



March 2025

FDA-Required REMS for Serious Drug Risks

Risk Evaluation and Mitigation Strategy (REMS) for opioid analgesic drug products¹ used in the outpatient setting to address their risks of addiction, abuse, and misuse, which can lead to overdose and death.

Dear **Professional Society/Licensing Board**:

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. We ask you to consider the development and/or distribution of training materials for your healthcare providers (HCPs) and encourage them to utilize the below resources and to successfully complete REMS-compliant training to improve their ability to prescribe and dispense these medications more safely. 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 now order pre-paid drug mail-back envelopes via the REMS website, <https://www.opioidanalgesicrems.com/home.html>, 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: <https://www.fda.gov/drugs/buying-using-medicine-safely/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 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 <https://www.opioidanalgesicrems.com/home.html> 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, <https://www.opioidanalgesicrems.com/home.html>, 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: <https://www.opioidanalgesicrems.com/home.html> 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.

What other options are there to help with my pain?

Opioids are not the only thing that can help you control your pain. Ask your healthcare provider if your pain might be helped with a non-opioid medication, physical therapy, exercise, rest, acupuncture, types of behavioral therapy, or patient self-help techniques.

What is naloxone?

- Naloxone is a medicine that treats opioid overdose. It is sprayed inside your nose or injected into your body.
- Use naloxone if you have it and call 911 or go to the emergency room right away if:
 - You or someone else has taken an opioid medicine and is having trouble breathing, is short of breath, or is unusually sleepy
 - A child has accidentally taken the opioid medicine or you think they might have
- Giving naloxone to a person, even a child, who has not taken an opioid medicine will not hurt them.

Where can I get naloxone?

- There are some naloxone products that are designed for people to use in their home.
- Naloxone is available in pharmacies. Ask your healthcare provider about how you can get naloxone. In some states, you may not need a prescription.
- When you get your naloxone from the pharmacy, **read the Patient Information** on how to use naloxone and ask the pharmacist if anything is unclear.
- Tell your family about your naloxone and keep it in a place where you or your family can get to it in an emergency.

How should I dispose of the opioid medicine?

When you no longer need your opioid medicine, dispose of it as quickly as possible to avoid any possibility of abuse or misuse by anyone else. The Food and Drug Administration recommends that you drop off your medicine at a drug take-back site or program or mail your medicine using a pre-paid drug mail-back envelope. If you cannot get to a drug take-back location or if a mail-back envelope is not available to you, your next best option is to immediately flush your medicine down the toilet. Find more information about disposal methods here: [Drug Disposal: Drug Take-Back Options | FDA](#)

Naloxone is never a substitute for emergency medical care. Always call 911 or go to the emergency room if you've used or given naloxone.

What things should I know about the specific opioid medicine that I am taking?

- Your health care provider has prescribed _____ for you. Read the Medication Guide for this medicine, which is information provided by your pharmacy.
- Remember this other important information about your opioid medicine:

Dosing instructions: _____

Any specific interactions with your medicines: _____

What if I have more questions?

- Read the Medication Guide that comes with your opioid medicine prescription for more specific information about your medicine.
- Talk to your healthcare provider or pharmacist and ask them any questions you may have.
- Visit: [Opioid Medications | FDA](#) for more information about opioid medicines.

What You Need to Know About Opioid Pain Medicines

This guide is for you! Keep this guide and the Medication Guide that comes with your medicine so you can better understand what you need to know about your opioid pain medicine. Go over this information with your healthcare provider. Then, ask your healthcare provider about anything that you do not understand.

What are opioids?

Opioids are strong prescription medicines that are used to manage severe pain.

What are the serious risks of using opioids?

- Opioids have serious risks of addiction, abuse, and misuse, which can lead to overdose.
- Too much opioid medicine in your body can cause your **breathing to stop** - which could lead to death. This risk is greater if you are taking other medicines that make you feel sleepy or people with sleep apnea.
- **Addiction** is when you crave drugs (like opioid pain medicines) because they make you feel good in some way. You keep taking the drug even though you know it is not a good idea and bad things are happening to you. Addiction is a brain disease that may require ongoing treatment.

Risk Factors for Opioid Abuse:

- You have:
 - » a history of addiction
 - » a family history of addiction
 - You take medicines to treat mental health problems
 - You are under the age of 65 (although anyone can abuse opioid medicines)
- **You can get addicted to opioids even though you take them exactly as prescribed, especially if taken for a long time.**
 - If you think you might be addicted, talk to your healthcare provider right away.
 - If you take an opioid medicine for more than a few days, your body becomes physically dependent." This is normal, and it means your body has gotten used to the medicine. You must taper off the opioid medicine (slowly take less medicine) when you no longer need it to avoid withdrawal symptoms.

How can I take opioid pain medicine safely?

- Tell your healthcare provider about **all** the medicines you are taking, including vitamins, herbal supplements, and other over-the-counter medicines.
- Read the Medication Guide that comes with your prescription.
- Take your opioid medicine exactly as prescribed.
- Do not cut, break, chew, crush, or dissolve your medicine. If you cannot swallow your medicine whole, talk to your healthcare provider.
- When your healthcare provider gives you the prescription, ask:
 - How long should I take it?
 - What should I do if I need to taper off the opioid medicine (slowly take less medicine)?
- Call your healthcare provider if the opioid medicine is not controlling your pain. Do not increase the dose on your own.
- **Do not share or give your opioid medicine to anyone else.** Your healthcare provider selected this opioid and the dose just for **you**. A dose that is okay for you could cause an overdose and death for someone else. Also, it is against the law.
- Store your opioid medicine in a safe place where it cannot be reached by children or stolen by family or visitors to your home. Many teenagers like to experiment with pain medicines. Use a lock-box to keep your opioid medicine safe. Keep track of the amount of medicine you have.
- Do not operate heavy machinery until you know how your opioid medicine affects you. Your opioid medicine can make you sleepy, dizzy, or lightheaded.

What should I avoid taking while I am taking opioids?

Unless prescribed by your healthcare provider, you should avoid taking alcohol or any of the following medicines with an opioid because it may cause you to stop breathing, which can lead to death:

- Alcohol: Do not drink any kind of alcohol while you are taking opioid medicines.
- Benzodiazepines (like Valium or Xanax)
- Muscle relaxants (like Soma or Flexeril)
- Sleep medicines (like Ambien or Lunesta)