From The Medical Letter on Drugs and Therapeutics

A New Abuse-Deterrent Opioid—Xtampza ER

The FDA has approved Xtampza ER (Collegium), a new extended-release, abuse-deterrent capsule formulation of oxycodone, for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Abuse-Deterrent Opioids

Five other abuse-deterrent opioid formulations were approved earlier, three as single-drug products and two in combinations with opioid antagonists.[1] Two of these products, Morphabond (morphine ER) and Targiniq ER (oxycodone ER/naloxone), have not yet been marketed. Zohydro ER (hydrocodone ER) was reformulated in 2015 to make abuse more difficult, but it has not received FDA approval as an abuse-deterrent opioid. No studies are available comparing the relative safety of these products.

No opioid formulation prevents consumption of a large number of intact dosage units, the most common method of abuse. Abuse-deterrent formulations have one or more properties that make their intentional nontherapeutic use more difficult, less attractive, or less rewarding.

Table 1. Pharmacology

Formulation	9, 13.5, 18, 27, 36 mg capsules[a]
Route	Oral
Tmax	4.5 hours[b]
Metabolism	Hepatic mainly by CYP3A4 and to a lesser extent by CYP2D6
Elimination	Primarily in urine as metabolites
Half-life	5.6 hours[c]

[a] Of oxycodone base. Equivalent to 10, 15, 20, 30, 40 mg of oxycodone HCl.

[b] With food; 3 hours later than with immediate-release oxycodone.

[c] With food; half-life of immediate-release oxycodone is 3.2 hours.

Table 2. Some Abuse-Deterrent Opioid Formulations

Drug	Abuse-Deterrent Mechanism	Cost[a]
Hydrocodone ER		
Hysingla ER (Purdue)	Resists crushing and breaking; tablets form a viscous gel whendissolved	$215.80
Zohydro ER (Pernix)[b]	Contains excipients that form aviscous gel when capsules are crushed or dissolved	404.90
Morphine ER/naltrexone		
Embeda (Pfizer)	Contains sequestered opioid antagonist, which is released if capsules are crushed or dissolved	178.50
Oxycodone ER		
OxyContin (Purdue)	Resists crushing and breaking; tablets form a viscous gel whendissolved	188.80
Xtampza ER (Collegium)	Microspheres resist effects of crushing and chewing; melted or dissolved contents of capsules are difficult to inject	202.20

Abbreviations: ER, extended-release; WAC, wholesaler acquisition cost or manufacturer's published price to wholesalers.

[a] Approximate WAC for 30 days' treatment at the recommended starting dosage for patients who are not opioid tolerant. WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. June 5, 2016. Reprinted with permission by First Databank, Inc. All rights reserved. ©2016. www.fdbhealth.com/policies/drug-pricing-policy.

[b] Not FDA-approved as having abuse-deterrent properties.

Pronunciation Key

Xtampza: ex tamp' zah

The New Formulation

Xtampza ER is available in capsules containing microspheres formulated with oxycodone base and inactive ingredients that make the formulation more difficult to manipulate for the purpose of abuse. Each capsule contains 9, 13.5, 18, 27, or 36 mg of oxycodone (equivalent to 10, 15, 20, 30 or 40 mg of oxycodone HCl, respectively).

Pharmacokinetics

The oral bioavailability of Xtampza ER is greater when taken with food (Cmax increased by 100-150% and AUC by 50-60% with a high-fat meal) (**Table 1**). In one pharmacokinetic study, crushing Xtampza ER capsules did not increase the Cmax or the AUC of oxycodone compared to intact capsules when both were taken with a high-fat meal. Crushing the capsules also did not compromise the extended-release properties of Xtampza ER, unlike OxyContin abuse-deterrent tablets (**Table 2**), which lost their extended-release properties when crushed.[2] In another study, crushing and snorting Xtampza ER capsules following a high-fat meal resulted in lower peak serum concentrations of oxycodone than taking intact capsules.[3]

Clinical Studies

A 12-week, randomized, double-blind trial in 740 patients with moderate to severe chronic low back pain compared Xtampza ER with placebo. The maximum dose was 144 mg/day (equivalent to 160 mg of oxycodone HCl). Patients treated with the active drug had significantly lower pain scores from week 2-12 than those who received placebo.[4]

Adverse Effects

Nausea, headache, constipation, somnolence, pruritus, vomiting, and dizziness, all typical opioid side effects, occurred commonly in the clinical trial in patients treated with Xtampza ER.

Pregnancy

As with other opioid analgesics, prolonged use of Xtampza ER during pregnancy can cause neonatal opioid withdrawal syndrome. Oxycodone is excreted in breast milk and can cause opioid effects in breastfed newborns.

Drug Interactions

Oxycodone is metabolized mainly by CYP3A4 and to a lesser extent by CYP2D6. Administration of Xtampza ER concurrently with drugs that inhibit CYP3A4 (or discontinuation of CYP3A4 inducers) can increase serum concentrations of oxycodone and could be fatal. Concurrent use of CYP3A4 inducers could decrease oxycodone serum concentrations and the analgesic effect of the drug.[5]

Dosage and Administration

The recommended starting dosage of Xtampza ER for opioid-naive patients is 9 mg every 12 hours. The capsules must be taken with food; patients should consume the same amount of food with every dose in order to ensure consistent plasma levels. For patients who have difficulty swallowing the capsules, their contents can be sprinkled on soft foods or into a cup, and then given orally or through a gastrostomy or nasogastric tube. The maximum daily dose of Xtampza ER is 288 mg (equivalent to 320 mg oxycodone HCl). The package insert contains dosing instructions for conversion from other oxycodone formulations or other opioids. Patients with hepatic impairment starting Xtampza ER should take one-third to one-half the usual dosage; they should not take the drug if the required dose is <9 mg. Patients should be monitored for respiratory depression for 72 hours after either starting treatment or increasing the dose.

Conclusion

Xtampza ER is the second extended-release abuse-deterrent formulation of oxycodone. How it compares to the abuse-deterrent formulation of OxyContin for prevention of misuse is unknown. Whether use of abuse-deterrent opioid products actually reduces overall opioid abuse remains to be determined.

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