



ANDA #####

## REMS MODIFICATION NOTIFICATION

APPLICANT NAME  
ADDRESS

Attention: CONTACT NAME  
TITLE

Dear CONTACT:

We refer to your Abbreviated New Drug Application (ANDA) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for PROPRIETARY NAME (ESTABLISHED NAME).

### **RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENT**

The REMS for extended-release and long acting (ER/LA) opioid analgesic products, of which DRUG is a member, was originally approved on July 9, 2012, and the most recent REMS modification was approved on May 26, 2017. The REMS consists of a Medication Guide, elements to assure safe use, and a timetable for submission of assessments of the REMS.

In accordance with section 505-1(g)(4)(B) of the FD&C Act, we have determined that your approved REMS for ER/LA Opioid Analgesics must be modified to ensure that training is made available healthcare providers involved in the treatment and monitoring of patients with pain and to implement an updated FDA Blueprint for Healthcare Provider (HCP) Education (to replace the current FDA Blueprint for Prescriber Education for ER/LA Opioid Analgesics) to ensure that the benefits of the drug outweigh the risks of adverse outcomes (addiction, unintentional overdose, and death) resulting from inappropriate prescribing, abuse, and misuse (see FDA Blueprint Appendix A). The updated FDA Blueprint for prescribers and other HCPs who are involved in the treatment and monitoring of patients with pain must include how to manage acute and chronic pain, along with when and how to safely integrate opioids and other pharmacological and nonpharmacological therapies in the management of pain. This modification is necessary to ensure HCPs have access to comprehensive information on how to manage pain, along with when and how to safely integrate opioid analgesics that are intended for use in an outpatient setting in the management of pain.

Additionally, in accordance with section 505-1(a)(2) of the FDCA, we have also determined that a REMS is necessary for immediate-release (IR) opioid analgesic products to ensure the benefits

of these drug outweigh the risks of adverse outcomes (addiction, unintentional overdose, and death) resulting from inappropriate prescribing, abuse, and misuse.

As discussed at the January 25, 2017, meeting held at FDA headquarters in Silver Spring, MD, in the interest of public health and to minimize the burden on the healthcare delivery system of having multiple unique REMS programs for drugs with similar, serious risks, FDA has determined that all application holders of opioid analgesics that are intended for use in an outpatient setting should work together, using the existing infrastructure of the ER/LA Opioid Analgesics REMS, to develop a shared system opioid analgesic REMS.

Your proposed modified REMS must include the following:

**Medication Guide:** As one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR 208. Pursuant to 21 CFR 208, FDA has determined that DRUG poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of DRUG. FDA has determined that DRUG is a product that has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use DRUG. FDA has also determined that DRUG is a product for which patient labeling could help prevent serious adverse events. The Medication Guide should have both common content applicable to all opioid analgesics, as well as product specific information that is necessary for safe and effective use of the drug. Under section 505-1 of the FD&C Act, FDA has also determined that a Medication Guide is necessary to ensure the benefits of the drug outweigh the risks of adverse outcomes (addiction, unintentional overdose, and death) resulting from inappropriate prescribing, abuse, and misuse.

Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed DRUG.

In addition, under 21 CFR 208.24(d), you are responsible for ensuring that the label of each container or package includes a prominent and conspicuous instruction to authorized dispensers to provide a Medication Guide to each patient to whom the drug is dispensed, and states how the Medication Guide is provided. You should submit marked up carton and container labels of all strengths and formulations with the required statement alerting the dispenser to provide the Medication Guide. We recommend one of the following statements, depending upon whether the Medication Guide accompanies the product or is enclosed in the carton (for example, unit of use):

- “Dispense the enclosed Medication Guide to each patient.” or
- “Dispense the accompanying Medication Guide to each patient.”

**Elements to Assure Safe Use:** Pursuant to 505-1(f)(1), we have also determined that elements to assure safe use are necessary to mitigate the serious risks of adverse outcomes (addiction, unintentional overdose, and death) resulting from inappropriate

prescribing, abuse, and misuse, listed in the labeling of the drug. In addition, we have determined that a Medication Guide and a communication plan are not sufficient to mitigate these serious risks.

