Abuse-Deterrent Formulations: A Private Payer View

FDA Public Meeting on Pre-Market Evaluation of Abuse-Deterrent Properties of Opioid Drug Products

October 31, 2016
BCBS Companies’ Efforts to Combat Opioid Addiction and Substance Use Disorder

– Promote the health and safety of our members and the communities in which we serve through public awareness and education of opioid risk
– Develop and adopt actionable policies and procedures that ensure safe prescribing of opioid medication and appropriate access to treatment for opioid use disorder
– Encourage and support the enactment of well-informed public policy to prevent prescription opioid misuse, abuse, fraud and diversion
BCBSA Engages

• Joined President Obama in Oct. 2015 White House meeting to address crisis
  – Announced production of PBS documentary, sponsored by BCBSA, to heighten awareness

• NGA declared opioid use one of Governors’ top five concerns in 2016
  – Called on private sector partners to commit to joining them to combat the “epidemic”
  – BCBSA steps forward to form executive-level workgroup to develop systemwide best practices and commit to leveraging BCBS data capabilities to enhance understanding of opioids prevalence and impact

• Hosted BCBSA Congressional briefing on Capitol Hill
  – Blue Cross and Blue Shield of Massachusetts, Blue Shield of California and BlueCross BlueShield of Western New York participated in briefing

• Have since continued the momentum through ongoing engagements as part of BCBSA’s opioid commitment
Pillars of BCBSA’s Commitment

**Emphasize Enduring Solutions**
Convene executive-level steering committee to develop best practices

**Increase Awareness**
Partner with WNED-TV (PBS) on an opioids documentary and community education

**Share Data Insights**
Leverage industry-leading data capabilities

Create Strategic Partnerships
Collaborate with organizations to affect change
Support for National and State Efforts

- Supportive of efforts from the White House, Congress, HHS, FDA and CDC to combat opioid addiction and substance use disorder

- We have been working with the DEA, ONDCP and NGA on developing solutions and identifying obstacles
  - Focus has been on prevention, education, fraud & diversion and those who need treatment

- Aligning our work with FDA Public Health Goals for Improved Use of Prescription Opioids:
  - Provide appropriate access to pain treatments for patients, including opioid drugs
  - Reduce the misuse and abuse of prescription opioids

- We view this as a multi-faceted problem that will take multiple solutions – no “silver bullets”
• Commend the Food and Drug Administration for its measured approach in taking steps to address our nation’s opioid epidemic through abuse-deterrent formulations (ADFs) of opioids.

• Generic ADF products should demonstrate that they are no less abuse-deterrent than their reference listed drug with respect to all potential routes of abuse.

• Appreciate that the FDA will continue to assess the state of science and we support a continued “look-back” for both brand and generic ADFs in the market to ensure that regulations are keeping up with our collective knowledge of the issue.

• Recommend that the FDA conduct post-market surveillance of ADF products (both brand and generic) to track potential increased abuse and whether there actually is a positive impact on the opioid epidemic by having more ADF products in the community.

• The cost of ADFs also should be monitored to ensure that these drugs (both brand and generic) are not resetting the market in a way that causes untenable cost burdens on patients and payers (both public and private)
Abuse-Deterrent Formulations: Our View

• We are strong supporters of maintaining access to appropriate treatment for individuals that need opioids for management of pain for acute or chronic conditions.

• Agree with FDA position that ADF technologies have not yet proven to be successful at deterring the most common form of abuse – swallowing a number of intact capsules or tablets.
  – Abuse-deterrent properties do not mean that there is no risk of abuse
  – Abuse-deterrent properties are defined as those properties shown to meaningfully deter abuse, even if they do not fully prevent abuse

• While creating a pathway for generic ADFs to enter the market is useful, we caution that more ADFs in the marketplace are not the silver bullet to solving our national opioid epidemic. For this reason, we oppose any sort of coverage mandates for ADFs.
Additional thoughts regarding ADFs

- So-called abuse-deterrent formulations (ADFs) may offer safety advantages over easily snorted and injected OPRs, but they do not render them less addictive.¹

- Opioid addiction, in both medical and nonmedical OPR users, most frequently develops through oral use²

- Some opioid-addicted individuals may transition to intranasal or injection use, but most continue to use OPRs orally³

- The significant cost of so-called ADF has the potential to markedly increase costs to the health care system, given their significant expense compared to current formulations which are often generic

- Does evidence exist showing ADFs decrease substance use disorder or reduce the long-term costs of substance use disorder?
  - Thus, ADFs should not be considered a primary prevention strategy for opioid addiction¹

- We will be monitoring ICER Study to review abuse-deterrent formulations of opioids (ADFs) as part of integrative pain management (March 2017)

Literature states that ADFs have limits in mitigating the opioid epidemic...

