4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-N-0951]

Reconsidering Mandatory Opioid Prescriber Education Through a Risk Evaluation and Mitigation Strategy in an Evolving Opioid Crisis; Public Workshop; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop; request for comments.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing the following public workshop entitled "Reconsidering Mandatory Opioid Prescriber Education Through a Risk Evaluation and Mitigation Strategy (REMS) in an Evolving Opioid Crisis." Convened by the Duke-Margolis Center for Health Policy and supported by a cooperative agreement between FDA and Duke-Margolis, the purpose of the public workshop is to give stakeholders an opportunity to provide input on aspects of the current opioid crisis that could be mitigated in a measurable way by requiring mandatory prescriber education as part of a REMS. We expect interested stakeholders to include healthcare providers, healthcare professional associations, pharmacists, pharmacy benefit managers, public and private insurers, patient organizations, Federal and State Agencies, providers of continuing education for healthcare professionals, and the public. A second public workshop is being planned to solicit input on additional issues associated with a move to mandatory prescriber education under a REMS, such as operational and technical issues related to such a system and what should be included in potential mandatory prescriber education.

DATES: The public workshop will be held on October 13, 2021, from 1 p.m. to 5 p.m. Eastern Time and October 14, 2021, from 1 p.m. to 4:05 p.m. Eastern Time. Submit either electronic or written comments on this public workshop by December 3, 2021. See the SUPPLEMENTARY INFORMATION section for registration date and information.

ADDRESSES: Due to the impact of the COVID-19 pandemic, these meetings will be held virtually to help protect the public and limit the spread of the virus.

You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before December 3, 2021. The https://www.regulations.gov electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of December 3, 2021. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2021-N-0951 for "Reconsidering Mandatory Opioid Prescriber Education Through a Risk Evaluation and Mitigation Strategy (REMS) in an Evolving Opioid Crisis." Comments filed and received in a timely manner (see ADDRESSES) will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469,

September 18, 2015, or access the information at:

https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Michie Hunt, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6153, Silver Spring, MD 20993, 301-796-3504, michie.hunt@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

As FDA continues to work to address the opioid crisis, we are reconsidering our current efforts to ensure prescriber education regarding opioids is being delivered in a way that is as efficient and effective as possible. As a part of this work, we are revisiting whether there is a need for a mandatory form of prescriber education linked to the prescribing of opioids. In 2012, FDA approved the Extended Release/Long Acting (ER/LA) Risk Evaluation and Mitigation Strategy (REMS), at the core of which was a requirement that sponsors of ER/LA opioid analgesics make an education program available for healthcare providers who prescribe ER/LA opioid analgesics (e.g., physicians, nurse practitioners, and physician assistants). The goal of the ER/LA opioid analgesic REMS was to reduce serious adverse outcomes resulting from inappropriate prescribing, misuse, and abuse of ER/LA opioid analgesics while maintaining patient access to pain medications. The adverse outcomes of concern included addiction, unintentional overdose, and death.

While developing the REMS requirements, FDA considered whether the education should be made mandatory for prescribers but decided against making mandatory education a

REMS requirement at the time. This was due to concerns about placing an undue burden on the healthcare delivery system, in part because the implementation of mandatory education through the REMS might have required a restricted distribution system. It is possible that given technological advances in the intervening years, including broader implementation of e-prescribing for controlled substances, there might be ways to lessen the burden associated with a restricted distribution system, including potential negative impact on patients who need opioids for pain management.

When the REMS was put in place in 2012, instead of mandatory education, FDA required that ER/LA opioid manufacturers make the training available to prescribers at no or nominal cost and that the training be accessible in a variety of different formats. FDA also recommended that the training be offered for continuing education (CE) credit. The REMS as implemented requires the training to conform to a blueprint (available at https://www.accessdata.fda.gov/drugsatfda_docs/rems/Opioid_analgesic_2018_09_18_FDA_Blueprint.pdf) developed by FDA that contains a high-level outline of the core educational messages to be included in the CE programs developed under the REMS. The initial education program included general and product-specific information about the ER/LA opioid analgesics; information on proper patient selection for use of these drugs; guidance for safely initiating therapy, modifying dosing, and discontinuing use of ER/LA opioid analgesics; guidance for monitoring patients; and information for counseling patients and caregivers about the safe use of these drugs.

