

Introduction

FDA's Opioid Analgesic REMS Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain

Background

In July 2012, FDA approved the Extended-Release and Long-Acting (ER/LA) Opioid Analgesic Risk Evaluation and Mitigation Strategy (ER/LA REMS) to ensure that the benefits of ER and LA opioid analgesics used in the outpatient setting outweigh the risks. That REMS was modified and the new *Opioid Analgesic REMS* includes, in addition to ER/LA opioid analgesics, all immediate-release (IR) opioids used in the outpatient setting that are not already covered by another REMS program. The *Opioid Analgesic REMS* is intended to support other national efforts underway to address the misuse and abuse of prescription opioid analgesics.

As part of the Opioid Analgesic REMS, all opioid analgesic companies must provide the following:

- Education for health care providers (HCPs) who participate in the treatment and monitoring of pain. For the purpose of the Opioid Analgesic REMS, HCPs will include not only prescribers, but also HCPs who participate in the treatment and monitoring of patients who receive opioid analgesics, including pharmacists and nurses.
 - Education will be offered through accredited continuing education (CE) activities. These activities will be supported by unrestricted educational grants from opioid analgesic companies.
- Information for HCPs to use when counseling patients about the risks of ER, LA, and IR opioid analgesic use.

To facilitate the development of CE educational materials and activities as part of the Opioid Analgesic REMS, FDA has also revised the education blueprint — originally designed to facilitate development of CE educational materials under the ER/LA REMS. FDA has completed the revisions to the *FDA Education Blueprint for Health Care Providers Involved in the Treatment and Monitoring of Patients with Pain* (FDA Blueprint), following publication of a draft version and consideration of received public comments.

The FDA Blueprint contains a high-level outline of the core educational messages that will be included in the educational programs developed under the Opioid Analgesic REMS. The FDA Blueprint focuses on the fundamentals of acute and chronic pain management and provides a contextual framework for the safe prescribing of opioid analgesics. The core messages are directed to prescribers, pharmacists, and nurses, but are also relevant for other HCPs who participate in the management of pain. The course work is not intended to be exhaustive nor a substitute for a more comprehensive pain management course.

Accrediting bodies and CE providers will ensure that the CE activities developed comply with the standards for CE of the Accreditation Council for Continuing Medical Education,^{1,2} or another CE accrediting body, depending on the target audience's medical specialty or health care profession.

FDA is making the FDA Blueprint, approved as part of the Opioid Analgesic REMS, available on the REMS@FDA Website (www.fda.gov/REMS), where it will remain posted for use by CE providers as they develop the CE materials and activities. A list of the REMS-compliant CE activities supported by unrestricted educational grants from the opioid analgesic companies to accredited CE providers will be posted at www.opioidanalgesicREMS.com as that information becomes available.

Reasons Why HCP Education Is So Important

Adverse outcomes of addiction, unintentional overdose, and death resulting from inappropriate prescribing, abuse, and misuse of opioids have emerged as major public health problems. It is critical that HCPs are knowledgeable about the risks associated with opioid analgesics as they pertain to their patients as well as from a public health perspective. The data continue to show problems associated with prescription opioid analgesics.

- In 2015, over 52,404 Americans died from drug poisonings, and of these, 24% or approximately 12,570 deaths involved opioid analgesics.³
- Based on the 2016 National Survey on Drug Use and Health (NSDUH), an estimated 11.5 million Americans aged 12 or older misused a prescription pain reliever in the past year — with hydrocodone, oxycodone, and codeine products being the most commonly reported.⁴
- The most common source of pain relievers in the 2016 NSDUH was “a friend or relative” (53%). “A physician’s prescription” was the second most common source, reported by approximately 35% of respondents.⁵

The nation is facing competing public health problems: the need to adequately treat a large number of Americans with acute and chronic pain and an epidemic of prescription opioid abuse.

¹ [Accreditation Council for Continuing Medical Education. 2016. Accreditation Requirements. Criteria for CME Providers-Accreditation Criteria.](#) Accessed July 2018.

² [Accreditation Council for Continuing Medical Education. 2016. Accreditation Requirements. Criteria for CME Providers-Standards for Commercial Support.](#) Accessed July 2018.

³ See https://www.cdc.gov/nchs/data/factsheets/factsheet_drug_poisoning.pdf. Accessed July 2018.

⁴ Substance Abuse and Mental Health Services Administration. (2017). *Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health* (HHS Publication No. SMA 17-5044, NSDUH Series H-52). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

⁵ Ibid.

