Abuse-Deterrent Formulations: A Private Payer View

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

BlueCross BlueShield Association

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"**

BCSBA Comments on FDA Draft Guidance: *General Principles for Evaluating the Abuse-Deterrence of Generic Solid Oral Opioid Drugs* - May 2016

- 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 use[2]
- Some opioid-addicted individuals may transition to intranasal or injection use, but most continue to use OPRs orally[3]
- 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 addiction[1]
- We will be monitoring ICER Study to review abuse-deterrent formulations of opioids (ADFs) as part of integrative pain management (March 2017)

1.Kolodny et al. Annu. Rev. Public Health 2015. 36:559–74

2. US FDA (Food Drug Admin.). 2013. Guidance for Industry: Abuse-Deterrent Opioids—Evaluation and Labeling. Silver Spring, MD: US FDA. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM334743.pdf

3. Katz et al. Tampering with prescription opioids: nature and extent of the problem, health consequences, and solutions. Am. J.Drug Alcohol Abuse 2011. 37:205–17

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

JAMA Psychiatry. 2015;72(5):424-430. doi:10.1001/jamapsychiatry.2014.3043.

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ABSTRACT

ABSTRACT | INTRODUCTION | METHODS | RESULTS | DISCUSSION | CONCLUSIONS | ARTICLE INFORMATION | REFERENCES

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 Alexander[5,6,7]

> 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-painkillller/

Speaking of blogs…

TheMatador
Bluelighter
Join Date: Dec 2008
Posts: 621

17-07-2009 18:42

From OpanaER - Mega Thread -
I believe it will be a good (harm reduction) reference to the following topics covered :

> Originally Posted by **johanneschimpo**
> *(1) make sure your snorting technique is good, so you don't waste anything, (2) try the high-fat meal ordeal, and/or (3) use some sort of CYP450 inhibitor. Of all those, #1 is definitely the most important. Hopefully somebody with a lot of tried and tested experience can chime in with something more specific for you.*

(1.1) I have had oxymorphone daily for quite some time in the form of OpanaER and OpanaIR tablets, OpanaER is much superior in my opinion especially for insuffulating for the simple reason OpanaIR tablets are only made in 5mg and 10mg pills, and they are bigger, about 1.5x as much powder as any OpanaER tablet, which go up to 40mg...So when you have a nice high dosage OpanaER Tablet that's the way to go. Say you have a 40mg OpanaER tablet for instance, your snorting ~6x less powder even if you had the highest OpanaIR tablets available (10mg) and ~12x less if you have the 5mg OpanaIR tabs
So when acquiring oxymorphone for insuffulation, OpanaER is the way to go if you get the half of the upper portion of the dosages available, which is the majority.

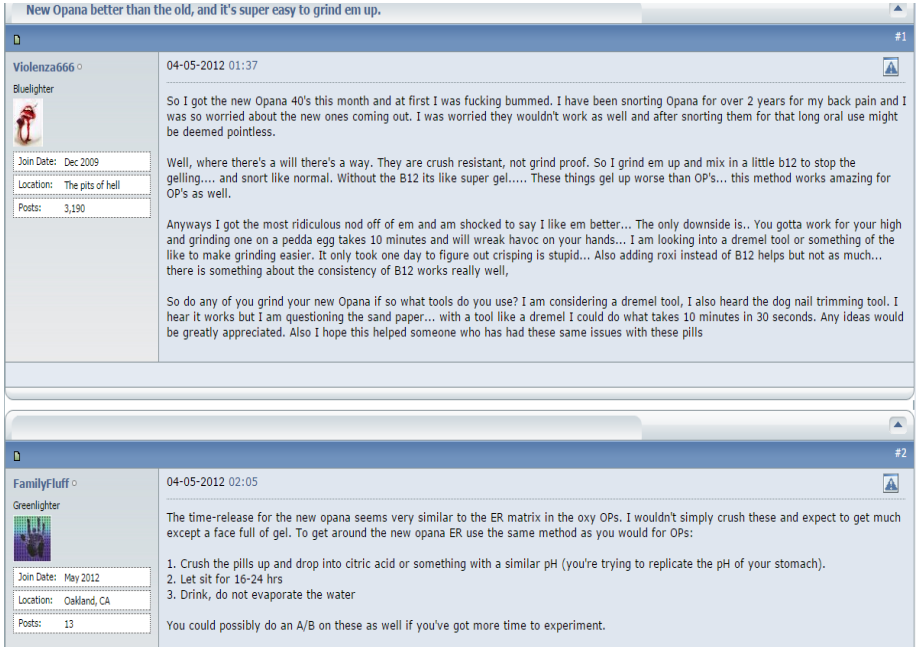
(1.2)When insuffulating OpanaER, since it is a time release pill it does gel to an extent, but not very badly, its actually something I really enjoy as well as many other Opana users I know and have talked to here on BL.
The reason is this: When you insuffulate OpanaER as opposed to Oxycontin, it has the ability to gels slightly which allows it to stay up in your nasal membranes for a very long time (it can stay up in your noses for hours if you desire (i have), you can control how long you would like to hold you dose up in your nose for the most part, and then swallow it down when you feel like it) and gives it a GREAT chance to absorb, it makes for a very strong and lengthy high, as opposed to Oxycontin dripping down your throat constantly
Don't get me wrong I like my Oxycontin, but after having Opana available it's no contest in my opinion, the fine powder that the Opana tablet creates sticks in the nasal membranes so perfectly, it makes for a far superior high than any Oxycontin high