Your REMS must include elements to mitigate these risks, including at least the following:

1. The applicant must ensure that training is provided to prescribers who prescribe DRUG and other healthcare providers involved in the treatment and monitoring of patients with pain. See draft FDA Blueprint Appendix A. The training must include successful completion of a knowledge assessment and proof of successful program completion. To assure access to DRUG and minimize the burden on the healthcare delivery system, FDA expects that the training will be conducted by accredited, independent continuing education providers to the extent practicable.
2. The applicant must provide to health care providers involved in the treatment and monitoring of patients with pain information that those health care providers can use to educate patients in the safe use, storage, and disposal of opioids.
3. The applicant must inform prescribers and other health care providers involved in the treatment and monitoring of patients with pain (e.g., pharmacists, nurses) of the existence of the REMS and the need to successfully complete the necessary training.

**Assessments:** Under section 505-1(g)(2)(C) of the FD&C Act, FDA can require the submission of a REMS assessment if FDA determines an assessment is needed to evaluate whether the REMS should be modified to ensure the benefits of the drug outweigh the risks or to minimize the burden on the healthcare delivery system of complying with the REMS.

FDA strongly recommends that applicants make provision in the shared system for joint assessments of the effectiveness of the REMS.

Because we have determined that a modified REMS as described above is necessary to ensure the benefits of ER/LA opioid analgesics that are intended for use in an outpatient setting outweigh their risks, you must submit a proposed REMS modification within 180 days of the date of this letter.

Submit the proposed modified REMS as a a Prior Approval supplement (PAS) to your ANDA.

Because FDA is requiring the REMS modifications in accordance with section 505-1(g)(4)(B), you are not required to submit an adequate rationale to support the proposed modifications, as long as the proposals are consistent with the modifications described in this letter. If the proposed REMS modification supplement includes changes that differ from the modifications described in this letter, an adequate rationale is required for those additional proposed changes in accordance with section 505-1(g)(4)(A).

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

**NEW SUPPLEMENT FOR ANDA #####/S-000  
PRIOR APPROVAL SUPPLEMENT  
PROPOSED MAJOR REMS MODIFICATION**

Prominently identify subsequent submissions related to the proposed REMS modification with the following wording in bold capital letters at the top of the first page of the submission:

**ANDA #####/S-000  
PROPOSED REMS MODIFICATION-AMENDMENT**

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

**SUBMISSION OF REMS DOCUMENT IN SPL FORMAT**

In addition to submitting the proposed modified REMS as described above, you can also submit the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, include the SPL file with your proposed REMS modification submission.

For more information on submitting REMS in SPL format, please email [REMS\\_Website@fda.hhs.gov](mailto:REMS_Website@fda.hhs.gov).

**OTHER**

We will be holding a teleconference on October 25, 2017, to provide further guidance and answer questions. It is important that you assign a representative to attend this meeting.

Note that the ER/LA Opioid Analgesics shared system REMS currently uses a Type V Drug Master File (DMF) for shared system REMS submissions. Additional information regarding the process for referencing the DMF will be provided during the teleconference referenced above.

If you have any questions, call CAPT Stacy Barley, REMS Coordinator, at (301) 796-2137.

Sincerely,

*{See appended electronic signature page}*

Trueman W. Sharp, M.D., M.P.H.  
Acting Deputy Director

ANDA #####  
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Office of Bioequivalence  
Office of Generic Drugs  
Center for Drug Evaluation and Research

ENCLOSURE:  
Appendix A

# **FDA Education Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain (May 2017)**

(Draft Revisions to FDA Blueprint for Prescriber Education  
for Extended-Release and Long-Acting Opioids)<sup>1</sup>

## **Section 1: The Basics of Pain Management**

### **I. 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.

Pain can be classified as follows:

1. Acute vs. chronic – Health care providers (HCPs) should be knowledgeable about the differences in the classification of pain based on how long it is expected to last.
2. Neuropathic vs. non-neuropathic – HCPs should be knowledgeable about the mechanisms underlying pain and the differences between nociceptive and neuropathic pain, and peripheral and central neuropathic pain.