Described in the 2011 report by the National Academies of Science, Engineering, and Medicine (NASEM), *Relieving PAIN in America, A Blueprint for Transforming Prevention, Care, Education, and Research*,⁶ 100 million Americans suffer from common chronic pain conditions; fewer than half of Americans undergoing surgery report adequate pain relief; and 60% of Americans visiting the emergency department with acute painful conditions receive analgesics.

The increasing availability of prescription opioids since the 1990's has been accompanied by an epidemic of opioid addiction. The Substance Abuse and Mental Health Services Administration's *National Survey of Drug Use and Health* has shown that most people who use prescription analgesics "nonmedically" obtain them from friends or family, who it is believed obtained the drugs from a doctor's prescription.⁷

Some of the immediate consequences of untreated or undertreated pain include reduced quality of life, impaired physical function, and high economic costs. Chronic pain is associated with physical disability, fear, anger, depression, anxiety, and reduced ability to carry out the roles of family member, friend, and employee. It is critically important that HCPs have all the information they need to properly treat their patients and safely manage their pain. It is also critical for HCPs to understand when opioid analgesics are the appropriate treatment and how to implement best practices to ensure their patients' safety. A 2017 report by NASEM, *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*, describes the challenges of providing adequate pain management and calls for the establishment of "comprehensive pain education materials and curricula" for HCPs.⁸

Having broad knowledge about how to manage patients with pain can create the opportunity for HCPs to consider *all* options for pain management, including nonpharmacologic and non-opioid pharmacologic options, and to reserve opioids for when non-opioid options are inadequate and when the benefits of the opioids are expected to outweigh the risks. This information can also aid HCPs in identifying and intervening when encountering obstacles that may reduce access to nonpharmacological and non-opioid medication options. Fully informed HCPs can help contribute to national efforts to address opioid addiction and reduce opioid misuse and abuse.

⁶ <http://www.nationalacademies.org/hmd/Reports/2011/Relieving-Pain-in-America-A-Blueprint-for-Transforming-Prevention-Care-Education-Research.aspx>. Accessed July 2018.

⁷ <https://www.samhsa.gov/data/sites/default/files/NSDUH-DeTubs-2016/NSDUH-DeTubs-2016.pdf>, Table 6.53A. Accessed July 2018.

⁸ <http://nationalacademies.org/hmd/Reports/2017/pain-management-and-the-opioid-epidemic.aspx>. Accessed July 2018.

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Purpose of the Opioid Analgesic REMS HCP Educational Effort

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, identifying risk factors for abuse and addiction
- 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
- 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
- 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 opioid use disorder

In addition, HCPs will gain an understanding of current information about safe opioid practices and about current Federal⁹ and State regulations, national guidelines,¹⁰ and professional organization¹¹ and medical specialty guidelines on treating pain and prescribing opioids. HCPs will also become familiar with the use of naloxone and with the importance of its availability for use by patients and caregivers both in the community and in the home.

⁹ For example, see <https://www.deadiversion.usdoj.gov/21cfr/cfr/2106cfrt.htm> and <https://www.deadiversion.usdoj.gov/21cfr/21usc/829.htm>. Accessed July 2018.

¹⁰ For example, see Dowell D, Haegerich TM, Chou R. 2016. [CDC Guideline for Prescribing Opioids for Chronic Pain](#) –United States, 2016. MMWR Recomm Rep 2016; 65 (No.RR-1): 1-49. Accessed July 2018.

¹¹ For example, see [Federation of State Medical Boards' Guidelines for the Chronic Use of Opioid Analgesics](#). Accessed July 2018.

Section 1: The Basics of Pain Management

I. THE NEED FOR COMPREHENSIVE PAIN EDUCATION

The FDA Blueprint was developed with two, competing, U.S. public health concerns in mind, (1) the large number of Americans with acute and chronic pain and (2) the epidemic of prescription opioid abuse.

1. Providing health care providers (HCPs) with a thorough understanding of the risks associated with opioids can give HCPs the opportunity to consider all pain management options, including nonpharmacologic and pharmacologic options, prescribing opioids only when non-opioid options are inadequate and when the benefits of using an opioid are expected to outweigh the risks.
2. When HCPs have information about the risks of opioid misuse and abuse, they will be better able to create opportunities for patient counseling and other strategies to reduce these risks.

II. DEFINITIONS AND MECHANISMS OF PAIN

Pain can be categorized according to its duration, underlying pathophysiology of the original insult, and whether a central sensitization component has developed. An understanding of these different categorizations can help direct therapeutic decisions.