After reviewing existing requirements and considering Advisory Committee recommendations obtained in 2016 about the ER/LA REMS, in 2018 FDA expanded the REMS to include both immediate release (IR) opioid analgesics and ER/LA opioid analgesics intended for use in an outpatient setting. The content of the blueprint was redesigned to contain principles of appropriate pain management, including the use of alternatives to opioids for the treatment of pain; the basic elements of addiction medicine; and the neurobiology, identification, and

management of opioid use disorder. The blueprint currently does not include principles for managing opioid use disorder, including treatment with buprenorphine. The revised Opioid Analgesic (OA) REMS also expanded the prescriber audience and requires that the OA manufacturers make training available to all members of the healthcare team involved in the management of patients with pain, including nurses and pharmacists. As with the ER/LA REMS, training under the OA REMS is voluntary.

Cumulatively, from February 28, 2013, through May 15, 2021, there have been 354,949 completers of REMS CE from the ER/LA REMS and the OA REMS. For context, there were approximately 1 million prescribers of opioid analgesics in 2019. In addition, although many public and private entities have independently implemented their own education programs and other interventions to encourage safe and effective prescribing practices for opioid analgesics, there is no nationwide standard. Therefore, these programs likely differ with regard to content, focus, and duration.

Following the creation and expansion of the REMS and other efforts, including the introduction of the Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain in 2016,[1] the estimated number of opioid analgesic prescriptions dispensed per capita in the United States has been steadily declining from a peak of 84 prescriptions per 100 residents in 2012 to 67 prescriptions per 100 residents in 2016; and 52 prescriptions per 100 residents in 2018. The rate dropped to 43 prescriptions per 100 U.S. residents in 2020, reflecting levels not seen since the early 1990s (44 prescriptions per 100 U.S. residents in 1992).[2] Despite this decrease in dispensing, multiple studies have reported patients received more opioid analgesic tablets than needed following surgical procedures. FDA's systematic review of studies published prior to 2019 showed that in articles reporting on the prescribing of excess tablets, 25 percent to 98 percent of the total tablets prescribed were

[1]Dowell, D., T.M. Haegerich, and R. Chou, "CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016". *JAMA*, (2016) 315(15):1624-1645.
[2]IQVIA Institute, "National Prescription Audit" extracted March 2021, U.S. Census Bureau.

reported to be excess, with most studies reporting that 50 percent to 70 percent of tablets went unused.[3] There are also concerns about continued opioid analgesic prescribing to vulnerable populations, such as children and adolescents following common dental and minor surgical procedures.

Despite this decline in opioid analgesic dispensing, overall opioid-involved overdose deaths have risen sharply since 2012, with opioids often seen in combination with other substances such as cocaine, methamphetamine, and benzodiazepines.[4, 5] This rise has been driven primarily by a surge in deaths initially involving heroin and then illicitly manufactured fentanyl and fentanyl analogues. Although these overdose deaths largely involve illicit substances, many users of illicit opioids are initially exposed to opioids through nonmedical use of prescription opioids.[6] Moreover, as of 2020, prescription opioids were involved in more than 16,000 fatal overdoses per year,[7] higher than the number seen at the peak of opioid analgesic dispensing in 2012.[8]

Against this background of a complex and intensifying crisis, FDA is reconsidering the need for mandatory prescriber training through a REMS and seeks input from stakeholders about the aspects of the opioid crisis that mandatory training through such a REMS could potentially mitigate. In light of the many available education programs and the lack of a nationwide standard, FDA is exploring the value of a single source for education on the appropriate use of opioids, on the risks of opioid abuse and misuse, and on the treatment of opioid use disorder to address multiple needs and reduce the burden on prescribers.