### **II. ASSESSING PATIENTS IN PAIN**

HCPs should be knowledgeable about how to fully assess each patient when initiating a pain management program. When appropriate, standardized scales can be used to help document pain characteristics and guide management decisions throughout treatment.

Important elements of an initial assessment include the following:

1. Patient History –A complete history should be obtained. As part of the history of the pain condition, include prior evaluation such as diagnostic studies and types of past prior pharmacologic and nonpharmacologic treatment attempts and response. Any history of substance use, psychiatric history, family history of substance abuse and psychiatric disorders should be obtained and documented.
2. Screening tools should be used to evaluate known risk factors for development of chronic pain after an acute injury or disease.
3. Screening tools should be used to evaluate the known risk factors for opioid use disorder or abuse (e.g., structured interview tools).
4. Pain assessment scales/tools – The nature of pain should be fully documented.

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<sup>1</sup> This document is part of the [Extended-Release and Long-Acting \(ER/LA\) Opioid Analgesics REMS Program](#) accessed April 12, 2017

5. Functional assessment scales – When pain or the associated disease interferes with physical or emotional function, disease specific or general quality of life scales should be used for documentation.
6. Physical Examination – A thorough physical exam should be conducted with any findings documented and followed that could influence analgesic choice or underlying pain condition.
7. Psychosocial Evaluation – This should be considered, particularly for patients with chronic pain.
8. Diagnostic Studies – Such studies should be considered to assist in determining cause of pain, particularly acute pain without clear precipitating event, or chronic pain not responding to conservative therapy.
9. Proper documentation – The overall treatment approach and plan should be well documented in the patient record. All patient interactions and treatment plans should be documented. Documentation can include written agreements/documentation and informed consent/patient provider agreements (PPAs).

## **Section 2: Creating the Pain Treatment Plan**

A comprehensive 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 treatment plan should also include goals related to pain interfering with life activities such as school, work, and social activities.

### **I. COMPONENTS OF AN EFFECTIVE TREATMENT PLAN**

1. The goals of treatment – It is important to establish a set of goals early in the course of treatment, including expectations about the following:
  - The degree of improvement in pain
  - The degree of improvement in function, where relevant
2. Possible constituents of the treatment plan – The HCP should be knowledgeable about which therapies can be used to manage pain and how these should be implemented.
  - Nonpharmacologic therapies – includes psychological, physical rehabilitative, surgical approaches; and complementary therapies
  - Pharmacologic therapies – non-opioid, opioid, and adjuvant medications
3. Patient/HCP interaction – There should be a plan for patient/prescriber/health care team interaction during treatment, including expectations about the following:
  - Patient responsibilities/compliance with the plan
  - Responsibilities of the prescriber and health care team
  - Plans for reviewing functional goals
  - Use of supplemental immediate release (IR) opioids for intermittent increases in pain

- Use of PPAs – HCPs should be knowledgeable about the role of PPAs
  - PPAs can help ensure that patients and caregivers understand the goals and the risks of treatment and how to use the medications safely.
  - PPAs can include commitments to return for follow-up visits, to comply with appropriate monitoring (such as random drug testing), and to safeguard the medication.

## **II. NONPHARMACOLOGIC THERAPIES**

A number of nonpharmacologic therapies are available that can play an important role in managing pain, particularly musculoskeletal pain and chronic pain.

- Psychological approaches – e.g., cognitive behavioral therapy
- Physical rehabilitative approaches – e.g., physical therapy, occupational therapy
- Surgical approaches
- Complementary therapies – e.g., acupuncture, chiropractic

HCPs should be knowledgeable about the range of available therapies, when they may be helpful, and when they should be used as part of a multidisciplinary approach to pain management.

