3rd Human Abuse Liability & Abuse-Deterrent Formulations Conference
November 2-3, 2016
Arlington, Virginia

Essential Elements of Legislation to Foster a Transition to Medications with Abuse-Deterrent Properties

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Conflict of Interest Disclosure

- CLAAD's funders include members of the pharmaceutical, addiction treatment, and laboratory industries, and are disclosed on its website, www.claad.org.
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Preview

- Background and context
- Federal legislation
- State legislation
- Discussion

Purpose

- New federal and state legislative sessions begin in January
- Pre-filing of bills has already begun in some states
- Federal abuse deterrence legislation, if any, would likely be part of PDUFA VI (current authorization ends Sept. 2017)
- Lack of consensus among stakeholders is a reason for legislators to abandon or oppose legislation
- Consensus recommendations from informed stakeholders should form the basis of legislative proposals

Comprehensive National Strategy

- Prescriber education (covering all controlled medications)
- Public awareness and patient counseling, including safe storage and responsible disposal
- Prescription monitoring programs
- Prosecution of criminals, rehabilitation of negligent prescribers
- Overdose rescues, interventions, and referrals to treatment
- Access to effective treatments for substance use disorder
- Development, use, and coverage of non-pharmacologic treatments; non-controlled, lower scheduled, and abuse-deterrent medications

Policy Goals: Reduce Unnecessary Exposure to and Risks of Controlled Medications

- Development and use (when appropriate) of alternatives to commonly abused medications
  - Non-pharmacologic treatments, *e.g.*, virtual reality
  - Non-controlled medications, *e.g.*, biologics
  - Lower risk (lower scheduled) controlled medications
  - Medications with abuse-deterrent properties and novel delivery systems
    - Extended release, immediate release
    - Brand, generic
    - Not just opioids for pain, not just opioids
- Broad market transition
- Regulatory clarity and flexibility
- Recognition of benefits (providers, patients, and public)
- Advance notice of transition deadline to ensure product availability, competition, and lower costs
- Public and private insurance coverage

Arguments in Favor of Opioids with Abuse-Deterrent Properties

Solid Oral Forms

- May help prevent unintentional overdose
  - Inexperienced persons who alter route of administration
  - Medical misuse, e.g., crushing to take with apple sauce
- May be less desirable for abuse
  - Lower black market demand
  - Less often diverted

Implants and Injectables

- May not be dispensed to patients for self-administration
- May reduce opportunities for diversion, misuse, abuse, and accidental exposure
- May offer continuous medication delivery and greater adherence to medication regimen
- May improve access and convenience, and help reduce stigma

Arguments Against Opioids with Abuse-Deterrent Properties

- "Abuse-deterrent" term is too broad. First-generation products do not prevent:
  - Euphoria, addiction
  - Interactions with other substances, *e.g.*, alcohol
  - All forms of manipulation for abuse or overdose by all means
- Can cost more than conventional counterparts; not yet available as generics
- Difficult to isolate public health benefits
  - Relatively slow market adoption
  - Not supported by adequate demand reduction
  - Impacted by price, purity, and availability of illicit substances
- Are additional opioids coming to market during an opioid overdose epidemic
  - Irrespective in intended safety improvements
  - Despite displacement of conventional opioids in many cases
- [Can yield profits manufacturers at a time of high anti-pharma sentiment]

Strongest Arguments in Favor of Opioids with Abuse-Deterrent Properties

- Any reduction in diversion, misuse, abuse, accidental exposure, overdose, or disease transmission is a positive outcome
- Current opioid analgesics with abuse-deterrent properties may help thwart the trajectory of abuse
  - Individuals who abuse opioids typically start with oral ingestion, move to crushing and snorting, continue to snorting of heroin, and finally, inject prescription opioids and heroin—as tolerance develops and it becomes more costly to maintain abuse patterns
  - Individuals who use altered routes of administration are at an increased risk for overdose and the exacerbation of substance use disorders
- Use of current products can help fund the development of next-generation products, which could prevent:
  - Euphoria, addiction
  - Interactions with other substances, e.g., alcohol
  - All forms of manipulation for abuse or overdose by all means

Federal Legislation

- 2013-2014: Stop Tampering of Prescription Pills (STOPP) Act, H.R. 486
- 2015: Stop Tampering of Prescription Pills (STOPP) Act, H.R. 2335
  - Requires FDA to deny approval to a new, non-abuse-deterrent oral opioid if an abuse-deterrent drug containing the same opioid is available
  - To be approved by the FDA, a generic version of an abuse-deterrent brand name drug must be at least comparably abuse-deterrent to the brand name drug
  - An approved generic drug is not bioequivalent to, and does not have the same therapeutic effect as, a brand name drug that becomes abuse-deterrent unless the generic drug is at least comparably abuse-deterrent
  - Approval of a generic oral opioid is withdrawn if the brand name drug is not abuse-deterrent and not available and there is an approved abuse-deterrent drug available that contains the same opioid in the same dose
  - Approval of an oral opioid is withdrawn if the drug is not abuse-deterrent and there is an approved abuse-deterrent drug available that contains the same opioid
    - Withdrawal of approval may be waived by the FDA for a drug intended for a special needs population
    - The FDA must delay withdrawal to give the drug sponsor an opportunity to obtain approval for an abuse-deterrent formulation of the drug

