

HEALTH

Reformulated opioids thwart misuse of the painkillers

The new tablets are harder to crush. Recent studies have found that substance abusers are steering clear of the drug.

By KEVIN B. O'REILLY, amednews staff. Posted Jan. 14, 2013.

More evidence is emerging to show that tamper-resistant formulations of extended-release analgesic opioids are improving public health by discouraging abuse.

The results should provide some reassurance to physicians concerned about the potential misuse of opioids by their patients, say doctors who specialize in pain treatment and addiction medicine.

Opioids contribute to an estimated 15,000 U.S. deaths and more than 340,000 emergency department visits annually, according to the Centers for Disease Control and Prevention.

Prompted by appeals from physicians and officials at the Food and Drug Administration for a harder-to-abuse pill to ease what many see as a public health crisis, drugmaker Purdue Pharma in August 2010 launched a tamper-resistant form of its best-selling painkiller oxycodone, marketed as OxyContin.

The change has made a dent in misuse of the drug, research shows. A study in the July 12, 2012, issue of *The New England Journal of Medicine* surveyed 103 patients entering U.S. treatment programs between 2009 and 2012. Before the crush-resistant form of oxycodone was marketed, 36% chose it as their primary drug of abuse. By 2012, just 13% said they principally abused oxycodone.

A much larger study, published Nov. 3, 2012, in the American Pain Society's *The Journal of Pain*, echoes the findings. Researchers examined surveys taken by more than 140,000 patients admitted to 357 U.S. treatment centers between June 2009 and March 2012. Among patients who said they abused a prescription opioid, the proportion misusing extended-release oxycodone fell by half, from 24% to 12%. Non-oral abuse through snorting, smoking or injection fell by 71%, said the study, which was funded in part by Purdue Pharma and Inflexxion Inc., a pharmaceutical risk-management corporation that developed the study assessment.

How tamper resistance works

Misuse of the reformulated drug is not impossible, but it is more difficult, said Simon H. Budman, PhD, co-author of the study in *The Journal of Pain* and CEO of Inflexxion.

"If there's a will, there's a way," he said. "If you really want to abuse these drugs, you can, but it may be time-consuming, quite inconvenient and you may lose a lot of that active ingredient."

He compared the traditional oxycodone pill to aspirin — easy to crush. The tamper-resistant pill is more like Skittles candy when smashed.

"If you take the reformulated product and hit it with a hammer, it becomes a flat tablet but not a fine powder," Budman said. "You don't get very far with that. ... The active molecule is embedded within those polymers and dissolves as it goes through the digestive tract."

Oral misuse of long-acting oxycodone — that is, simply swallowing more pills — also fell by 27%, *The Journal of Pain* study found. Yet researchers discovered that people intent on abusing opioids switched to the nonresistant, extended-release form of oxymorphone, marketed as Opana by Endo Pharmaceuticals. Abuse of that drug skyrocketed by 196%, to 5.5% of opioid abusers, after the abuse-deterrent oxycodone was launched.

In March 2012, Endo released its own tamper-resistant formulation of oxymorphone. In a Nov. 30, 2012, news release, the company cited surveillance data on substance abusers and from U.S. poison control centers showing a 59% decline in misuse of its crush-resistant pill.

Meanwhile, Michael Schiesser, MD, an addiction-medicine specialist in Bellevue, Wash., said the tamper-resistant prescription opioids have sparked an upsurge in the use of an illicit opiate — heroin.

A "no-brainer" alternative

When physicians decide that a long-acting opioid analgesic is the right choice for a patient, prescribing these new abuse-deterrent formulations "should be a no-brainer" in terms of public health effects, said Lynn R. Webster, MD, president-elect of the American Academy of Pain Medicine.

"You cannot, *a priori*, determine who is going to abuse the drug and, more importantly, you can't tell when the drug is going to be diverted to nonmedical use," Dr. Webster said. "Sixty percent of the drugs used nonmedically are diverted, stolen or given away. So don't just give it to high-risk patients. You have to give it to all patients so that if it is diverted, then that other

population is somewhat protected.”

Abuse-deterrent formulations could help reduce hepatitis C, HIV and other injection-related diseases as well as overdose deaths, said Andrew Kolodny, MD, chair of the Dept. of Psychiatry at Maimonides Medical Center in New York City and president of the advocacy group Physicians for Responsible Opioid Prescribing. He said the FDA should require all long-acting opioid tablets on the market to have some form of abuse deterrence.

In December 2012, a federal judge dismissed Endo’s lawsuit against the FDA that sought to prevent approval of a generic form of oxycodone that is not crush-resistant. The company had argued that form of the drug is unsafe and asked the agency to decide on the matter before the generic hit the market on Jan. 1. The FDA says it will decide on that matter by May. U.S. District Judge Reggie B. Walton agreed with the agency that putting off the decision until then does not constitute an undue delay.

Although the abuse-deterrent painkillers provide doctors and patients with a better alternative, Dr. Kolodny said they are insufficient to address what he termed an “epidemic” of opioid overprescribing.

“Many prescribers may assume that the tamper resistance makes them less addictive, which is totally false and could potentially lead to more overprescribing and more new cases of opioid addiction,” he said. “Tamper-resistant formulations are a very small part of the solution.”

ADDITIONAL INFORMATION:

The impact of opioid tamper-proof tables

Among opioid-abusing patients seeking treatment for substance-use disorders, misuse of extended-release oxycodone fell by half after a reformulated, abuse-resistant version came on the market in August 2010. Oral and nonoral forms of abuse declined.

Type of abuse	Drop in abuse
Any form	49%
Ingested orally	27%
Administered nonorally	71%

Source: “Abuse Rates and Routes of Administration of Reformulated Extended-Release Oxycodone: Initial Finding From a Sentinel Surveillance Sample of Individuals Assessed for Substance Abuse Treatment,” *The Journal of Pain*, Nov. 3, 2012 (www.ncbi.nlm.nih.gov/pubmed/23127293/)

WEBLINK

“8 Reliable Principles to Safe Opioid Prescribing,” American Medical Association webinar, Nov. 1, 2012 (eventcenter.commpartners.com/se/Meetings/Playback.aspx?meeting.id=222877)

“Effect of abuse-deterrent formulation of OxyContin,” *The New England Journal of Medicine*, July 12, 2012 (www.ncbi.nlm.nih.gov/pubmed/22784140/)

“Abuse Rates and Routes of Administration of Reformulated Extended-Release Oxycodone: Initial Finding From a Sentinel Surveillance Sample of Individuals Assessed for Substance Abuse Treatment,” *The Journal of Pain*, Nov. 3, 2012 (www.ncbi.nlm.nih.gov/pubmed/23127293/)

Copyright 2013 American Medical Association. All rights reserved.

RELATED CONTENT

- » **Chronic pain medicines should come with behavioral pacts** Jan. 14
- » **Are opioids only for patients with “severe pain”?** Aug. 20, 2012
- » **FDA opioid safety plan focuses on physician education** July 23, 2012
- » **More newborns showing ill effects of maternal opioid use** May 21, 2012
- » **Prescribing opioids after minor surgery can lead to long-term use** March 26, 2012
- » **More help sought to fight opioid abuse** Nov. 28, 2011