## **III. GENERAL PRINCIPLES OF PHARMACOLOGIC ANALGESIC THERAPY**

Pain can arise from a broad variety of causes. A number of analgesics are available that can be used to manage the symptoms of pain. HCPs should be knowledgeable about the range of analgesics available and the types of pain that may be responsive to those analgesics.

### **A. Non-opioid analgesics and adjuvant medications**

HCPs should be knowledgeable about the pharmacologic alternatives to opioid analgesics that can be used for pain management, including non-opioid analgesics and adjuvant medications. The following are examples of non-opioid analgesics and adjuvant medications that can be used to manage pain. (This list is not all-inclusive.)

1. Non-steroidal anti-inflammatory drugs (NSAIDs) and acetaminophen
2. Antiepileptic drugs
3. Antidepressants
4. Local and regional anesthetics
5. Other miscellaneous adjuvant medications

When using non-opioid analgesics and adjuvant 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
7. Drug-drug interactions – both pharmacodynamic and pharmacokinetic

## **B. Opioid analgesics**

HCPs should be knowledgeable about the risks associated with opioid analgesics as they pertain to their patients and from a public health perspective.

1. Epidemic of prescription opioid drug abuse – HCPs should be knowledgeable about the extent of the problem. HCPs should understand that most of the opioids available for misuse and abuse in the community originate from prescriptions for individual patients.
2. Paradigm shift in opioid prescribing – HCPs should be knowledgeable about existing information about safe opioid practices, current federal and state regulations, and guidelines on opioid prescribing<sup>2,3,4</sup> and the use of naloxone.

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 for misuse, abuse, addiction, overdose, and death
  - b. Importance of prescription drug monitoring programs (PDMPs)<sup>5</sup>
  - c. DSM V criteria for opioid use disorder 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)<sup>6</sup>
  - d. The concepts of tolerance and physiological dependence and how they differ from opioid use disorder (addiction)
  - e. Some opioid analgesics are only safe for opioid-tolerant patients
2. Mechanism of action and analgesic effect – opioid receptors and opioid action
  - Types of opioids (synthetic phenylpiperidines, synthetic pseudo piperidines, naturally occurring alkaloids)
3. Indications and uses for pain management

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<sup>2</sup> [2013 Federation of State Medical Boards Model Policy on the Use of Opioid Analgesics in the Treatment of Chronic Pain](#) accessed on February 22, 2017.

<sup>3</sup> [Dowell D, Haegerich TM, Chou R. CD Guideline for Prescribing Opioids for Chronic Pain –United States, 2016. MMWR Recomm Rep 2016; 65 \(No.RR-1\): 1-49](#) accessed February 22, 2017.

<sup>4</sup> [SAMHSA Opioid Overdose Prevention Toolkit, updated 2016](#) accessed February 22, 2017.

<sup>5</sup> [SAMHSA Prescription Drug Monitoring Programs: A Guide for Healthcare Providers](#) accessed April 12, 2017.

<sup>6</sup> [American Psychiatric Association DSM-5-Opioid Use Disorder Diagnostic Criteria](#) accessed April 12, 2017.

