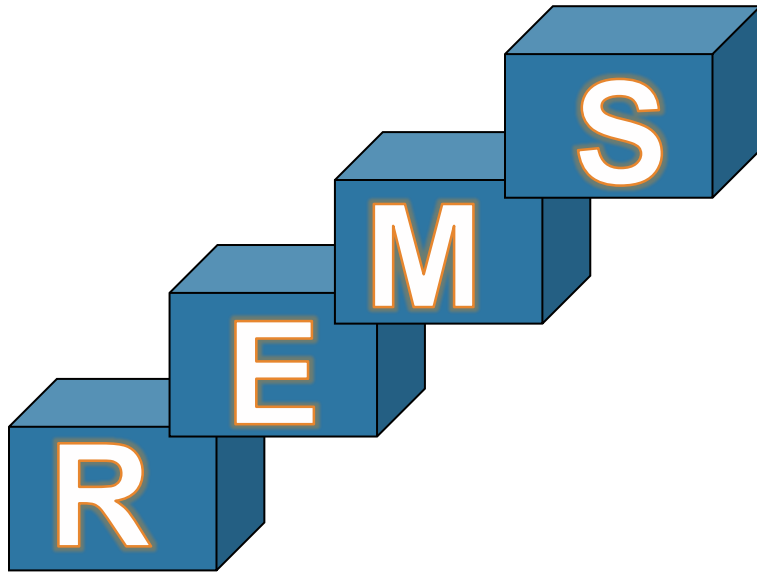


Development of the 2012 Extended Release and Long-Acting (ER/LA) Opioid Analgesic REMS

FDA Informs Sponsors a REMS is Needed



February 6, 2009

FDA notified holders of ER/LA opioid analgesics that their products would require a REMS to ensure that the benefits of those products continued to outweigh their risks.

March 3, 2009

FDA met with the application holders to discuss the REMS design to manage the risks while considering the burden on the health care system.

Stakeholder Input: Public Docket

FDA opened a public docket on April 20, 2009.

FDA is interested in obtaining information and public comment on the following issues:

- a. Elements of the REMS
- b. System Issues

FDA received 2617 comments on the proposed REMS.

Federal Register / Vol. 74, No. 74 / Monday, April 20, 2009 / Notices 17967

Agency: To discuss the annual strategic plan updating process and services and supports activities.

Place: In Person: National Institutes of Health, William H. Natlicher Conference Center, 43 Center Drive/Building 48, Conference Rooms E4.F2, Bethesda Campus, Bethesda, MD 20892.

Videocast: <http://videocast.nih.gov>.

Contact Person: Ms. Lina Perez, Office of Autism Research Coordination, Office of the Director, National Institute of Mental Health, NIH, 1001 Executive Boulevard, Bethesda, MD 20892-7060, (301) 443-0840.

93.282, Mental Health National Research Service Awards for Research Training, National Institutes of Health, HHS.

Date: April 13, 2009.

Resender: Spaeth, Director, Office of Federal Advisory Committee Policy, (FR Doc. E9-0033 Filed 4-17-09; 8:45 am)

BILLING CODE: 4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUMMARY: The Food and Drug Administration (FDA) is announcing a public meeting to obtain input on developing Risk Evaluation and Mitigation Strategies (REMS) for certain opioid drugs. The REMS would be intended to ensure that the benefits of these drugs continue to outweigh certain risks. The agency has long been concerned about adverse events associated with this class of drug and has taken steps in cooperation with drug manufacturers to address these risks. [We intend to use the comments, REMS](#)

The screenshot shows the 'regulations.gov' website interface. The main heading is 'Risk Evaluation and Mitigation Strategies for Certain Opioid Drugs'. Below this, there is a 'Docket Folder Summary' section with a 'View all documents and comments in this Docket' link. A 'Comments Received' badge is prominently displayed on the right side, showing '2,617 Comments Received'. The badge is circled in red. Below the badge, there is a 'Sign Up for Email Alerts' button. The main content area lists several documents, including 'Risk Evaluation and Mitigation Strategies for Certain Opioid Drugs, Notice of Public Meeting' and 'Public Meeting Risk Evaluation and Mitigation Strategies for Certain Opioid Drugs, May 28, 2009'. Each document entry includes a 'Comment Period Closed' date and time.

campus can fill up quickly. The NIH campus is also accessible via the metro Red Line, Medical Center Station. The Natlicher Conference Center is a 5-minute walk from the Medical Center Metro Station. Additional NIH campus visitor information is available at: <http://www.nih.gov/about/visitor/index.htm>. Information about the IACCT and a registration link for this meeting are available on the Web site: <http://www.iacct.hhs.gov>.

