Abuse and route of administration prevalence for tapentadol products within the NAVIPPRO® ASI-MV® surveillance system

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Background
Tapentadol is a centrally acting analgesic that differs from other opioids in that it has two mechanisms of action: µ opioid receptor agonism and norepinephrine reuptake inhibition. Tapentadol has a lower affinity to the µ opioid receptor compared to morphine, suggesting a possible sparing effect on µ opioid receptors in non-opioid tolerant states. Tapentadol may not be significantly rewarding compared to other opioids, and thus may lead to a lower abuse potential for tapentadol products. Tapentadol is available as an immediate-release (IR) product (Nucynta® ER) and an extended-release (ER) product (Nucynta® ER/LA) (Figure 1). The route of administration (ROA) is an important factor for tapentadol, as well as the release of technology designed with abuse-deterrent characteristics in the ER version of the product, which may cause abuse and route of administration (ROA) profiles for tapentadol-based products to differ from other opioids currently on the market, particularly those which are not abuse-deterrent (ADTs).

Methods
Sample
Abuse patterns were evaluated for tapentadol as a compound, and separately for the products Nucynta® ER and Nucynta® ER/LA, compared to other opioids (Table 1). Comparator groups included ER or long-acting (LA) opioids with abuse-deterrent technology, ER/LA opioids without abuse-deterrent technology, and oxycodone ER products with abuse-deterrent technology. Prevalence of past 30-day abuse and abuse via specific routes of administration were calculated among a sample of 270,695 adults assessed for substance abuse treatment problems. This analysis aimed to evaluate overall abuse of tapentadol products (Nucynta® and Nucynta® ER) and abuse of these products via different ROA using various denominators that account for community exposure or availability. Abuse was evaluated among a high-risk population of adults assessed for substance abuse treatment problems.

Results
Abuse of Tapentadol and Comparator Opioids

Sample demographics:
- 63.8% male
- 62.8% Caucasian
- 48.1% between 21 and 34 years old
- 63.6% completed some college or more
- 29.5% indicated a chronic medical problem

Among the total study sample, abuse of tapentadol products was low. Abuse of ADF ER/LA opioids and oxycodone ER ADF products was greatest during 2013 and lower in subsequent years. Conversely, abuse of non-ADF ER/LA opioids was lower during 2012–2014 and greater in 2015 and 2016 (Figure 1). Considering prescription availability, abuse of oxycodone ER ADF products and ADF ER/LA opioids were greater than each of the other comparators. Abuse adjusted for the prescribed availability of ADF ER/LA opioids and oxycodone ER ADF products was greatest in 2013 and 2014 and lower in the two subsequent years. Abuse of non-ADF ER/LA opioids was relatively consistent from 2014 through 2016 (Figure 2). Prescription tablet adjusted-estimates were similar to abuse prevalence adjusted for total prescriptions dispensed. Of note, the prescribed availability of each comparator was approximately 5 to 8 times greater than that of tapentadol products.

Abuse and route of administration (ROA) prevalence for tapentadol products was greatest during 2013 and lower in subsequent years. Conversely, abuse of non-ADF ER/LA opioids used illicit ROA during 2012-2014 and greater in 2015 and 2016 (Figure 3). The ROA profile of Nucynta® ER, a product containing abuse-deterrent characteristics, more closely resembled the unsubstituted tapentadol HCI in healthy male subjects. Abuse of Nucynta® ER compared to non-ADF ER/LA opioids, including injection and snorting more frequently than the prescribed route of swallowing whole (27%) (Figure 4).

The most frequently used ROA among abusers of both Nucynta® (61% of abusers) and Nucynta® ER (83%) was the prescribed route of swallowing whole. Swallow whole was also the most frequently indicated route among abusers of the abuse-deterrent comparator categories ADF ER/LA opioids (50%) and oxycodone ER ADF products (50%). However, prevalences of ADF ER/LA opioids used illicit ROA including injection (50%) and snorting (41%) more frequently than the prescribed route of swallowing whole was 27% (Figure 5).

When considering prescription availability, abuse via swallowing whole was greatest for Nucynta®, Nucynta® ER, and the ADF comparator categories. Prescription-adjusted ROA prevalence estimates for non-ADF ER/LA opioids were greatest for illicit routes including injection and snorting (Figure 4).

On a yearly basis, abuse of ADF ER/LA opioid products was most frequently via the prescribed route of swallowing whole and remained relatively consistent year to year. Injection was the second most prevalent ROA indicated for these products each year from 2013 through 2016.

A greater proportion of those abusing non-ADF ER/LA opioid products injected these products during the early years of the study period (2012 & 2013) followed by a lower proportion in subsequent years (2014—2016). Conversely, the proportion of abusers using these products via snorting was lowest in 2015 and greater in each succeeding year through 2016.

Conclusions
Abuse of tapentadol products, including Nucynta® and Nucynta® ER, was low within the ASI-MV network both unadjusted and adjusted for prescription and tablet availability.

Abuse of tapentadol products was predominantly via the prescribed route of swallowing whole. The ROA profile of Nucynta® ER, a product containing abuse-deterrent characteristics, more closely resembled the unsubstituted tapentadol HCI in healthy male subjects. Abuse of tapentadol products compared to opioids without abuse-deterrent technologies. ADF ER/LA opioids were more commonly abused using the prescribed route of swallowing whole with lower abuse via illicit ROA compared to non-ADF ER/LA opioids. Conversely, abuse of non-ADF ER/LA opioids used illicit ROA including injection and snorting more frequently than the prescribed route of swallowing whole.

Nucynta® ER was designed with abuse-deterrent properties, but does not have FDA approved abuse-deterrent labeling. Additional research examining abuse patterns of opioids with abuse-deterrent FDA labeling compared to those containing abuse deterrent technology but without labeling may aid in further understanding the impact ADF technologies and subsequent FDA labeling may have on abuse levels and ROA patterns of opioid products.

References

Table 1. Comparator Groups

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Figure 1. Yearly past 30-day abuse per 100 assessments

Figure 2. Yearly past 30-day abuse, adjusted for prescription volume

Figure 3. Aggregate study period ROA, percentage among abusers*

Figure 4. Aggregate study period ROA, adjusted for prescription volume

Figure 5. Yearly ROA for non-ADF ER/LA opioid products, percentage among abusers*

Figure 6. Yearly ROA for non-ADF ER/LA opioid products, percentage among abusers*