- Acute vs. chronic pain vs palliative care vs breakthrough cancer pain
4. Routes of administration and formulations used in pain management
    - a. Formulations – immediate release (IR) vs extended release (ER) vs long-acting (LA)
    - b. Transdermal patches and important interactions with heat, magnetic resonance imaging (MRI) risk with some transdermal patches
    - c. Abuse-deterrent formulations (ADFs)
      - Definition of ADF – These drugs make abuse by certain routes more difficult, but do not prevent abuse or alter risk for addiction
      - Most common methods of opioid abuse
      - Guidance for Industry, Abuse-deterrent opioids – evaluation and labeling<sup>7</sup>
      - FDA-approved ADF products currently available
  5. Initial dosing, dose titration, dose tapering (when appropriate) for analgesia
    - a. Relative potency vs. conversion factors – HCPs should have knowledge of the concepts and limitations of the conversion charts in labeling and the concepts and limitations of equianalgesic dosing tables in literature
    - b. Variability of response
    - c. Special populations – HCPs should be knowledgeable about additional factors to consider when managing pain in the following settings.
      - Opioids during pregnancy and neonatal abstinence syndrome – HCPs should discuss the potential risks and benefits of opioids during pregnancy, including the need to anticipate and treat neonatal opioid withdrawal syndrome
      - Dosage adjustment for renal and hepatic impairment
      - Opioid use in children and adolescents
      - Opioid use in older adults
      - Sleep disorders and opioids
      - Common and uncommon psychiatric disorders, pain, and opioids
  6. Contraindications
  7. Adverse Events
    - Medication errors
    - Serious adverse drug reactions
    - Common adverse drug reactions
  8. Drug-drug interactions – both pharmacodynamic and pharmacokinetic
    - Pharmacokinetic interactions based on metabolic pathway
    - Drugs that have pharmacokinetic and not just pharmacodynamic interactions with alcohol
    - Concerns with particular drug-drug interactions
      - Benzodiazepines and other central nervous system depressants

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<sup>7</sup> See FDA guidance for industry [Abuse-Deterrent Opioids—Evaluation and Labeling](#). accessed April 12, 2017.

- Monoamine oxidase inhibitors
  - Antidiuretic hormone drugs
9. Safe use of opioids
- a. Strategies to prevent opioid overdose/death
    - Dosing instructions
    - Safe storage
      - Risk of accidental exposure/ingestion by household contacts, especially children/teens
      - Risk of theft
    - Proper disposal of used (e.g. transdermal patches) and unused opioids
    - Encouraging availability of naloxone for all patients with opioid prescriptions
    - Seeking emergency medical treatment if an opioid overdose occurs
  - b. Pain management after an opioid overdose – HCPs should recognize that patients who have survived an opioid overdose are at much greater risk for future overdoses.
  - c. 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.

##### **A. Initiating treatment with opioids – acute pain**

1. Patient selection – when is an opioid necessary?
2. Dosing
  - a. As needed vs. around-the-clock
  - b. Matching expected duration of pain with quantity of analgesic prescribed
  - c. Using lower doses as long as possible, avoiding ER/LAs when pain is not expected to be present for an extended period of time and can be suitably managed with an IR
3. HCPs should prescribe and discuss the use of naloxone products as a means of avoiding death due to overdose
4. Periodic review and monitoring for patients on opioid analgesics
5. Screening tools for risk of abuse

##### **B. Initiating treatment with opioids – chronic pain**

1. Patient selection
  - a. Chronic pain vs. palliative care
  - b. HCPs should know which products and which doses are indicated for use in only opioid-tolerant patients

- c. Screening tools for known risk factors for abuse
2. Dosing
    - a. As needed vs. around-the-clock – HCPs should consider as needed dosing before initiating around-the-clock treatment.
    - b. HCPs should be knowledgeable about the warning signs and symptoms of significant respiratory depression from opioids and monitor patients closely, especially at the time of treatment initiation and dose increases.
    - c. Initial dose – HCPs should be knowledgeable about how to determine a safe initial dose and how to follow patients initiating an opioid analgesic regimen.
    - d. Titration – HCPs should know the safe interval for titration of an opioid dose taking into consideration the half-life of the product and the amount of all opioid medication used.
    - e. Safe conversion from other opioids – HCPs should be knowledgeable about the concepts and limitations of the conversion charts in labeling and the concepts and limitations of equianalgesic dosing tables in literature.
  3. Considerations in opioid selection
    - a. When to go from IR to ER/LA – HCPs should be knowledgeable about when it is appropriate to prescribe IR and ER/LA opioid analgesics.
    - b. Special precautions with methadone – HCPs should know that methadone has a longer half-life than the duration of analgesia, dosing multiple times per day for pain results in accumulation, and can prolong the QT interval.
    - c. Products restricted to opioid-tolerant patients – HCPs should be knowledgeable about the important information for each analgesic, including which opioids are indicated for use in only opioid-tolerant patients for safety reasons.
  4. HCPs should prescribe and discuss the use of naloxone products as a means of avoiding death due to overdose.
  5. When an IR should be added to an ER/LA analgesic – HCPs should be knowledgeable about when and how to supplement pain management with IR analgesics, opioids and non-opioids.

