Opioid Prescribing Practices and Pain Management: Role of FDA

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Disclosure Statement

I have no financial relationships with proprietary entities that produce health care goods and services

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

• FDA is addressing the needs of the pain patient and the need to confront opioids abuse seriously
• FDA has a critical regulatory role it plays
  – Education of prescribers
  – Science-based development of abuse-deterrent formulations of opioids
  – Hydrocodone combination product upscheduling
  – Zohydro approval
  – ER-LA opioid relabeling and PMRs
• Additional role supporting important non-regulatory activities through collaboration and resources
• Actions are aimed at supporting improved use while avoiding stigmatizing pain patients and their needs
Central Theme: Search for Balance

- Prescription opioid analgesics are essential to the effective treatment of pain.
- Prescription opioid analgesics are at the center of a major public health crisis of addiction, misuse, abuse, overdose, and death.
FDA Regulatory Activities on Opioids (Selected)

1) ER-LA OPIOID REMS, RE-LABELING AND PMR REQUIREMENT
2) ABUSE-DETERRENT FORMULATIONS DEVELOPMENT
3) HYDROCODONE: UPSCHEDULING AND ZOHYDRO APPROVAL
ER-LA Opioid REMS, Re-labeling and PMR Requirements
ER/LA Opioid REMS

Go to FDA.GOV and type opioid REMS in search box

or

Focus on Prescriber Education

• Patient-Prescriber interaction critical opportunity to improve opioid use
  – Better discussions about use of opioids
  – Better discussion about how to avoid adverse effects of opioids
  – Better discussion about how to store and dispose of opioids

• Opioid prescribing is challenging

• Educating prescribers represents targeted opportunity to improve opioid use
Opioids: FDA Risk Evaluation and Mitigation Strategy (REMS)

- Focus is long-acting and extended-release opioids (ER/LA opioids)
- Goals:
  - Reduce inappropriate prescribing, misuse and abuse
  - Minimize the burden on the healthcare system by encouraging a single shared system
- Manufacturers required to make educational materials available for prescribers and patients based on FDA-approved materials
  - CE for prescribers to encourage participation
Opioids REMS In Context

• Opioid REMS: proposed education for prescribers is not mandatory
• Paired with a separate Administration goal in ONDCP plan to link mandatory effective prescriber training to DEA registration to prescribe controlled substances
  – Legislation required
ER/LA REMS: Recent Actions

- Initial assessment
- Continuing Education materials now available
- FDA ‘Letter’ to prescribers highlighting availability of REMS educational materials
  - Take advantage of the CE materials now available at low (or no) cost
  - Know and apply the information in the latest approved labels
  - Educate patients on opioids use, risks and proper storage/disposal
What is SCOPE of Pain?

SCOPE of Pain is a series of continuing medical education/continuing nursing education activities designed to help you safely and effectively manage patients with chronic pain, when appropriate, with opioid analgesics. Our program consists of:

- A 3-module web-based activity;
- 10 live conferences held around the US that will include Policy and Resource Panels; and
- Train-the-trainer sessions and a subsequent trainer-delivered series of four community health center based grand rounds workshops.

The FDA has mandated manufacturers of extended release/long-acting (ER/LA) opioid analgesics, as part of a comprehensive Risk Evaluation and Mitigation Strategy (REMS), to make available comprehensive prescriber education in the safe use of these medications based on the FDA curriculum known as the Blueprint for Prescriber Education for Extended Release and Long-Acting Opioid (ER/LA) Analgesics. Our curriculum covers all aspects of this blueprint and more to provide a comprehensive educational program.

Who is this for?

Physicians, nurse practitioners, physician assistants, registered nurses, nurses, dentists, and pharmacists

Watch an introductory video with Dr. Barry Manuel

Why do I need SCOPE of Pain training?

Chronic pain affects approximately 100 million in the US, making it one of the most common reasons for patients to seek medical care. Unfortunately, pain management, including the appropriate use of opioids, is not well covered in medical training. Moreover, there are inadequate numbers of pain management specialists to help generalist providers manage these patients.

