

FDA Approval of Extended-Release Oxycodone for Children With Severe Pain

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In a highly controversial decision, the Food and Drug Administration (FDA) approved, in August 2015, extended-release oxycodone for use by children between 11 and 16 years old with “pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate.”¹ For the first time, doctors are provided specific dosing guidance for pediatric patients who must already be responding to and tolerating a minimum opioid dose equal to at least 20 mg oxycodone per day before they can be prescribed an equivalent dose of extended-release oxycodone.¹ With this decision, on-label prescribing of extended-release oxycodone to children has become a possibility. Previously, it was only prescribed off-label in the pediatric setting, even though the practice was common and generally accepted. Although the potential risks of increased opioid addiction and abuse among youth are a legitimate concern, they are outweighed by the tangible benefits of the new pediatric safety and dosing instructions. The approval provides health care practitioners with evidence-based information to use extended-release oxycodone more safely in pediatric patients.

DIVERSE PERSPECTIVES

Extended-release oxycodone allows dosing every 12, as opposed to every 4 to 6 hours.¹ In pediatric patients who require opioid treatment to manage pain, extended-release opioids may be a useful alternative because they require fewer doses per day. Reduced complexity in dosing may in turn help improve medication adherence and quality of life.² For patients experiencing inadequately controlled chronic severe pain, use of long-acting prescription opioids may help to provide more effective pain relief.²

Since the 1990s, the FDA has encouraged pharmaceutical companies to conduct clinical trials to determine safety and efficacy of their drugs in children.¹ One such incentive is a short-term extension of patent exclusivity for products specifically approved by the FDA for pediatric use. In this study, the manufacturer investigated extended-release oxycodone for prolonged use among children who experienced significant trauma or severe pain from cancer or after major surgeries.³ The analysis

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ultimately fully supported such indications in children aged 11 to 16 years, and provided additional and specific information regarding proper prescription.³

For the FDA, the approval serves 2 purposes: curbing the current practice of off-label prescription to children, and providing prescription guidelines informed by clinical trials specifically designed for children.³ Off-label prescribing, without specific instructions for pediatric use, may not only adversely affect patient health, but may also increase inadvertent overprescription of a powerful opioid.

Previously, physicians relied on their own experiences and results of clinical trials with adult subjects when prescribing extended-release oxycodone to children. "Since the drug was [already] being used to treat children, we wanted prescribers to have the information they needed to ensure safety and efficacy," said an FDA spokesman.⁴ The FDA believes that the approval will lead to more responsible and educated prescribing of an opioid in a particularly vulnerable population.

Yet, the recent approval also elicited sharp criticism from some elected officials (eg, Vermont governor⁵) and addiction specialists (eg, director of Physicians for Responsible Opioid Prescribing⁴) concerned about prescription opioid misuse. Half of drug overdose deaths, the leading cause of injury death in the United States, are due to prescription drugs; almost three-quarters of which involve opioids.⁶ The National Institute on Drug Abuse noted a connection between opioid use and heroin addiction. Nearly three-quarters of new heroin users initially began using prescription opiates for nonmedical reasons.⁶

Another concern is that adolescents may be even more susceptible to opioid addiction than adults.⁴ Surveys show that young people

underestimate the power of prescription opiates.⁷ Moreover, 70% of people, and more than half of teens, who have misused prescription opiates obtained these drugs from a patient to whom they were prescribed.⁷ Although the FDA has stressed the importance of secure location, there is limited ability to enforce safe storage of extended-release oxycodone once it is prescribed.

The oft-unstated concerns of the critics are that the pediatric-specific approval will allow the manufacturer to target doctors to promote the use of extended-release oxycodone among children.⁴ Under the Federal Food, Drug, and Cosmetic Act, it is legal for pharmaceutical companies to promote their products only for on-label use. Although the manufacturer has promised that it will not promote extended-release oxycodone to pediatricians or other physicians, critics remain concerned about increased opioid misuse given the legality of on-label promotion of pediatric use of extended-release oxycodone.⁴

MEASURES REDUCING OPIOID MISUSE

Allaying fears of, and addressing the potential for, opioid abuse are therefore of utmost importance. The FDA has encouraged reformulation of the original extended-release oxycodone to better resist being crushed or dissolved to deter abuse by nasal or intravenous routes.¹ In the 2 years after the manufacturer's reformulation, abuse of extended-release oxycodone declined, while abuse of generic oxycodones increased.¹ The FDA has announced that it will no longer accept applications for generic versions of extended-release oxycodone.¹ The FDA has also implemented numerous Risk Evaluation and Mitigation Strategies and relabeled the package inserts for opioids.¹ Additionally, the FDA continues to work with

state policymakers and the Obama administration to combat opioid abuse, including better education and prevention strategies.⁶

The FDA has also required the manufacturer to conduct postapproval analyses, mandating a comprehensive analysis and annual reporting for 3 years of adverse events, such as respiratory depression, overdoses, and accidental exposure, in pediatric patients.¹ The manufacturer also will have to report nationally representative data on the volume of and indications for pediatric prescription of extended-release oxycodone, as well as the types of prescribing clinicians.¹ The postmarketing data, much more comprehensive than any data that could have been gathered through off-label prescriptions, could help us better address the problem of prescription drug abuse in adolescents.

CONCLUDING THOUGHTS

The FDA approval would unlikely expand the pattern of use of the medication or increase misuse.¹ For years, extended-release oxycodone has already been prescribed off-label to extremely ill children in severe pain from cancer, major surgeries, or other trauma. Children are not treated with opioids very often and they are usually prescribed only for a limited period of time under close supervision by health care professionals. Moreover, the new label specifies that extended-release oxycodone should be used only for children 11 years or older in severe pain who have already been on an opioid for at least 5 days.¹ It is not supposed to be prescribed to children as a first-line opioid or for short-term pain.

The FDA acknowledges that the approval represents a delicate balance between evidence-based safe use and potential misuse of opioids. As one FDA official noted,

“the point is that seriously ill children deserve evidence-based medicine. They shouldn’t be experimented on...”⁴ A pediatric oncologist minced no words: “Just because extended-release oxycodone has been abused or prescribed inappropriately doesn’t mean we should deprive the children who need the drug ... [it is] our obligation to have the best level of evidence for its use in children.”⁴

The FDA approval is a step in the right direction for medication safety. Children and teens with severe pain will now have an additional on-label treatment option, with specific dosing guidance supported by clinical trials. Although critics of the FDA decision are concerned about the potential for abuse, physicians and communities must do their part to prevent overuse and misuse through proper prescribing, increased education, and safe storage of opioids within the home.

ABBREVIATION

FDA: Food and Drug Administration

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