Recreational drug user preferences: Egalet® opioids have low abuse and tampering attractiveness relative to marketed opioids

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INTRODUCTION

While opioids remain a cornerstone of effective pain management, abuse of prescription opioids is a major problem [1]. Extended release (ER) preparations have been considered to have a lower abuse potential because the slow release and lower maximum concentrations of drug are less likely to result in euphoria. However, ER products are abused, and tampering to alter method of ingestion and destroy the slow-release properties is a major part of this problem. To limit misuse and abuse, an abuse deterrent product should ideally be resistant to physical (e.g. crushing, melting) and chemical (e.g. dissolution and extraction) manipulations [1].

Egalet a/s has several opioid products in development using the novel proprietary Egalet® technology, with the aim to build the above mentioned abuse deterrent properties into the formulations. Results have demonstrated that Egalet® opioids maintain their ER properties across a wide range of solvents including ethanol, and are resistant to physical and chemical attempts to alter the slow-release properties of the drug [2].

The Egalet® formulations are based on an injection molded polymer system consisting of an erodible matrix partly covered with a water-impermeable, non-erodible shell (Figure 1). The well-defined fixed surface erosion area at both ends of the cylindrical tablet allows a tightly controlled, extended release for up to 12 hours and a potential for once-daily dosing.

The ER and abuse deterrent properties are expected to reduce the attractiveness of the Egalet® products for tampering and abuse.

Figure 1. Cross section of an Egalet® opioid tablet

The opioid is dispersed in a matrix (light grey) partly covered by an essentially non-erodible shell (dark grey). The opioid is released by erosion of the matrix.

METHODS

A non-interventional, single-session research study was conducted to evaluate the attractiveness for tampering and abuse of three Egalet® opioid tablets compared to seven marketed opioid formulations of morphine, oxycodone, hydrocodone, and fentanyl.

Subjects were 18 years of age or older, were current or recent recreational (non-medical) opioid users, and provided examples of pharmaceutical opioid tampering with at least 2 different products.

After collecting information about tampering history and preferences, the study included for each product open-ended questions related to tampering methods, assessments of opioid attractiveness (OAS) [3], value of product scale (VPS) and likelihood to tamper scale (LTS), as well as ranking of overall desirability and estimated street value [4].

The opioid products were presented to the subjects one at a time using standardized drug information cards (DICs). Each DIC included photographs of the products and information of the drug's brand/street name(s), active ingredient, doses, solubility, potency relative to morphine, and physical/release properties. Since the Egalet® products have not yet been marketed, placebos for the Egalet® opioids were provided alongside the DICs.

RESULTS

Of 20 subjects completing the interview and included in the analysis (Per Protocol), 17 were male and 3 female, from 25 to 49 years of age. All subjects had previously tampered with an opioid product, and oxycodone was reported as the preferred opioid. The most common routes of administration were oral ingestion of the intact product (45%), intranasal use (snorting), and oral chewing (25% each). The 4 most common tampering methods used previously were crushing (95%), removal of coatings or layers (80%), chewing, and dissolving in water for oral intake (75% each). None of the subjects would be willing to spend more than 1 hour tampering with a pharmaceutical product for abuse (Table 1).

Table 1. Time Willing to Spend Tampering (n=20)

	Unspecified pharmaceutical product for abuse	30 mg morphine or 15 mg oxycodone	200 mg morphine or 100 mg oxycodone
Time	*Number of subjects (%)*		
3 minutes	8 (40%)	9 (45%)	3 (15%)
10 minutes	8 (40%)	8 (40%)	5 (25%)
30 minutes	4 (20%)	3 (15%)	8 (40%)
1 hour	0	0	4 (20%)
≥ 3 hours*	0	0	0

Questions: In general, what's the maximum amount of time you'd be willing to spend tampering with [*a pharmaceutical product / 30 mg of morphine or 15 mg of oxycodone / 200 mg of morphine or 100 mg of Oxycodone*]? (select one).
* the options given in the questionnaire were: 3 hours, 10 hours, 24 hours, and more than 24 hours.

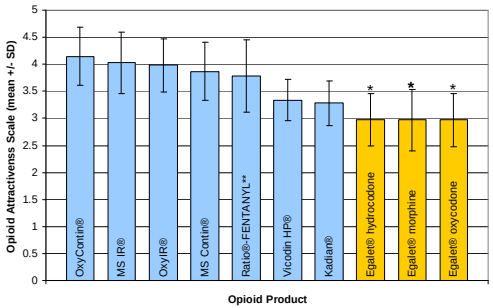

Figure 2. Opioid Attractiveness Scale (n=20)

Subjects were instructed to rate the attractiveness of each of 16 drug features on a 5-point verbal rating scale with the anchors 1=Extremely Unattractive to 5=Extremely Attractive. For each product the mean score was calculated by dividing the sum of scores by the number of items.