Federal Legislation

- 2015: Promoting Access for Treatments Ideal in Enhancing New Therapies (PATIENT) Act, H.R. 1353
  - Incentivizes drug manufacturers by allowing for an additional 24 months of market exclusivity for improved medications
  - Improvements could include enhanced safety, patient adherence, fewer side effects, or new indications
  - The additional 24 months would bring the exclusivity period to 9 years for orphan drugs, 7 years for new chemical drugs, and 5 years for "other" drugs

Federal Legislation

- 2016: Curb Opioid Misuse By Advancing Technology (COMBAT) Act, H.R. 5127
  - Provides incentives to develop new abuse-deterrent technologies (no reference to schedule)
    - Approval based on new clinical abuse potential studies
    - FDA labeling of abuse-deterrent properties
  - Additional 12 months of data exclusivity (total of four years) for new ("other") drugs
  - Additional 60 days of data exclusivity (total of 240 days) for patent-challenge generics
  - Creates a new class of ADF that can breach the exclusivity of an approved product, including FDA-labeled ADFs
  - Does not require the second-in-time ADF to have a new, different, or more abuse-deterrent technology

Recommendations: Federal Legislation

- Incentivize the development of abuse-deterrent controlled medications
  - Grant a bonus period of exclusivity (TBD) to developers that obtain FDA approval and abuse-deterrent labeling
    - New chemical (5 years standard)
    - "Other" (3 years standard)
    - Patent challenge (180 days standard)
- Eventually transition the highest-risk, non-abuse-deterrent controlled medications off the market
  - Mandate all non-abuse-deterrent, Schedule II, solid-form products be reformulated and approved with abuse-deterrent labeling by a realistic deadline (TBD)
  - After a realistic deadline (TBD), deny applications for non-abuse-deterrent, Schedule II, solid-form controlled medications unless a drug shortage or significant unmet need exists
- Require coverage by federal health programs
- Address delivery systems separately, recognizing that the framework for evaluating manipulation of oral opioids is not tailored to injectables and implants

State Legislation: Study (Utah)

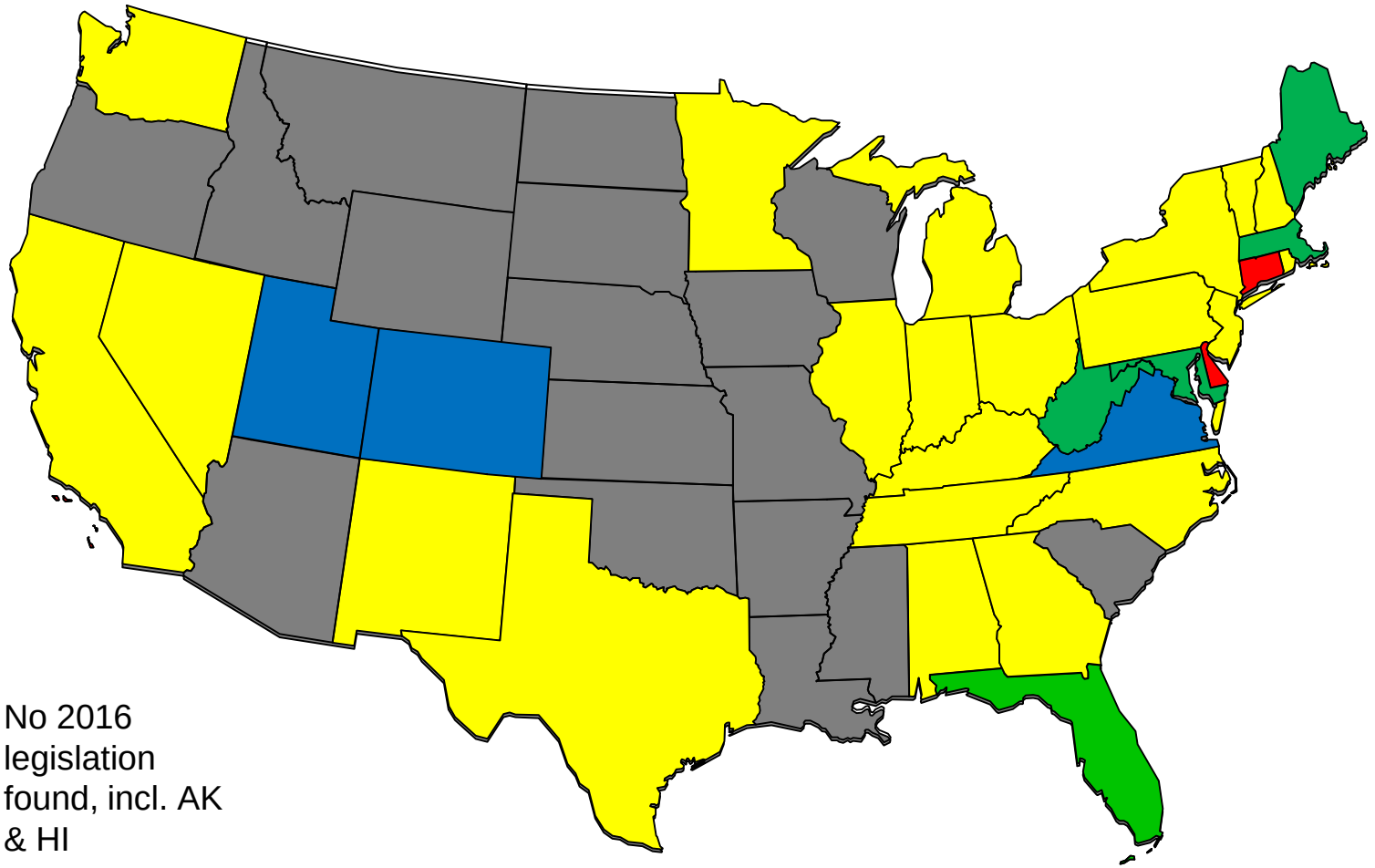
- Applied to:
  - Opioid analgesics
  - With FDA abuse-deterrent labeling
- Looked at:
  - Barriers to use
  - Efficacy of use
- Conclusions:
  - Abuse rates of ER oxycodone decreased after the release of the abuse-deterrent form
  - An increase in the abuse of other non-abuse-deterrent opioids after the release of abuse-deterrent ER oxycodone may indicate that increasing the number of abuse-deterrent formulations will further reduce abuse
  - There was an increase in the rate of heroin abuse corresponding with the release of abuse-deterrent ER oxycodone; however, economic factors, such as availability and price, may influence abuse patterns
  - Formulary coverage, prior authorization, and out-of-pocket cost have been cited as barriers in early discussions of abuse-deterrent opioids
  - Outcome data demonstrating superiority of one drug (e.g,. oxycodone, morphine) or formulation (e.g., abuse-deterrent, non-abuse deterrent) over another will alter the cost sharing of opioids