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[3]Mallama, C.A., C. Greene, A.A. Alexandridis, et al. "Patient-Reported Opioid Analgesic Use After Discharge From Surgical Procedures: A Systematic Review." (2021) *Pain Medicine,* doi: 10.1093/pm/pnab244.
[4]National Institute on Drug Abuse, "Overdose Death Rates." (2021) (Available at: https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates) (accessed August 20, 2021).
[5]Mattson C.L., L.J. Tanz, K. Quinn, et al, "Trends and Geographic Patterns in Drug and Synthetic Opioid Overdose Deaths--United States, 2013-2019." *Morbidity and Mortality Weekly Report*, (2021) 70(6):202-207.
[6]Compton, W.M., C.M. Jones, and G.T. Baldwin, "Relationship Between Nonmedical Prescription-Opioid Use and Heroin Use." *New England Journal of Medicine*, (2016) 374:154-163.
[7]Ahmad, F.B., L.M. Rossen, and P. Sutton, "Provisional Drug Overdose Death Counts." National Center for Health Statistics, 2021. (Available at: https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm) (accessed 8/20/2021).
[8]National Institute on Drug Abuse, "Overdose Death Rates." January 29, 2021. (Available at: https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates)

II. Topics for Discussion at the Public Workshop

1. How could mandatory prescriber education through a REMS improve appropriate opioid prescribing, pain management, and the treatment of opioid use disorder?

a. Please specifically discuss the value of such a system in light of existing continuing education requirements, the wide array of available educational programs (including currently available OA REMS educational offerings), and other interventions by Federal Agencies, States, healthcare systems, retail pharmacies, payers, pharmacy benefit managers, and other public and private organizations. Could mandatory education under a REMS make prescriber education more consistent, efficient, and effective?

b. Please specifically discuss how a mandatory REMS educational program could address the needs for prescriber education on the overprescribing of opioids for acute pain.

c. Please specifically discuss how a mandatory REMS educational program could address the needs for prescriber education on the treatment of opioid use disorder.

2. What are the important core competencies, knowledge gaps, clinical challenges, or misunderstandings among practitioners that could be addressed through mandatory education under a REMS to help improve patient outcomes and mitigate the current crisis?

a. Please comment specifically on any key knowledge gaps or core competencies related to screening, diagnosis, or treatment of opioid use disorder or substance use disorder that should be incorporated into mandatory education for opioid prescribers.

3. If FDA were to implement a mandatory prescriber education program, please discuss what appropriate program goals might be. How could we measure the impacts of such a program and determine whether it is meeting its goals?

4. Regarding the implementation of such a mandatory REMS educational system:

a. Please discuss challenges you foresee in the implementation of a mandatory REMS educational system.

b. What can we learn about the implementation of prescriber education from existing educational programs in pain management, in opioid risk reduction, and in the treatment of opioid use disorder?

5. What could be unintended consequences of mandatory opioid prescriber education through a REMS and are there ways to identify and address them?

Although not specifically discussed at this Public Workshop, FDA is interested in obtaining input on additional issues, including:

a. The continuing education delivery approaches, methods, and information technology platforms that should be considered to maximize the acceptability and effectiveness of mandatory prescriber education.

b. Any technological advances since 2012 that would make the delivery of mandatory training more efficient and reduce burden on the healthcare system.

III. Participating in the Public Workshop

Registration: To register for the public workshop, please visit the following website: http://events.constantcontact.com/register/event?llr=4fyj4myab&oeidk=a07eifbycnsfd5b6b1f. Please provide complete contact information for each attendee, including name, title, affiliation, address, email, and telephone.

Registration is free. Persons interested in attending this public workshop must register by 4:05 p.m. Eastern Time on October 14, 2021. Registrants will receive confirmation when they have been accepted. Registered participants will be sent technical system requirements in advance of the event. We recommend that you review these technical system requirements prior to joining the virtual public workshop. The workshop will be recorded, and the recording will be available after the workshop at https://healthpolicy.duke.edu/events/fda-public-workshop-opioid-prescriber-education.

There will be live closed captioning for this event. If you need other special accommodations due to a disability, please contact Michie Hunt (see FOR FURTHER

INFORMATION CONTACT) no later than October 4, 2021, or the Duke-Margolis Center for Health Policy at margolisevents@duke.edu.

FDA has verified the website addresses in this document, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

Dated: September 2, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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