(1.3 When preparing your OpanaER tablet for insuffulation, DO NOT wipe it off with water, or put it in your mouth like Oxycontin to remove the coating. This makes the pill gel slightly most of the time and your powder is all wet as a result. The powder in Opana is less dence then in an Oxycontin, so that's a factor.

(1.4)To remove the outer film of your OpanaER tablet simply grab a nice handy sharp knife, a nice razor blade, or even scissors have worked pretty damn good for me in a pinch
Then you just grab your OpanaER tablet that now has have its film coating carefully shaved off
I think everyone knows what to do after that

(2) A fatty meal a half hour before you dose, or even with your dose when I don't want to wait is always great, whether I'm taking it in the ER form for pain, or IR for insuffalation. I almost always try to eat some kind of food (preferably with a portion of healthy fat) , it helps everytime and has been documented to raise the BA up to 50%

(3) I don't know much about CYP450 inhibitors yet unfortunately and don't have access to sourced information on the subject yet, do you by chance happen to have a chart available JC? and/or possibly know of any common ones?
EDIT: CYP450 inhibitors off the top of my head, diphenhydramine (Benadryl), cimetidine (Tagamet)
...For further info check out JC's CYP450 chart
Thanks again JC



New Opana better than the old, and it's super easy to grind em up.

#1

Violenza666
Bluelighter
Join Date: Dec 2009
Location: The pits of hell
Posts: 3,190

04-05-2012 01:37

So I got the new Opana 40's this month and at first I was fucking bummed. I have been snorting Opana for over 2 years for my back pain and I was so worried about the new ones coming out. I was worried they wouldn't work as well and after snorting them for that long oral use might be deemed pointless.

Well, where there's a will there's a way. They are crush resistant, not grind proof. So I grind em up and mix in a little b12 to stop the gelling.... and snort like normal. Without the B12 its like super gel..... These things gel up worse than OP's... this method works amazing for OP's as well.

Anyways I got the most ridiculous nod off of em and am shocked to say I like em better... The only downside is.. You gotta work for your high and grinding one on a pedda egg takes 10 minutes and will wreak havoc on your hands... I am looking into a dremel tool or something of the like to make grinding easier. It only took one day to figure out crisping is stupid... Also adding roxi instead of B12 helps but not as much... there is something about the consistency of B12 works really well,

So do any of you grind your new Opana if so what tools do you use? I am considering a dremel tool, I also heard the dog nail trimming tool. I hear it works but I am questioning the sand paper... with a tool like a dremel I could do what takes 10 minutes in 30 seconds. Any ideas would be greatly appreciated. Also I hope this helped someone who has had these same issues with these pills

#2

FamilyFluff
Greenlighter
Join Date: May 2012
Location: Oakland, CA
Posts: 13

04-05-2012 02:05

The time-release for the new opana seems very similar to the ER matrix in the oxy OPs. I wouldn't simply crush these and expect to get much except a face full of gel. To get around the new opana ER use the same method as you would for OPs:

1. Crush the pills up and drop into citric acid or something with a similar pH (you're trying to replicate the pH of your stomach).
2. Let sit for 16-24 hrs
3. Drink, do not evaporate the water

You could possibly do an A/B on these as well if you've got more time to experiment.

> Originally Posted by **Squrll402**
> *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 or 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 will moist with a cloth removing the coating. You will be left with a white pill. Put your desired amount in a spoon. I use a gas stove and heat the spoon with the pill 20 seconds. Then mash down the hot pill with the top of your rig. Continue until pill is flattened in the spoon. Heat mashed pill in spoon until it is a golden brown or blackish color. Golden brown is preferred. Immediately put about 150-200 cc's, or one and a half to two milliliters of water in the spoon on top of the pill. Immediately stir water and pill until pill is gone and it has formed a liquid, Amber color to pure black in color. Put cotton in liquid to filter it and draw up in rig. It will be very dark especially until u get the hang of it. When injecting, the only way to know if there's blood in the rig is to watch the tiny air bubbles in the rig, when they fill in you've hit a vein. Inject. The rush will be very intense. Opana is extremely strong so know your tolerance or start with 5 mgs or less. This is not healthy to do by any means.*