(Catalogue of Federal Domestic Assistance Program Nos. 93.242, Mental Health Research Grants; 93.281, Scientific Development Award, Scientific Development Award for Clinicians, and Research Scientist Award;

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
(Docket No. FDA-2009-N-0143)

Risk Evaluation and Mitigation Strategies for Certain Opioid Drugs; Notice of Public Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public meeting; request for comments.

706-3448, FAX: 301-847-3752, or Anne Henig, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg 51, rm. 6176, Silver Spring, MD 20903-0002, 301-796-3442, FAX: 301-847-8753, email: CpoidREMS@fdh.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDAAA (Public Law 110-85) created section 505-1 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355-1). Under section 505-1 of the act,

Stakeholder Input: Public Meetings

| February 9, 2009 | May 4-5, 2009 | May 27-28, 2009 | December 4, 2009 | July 22-23, 2010 |
|---|---|---|---|---|
| <p>Discuss the regulatory process and standards for review and approval of opioid products.</p> | <p>Obtain comments and opinions regarding the development of an opioid REMS</p> | <p>Hear about experiences with opioid drugs and suggestions for a REMS for ER/LA opioid products.</p> | <p>Hear from industry about their views on the specific features of the REMS.</p> | <p>Joint Meetings of ALSDAC and DSaRM to discuss FDA's proposal for a class-wide REMS for ER/LA opioids</p> |

Some Considerations in Developing the REMS

1 Scope of the REMS

2 Impact on the Health Care System

3 Impact on Patient Access to the Drug

Some Highlights of Stakeholder Comments (1)

- Size** Largest and most complex program of its kind
- Drugs** If the REMS only applies to ER/LA opioids, there will be shifts in prescribing to IR products or other potentially less effective pain relievers. Methadone should have a separate REMS.
- Prescriber Education** Many comments supported prescriber education but comments were divided as to whether such education should be mandatory.
- Include safe use, storage, and disposal of opioid medications, pain management, benefits and risks of opioid treatment.
 - If education is mandated, REMS certification should be linked to DEA registration to maximize participation, minimize cost, and streamline the prescription process.

Some Highlights of Stakeholder Comments (2)

Prescriber Certification

Individual prescriber enrollment and real time verification of prescriber training at pharmacy level could cause “opting out.” Consider linking certification to DEA registration or state requirements (e.g. state Medical Board Licensure).

Patient Education and Certification

Patient education is vital to the safe use of REMS drugs. A REMS that employs a patient registration system would be overly burdensome and create a stigma for pain patients that could adversely affect patient access to necessary medications.

Program Evaluation

It is critical to assess the effectiveness of the program and its impact on appropriate access to pain medications.

Other

Less restrictive elements should be implemented first to determine if they are effective in mitigating risk while preserving access.

Balancing Risk, Burden, and Patient Access

ETASU shall be commensurate with the specific serious risk listed in the labeling of the drug and considering such risk,

- Not be unduly burdensome on patient access to the drug
- And to the extent practicable minimize the burden on the health care delivery system



April 19, 2011

FDA sent REMS notification letters to application holders of ER/LA opioid analgesics. The notification letters specified requirements for

- Prescriber training/education
- Assessment plan and timetable for submission of assessments
- Medication Guide
- Patient Education Materials

Focus of the REMS was education and ER/LA products.

Prescriber Education

NDA #####

APPENDIX A: CONTENT OF EDUCATION PROGRAM

The training for prescribers required by the elements to assure safe use must contain the following content:

- I. General information for safe opioid prescribing
 - a. Patient selection and assessment
 - i. Determine goal of therapy
 - ii. Assessment of the risk of abuse, including history of substance abuse and serious mental illness
 - iii. When relevant, determining if patient is opioid tolerant
 - b. Considerations when prescribing opioids
 - i. Pharmacokinetics and potential for overdose
 - ii. Addiction, abuse, and misuse
 - iii. Intentional abuse by patient or household contacts
 - iv. Interactions with other medications/substances
 - c. Managing patients taking opioids
 - i. Establishing goals for treatment and evaluating pain control
 - ii. Use of Patient Provider Agreements (PPAs)
 - iii. Adherence to a treatment plan
 - iv. Recognizing aberrant behavior
 - v. Managing adverse events
 - d. Initiating and modifying dosing of opioids for chronic pain
 - i. As first opioid
 - ii. Converting from one opioid to another
 1. Converting from immediate-release to extended-release and long-acting products
 2. Converting from one extended-release and long-acting product to another
 - iii. Titrating to effect/tolerability
 - iv. How to deal with missed doses

- Prescriber education program includes
 - General information about the use of the class of ER/LA opioid analgesics to aid in patient selection and counseling
 - Specific drug information
 - Information about how to recognize the potential for and evidence of addiction, dependence, and tolerance
 - Training conducted by accredited, independent CME providers
- Training is not mandatory under REMS.
 - FDA supported mandatory training linked to DEA registration as proposed in the Administration's comprehensive plan to address the epidemic of prescription drug abuse in April 2011.

ACCME and FDA Collaboration



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Accreditation Criteria

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The Accreditation Criteria are divided into three levels. To achieve Provisional Accreditation, a two year term, providers must comply with Criteria 1, 2, 3, and 7–12. Providers seeking full Accreditation or reaccreditation for a four-year term must comply with Criteria 1–13. To achieve Accreditation with Commendation, a six-year term, providers must comply with all Accreditation Criteria.

NEED MORE HELP?
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312.527.9200

EDUCATIONAL RESOURCES
How would you explain the ACCME 2005 Accreditation Criteria for accredited CME in general?

- FDA worked with the Accreditation Council for Continuing Medical Education (ACCME) and other accrediting bodies and CE providers.



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HOME » REQUIREMENTS » ACCREDITATION REQUIREMENTS CME PROVIDERS » STANDARDS FOR COMMERCIAL SUPPORT: STANDARDS TO ENSURE INDEPENDENCE IN CME ACTIVITIES

Standards for Commercial Support: Standards to Ensure Independence in CME Activities

Standard 1: Independence

STANDARD 1.1 A CME provider must ensure that the following decisions were made free of the control of a commercial interest. (See www.accme.org for a definition of a "commercial interest" and some exemptions.) (a) Identification of CME needs; (b) Determination of educational objectives; (c) Selection and presentation of content; (d) Selection of all persons and organizations that will be in a position to control the content of the CME; (e) Selection of educational methods; (f) Evaluation of the activity.

NEED MORE HELP?
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EDUCATIONAL RESOURCES
What do I need to know about the role of employees of commercial interests in the planning and delivery of continuing medical education activities?

- Goal was to help ensure that CE programs developed to comply with the REMS would be in
 - compliance with ACCME accreditation criteria and
 - standards for commercial support.

FDA Lessons Learned re: CME

FDA and the CME community had different expectations for
The Blueprint for Prescriber Education

FDA

- FDA creates a *high level outline* to guide content of the Blueprint.
- FDA expected the *application holders to work together to develop the draft content* for FDA review and approval.
- This is analogous to how we handle the prescribing information in the label, i.e., sponsors may develop the draft, but FDA controls the content.

CME Community

- *FDA would develop the Blueprint* for CE providers to use to develop the actual CE content.
- Application holders provide FDA with information about the scope of the content.
- CME Community wanted to be sure that the FDA “controlled” the content of the professional education.

FDA Blueprint Available for Public Comment

- November 7, 2011 “Blueprint for Prescriber Education for Long-Acting/Extended-Release Opioid Class-Wide REMS”



- FDA received comments from about 65 individuals or organizations.
- Most comments were favorable and offered specific edits.
- The negative comments focused primarily on the REMS being ineffective in addressing the problem because
 - completion of the REMS training by prescribers is voluntary
 - industry is involved
 - the ER/LA opioid analgesic focus is too narrow

REMS Approval

- FDA considered comments received and approved the ER/LA Opioid Analgesics REMS on July 9, 2012 .
- The REMS included a
 - A Patient Counseling Document for a prescriber to give to a patient
 - One-page Medication Guide
- Final FDA “blueprint”
 - Posted on FDA website for accredited CE providers to develop training supported by independent educational grants from ER/LA opioid manufacturers.
 - Content focuses on safe prescribing of ER/LA opioid analgesics.
 - Directed to prescribers of ER/LA opioid analgesics but may be relevant for other healthcare professionals.