When defining, and classifying pain, the following should be taken into consideration:

1. Biological significance of pain (survival value)
2. Relationship between acute and chronic pain
3. Distinction between nociceptive and neuropathic pain

III. ASSESSING PATIENTS IN PAIN

HCPs should be knowledgeable about how to assess each patient when initiating a pain management program. When appropriate, evidence-based, standardized scales and tools can be used to document pain characteristics and guide management decisions throughout treatment, noting the strengths and weaknesses regarding specificity and sensitivity of these scales.

Important elements of an initial assessment should include the following:

1. Patient history

2. Screening tools to evaluate the known risk factors for development of chronic pain after an acute injury or disease
3. Screening tools to evaluate the known risk factors for opioid use disorder (OUD) or abuse
4. Queries of state prescription drug monitoring programs (PDMPs)
5. Pain assessment scales/tools
6. Functional assessment scales
7. Physical examination
8. Family planning, including information about use of contraceptives, pregnancy intent/status and plans to breastfeed
9. Psychological and social evaluation
10. Diagnostic studies when indicated

Section 2: Creating the Pain Treatment Plan

A comprehensive pain treatment plan should be developed and customized to the needs of the individual patient. The treatment plan should include the types of therapies planned, the goals of treatment, and an explanation of the patient and prescriber roles and responsibilities. The goals of treatment should be based on (1) expected outcomes of pain reduction; (2) improvement in functional outcomes impaired by pain (e.g., activities of daily living); and (3) quality of life.

If HCPs encounter potential barriers to managing patients with pharmacologic and/or nonpharmacologic treatment options, such as lack of insurance coverage or inadequate availability of certain HCPs who treat patients with pain, attempts should be made to address these barriers. The overall treatment approach and plan should be well documented in the patient record, including written agreements and informed consent/patient provider agreements (PPAs) that reinforce patient-provider responsibilities and avoid punitive tones.

I. COMPONENTS OF AN EFFECTIVE TREATMENT PLAN

1. The goals of treatment, including the degree of improvement in pain and function when function has been impaired by pain
2. Possible constituents of the treatment plan, including nonpharmacologic approaches and pharmacologic therapies
3. Patient/prescriber/health care team interactions, including

- Patient responsibilities/compliance with the plan
- Responsibilities of the prescriber and health care team, including patient monitoring
- Plans for reviewing functional goals
- Use of supplemental medication for intermittent increases in pain
- Use of PPAs

II. GENERAL PRINCIPLES OF NONPHARMACOLOGIC APPROACHES

Pain can arise from a wide variety of causes. There are a number of nonpharmacologic and self-management treatment options that have been found to be effective alone or as part of a comprehensive pain management plan, particularly for musculoskeletal pain and chronic pain. Examples include, but are not limited to, psychological, physical rehabilitative, and surgical approaches, complementary therapies,¹² and use of approved/cleared medical devices for pain management. HCPs should be knowledgeable about the range of treatment options available, the types of pain that may be responsive to those options, and when they should be used as part of a multidisciplinary approach to pain management. HCPs should also be aware that not all nonpharmacologic options have the same strength of evidence to support their utility in the management of pain, and some may be more applicable for some conditions than others.

III. GENERAL PRINCIPLES OF PHARMACOLOGIC ANALGESIC THERAPY

A variety of analgesics, including non-opioid and opioid medications, are available for use to manage pain symptoms. HCPs should be well informed about the range of analgesics available and the types of pain that may be responsive to those analgesics.

A. Non-opioid medications

When using non-opioid medications in pain management, HCPs should be knowledgeable about the following:

1. Mechanism of action of analgesic effect
2. Indications and uses for pain management
3. Routes of administration and formulations used in pain management
4. Initial dosing, dose titration, dose tapering (when appropriate) for analgesia
5. Contraindications
6. Adverse events, with emphasis on labeled warnings
7. Drug interactions — both pharmacodynamic and pharmacokinetic

B. Opioid analgesic medications

Opioid analgesic medications can be used successfully as a component of pain management. However, opioids carry risks not present with most non-opioid analgesics, specifically the risks

¹² For example, see <https://nccih.nih.gov>. Accessed July 2018.

of addiction, abuse and misuse, which can lead to respiratory depression, overdose and death. Therefore, it is the responsibility of HCPs to be knowledgeable, not just about the presence of such risks, but about how to weigh these risks before prescribing an opioid and about how to properly manage patients who are prescribed opioids, both for short-term and long-term use. When using opioid analgesics as part of pain management, HCPs should be knowledgeable about the following:

1. General precautions
 - a. Even at prescribed doses, opioid analgesics carry the risk of misuse, abuse, opioid use disorder, overdose, and death
 - b. Importance of the appropriate use of PDMPs¹³ and their use as a clinical decision support tool
 - c. DSM-5 (R) criteria (or the most recent version) for OUD and the concepts of abuse (taking an opioid to get high) vs. misuse (taking more than prescribed for pain or giving to someone else in pain)¹⁴
 - d. The concepts of tolerance and physiological dependence and how they differ from OUD (addiction)
 - e. Recognition that some opioid analgesics (e.g., Transmucosal Immediate Release Fentanyl products, some ER/LA products) are safe only for opioid-tolerant patients
2. Mechanism of action and analgesic effect
3. Types of opioids (full agonists, partial agonists)
4. Indications and uses for pain management
5. Range of opioid analgesic products available for pain management and their related safety concerns
 - a. Routes of administration including oral, transmucosal, transdermal
 - b. Release characteristics of immediate release (IR), extended-release (ER), long-acting (LA)
 - c. Abuse-deterrent formulations (ADFs)
 - Definition of ADF based on the FDA guidance for industry, *Abuse-Deterrent Opioids – Evaluation and Labeling*¹⁵
 - Recognition that all ADFs have the same potential for addiction and overdose death as non-abuse-deterrent opioids
 - How to understand FDA-approved ADF product labeling
6. Initial dosing, dose titration, dose tapering (when appropriate) for analgesia
 - a. Concepts and limitations of the conversion charts in labeling and the limitations of relative potency or equianalgesic dosing tables in literature

¹³ [SAMHSA Prescription Drug Monitoring Programs: A Guide for Healthcare Providers](#). Accessed July 2018.

¹⁴ [American Psychiatric Association DSM-5-Opioid Use Disorder Diagnostic Criteria](#). Accessed July 2018.

¹⁵ See FDA guidance for industry [Abuse-Deterrent Opioids – Evaluation and Labeling](#). Accessed July 2018.

- b. Interindividual variability of response
 - c. Special populations
 - Pregnant, postpartum, breastfeeding, and neonatal opioid withdrawal syndrome
 - Renal and hepatic impairment
 - Children and adolescents
 - Genetic and phenotypic variations
 - Older adults
 - Sleep disorders
 - Common and uncommon psychiatric disorders
7. Contraindications
8. Adverse Events
- a. Medication errors
 - b. Periods of greater risk for significant respiratory depression, including at treatment initiation and with dose increases
 - c. Serious adverse drug reactions (including overdose and death)
 - d. Labeled warnings
 - e. Common adverse drug reactions
9. Drug interactions
- a. Pharmacokinetic interactions based on metabolic pathway
 - b. Pharmacokinetic and pharmacodynamic interactions with alcohol
 - c. Concerns with particular drug–drug interactions, including, but not limited to:
 - Benzodiazepines and other central nervous system depressants, including alcohol
 - Monoamine oxidase inhibitors
 - Antidiuretic hormone drugs
10. Key safety strategies for use with opioid medications
- a. Dosing instructions including daily maximum
 - b. Safe storage to reduce risk of accidental exposure/ingestion by household contacts, especially children/teens and to reduce risk of theft
 - c. Naloxone products for use in the home to reduce risk of overdose deaths in patients and household contacts
 - d. Proper disposal of used (e.g., transdermal systems) and unused opioids
 - e. Pain management after an opioid overdose
 - f. Driving and work safety

IV. MANAGING PATIENTS ON OPIOID ANALGESICS

HCPs should be knowledgeable about the appropriate use of opioids in patients with acute and chronic pain, including the importance of balancing potential benefits with the risks of serious adverse outcomes such as overdose and death.

A. Initiating treatment with opioids — acute pain

1. Patient selection — consider when an opioid is an appropriate option and consult the PDMP
2. Dosing — as needed vs. around-the clock dosing, prescribing an appropriate quantity based on the expected duration of pain, i.e., the least amount of medication necessary to treat pain and for the shortest amount of time
3. Naloxone for home use — prescribe and discuss the use of naloxone products and the various means of administration
4. Screening tools for risk of abuse

B. Initiating treatment with opioids — chronic pain

1. Patient selection
 - a. Differences in benefit and risk and expected outcomes for patients with chronic pain, palliative care, or end-of-life care
 - b. Differences in initiating treatment in opioid nontolerant vs. opioid-tolerant patients
2. Dosing
 - a. As needed vs. around-the-clock
 - b. How to determine a safe initial dose
 - c. Safe conversion from other opioids
3. Considerations in opioid selection
 - a. IR or ER/LA
 - b. Special precautions with methadone
 - c. Products restricted to opioid-tolerant patients
4. When and how to use an opioid or non-opioid analgesic to supplement pain management