Challenges in the Current Environment

Provider Education Needed

Drug Manufacturers

Coverage of ADFs

Provider Education Needed

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April 2016 - Volume 32 - Issue 4 - p 279–284
doi: 10.1097/AJP.0000000000000268
Original Articles

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

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

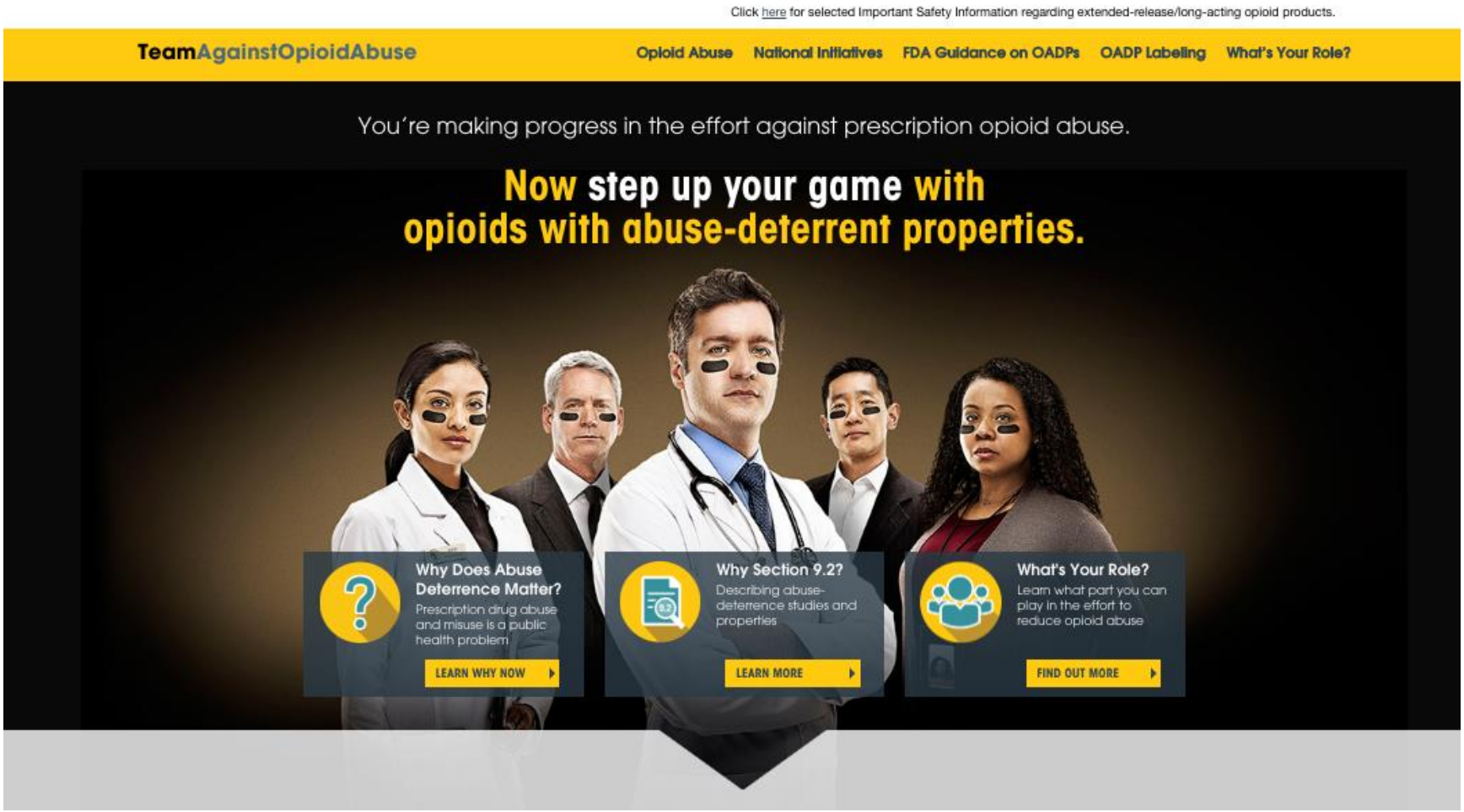
licit to the illicit market when this practice is common at all levels of the pharmaceutical supply chain. Most physicians supported clinical and regulatory interventions to reduce prescription opioid abuse, including the use of patient contracts (98%), urine drug testing (90%), requiring prescribers 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 critieria
- 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