Partly in response to the problem of under-treatment of pain, over the past decade...
ER-LA Opioid REMS, Re-labeling and PMR Requirement
Labeling Language

Old Language
• Xxx is indicated for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time

New Language
• Xxx is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate
Labeling Language (cont)

Old Language: Not for use:
• As an as-needed analgesic
• For pain that is mild…
• For acute pain
• For postoperative pain…

New Language: Not for use:
• Because of the risks of addiction, abuse and misuse of opioids, even at recommended doses and because of the greater risks of overdose and death with extended-release formulations, reserve Xxx for use in patients for whom alternative treatment options…are ineffective, not tolerated, or would otherwise be inadequate to provide sufficient management of pain
• As an as-needed analgesic
Additional Label Changes

• Boxed warning: increased emphasis on risks, including abuse, overdose, death, and Neonatal Opioid Withdrawal Syndrome

• Urges prescribers to ‘assess each patient’s risk’ for abuse before prescribing and to ‘monitor all patients regularly for the development of abuse’
Goals of labeling changes

- Move away from an indication based on a subjective severity scale
- Move towards individual assessment of the impact of the patient’s pain, to determine both whether or not it is severe enough to warrant ER-LA opioids and whether alternatives would be inadequate
- Highlight risks of ER-LA opioids
Next Steps

• Companies have 30 days to submit responses to letters

• FDA working to change Medication Guide, Blueprint, Patient Medication Information to reflect new language
Post-Marketing Requirements

• Studies and trials to be conducted by manufacturers of the ER-LA opioids to better assess the known risks of abuse, abuse, hyperalgesia, overdose and death when ER-LA opioids are used long-term

• More data are needed on the relationship between opioid dose and duration and these risks

• Part of overall risk-benefit profile
Next Steps

- FDA has process for tracking PMR conduct
- Initial timeline for studies created
  - Ongoing discussions with sponsors
  - Goal is to encourage sponsors to work together
Other Regulatory Actions
FDA Science-Driven Actions on Specific Opioids

• Oxycontin and Opana ER: decisions regarding abuse-deterrent properties of specific formulations

• Hydrocodone
  – Announced intent to recommend increased restrictions (‘upscheduling’) of hydrocodone combination products
  – Approval of Zohydro (single-entity hydrocodone)
Development of Abuse-Deterrent Opioids
Abuse-Deterrent Opioids
Guidance

• Goals: support development of abuse-deterrent formulations while supporting important role generics play in US healthcare

• Guidance on their development was promised as part of ONDCP Rx Drug Abuse Plan (2011)

• Guidance on their development mandated under FDASIA*
  – Goal date January 9, 2013

* Food and Drug Administration Safety and Innovation Act
Abuse-Deterrent Opioids Draft Guidance: Purpose

• Reflects the state of the science of abuse deterrence (relatively new), and the need to take flexible while still taking a rigorous, science-based approach in evaluation and labeling of drugs as data accumulates
Highlights of Guidance

• Lays out development roadmap:
  – Scientific Studies relevant to assessing impact of formulation on abuse
  – Assessments FDA will use when looking at study data
  – Impact of data on labeling, including claim for abuse-deterrence
    • Aim to incentivize new ADF development
• Identifies areas additional scientific needs
Issues

• Does not address how FDA will approach generics evaluation, approval, and withdrawal
• Does not set ‘bright line’ standard of what constitutes meaningful ‘abuse deterrence’
  – Will need more experience before we can set such a standard
    • To date, two decisions have been made wrt specific formulations based on the totality of the data available to FDA
  – Need more data on the link between non-clinical and pre-market studies and post-market impact on abuse, overdose, and death
Next Steps

• Principles in Guidance applied to decision-making: Oxycontin and Opana ER
• Scientific Meeting held to discuss draft Guidance September 31-October 1, 2013
  – Included discussion of FDA work on generics
• Review of comments to Docket
• FDA work on applications of Guidance to generics development
FDA Non-Regulatory Activities on Opioids
Analgesics Use: an Opportunity for Non-Regulatory ‘Safe Use’ Approach

• Medicines are essential for the treatment of an important human condition (pain)
• Pain has both medical and social aspects to its treatment
  – No single entity or institution ‘owns’ the problem
• Multiple TX modalities exist, including several classes of drugs (Rx and OTC): opiates, NSAIDs, APAP….
  – The available drugs all have ‘challenges’
• Complex regulatory and legal issues
Example of Safe Use Activity: Disposal of Fentanyl Patches

• More than 60,000 young children end up in emergency rooms each year because they got into medicines while their caregiver wasn't looking.
Fentanyl Patch

• A 2 year-old boy and his family were visiting his relative in a nursing home.
  – Two days after the visit, the child was found unconscious, in respiratory arrest, and unable to be resuscitated.