C. Ongoing management of patients on opioid analgesics

1. Periodic review of pain and functional goals
2. Review adverse events at each visit
 - Eliciting signs or symptoms of opioid abuse
 - Screening for endocrine function may be recommended

- Importance of adverse event reporting and mechanisms to report
3. Review refill history/review PDMP
 4. How to determine when an opioid analgesic is no longer necessary/beneficial

D. Long-term management

1. Evaluation of the patient with worsening pain for changes in underlying condition and for signs of OUD before increasing opioid dosage
2. Changing opioid medications
 - Concept of incomplete cross-tolerance when converting patients from one opioid to another
 - Concepts and limitations of the conversion charts in labeling and the limitations of relative potency or equianalgesic dosing tables in literature
3. Monitoring of patient adherence to the treatment plan, especially regarding misuse and abuse:
 - Perform medication reconciliation — recognize, document, and address aberrant drug-related behavior
 - Determine if nonadherence is due to inadequate pain management
 - Understand the utility and interpretation of urine drug testing (e.g., screening and confirmatory tests) and use as indicated
 - Screen and refer for substance use disorder treatment when concerns arise

E. How to recognize and intervene upon suspicion or identification of an OUD

HCPs should understand how to monitor patients taking opioid analgesics and identify the signs and symptoms of opioid misuse, abuse, and OUD and be knowledgeable about how to begin the process of intervention upon suspicion of an OUD.

F. When to consult with a pain specialist

HCPs should be knowledgeable about when referral to a pain management specialist is indicated, including identifying patients at high risk for OUD and patients unable to achieve adequate pain management.

G. Medically directed opioid tapering

HCPs should be knowledgeable about how to safely taper opioid analgesics, including how to recognize and manage signs and symptoms of opioid withdrawal. HCPs should be knowledgeable about the particular risks associated with tapering during pregnancy.

H. Importance of patient education

HCPs should recognize their role in reducing the risks associated with opioid analgesics through patient education at initiation of an opioid and throughout long-term management.

1. Inform patients about pain management expectations and managing pain through different pharmacologic and nonpharmacologic modalities.
2. Use the *Patient Counseling Guide: What You Need to Know About Opioid Pain Medicines* as part of discussion with patients and caregivers when prescribing opioid analgesics.
3. Counsel the patient about the following:
 - a. Importance of adherence to prescribed dosing regimen
 - b. Patients should use the least amount of medication necessary to treat pain and for the shortest amount of time
 - c. The risk of serious adverse events that can lead to death
 - d. The risk of addiction that can occur even when product is used as recommended
 - e. Known risk factors for serious adverse events, including signs and symptoms of overdose and opioid-induced respiratory depression, GI obstruction, and allergic reactions, among others
 - f. The most common side effects, along with the risk of falls, working with heavy machinery, and driving
 - g. When to call the prescriber (e.g., managing adverse events, ongoing pain)
 - h. How to handle missed doses
 - i. The importance of full disclosure of all medications and supplements to all HCPs and the risks associated with the use of alcohol and other opioids/benzodiazepines
 - j. Product-specific concerns, such as not to crush or chew ER products; transdermal systems and buccal films should not be cut, torn, or damaged before use, etc.
 - k. How to safely taper dose to avoid withdrawal symptoms
 - l. Safe storage and disposal, risks of theft by family members and household visitors
 - m. Never share any opioid analgesic with another person
 - n. How and when to use naloxone products and their various means of administration
 - o. Seeking emergency medical treatment if an opioid overdose occurs
 - p. How to report adverse events and medication errors to FDA (1-800-fda-1088 or via <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>)

V. ADDICTION MEDICINE PRIMER

HCPs should be knowledgeable about the basic elements of addiction medicine and be familiar with the definition, neurobiology, and pharmacotherapy of OUDs. In particular, stigmatizing or blaming language should be replaced with language that acknowledges that addiction,

reclassified as *substance use disorder*¹⁶ in the revised Diagnostic Statistical Manual–V, is a disease. The term *opioid use disorder*¹⁷ should be used when referring to the use of opioids, rather than other substances.

It should also be noted that there may be a different approach with a patient who misuses an opioid analgesic by taking the product differently than prescribed for the purpose of managing pain, in contrast to the patient who abuses an opioid analgesic with the intent of getting high. HCPs should be familiar with the following:

1. The neurobiology of OUD (addictive cycle)
2. Use of screening tools to identify patients at risk, based on known risk factors, and to identify patients developing signs of opioid dependence or addiction as early as possible.
3. Management of OUD, including the types of pharmacologic and nonpharmacologic treatments available and when to refer to an addiction medicine specialist.

¹⁶ Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, (Copyright 2013). American Psychiatric Association.

¹⁷ Id.