Original Investigation | May 2015

Abuse-Deterrent Formulations and the Prescription Opioid Abuse Epidemic in the United States Lessons Learned From OxyContin

Theodore J. Cicero, PhD; Matthew S. Ellis, MPE

[+] Author Affiliations


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ABSTRACT

Importance In an effort to reduce wide-scale abuse of the proprietary oxycodone hydrochloride formulation OxyContin, an abuse-deterrent formulation (ADF) was introduced in 2010. Although the reformulation produced an immediate drop in abuse rates, a definite ceiling effect appeared over time, beyond which no further decrease was seen.

Objective To examine the factors that led to the initial steep decline in OxyContin abuse and the substantial levels of residual abuse that have remained relatively stable since 2012.

Conclusions and Relevance Abuse-deterrent formulations can have the intended purpose of curtailing abuse, but the extent of their effectiveness has clear limits, resulting in a significant level of residual abuse. Consequently, although drug abuse policy should focus on limiting supplies of prescription analgesics for abuse, including ADF technology, efforts to reduce supply alone will not mitigate the opioid abuse problem in this country.
...and should not be considered a primary prevention strategy for opioid addiction

The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction

Andrew Kolodny,1,2,3 David T. Courtwright,4 Catherine S. Hwang,5,6 Peter Kreiner,1 John L. Eadie,1 Thomas W. Clark,1 and G. Caleb Alexander5,6,7

Some opioid manufacturers have reformulated OPRs to make them more difficult to misuse through an intranasal or injection route. These so-called abuse-deterrent formulations (ADFs) may offer safety advantages over easily snorted and injected OPRs, but they do not render them less addictive. Opioid addiction, in both medical and nonmedical OPR users, most frequently develops through oral use (85). Some opioid-addicted individuals may transition to intranasal or injection use, but most continue to use OPRs orally (47). Thus, ADFs should not be considered a primary prevention strategy for opioid addiction.
Clinicians weigh in regarding FDA guidance from March 2016:

“The greater concern is whether the tamper resistance and abuse deterrence of the original formulation is sufficient. Many people abuse and misuse opioids orally, in which case tamper resistance will be essentially ineffective,” said Dr. Lewis Nelson, an emergency medicine specialist at the New York University Langone Medical Center.

“The Internet is filled with videos and blogs demonstrating ways to bypass the tamper resistant mechanisms to release drug for abuse by other routes … This effort cannot be relied upon as the major approach to reducing opioid abuse,” he said.¹

¹ https://www.statnews.com/pharmalot/2016/03/24/opioid-fda-generics-painkilller/
Speaking of blogs...

To inject the abuse deterrent opana er’s it is simple. Depending on your tolerance cut off the amount you want to inject with a razor. Regular users one half to one quarter a 40 mg pill. Remove coating by either putting the pill in ur mouth or rubbing some water on it. Wipe the pill with a moist cloth removing the coating. You will be left with a white pill. Put your desired amount in a spoon. I use a glass stow and heat the spoon with the pill 20 seconds. 

*To remove the pill that is stuck* you can put it in a little bit of 100% olive oil and rub the pill very well until it is gone. 

Inject the pill in ur arm. The pill will expand in ur arm and the pills will be very strong. After 1 hour it will be hard to see ur pill.

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To use the abuse deterrent opana er's:

1. Crush the pills up and drop into urine acid or something with a similar pH (you're trying to replicate the pH of your stomach).
2. Mix it up for 20 secs.
3. Drink, don't reconstitute the water.

You could possibly do an A/B test on these as well if you've got more time to experiment.
Challenges in the Current Environment

- Provider Education Needed
- Drug Manufacturers
- Coverage of ADFs
Primary Care Physicians’ Knowledge And Attitudes Regarding Prescription Opioid Abuse and Diversion

Hwang, Catherine S. MSPH; Turner, Lydia W. MHS; Kruszewski, Stefan P. MD; Kolodny, Andrew MD; Alexander, G. Caleb MD, MS

Abstract

Objectives: Physicians are a key stakeholder in the epidemic of prescription opioid abuse. Therefore, we assessed their knowledge of opioid abuse and diversion, as well as their support for clinical and regulatory interventions to reduce opioid-related morbidity and mortality.

Materials and Methods: We conducted a nationally representative postal mail survey of 1000 practicing internists, family physicians, and general practitioners in the United States between December 2005 and July 2006.

Results: The adjusted response rate was 58%, and all physicians (100%) believed that prescription drug abuse was a problem in their communities. However, only two-thirds (66%) correctly reported that the most common route of abuse was swallowing pills whole, and nearly one-half (46%) erroneously reported that abuse-deterrent formulations were less addictive than their counterparts. In addition, a notable minority of physicians (25%) reported licit to the illicit market when this practice is common at all levels of the pharmaceutical supply chain. Most physicians supported clinical and regulatory interventions to reduce prescription opioid abuse, including the use of patient contracts (98%), urine drug testing (90%), requiring prescribers to check a centralized database before prescribing opioids (88%), and instituting greater restrictions on the marketing and promotion of opioids (77% to 82%). Despite this, only one-third of physicians (33%) believed that interventions to reduce prescription opioid abuse had a moderate or large effect on preventing patients’ clinically appropriate access to pain treatment.

