



FDA Perspective on Development of Abuse Deterrent Opioids: Have They Made Difference?

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The opinions and information in this presentation are my own and do not necessarily reflect the views and policies of the FDA

Outline

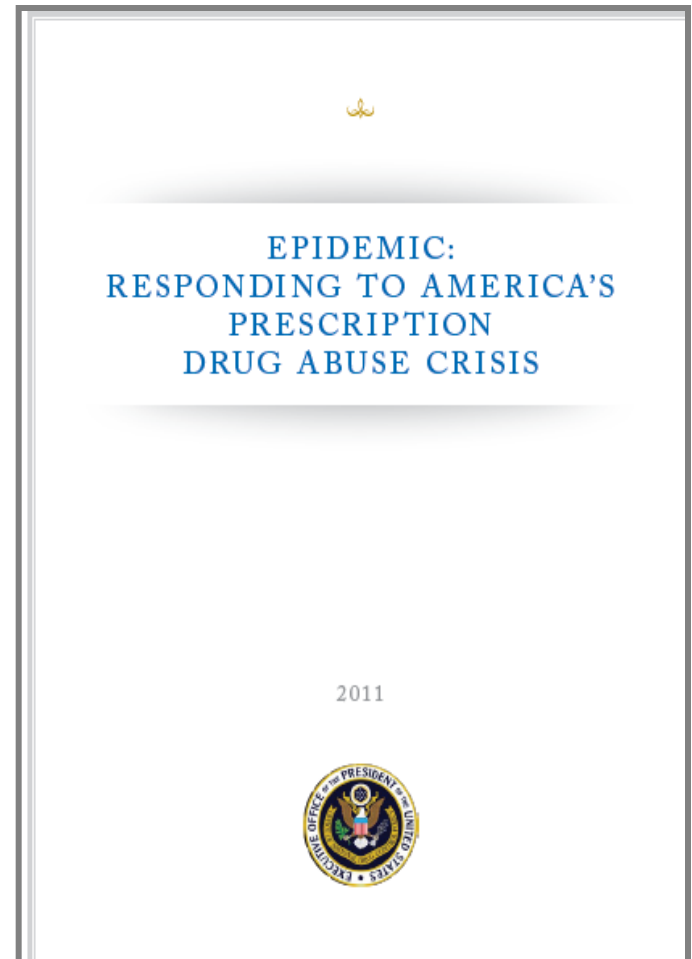
- Context: FDA Efforts to Address Prescription Opioids Abuse
- Supporting the Development of Abuse-Deterrent Formulations of Opioids
 - Policy Framework and Goals
 - Draft Guidances
 - Remaining Scientific, Policy and Process Issues
- Have Abuse-Deterrent Formulations of Opioids Made a Difference?
- Where are we Headed?

Overall Message

- The work on abuse-deterrent formulations of opioids is taking place within a larger policy framework aimed at addressing opioid abuse
- Use of abuse deterrent formulations is still limited, impacting the assessment of their actual impact on abuse and misuse
- FDA remains committed to incentivizing development and use of abuse-deterrent formulations of opioid as one part of the larger strategy by FDA and HHS to confront opioid abuse

FDA Part of Larger Governmental Response to Opioids Abuse

- Issued April 2011 - National Drug Abuse Prevention Plan
- Four major areas of focus to reduce prescription drug abuse and other harm from drugs
 - Education
 - Monitoring
 - Proper medication disposal
 - Enforcement





FDA Support for HHS Secretary's Initiative to Combat Opioid Abuse

- Improving opioid prescribing practices to reduce opioid use disorders and overdose
- Expanding use and distribution of naloxone
- Expanding Medication-assisted Treatment (MAT) to reduce opioid use disorders and overdose

FDA Public Health Goals for Improved Use of Prescription Opioids

- Provide appropriate access to pain treatments for patients, including opioids drugs
- Reduce the misuse and abuse of prescription opioids



FDA Activities to Improve Safe Use of Opioids and Reduce Prescription Opioid Abuse

- Improving the use of opioids through careful and appropriate regulations
- Improving the use of opioid through education of prescribers and patients
- Improving the safe use of opioids through partnership and collaboration
- **Improving the treatment of pain through improved science**



Drugs

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Drug Safety and Availability

Information by Drug Class

Resources for You

- [Opioid Medications](#)
- [Timeline of Key Opioid Actions](#)
- [Questions and Answers: REMS for Extended-Release and Long-Acting Opioids](#)
- [FDA Encourages Prescribers to Seek Training to Safely Prescribe Opioids](#)

Attention Prescribers: FDA seeks your help in curtailing the U.S. opioid epidemic

FDA is asking all prescribers of opioids to ensure they have thorough knowledge of the FDA-approved product labeling for the opioids they prescribe, and to ensure they have adequate training in opioid therapy. Below is our Open Letter to prescribers. We encourage all prescribers to help curb our nation's opioid epidemic!

[View and print full article - Attention Prescribers: Curtailing Opioid Epidemic \[PDF - 137KB\]](#)

Summary & Introduction	Take Training	Know Opioid Labels	Key Label Examples	Educate Patients	Conclusion
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Summary

- In light of the expanding opioid epidemic in the U.S., FDA urges prescribers to take advantage of training on opioid prescribing, available as of March 1, 2013. This voluntary training will be provided at little to no cost through accredited continuing education activities supported by independent education grants.
- Taking advantage of training opportunities on opioid therapy, now and in the future, is one of three key roles that FDA sees for prescribers in helping to curtail this pervasive problem. The other two are: knowing the content of the most current drug labels for the opioids they prescribe, and educating patients about the appropriate use of opioids, their potential risks, and proper disposal techniques.
- FDA-approved drug labels are frequently updated based on additional science, new benefit-risk information, or public health implications regarding the medication. Labels of extended release and long-acting opioid drugs were changed in July, 2012.