Patient Specific Information

The DOs and DON'Ts of Extended-Release / Long-Acting Opioids

DO:

- Read the Medication Guide
- Take your medicine exactly as prescribed
- Store your medicine away from children and in a safe place
- Flush unused medicine down the toilet
- Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088

Call 911 or your local emergency service, right away, if:

- You have trouble breathing

DO NOT:

- Take your medicine more often than prescribed
- Stop your medicine suddenly without talking to your doctor
- Drink alcohol while taking your medicine
- Take your medicine if you are pregnant or trying to get pregnant
- Take your medicine if you are breastfeeding

FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics 06/2015

Why Prescriber Education is Important

Health care professionals who prescribe extended-release (ER) and long-acting (LA) opioid analgesics (hereafter referred to as ER/LA opioid analgesics) are in a key position to balance the benefits of prescribing ER/LA opioid analgesics to treat pain against the risks of serious adverse outcomes including addiction, unintentional overdose, and death. Opioid misuse and abuse, resulting in injury and death, has emerged as a major public health problem.

- Based on the 2010 National Survey on Drug Use and Health, public health experts estimate more than 35 million Americans age 12 and older used an opioid analgesic for non-medical use some time in their life—an increase from about 30 million in 2002.³
- In 2009, there were nearly 343,000 emergency department visits involving nonmedical use of opioid analgesics.⁴
- In 2008, nearly 36,500 Americans died from drug poisonings, and of these, nearly 14,800 deaths involved opioid analgesics.⁵
- Improper use of any opioid can result in serious side effects including overdose and death, and this risk can be greater with ER/LA opioid analgesics.

Appropriate prescribing practices and patient education are important steps to help address this public health problem. Health care professionals who prescribe ER/LA opioid analgesics have a responsibility to help ensure the safe and effective use of these drug products. ER/LA opioid analgesics should be prescribed only by health care professionals who are knowledgeable in the use of potent opioids for the management of pain.

The expected results of the prescriber education in this REMS are that the prescribers will:

- Understand how to assess patients for treatment with ER/LA opioid analgesics.
- Be familiar with how to initiate therapy, modify dose, and discontinue use of ER/LA opioid analgesics.
- Be knowledgeable about how to manage ongoing therapy with ER/LA opioid analgesics.
- Know how to counsel patients and caregivers about the safe use of ER/LA opioid analgesics, including proper storage and disposal.
- Be familiar with general and product-specific drug information concerning ER/LA opioid analgesics.

I. Assessing Patients for Treatment with ER/LA Opioid Analgesic Therapy

- Prescribers should consider risks involved with ER/LA opioid analgesics and balance these against potential benefits. Risks include:
 - Overdose with ER/LA formulations, as most dosage units contain more opioid than immediate-release formulations.

³Substance Abuse and Mental Health Services Administration. 2011. Results from the 2010 National Survey on Drug Use and Health. Detailed Table, Table 7.1a. Rockville, MD. <http://www.samhsa.gov/2k11/NSDUH/Tables/Sec7/Tab7a1a45.htm#Tab7a1a>. Accessed on May 29, 2015.

⁴Substance Abuse and Mental Health Services Administration. 2011. Drug Abuse Warning Network, 2009: National Estimates of Drug-Related Emergency Department Visits, Table 19. Rockville, MD. <http://www.samhsa.gov/2k11/DAWN2009/DAWNED011M/DAWN2009ED.htm#Tab19>. Accessed on May 29, 2015.

⁵Vivner M, Chen LH, Mauck DM, Anderson RN, and Minino AM. 2011. Drug Poisoning Deaths in the United States, 1980–2008. In U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics. *NCHS Data Brief, No 87*. December 2011. Hyattsville, MD. <http://www.cdc.gov/nchs/data/ndb/087.pdf>. Accessed on May 29, 2015.

Summary

- Pharmaceutical companies, FDA, medical specialty groups, CME accreditors and accredited providers collaborated to include CME as a component of the ER-LA opioid analgesic REMS.
- Multiple companies successfully collaborated on the establishment, governance and operational aspects of a shared system REMS program with a CME component
- Lessons learned from creating the ER-LA opioid analgesic REMS CME program can be applied to the developing REMS requirements for immediate-release opioid analgesics.