

FDA Gives 'Tentative' Approval to Abuse-Deterrent *Xtampza ER*

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The US Food and Drug Administration (FDA) has granted tentative approval of an extended-release abuse-deterrent oxycodone (*Xtampza ER*, Collegium Pharmaceutical Inc) for the management of chronic pain, the company has announced.

The tentative go-ahead follows the [unanimous decision](#) of the FDA's Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee in September to support approval of the product for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternatives are inadequate.

The approval of the New Drug Application (NDA) is tentative because while the FDA has determined that the drug meets all of the required quality, safety, and efficacy standards for approval, patent litigation filed earlier this year by Purdue Pharma LP means that it is subject to an automatic stay of up to 30 months, the company notes in their statement.

Purdue claims that *Xtampza ER* infringes three Orange Book-listed patents that were recently found to be invalid by the US District Court for the Southern District of New York and are currently under appeal, according to the press release. If Collegium receives a court order that the listed patents are invalid or not infringed, or if Collegium settles the Purdue litigation before the expiration of the 30-month period, the FDA can then provide final approval of *Xtampza ER*, at which point the product can be marketed, it said.

"We are very pleased that the FDA has granted tentative approval for *Xtampza ER*," said Michael Heffernan, chairman and CEO, Collegium, in a press release. "The FDA has recognized that *Xtampza ER* has abuse-deterrent properties consistent with FDA's final guidance titled, *Guidance for Industry: Abuse-Deterrent Opioids — Evaluation and Labeling*."

"We remain confident that *Xtampza ER* does not infringe the three patents that Purdue has asserted against us," said Heffernan. "We intend to vigorously defend ourselves against these claims."

The products novel abuse-deterrent technology may offer an alternative for patients with chronic pain who have trouble swallowing. During the advisory committee meeting, representatives from the Canton, Massachusetts, based Collegium showed that the medication could be given by breaking open the capsule and pouring the oxycodone microspheres into a feeding tube or sprinkling them onto soft food or directly into the mouth.

"We've seen data suggesting the prevalence of dysphagia is substantial in chronic pain patients," said panelist Brian Bateman, MD, MSc, assistant professor of anesthesia at Harvard Medical School, during the advisory committee review. "This will meet that clinical need."

Unlike the abuse-deterrent form of *OxyContin* (Purdue), *Xtampza ER* does not get sticky when wet and cannot be transformed into an immediate-release form, even if it is crushed or chewed.



Xtampza ER microspheres. Courtesy Collegium Pharmaceutical

Committee members also said that the company had convincingly proven that this formulation would prevent abuse by inhalation or injection. "The abuse deterrence is very promising," said Anita Gupta, DO, PharmD, vice chair of the Division of Pain Medicine and Regional Anesthesiology at Drexel University College of Medicine, Philadelphia, Pennsylvania. "It's progress in the right direction."

Abuse Deterrence

After crushing and/or dissolving a prescription analgesic drug, abusers try to take it orally or snort or inject it to rapidly release the drug and get a "high." Collegium developed Xtampza using its proprietary *DETERx* technology platform to address these common methods of abuse.

Xtampza ER may also be beneficial for well-meaning patients and loved ones, Bill McCarberg, MD, a founding member of the Chronic Pain Management Program at Kaiser Permanente and president of the Western Pain Society, said in the press release. "Patients or their caregivers often inadvertently crush their medication to facilitate swallowing, which is dangerous with currently marketed ER products."

With a final approval, this new product may provide a unique ER, abuse-deterrent treatment option for the large unmet need of patients with chronic pain and dysphagia, said Dr McCarberg.

Such an approval would make Xtampza ER the fifth approved abuse-deterrent ER opioid. The others are OxyContin, *Targiniq* (oxycodone and naloxone extended-release tablets; Purdue), *Embeda* (morphine sulfate and naltrexone ER capsules; Pfizer), and *Hysingla ER* (hydrocodone ER tablets; Purdue).

Collegium conducted several studies — including in vitro pharmacokinetic studies and randomized human trials — to prove the safety and efficacy of Xtampza ER and to show that its abuse-deterrent technology worked.

The FDA's main concern was whether patients would follow directions to take the medication with food. Less bioavailability with fasting created the potential for adverse events, including overdose.

To better assess how the drug would work in the real world, the company conducted a phase 3 enriched-enrollment, randomized withdrawal, double-blind, placebo-controlled trial comparing Xtampza ER with placebo. The 193 Xtampza ER recipients and 196 placebo patients were opioid-naïve or opioid experienced and had moderate-to-severe, chronic lower-back pain for at least 6 months. Those taking Xtampza ER had statistically significantly lower pain scores after 12 weeks.

Patients also kept meticulous electronic food diaries. The company concluded that medication effectiveness varied little with different diets. And no adverse events were associated with either eating or not eating.

Members of the advisory panel [voted 23 to 1 against](#) allowing Purdue Pharma's *Avridi*, the first immediate-release oxycodone tablet to come with abuse-deterrent properties. The panel recommended that the FDA decline approval on the basis of concerns that delayed analgesia due to the antiabuse technology seen when it was taken with food may lead to increased overdose risk.