



Abuse Deterrent Formulations in the States

Abuse deterrent opioids are a recent reformulation of necessary pain medication that uses new technology to reduce or deter abuse of the medications through various means such as making the medication harder to crush and snort or melt and inject. The FDA has endorsed the development of these new reformulations of pain medications as a high public health priority. To date, there are 5 pain medications that have been approved with the FDA's Abuse Deterrent Formulation label, and there are around 30 others in development or awaiting the FDA's review.

To date, 3 states have passed legislation that ensures opioids with ADF technology are treated "no less favorably" than those without it. This legislation provides states with another tool to fight prescription drug abuse, improve the public health of their communities, and ultimately save lives.

Massachusetts Abuse-Deterrent Opioid Law – Passed in August 2014

The provisions of the Massachusetts law on abuse-deterrent opioids was part of a larger piece of legislation dealing with substance abuse recovery; the legislation required an existing state commission (the Massachusetts Drug Formulary Commission) to create a drug formulary of interchangeable abuse-deterrent opioids that are chemically equivalent substitutions for non-abuse-deterrent opioid drugs. The Commission was charged with reviewing information in the drug applications made to the U.S. Food and Drug Administration and other regulatory guidance when making its determination of substitution.

Upon publication of the Drug Formulary Commission's list of interchangeable abuse-deterrent drugs, the law requires: 1) Pharmacists to dispense an interchangeable abuse-deterrent drug unless a physician has indicated that a substitution should not be made; 2) Insurance carriers to cover abuse-deterrent drugs listed on the formulary in the same manner that they cover non-abuse-deterrent drugs; and 3) Insurance carriers to refrain from imposing additional cost burdens on consumers who receive abuse-deterrent drugs.

Maryland Abuse-Deterrent Opioid Law – Passed in May 2015

The provisions of the Maryland law require insurers to provide coverage for: at least two branded abuse-deterrent opioids (containing different analgesic ingredients) on the lowest cost tier for brand name prescription drugs covered by the insurer; and at least two generic abuse-deterrent opioids (containing different analgesic ingredients) on the lowest cost tier for generic drugs covered by the insurer.

The law also prohibits insurers from requiring use of an opioid analgesic without abuse-deterrent properties prior to providing coverage for an abuse-deterrent opioid, as defined in the law. However, insurers still retain the right to use utilization review, including prior authorization, prior to approving coverage for an abuse-deterrent opioid as long as the same utilization review criteria are applied to the coverage of opioids without abuse-deterrent properties.

Under the law, an abuse-deterrent opioid is defined as a brand or generic opioid analgesic drug product approved by the federal Food and Drug Administration with abuse-deterrent labeling claims that indicate the drug product is expected to result in a meaningful reduction in abuse.

The law applies to all health insurance policies issued or renewed on or after January 1, 2016.

Maine Abuse-Deterrent Opioid Law – Passed in August 2015

The Maine law requires that all health insurance carriers offering individual and group health plans in the state to cover abuse-deterrent opioid analgesic drug products as preferred drugs on any formulary, preferred drug list, or other list of drugs used by the carrier.

Coverage for abuse-deterrent opioid analgesic drug products must be provided on a basis not less favorable than that for opioid analgesic drug products that are not abuse-deterrent covered by a health plan.

The law applies to brand or generic opioid analgesic drug products approved by the FDA with abuse-deterrent labeling claims that indicate the drug product is expected to result in a meaningful reduction in abuse.

The terms of coverage for abuse-deterrent opioid analgesic drug products, which includes cost sharing and utilization management requirements, must be at parity with the coverage terms of non-abuse-deterrent opioid analgesic drug products covered by a health plan. Insurers cannot increase enrollee cost sharing to achieve compliance with the legislation.

The law applies to all policies and contracts issued or renewed on or after January 1, 2016.

Overview of FDA Guidance for Industry: Abuse-Deterrent Opioids – Evaluation and Labeling¹

- FDA considers the development of opioid analgesic drug products with abuse-deterrent properties a high public health priority.
- For purposes of the guidance, FDA defines **abuse-deterrent properties** as those properties shown to meaningfully deter abuse, even if they do not fully prevent abuse.
- FDA will allow labeled abuse-deterrent properties and associated claims if 1) the product has attributes intended to discourage its abuse that have undergone studies in one or more FDA-specified categories, **and** 2) the results of those studies meet or exceed the current FDA performance criteria and, therefore, are expected to result in or have demonstrated a meaningful reduction in its abuse.

In April 2015, FDA released its Guidance for Industry¹ to provide a framework for a) how to conduct studies of drug products designed to be abuse-deterrent, and b) how FDA will evaluate study results to allow labeled abuse-deterrent properties and associated claims of potential or proven impact on the product's abuse.