• “Tape” in the child’s throat.
  – Fentanyl levels were detected on autopsy.
  – “Tape" was a used fentanyl patch with significant drug left in it.
Fentanyl Patch

To date FDA has received 26 reports of children being accidentally exposed to fentanyl patches. 10 of these cases were fatal.

The fentanyl patch is one of a few potent medications that can be fatal in a single dose, if used erroneously or inappropriately. Used patches contain enough residual drug to harm or cause death of a child.
Safe Use Actions On Fentanyl Patches

• In addition to regulatory work (recently announced changes in packaging)

• Worked to revise FDA web information
  – Consumer message*
  – Disposal information and Flush list drugs**

• Sent letter to stakeholders

• Created Webinar on disposal to hospice care

• Created Wiki sites

• Social media

*http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm300803.htm
Many Other Non-Regulatory Activities

• Collaborating in the creation, testing and sharing of model Patient Provider Agreement

• Supporting research into opioids use and abuse through Cooperative Agreements
  – Brandeis Center of Excellence work on surveillance database
  – Work by several groups to identify successful strategies to affect patients choices
FDA Work Within Larger Governmental Response

• Revising 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 Work: FDASIA Report on Rx Drug Abuse*

Section 1122 of the Food Drug and Cosmetics Act (FDASIA) requires the Secretary of HHS, in coordination with other Federal agencies, as appropriate, to review current Federal initiatives and provide a report within one year identify gaps and opportunities with respect to

1) ensuring the safe use of prescription drugs with the potential for abuse; and

2) the treatment of prescription drug dependence

* Addressing Prescription Drug Abuse in the United States Current Activities and Future Opportunities, 2013
FDASIA Report on Rx Drug Abuse

1) Epidemiology and Drivers of Prescription Drug Abuse in the United States

2) Current Prescription Drug Abuse Activities and Opportunities to Enhance Activities
   - Surveillance
   - Drug Abuse Prevention
   - Patient and Public Education
   - Provider Education
   - Clinical Practice Tools
   - Regulatory and Oversight Activities
   - Drug Abuse Treatment
   - Overdose Prevention
Opportunities Identified

1. Databases and analysis
   1. Support efforts to increase provider use of prescription drug monitoring programs (PDMPs)
   2. Strengthen surveillance systems and capacity
   3. Improve analytic tools for regulatory and oversight purposes
   4. Leverage HIT to improve clinical care and reduce abuse

2. Education
   1. Build the evidence-base for prescription drug abuse prevention programs
   2. Enhance coordination of education programs among federal agencies
   3. Further develop targeted education programs
Opportunities Identified (cont)

3. Tools
   1. Expand Screening, Brief Intervention, and Referral to Treatment services
   2. Synthesize pain management guideline recommendations and incorporate into clinical decision support tools
   3. Collaborate with insurers and pharmacy benefit managers on claims review and on programs to improve oversight of high-risk prescribing

4. Treatment
   1. Continue efforts to integrate drug abuse treatment and primary care
   2. Expand efforts to increase access to medication-assisted treatment
   3. Prevent opioid overdose through new formulations of naloxone
FDASIA Report and Access

• Tools lacking to assess impact of policies and regulations on access to pain treatment

• FDASIA report “Opportunities to Enhance Surveillance Activities”:
  – “Examine potential unintended consequences that may result of interventions aimed at reducing prescription drug abuse, such as a decrease in legitimate access to pain treatment”
We Know FDA Is One of Many Stakeholders

**FDA**
evaluates benefits/risks for the population

**Provider**
evaluates benefits/risks for a patient

**Patient**
evaluates benefits/risks in terms of personal values
We Are Listening: Extensive Public Input

- Zohydro Advisory Committee December 7, 2012
- Hydrocodone Upscheduling Advisory Committee January 24-25, 2013
- Part 15 hearing on Opioid labeling February 7-8, 2013
- Extensive Public Comment
  - Hydrocodone Docket: 768 comments
  - PROP Citizen’s Petition Docket: 1923 comments
Summary

• We take our role seriously, have significantly expanded our activities to address opioids
  – Improved use of opioids
  – Appropriate access

• 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, in support of our public health mission