Q4 2019) to 36.37 (Q3 2016) mentions per 100,000 prescriptions (Figure 2B). Overall, quarterly Xtampza ER NMU rates per 100,000 prescriptions dispensed were significantly lower than quarterly rates observed for other oxycodone ER NMU (with

![Figure 2](https://example.com/figure2.png)

**Figure 2** Quarterly (Q3 2016-Q4 2019) rates of past 30-day NMU (A) per 100 ASI-MV assessments, (B) per 100,000 prescriptions dispensed, and (C) per 1,000,000 units dispensed for Xtampza ER and comparator oxycodone products.

**Note:** Xtampza ER was added to the ASI-MV in Q3 2017.

**Abbreviations:** ER, extended-release; IR, immediate-release; ASI-MV, Addiction Severity Index-Multimedia Version; NMU, nonmedical use.
the exception of Q4 2017), but not consistently significantly lower than oxycodone IR NMU rates.

The units dispensed adjusted rate of past 30-day Xtampza ER NMU was lowest in Q4 2018 (0.77) and highest in Q4 2017 (5.32). Other oxycodone ER past 30-day NMU adjusted for units dispensed ranged from 6.32 (Q4 2019) to 9.56 (Q2 2019). Oxycodone IR past 30-day NMU adjusted for units dispensed ranged from 2.33 (Q4 2019) to 4.86 (Q3 2016) (Figure 2C). Overall, Xtampza ER NMU rates per 1,000,000 units dispensed were significantly lower than quarterly rates observed for other oxycodone ER NMU but not significantly lower than oxycodone IR NMU rates.

Nonmedical users of Xtampza ER were significantly less likely to report any non-oral route of administration (28.8%) compared to nonmedical users of other oxycodone ER products (57.9%; Chi-square 18.57, \(p<0.001\)) and nonmedical users of oxycodone IR products (60.1%; Chi-square 52.47, \(p<0.001\)) (Table 3). Specifically, snorting and injecting were reported less frequently for Xtampza ER NMU (17.8% and 6.8%, respectively) compared to other oxycodone ER NMU (31.9% reported snorting and 21.9% reported injecting) and oxycodone IR NMU (40.6% reported snorting and 15.5% reported injecting).

The significant disproportionality in routes of administration between the study groups is further illustrated in the PRR analysis using Xtampza ER as the reference group (Figure 3). All ratios were less than 1.0 which indicates the ratio of the comparator group was higher than that of Xtampza ER. The PRR for other oxycodone ER was statistically significant for the evaluation of any non-oral route versus swallowing whole and for the evaluation of injection versus swallowing whole. The PRR for oxycodone IR was statistically significant for all comparisons except for injection versus swallowing whole. These data suggest that Xtampza ER is less likely to be used via a non-oral route (including injection) than swallowing, compared to other oxycodone ER medications and less likely to be used via any alternate route, any non-oral route, or snorting compared to oxycodone IR.

### Discussion

This study analyzed 192,810 assessments from the ASI-MV network for Xtampza ER and oxycodone opioid comparator groups from 01 July 2016 through 31 December 2019. The ASI-MV is a standardized, validated clinical tool used for substance abuse evaluation and