Examples of abuse-deterrent technologies¹:

- 1. Physical or Chemical Barriers** – barriers to prevent chewing, crushing, cutting, grating, or grinding, or barriers that resist extraction of the opioid from the formulation using common solvents like water or alcohol. Physical and chemical barriers can change the physical form of an oral drug to make it less amenable to abuse.
- 2. Agonist/Antagonist Combinations** – additives that can interfere with, reduce, or defeat the euphoria associated with abuse. For example, an antagonist can be walled off and only released when the product is manipulated for abuse.
- 3. Aversion** – drug substances can be combined with noxious substances in such a way as to produce an unpleasant effect if the dosage form is manipulated or a higher dosage than directed is used.
- 4. Delivery System** – certain drug release designs or methods of drug delivery that can offer resistance to abuse.
- 5. New Molecular Entities (NME) and Prodrugs** – NMEs could cross the blood-brain barrier slowly, reducing euphoria. A prodrug could lack opioid activity until it has undergone transformation in the gastrointestinal tract and, therefore, would be unattractive for intranasal or intravenous abuse.
- 6. Combination** – two or more of the above methods could be combined to deter abuse.
- 7. Novel Approaches** – novel approaches or technologies to deter abuse that are not captured in the previous categories.

The FDA Guidance designates four categories of studies to evaluate abuse-deterrent characteristics of an opioid analgesic drug product:

Category of Study	Description of Study	Primary Purpose of Study
Category 1	Laboratory (in vitro) Manipulation and Extraction Studies	Evaluate the ease of defeating physical and chemical properties of the formulation
Category 2	Pharmacokinetic (PK) Studies	Compare PK profiles of intact and manipulated product with those of a suitable comparator
Category 3	Clinical Abuse Potential Studies	Assess abuse-related measures (eg, drug liking, willingness to take again)
Category 4	Postmarket (Epidemiology Studies)	Assess real-world impact using post-marketing outcome data

In general, information on labeled abuse-deterrent properties and associated claims will be found in the Summary at the end of Section 9.2 of the drug product's "Full Prescribing Information" and will be based on data from more than one category.

¹ FDA Guidance for Industry: Abuse-Deterrent Opioids – Evaluation and Labeling, April 2015
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334743.pdf>

Rally shines a light on issue that needs it

by The Oklahoman Editorial Board Published: September 4, 2015

MOTOR vehicle accidents take hundreds of lives in Oklahoma every year, which is one reason why newspapers and other media outlets regularly report on them. Readers and viewers can relate — after all, so many people drive the state's roads and highways every day for work or pleasure.



Gail Box, whose son died from a prescription drug overdose, speaks Monday at a rally at the state Capitol. [Photo by Jim Beckel, The Oklahoman]

Yet we hear far less about a greater killer: drug overdoses, particularly those involving prescription drugs. The lower profile is understandable, given that these deaths generally occur in private settings and family members are reluctant to let others know that an overdose is what claimed their loved one. But it merits real attention: Oklahoma has a major prescription drug problem!

This was one of the messages from a rally Monday at the state Capitol, hosted by the state Health Department and the Coalition Against Rx Drug Epidemic (CARE). The rally was meant to raise awareness and provide resources for those whose lives have been affected by prescription drug abuse.

How bad is it? A report this year by Trust for America's Health ranked Oklahoma sixth-highest for drug overdose deaths, at a rate of 20 per 100,000 people. Since 2003, Oklahoma has seen the number of overdose deaths from powerful prescription drugs more than double, and the number of deaths from painkillers hydrocodone and oxycodone more than quadruple.

A state Health Department analysis found that from 2007 to 2012, more overdose deaths in Oklahoma involved hydrocodone or oxycodone than alcohol, meth, cocaine, heroin and all other illicit drugs combined.

One leader of the awareness effort is Gail Box, whose son Austin died of an overdose four years ago. A University of Oklahoma football player, Box had five prescription painkillers and an anti-anxiety drug in his system when he died. He had been prescribed a limited amount of painkillers after injuring his back in 2010. His dependence grew; his parents never knew there was a problem.

Gail Box said Monday there is guilt in not having recognized signs of the addiction, but that she also wishes her son would have felt he could tell her he had a problem.

"I think that we put so much shame on those suffering from addiction," she said. "We need to lift that veil of shame. We need to let people know it's OK to ask for help."

We see that veil of shame in the state's efforts to address its many mental health challenges. There is a stigma associated with telling a friend that you're feeling depressed, or that you're seeing a doctor for a mental health issue, or that a loved one died by suicide. Getting past that stigma is paramount if real strides are to be made.

The same is true with prescription drug abuse. It's OK to ask for help. Former Oklahoma State basketball coach Sean Sutton, who became addicted to prescription drugs, says he has a responsibility to educate others — "people that might be trapped or stuck in addiction, that there's a way out, that you can't do it alone," he said in a 2013 interview.

Monday's rally placed a spotlight on a problem that's usually in the shadows. But prescription drug abuse takes too great a toll on Oklahomans and their families to remain there. If you have a problem, or know someone who may, the 211 help line can offer referrals. Don't wait another day.