Dear Healthcare Provider Letter #2

FDA-Required REMS for Serious Drug Risks

Risk Evaluation and Mitigation Strategy (REMS) for opioid analgesic drug products[1] used in the outpatient setting to address their risks of addiction, abuse, and misuse, which can lead to overdose and death.

Dear Healthcare Provider:

You are receiving this letter because you are either registered with the Drug Enforcement Administration (DEA) to prescribe Schedule II, III, IV opioid analgesics and/or you are involved in the management or support of patients with pain and their caregivers. The purpose of this letter is to inform you about the Opioid Analgesic REMS that is required by the U.S. Food and Drug Administration (FDA) for opioid analgesic drug products used in the outpatient setting. Under the conditions of the REMS, the following resources are available:

1. Safe Disposal of Unused Opioid Analgesics—Pre-Paid Drug Mail-Back Envelopes

Counseling patients on the options for safe disposal of unused opioid analgesics is a critical component of the Opioid Analgesic REMS to avoid nonmedical use, opioid use disorder (OUD), and overdose. To support the availability of safe disposal systems, opioid analgesic manufacturers are providing pre-paid drug mail-back envelopes that can be given to patients with their opioid analgesic prescriptions upon request to pharmacies and other dispensers that dispense opioid analgesics for outpatient use.

Pharmacies and other opioid dispensing sites can order pre-paid drug mail-back envelopes via the REMS website, www.opioidanalgesicrems.com, or by calling 1-800-503-0784 starting March 31, 2025.

Disposal options include drug take-back sites or programs and pre-paid drug mail-back envelopes. If these options are not available, the next best option is for patients to immediately flush their opioid analgesics down the toilet. More information on safe disposal methods is available at: www.fda.gov/safe-disposal-medicines.

2. REMS-Compliant Accredited Continuing Education (CE)

REMS-compliant training is a critical component of the Opioid Analgesic REMS and focuses on pain management and creating a pain treatment plan. The FDA developed specific core concepts to be communicated to a broad range of Health Care Providers (HCPs) in the **Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain** ("FDA Blueprint"). This "**FDA Blueprint**" is being used to develop training that includes accredited CE courses or training offered by academic institutions/learned societies. The "**FDA Blueprint**" is available at: https://www.fda.gov/media/173774/download?attachment

Following completion of educational activities under the Opioid Analgesic REMS, HCPs should be knowledgeable about the following.

- The fundamental concepts of pain management, including definitions and mechanisms of pain
- How to assess patients in pain, and identify risk factors for substance use disorders

- The range of therapeutic options for managing pain, including nonpharmacologic approaches and pharmacologic (non-opioid and opioid analgesics) therapies
- How to integrate opioid analgesics into a pain treatment plan individualized to the needs of the patient and evaluate for functional improvement
- How to safely and effectively manage patients on opioid analgesics in the acute and chronic pain settings, including initiating therapy, titrating, and discontinuing use of opioid analgesics
- How to counsel patients and caregivers about the safe use of opioid analgesics, including proper storage and disposal (e.g., drug take-back sites or programs and mail-back envelopes)
- How to counsel patients and caregivers about the use of naloxone for opioid overdose
- When referral to a pain specialist is appropriate
- The fundamental elements of addiction medicine
- How to identify and manage patients with OUD

REMS-compliant accredited CE is available. Visit www.opioidanalgesicrems.com for a listing of available REMS-compliant training.

3. The Opioid Analgesic REMS Patient Guide & Medication Guide

Enclosed with this letter is the **Patient Guide** that was developed under the REMS. It was specifically designed to assist **you** with conducting important conversations about safety with patients for whom an opioid analgesic may be prescribed. It contains important safety information common to the drug products subject to this REMS and options for safe disposal of opioid medicines. The **Patient Guide** should be provided to the patient or their caregiver at the time of prescribing. The **Patient Guide** is also available on the REMS website, www.opioidanalgesicrems.com, or ordered by calling the REMS Call Center at 1-800-503-0784.

Adverse Event Reporting

To report all suspected adverse reactions associated with the use of the opioid analgesics, contact:

- the FDA MedWatch program:
  - by phone at 1-800-FDA-1088 (1-800-332-1088) or
  - online at www.fda.gov/medwatch, or
- the pharmaceutical company that markets the specific product

More information about this REMS can be obtained at: www.opioidanalgesicrems.com or by calling the Opioid Analgesic REMS Call Center at 1-800-503-0784.

Sincerely,
The Opioid Analgesic REMS Program Companies

[1]**The branded and generic drug products subject to this REMS include *all*:** a) oral dosage forms of extended-release and immediate-release opioids containing: codeine and codeine analogs, hydrocodone, hydromorphone, levorphanol, meperidine, morphine, oxycodone, oxymorphone, pentazocine, tapentadol and tramadol; b) fentanyl, butorphanol and buprenorphine-containing intranasal, buccal and transdermal delivery systems; and c) methadone tablets and solutions that are indicated for use as analgesics.