| Table 3 Prevalence of Nonmedical Use (NMU) for Xtampza ER and Comparators by Route of Administration (7/1/2016–12/31/2019) |
|---------------------------------------------------------------|
| **Past 30-Day Xtampza ER NMU** | **Past 30-Day Other Oxycodone ER NMU** | **Past 30-Day Oxycodone IR NMU** |
| n | % | n | % | n | % |
| **Total NMU Mentions** | 73 | 100.0 | 4114 | 100.0 | 31,281 | 100.0 |
| **Route of Administration** | | | | | | |
| **Any Oral** | | | | | | |
| Swallow whole | 45 | 61.6 | 3261 | 79.3 | 21,977 | 70.3 |
| Chew then swallow | 38 | 52.1 | 2262 | 55.0 | 15,498 | 49.5 |
| Dissolve like a cough drop | 5 | 6.8 | 658 | 16.0 | 4287 | 13.7 |
| Dissolved in liquid then drank | 2 | 2.7 | 230 | 5.6 | 1489 | 4.8 |
| **Any non-oral** | 21 | 28.8 | 2380 | 57.9 | 18,787 | 60.1 |
| **Chi-square, Any Non-Oral (p-value)** | Index Group | 18.57 (<0.001) | 52.47 (<0.001) |
| Snort | 13 | 17.8 | 1314 | 31.9 | 12,696 | 40.6 |
| Smoke | 3 | 4.1 | 165 | 4.0 | 1250 | 4.0 |
| Inject | 5 | 6.8 | 901 | 21.9 | 4841 | 15.5 |
| Other | 8 | 11.0 | 189 | 4.6 | 685 | 2.2 |

**Notes:** *Total NMU mentions are the total number of products within each drug group/category that respondents endorsed for past 30-day NMU. Assessments may have endorsed multiple drugs in any category and product/comparator categories are not mutually exclusive. **Multiple drugs and multiple routes of administration for each drug could be selected by respondents for each product/comparator. Any mention of any route of administration for each product/opioid group is included. Thus, the total number of routes may be greater than total NMU mentions. Italic font indicates statistically significant finding. Results in bold represent the collective categories of oral and non-oral routes of administration while results in regular font represent subsets within each group (subsets are not mutually exclusive).

**Abbreviations:** ER, extended-release; IR, immediate-release; NMU, nonmedical use.
treatment planning which also allows for the study of opioid NMU within a high-risk population.

While all quarterly rates of past 30-day NMU adjusted for the volume of ASI-MV assessments and almost all drug utilization adjusted rates were lowest for Xtampza ER, many did not reach statistical significance likely due to the small number of Xtampza ER NMU cases reported (n=73) and low volume of prescriptions and units dispensed, particularly during introduction of the product to the market.

Additionally, all ratios from the PRR analysis were less than 1.0, indicating that rates of use of any alternate route, any non-oral route, snorting, and injecting were higher for other oxycodone ER and oxycodone IR than for Xtampza ER. The PRR between Xtampza ER and other oxycodone ER suggests a lower likelihood of Xtampza ER being used via any alternate route by 22%, any non-oral route by 31%, snorting by 43%, and injecting by 51%. These ratios were statistically significant for all except injection, despite it having the most remarkable ratio (PRR 0.489, CI 0.2142, 1.1141). In this study, oxycodone IR products accounted for 93.4% of all opioid prescriptions dispensed and had the highest proportion of non-oral routes (60.1%), including snorting (40.6%). This product group by far is the most widely available opioid medication and is the first-line therapy for treatment of acute pain. This is also a group of products that are easily manipulated for non-oral routes of administration which is an important consideration for any prescriber.

Opioid prescribing behaviors vary and cannot be ignored as a confounder when evaluating rates of opioid NMU and routes of administration. A recent study described the variability in prescribing ADF products using data from 2018. The rate of ADF prescribing per 1000 adult recipients of opioid analgesics was nearly twice
Conclusion

The ability to provide effective pain management therapy while reducing the risk of opioid misuse and abuse continues to be a challenge for medical professionals. Oxycodone-containing products are some of the most commonly prescribed opioids. Xtampza ER had significantly lower rates of NMU than other oxycodone ER products and oxycodone IR products, as well as significantly lower rates of non-oral NMU than oxycodone IR products, in a population of individuals seeking substance abuse treatment. Understanding NMU profiles of different opioid medications is important for prescribers as they balance opioid NMU risks with effective pain therapy.

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Disclosure

JLG, RSR, and TDG are employees of and SFB is a consultant to Inflexxion, a division of Integrated Behavioral Health. The authors report no other conflicts of interest in this work.

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