Introduction

Misuse and abuse of prescription opioids has reached epidemic proportions in the U.S. While much of the problem is attributable to illicit use, appropriate use of medications for pain may also lead to unnecessary adverse events, addiction, and death for some patients. *No group can be more effective in reducing this trend than our nation's front-line health care professionals, especially physicians and other prescribers.*

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Improving the Development and Use of Abuse-Deterrent Formulations of Opioids

Twin Goals for Abuse Deterrent (AD) Formulations of Opioids

- Incentivize the development of opioid medications with progressively better abuse-deterrent properties and support their widespread use
- Assure appropriate development and availability of generics, reflecting their importance in US healthcare

Essential Features of Successful AD Formulations

- The product must deliver a consistent and effective dose of opioid when used as labeled
- The product's potentially abuse-deterrent properties can be expected to, or actually does, result in a significant reduction in that product's abuse potential
 - Two stages
 - Labeling must be based on scientific data
 - Labeling based on pre-market studies needs confirmed using post-market data



Regulatory Activities Related to AD Opioids

Developing Guidance on AD Formulations

- Advisory Committees
 - Topic at several meetings: 2008 through 2014
 - Meeting on Draft Guidance in 2014
 - Tone generally conservative about data needed to conclude a new formulation is abuse-deterrent
 - <http://www.fda.gov/drugs/newsevents/ucm408607.htm>
- Public/Congressional interest in issue pronounced....

Guidance on AD Opioid Formulations

- Promised as part of Office of National Control Policy (ONDCP) Rx Drug Abuse Plan (2011)
 - Draft guidance release for comment: January 9, 2013
 - Final Guidance released April, 2015
 - <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm334743.pdf>

Regulatory Activity Related to AD Opioids: Development

- 5 products given abuse-deterrent claims in label
 - OxyContin (oxycodone, crush/extraction resistant):
April, 2013
 - Targeniq (oxycodone hydrochloride and naloxone, naloxone aversive): July, 2014
 - Embeda (morphine/naltrexone, naltrexone is aversive/precipitates withdrawal when abused):
October, 2014
 - Hysingla (hydrocodone, crush/extraction resistant):
November, 2014
 - MorphaBond (morphine sulfate, crush/extraction resistant): October, 2015

Regulatory Activity Related to AD Opioids: Development (Cont)

- Manufacturers working on new technologies:
- >30 active INDs being discussed with CDER
 - New technologies being explored

Next Steps: Generics Abuse-Deterrent Opioids Guidance

- Generic products represent a significant fraction of all prescriptions in the US today
- No current guidance for ANDA sponsors or reviewers
- A generic opioid product should be no less abuse-deterrent than its RLD under the manipulation conditions and routes of abuse that are practiced by drug abusers
 - This will ensure abusers do not seek out generics as easier to abuse



Assessment Activities Related to AD Opioids

Need for Assessment

- Current labels based on clinical and in vitro data to predict the formulation will reduce abuse
- Real-world assessment needed (and ongoing)
- **DECIDE WHAT WORKS AND WHAT DOESN'T**

Assessment: Market Challenges

- Opioids market still dominated by non-AD formulations
- Market Share for AD Opioids limited:
 - AD formulation of OxyContin made up around 25% of the ERLA opioids market in 2014
 - ERLA opioids comprised around 10% of the total opioids market
 - Other AD opioids with limited market share to date

Assessment: Data Challenges

- Databases often don't collect information on individual products (e.g., generic vs brand name) and formulations (e.g., liquid, solid oral, patch)
- Patients abuse multiple products (and substances)
- Many other activities going on to address prescription opioid abuse, complicating conclusions about cause and effect



Future for AD Opioids

Future for AD Opioids Where We're Headed?

- **Early:** market has a small number of AD products using early AD technology
 - Case by case decision-making
- **Intermediate:** multiple products approved as abuse deterrent using various technologies
 - Fuller set of regulatory issue identified,
 - Guidance outlining FDA's approach for brand name and generic development is refined
 - Actions potentially shift to class-wide scope
- **Late:** AD formulations of all major opioids marketed
 - Focus is on supporting iterative improvement in AD technologies

Future for AD Opioids

How Will We Get There?

- **Progressively Series of Regulatory Actions**
 - Giving a labeling claim for specific products
 - Also blocking the approval of other drugs that lack the same (or better) abuse-deterrent properties
 - Also, taking action against existing products with the same opioid
 - Also, taking action against existing products, including those with different opioids

Challenges in Getting to the Future for AD Opioids

- Incentivizing innovation: Primary incentive FDA has available is labeling
- Encouraging iterative development of effective abuse-deterrent formulations
 - Challenge to assess impact of individual formulations
 - Challenge to encourage uptake of effective products by payers
- Managing expectations: abuse-deterrent opioids will not ‘prevent’ abuse, and are not ‘silver bullets’

Summary

- FDA is working across many areas to address prescription opioid abuse, including the development and assessment of AD opioids
 - Encourage the development of new abuse-deterrent products to treat pain that will offer improved safety and efficacy
 - Ensure the assessment of these new products as the science improves
- Within this broadened range of activities, our regulatory mission remains at the heart of FDA role in opioids
 - FDA will act within its authorities, based on science,²⁷ in support of our public health mission