** Significantly different from all other opioid products (ANOVA, p≤0.003). Egalet® products did not differ from one another.*

*** Ratio®-FENTANYL transdermal patch.*

For all scales including OAS, VPS, LTS, and the VPS-LTS index (cross product of VPS and LTS), the Egalet® opioid products were ranked lowest (Figure 2,3). Likewise, for Overall Desirability (Figure 4) and Estimated Street Value, the Egalet® opioids were ranked as the least desirable and as having the least street value. OxyContin® was consistently the most attractive or among the most attractive drugs. Other high ranking opioids were IR oxycodone and morphine products followed by ER morphine products.

DISCUSSION

The amount of time abusers would be willing to spend tampering has not previously been reported. In this study it was found that the higher the dose, the greater the willingness to spend time on tampering; yet regardless of dose the maximum duration of time subjects were willing to spend on tampering was 1 hour. This information is critical for choosing the appropriate design of in vitro studies to test tamper deterrence.

The study by Butler and co-workers [3] concluded that the OAS scale represents a significant tool in assessing what makes a prescription opioid attractive or unattractive for abuse and for identifying differences between different products. This study provided valuable information on the relative risk of abuse for the products tested, with the three Egalet® opioids having the lowest attractiveness.

However, drug users' preferences may be based on past experience [4], and factors such as availability, price, and formulation and dosage strengths may also have an impact on attractiveness. Since the Egalet® products are not yet available on the market, this may have contributed to the lower ranking compared to well-known products. However, the subject's opioid preference at baseline was not significant in any of the analyses.

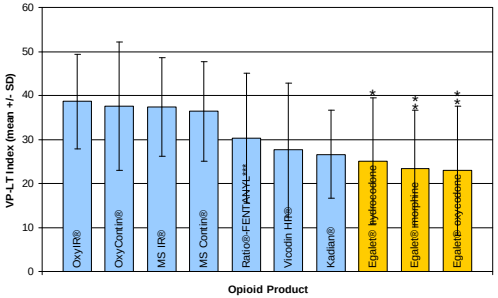

Figure 3. Value of Product – Likelihood to Tamper Index (n=20)

The Value of Product – Likelihood to Tamper Index was created as the cross product of the Value of Product scale ("[Product name] would be highly valuable to me") and Likelihood to Tamper scale ("I, or someone I know, would definitely tamper with [Product name]") both rated on a 7-point Likert scale with the anchors 1= Strongly Disagree to 7=Strongly Agree.

** Significantly different from OxyIR®, OxyContin®, MS IR®, and MS Contin® (ANOVA, p<0.001). Egalet® products did not differ from one another.*

*** Significantly different from OxyIR®, OxyContin®, MS IR®, MS Contin®, and Ratio®-FENTANYL (ANOVA, p≤0.017). Egalet® products did not differ from one another.*

**** Ratio®-FENTANYL transdermal patch.*

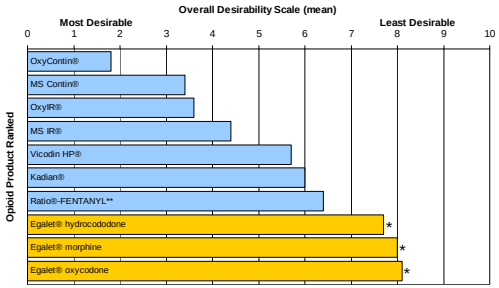

Figure 4. Subject Ranking of Overall Desirability (n=20)

Subjects ranked the products from most desirable (1) to least desirable (10) taking into account all information including the available strengths.

** Significantly different from all other opioid products (pairwise comparison by Wilcoxon rank-sum test, p<0.05) other than ratio®-FENTANYL. Variability was relatively large but similar for all products.*

*** Ratio®-FENTANYL transdermal patch.*

Rankings for Estimated Street Value were similar.

CONCLUSIONS

- The Egalet® opioids were found by recreational opioid users to be the least attractive of the opioid products included in the study
- No subjects would spend 1 hour tampering with a low-dose opioid product for abuse while 20% of subjects would spend up to 1 hour tampering with a high-dose opioid
- The Egalet® opioid products may be strong candidates for a novel abuse deterrent generation of opioid products

References

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[3] Butler SF, Benoit CM, Budman SH, et al. Development and validation of an opioid attractiveness scale: a novel measure of the attractiveness of opioid products to potential abusers. Harm Reduct J 2006;3:5

[4] Sellers EM, Schuller R, Myroslava K, et al. Relative abuse potential of opioid formulations in Canada: A structured field study. J Opioid Manage 2006;2(4):219-27