Discussion: Although physicians are unaware of some facets of prescription opioid-related morbidity, most support a variety of clinical and regulatory interventions to improve the risk-benefit balance of these therapies.
Observations on Terminology

• The terms used when discussing the opioid crisis are used inconsistently, vary by stakeholder, and are often incorrectly interchanged

• The American Society of Addiction Medicine defines addiction as a primary, chronic and relapsing brain disease characterized by an individual pathologically pursuing reward and/or relief by substance use and other behaviors
  – However, there is no DSM-V or ICD-9/10 code for addiction
  – The DSM-V combined substance abuse and substance dependence into a single “substance use disorder” (SUD) defined by the substance and graded on a continuum, based on the number of 11 criteria present (mild, moderate, severe) e.g., Mild Opioid Use Disorder for as few as two criteria

• The AMA testimony, backgrounders, and other discussions refer to “inappropriate prescribing,” but do not define “appropriate prescribing.”

• An AAFP policy statement uses the terms misuse, abuse & overdose, and their journal articles have defined misuse as hazardous use, substance abuse, and substance dependence

• Many other instances exist, and the intended use of a term in state/federal policy could conflict with diagnosis or payment codes, complicating UM, compliance, and research/evaluation
Some manufacturers eagerly pushing ADFs as the solution
That same manufacturer’s take on assigning roles and responsibilities...

<table>
<thead>
<tr>
<th>Role</th>
<th>Action Steps</th>
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<tbody>
<tr>
<td><strong>Prescribers</strong></td>
<td>- Complete REMS compliance training(^1)</td>
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<tr>
<td></td>
<td>- Consult section 9.2 to determine abuse-deterrence status of an opioid product(^2)</td>
</tr>
<tr>
<td></td>
<td>- Prescribe opioids appropriately(^1)</td>
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<tr>
<td><strong>Pharmacists</strong></td>
<td>- Increase awareness of prescription drug abuse and misuse and the availability and benefits of opioids with abuse-deterrent properties(^3)</td>
</tr>
<tr>
<td></td>
<td>- Consult section 9.2 to determine abuse-deterrence status of an opioid product(^1)</td>
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<tr>
<td><strong>Payers</strong></td>
<td>- Form partnerships with stakeholder agencies to develop reimbursement strategies that ensure patients in pain receive opioids with abuse-deterrent properties when appropriate(^4)</td>
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<tr>
<td><strong>Policymakers</strong></td>
<td>- Provide guidance to the pharmaceutical industry on the development of abuse-deterrent drug formulations and on postmarket assessment of their performance(^5)</td>
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<tr>
<td><strong>Pharmaceutical Manufacturers</strong></td>
<td>- Develop abuse-deterrent opioid formulations(^6)</td>
</tr>
<tr>
<td><strong>Patients</strong></td>
<td>- Take appropriate action to safeguard prescription opioids from abuse, misuse, and diversion and ensure their proper disposal(^7)</td>
</tr>
<tr>
<td><strong>Parents and Community Leaders</strong></td>
<td>- Educate children about the risks associated with prescription opioids(^8)</td>
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State Activity on ADFs

2016 Legislative Landscape: Abuse-Deterrent-Formulation (ADF) Drugs

ADF Legislation Introduced But Did Not Pass (Or Has Not Progressed Yet)

ADF Study Bill Passed
- 2014 ADF Legislation Passed
- 2015 ADF Legislation Passed
- 2016 ADF Legislation Passed

No ADF Legislation Introduced

Note: Map is as of May 11, 2016.

Some states are taking a cautious approach

"While the intent of this bill is laudable, research on the impacts of utilizing abuse-deterrent drugs is in its infancy. The effectiveness of such drugs is currently under review, and it is simply too early to tell whether it would achieve its intended effects... abuse-deterrent opioid drugs are approximately two to three times more expensive on a daily basis than opioid drugs that lack abuse-deterrent properties, thus resulting in increased, and unplanned, costs to the State and consumers."

GOVERNOR ANDREW CUOMO (D-NY)
Veto message for AB 7427-A (no. 284), December 11, 2015

"In addition to the lack of clarity regarding the efficacy of these drugs, abuse-deterrent opioids cost approximately three times more than opioids without these formulations. By all accounts, this bill will cost the State over $11 million each year, the benefits of which, as noted, are still uncertain."

GOVERNOR CHRIS CHRISTIE (R-NJ)
Veto message for AB 4271, January 19, 2016
Closing Thoughts

• A multi-faceted approach will be necessary to even begin to tackle this epidemic – no single solution is going to be the answer

• Collectively we need to consider how to prevent addiction while also building supports for those who need treatment

• ADFs are still unproven, and while they may benefit some individuals the fact remains that they can still be abused
  – Evidence needs to catch up with the marketing of ADFs

• Incentives should be in place to encourage the development of innovative, effective, abuse-deterrent products but more proof is needed before any widespread coverage will be embraced

• Education on ADFs is essential
Contact Information

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