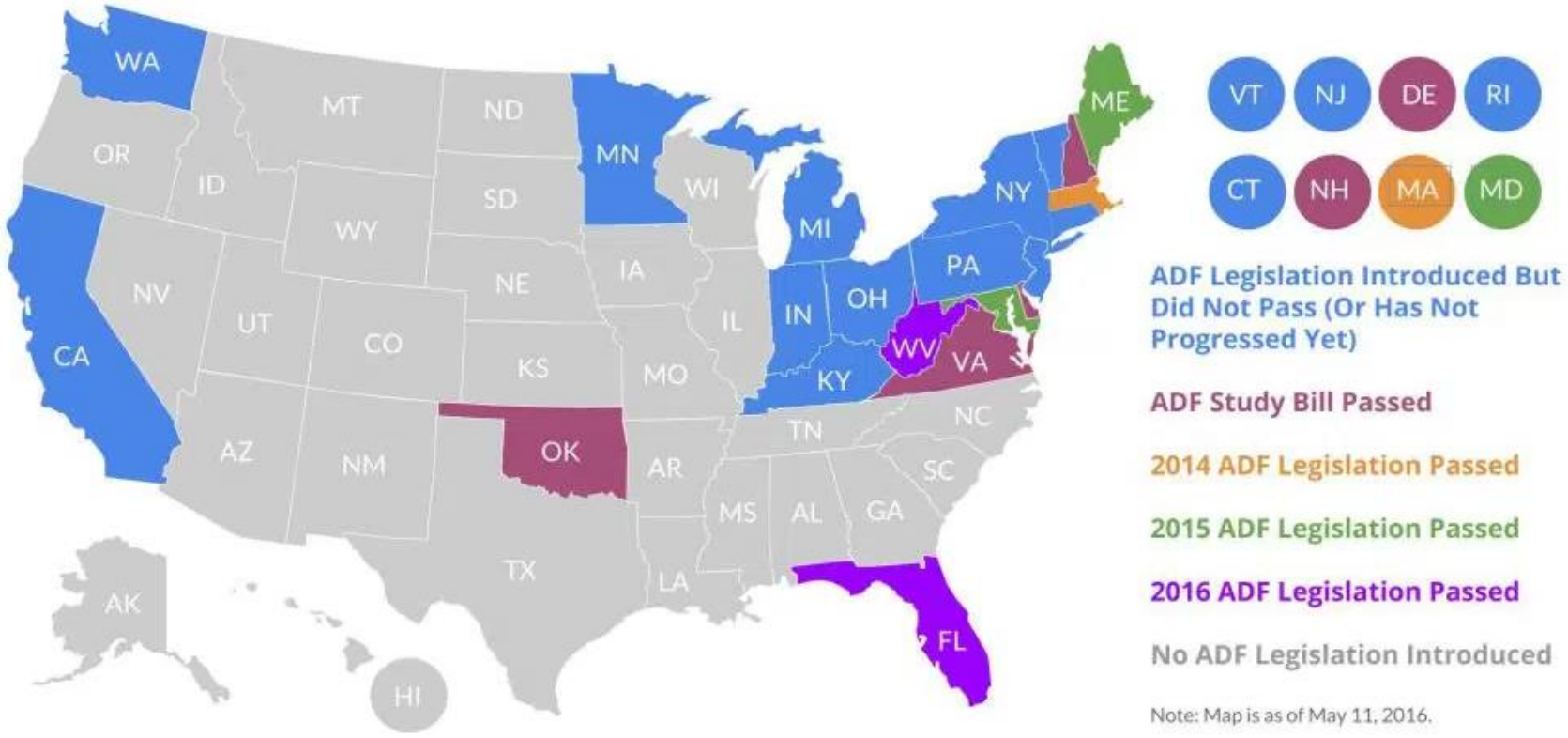
That same manufacturer's take on assigning roles and responsibilities…

Some Action Steps for Helping Reduce Prescription Opioid Abuse

Prescribers	• Complete REMS compliance training[2] • Consult section 9.2 to determine abuse-deterrence status of an opioid product[4] • Prescribe opioids appropriately[1]
Pharmacists	• Increase awareness of prescription drug abuse and misuse and the availability and benefits of opioids with abuse-deterrent properties[1] • Consult section 9.2 to determine abuse-deterrence status of an opioid product[4]
Payers	Form partnerships with stakeholder agencies to develop reimbursement strategies that ensure patients in pain receive opioids with abuse-deterrent properties when appropriate[1,2]
Policymakers	Provide guidance to the pharmaceutical industry on the development of abuse-deterrent drug formulations and on postmarket assessment of their performance[1]
Pharmaceutical Manufacturers	Develop abuse-deterrent opioid formulations[1-4]
Patients	Take appropriate action to safeguard prescription opioids from abuse, misuse, and diversion and ensure their proper disposal[1]
Parents and Community Leaders	Educate children about the risks associated with prescription opioids[1]

State Activity on ADFs

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



https://www.multistate.com/insider/2016/05/states-address-opiod-epidemic-with-abuse-deterrent-formulation-legislation/

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

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