State Legislation: Coverage (West Virginia)

- Applies to:
  - Opioid analgesics (agonists)
  - With FDA abuse-deterrent labeling
- Insurers shall provide coverage for at least one abuse-deterrent opioid for each active ingredient
- Cost-sharing for brand name abuse-deterrent opioids shall not exceed the lowest tier for brand name drugs on the plan's formulary
- Cost-sharing for generic abuse-deterrent opioids covered pursuant to the ADF law shall not exceed the lowest cost-sharing level applied to covered generics
- Insurers may not require a patient first to use a non-abuse-deterrent opioid before covering an abuse-deterrent opioid on the formulary
- Preauthorization for a covered abuse-deterrent opioid is permitted if the same requirements are applied to non-abuse-deterrent opioids with the same type of drug release, immediate or extended

State Abuse Deterrence Legislation

October 2016



No 2016 legislation found, incl. AK & HI

Study Bill Not Passed

Study Law Passed

Coverage Law Passed

Coverage Bill Not Passed (or Vetoed)

Recommendations: State Legislation

- Advance coverage of brand and generic opioid analgesics with FDA abuse-deterrent labeling
- Address delivery systems separately, recognizing that the framework for evaluating manipulation of oral opioids is not tailored to injectables and implants
- Integrate efforts and revise bills (or amend laws) as other abuse-deterrent products come to market, *e.g.*, stimulants or benzodiazepines that do not interact with other substances

2017 State Pre-Filing

- No pre-filed bills regarding abuse deterrence found for 2017
- November and December are the busiest months for pre-filing bills
- 24 states accept proposals in the last two months of 2016
  - November (15 states): Mississippi (Nov. 1), Vermont (Nov. 1), Kansas (Nov. 8), New Jersey (Nov. 8), Connecticut (Nov. 9), Tennessee (Nov. 9), Texas (Nov. 9), Arizona (Nov. 14), Arkansas (Nov. 14), Georgia (Nov. 15), Maryland (Nov. 15), New York (Nov. 15), Oklahoma (Nov. 15), Rhode Island (Nov. 15), and Utah (Nov. 15)
  - December (9 states): Missouri (Dec. 1), South Carolina (Dec. 1), Washington (Dec. 1), Wyoming (Dec. 1), Maine (Dec. 7), Indiana (Dec. 10), South Dakota (Dec. 11), West Virginia (Dec. 15), and New Mexico (Dec. 15)

Conclusion

- Thanks to ExL Events and conference sponsors
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- Thank you
- Questions and discussion