**C. Periodic review and monitoring for patients on opioid analgesics**

1. Review pain and functional goals – HCPs should evaluate patients periodically and determine if the therapy is achieving the desired goals.
2. Review adverse events – HCPs should review adverse events at each visit, with a particular focus on changes.
  - Screening for endocrine function may be recommended
3. Review refill history/reviewing PDMP – HCPs should review the patient’s refill history and refer to the state PDMP(s) available at each visit watching for evidence that the patient may have a developing problem.

4. How to determine when opioid analgesic no longer necessary/beneficial – HCPs should be knowledgeable about when the use of an opioid analgesic should be discontinued based on an integrated assessment of the goals of treatment, adverse events, and any evidence of aberrant drug use behaviors.

#### **D. Long-term management**

1. Evaluating the patient with worsening pain – Before increasing opioid dosage, HCPs should be knowledgeable about the need to reassess the underlying condition in patients with worsened pain and consider whether any signs of abuse are present.
2. Opioid rotation – When managing patients with chronic pain and long-term opioid therapy, HCPs should be knowledgeable about when it can be helpful to change the opioid, understand the safety concerns that can arise based on the following concepts, and follow the patient closely for signs and symptoms of respiratory depression and sedation until a stable dose of the new analgesic is established.
  - a. HCPs should be knowledgeable about the concept of incomplete cross-tolerance when converting patients from one opioid to another.
  - b. HCPs should be knowledgeable about the concepts and limitations of the conversion charts in labeling and the limitations of equianalgesic dosing tables in literature.
  - c. HCPs should monitor patient adherence to the treatment plan, especially with regard to misuse and abuse by the following:
    - Recognizing, documenting, and addressing aberrant drug related behavior
    - Differentiating abuse-related behavior from inadequate pain management
    - Understanding the utility and interpretation of urine drug testing (e.g., screening and confirmatory tests), and using it as indicated
    - Screening and referring for substance abuse treatment as indicated
    - Performing medication reconciliation as indicated

#### **E. When to consult with a pain specialist**

HCPs should be knowledgeable about when to appropriately refer high-risk patients to pain management specialists and when to refer patients who have not been able to achieve adequate pain management.

#### **F. 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.

#### **G. Importance of patient education**

HCPs should be knowledgeable about their role in reducing the risks associated with opioids through patient education at initiation of an opioid and during long-term management of patients taking opioids.

1. HCPs should counsel the patient on how to take the opioid analgesic as prescribed.
2. HCPs should inform patients about pain management expectations and managing pain through different modalities (non-opioids, rest, physical therapy, occupational therapy, etc.) when appropriate.
3. HCPs should be aware of and use the *Patient Counseling Document* and *Medication Guide* as part of discussion with patients and caregivers when prescribing opioid analgesics.
4. HCPs should counsel the patient about the following:
  - a. Serious adverse events that can lead to death and that can occur even when product is used as recommended
  - b. Known risk factors for serious adverse events, including signs and symptoms of overdose and opioid-induced respiratory depression, GI obstruction, allergic reactions, among others
  - c. Most common side effects (e.g., constipation, nausea, headache, dizziness), and the risk of falls, working with heavy machinery, and driving
  - d. When to call the prescriber (e.g. managing adverse events, ongoing pain)
  - e. The importance of adherence to dosing regimen, how to handle missed doses, and need to contact prescriber should pain not be controlled
  - f. The importance of telling the prescriber about all of the medications they are taking and not adding other CNS depressants/other opioids/benzodiazepines without discussing these with the prescriber as the combination has the potential to cause overdose and death
  - g. Product-specific concerns, such as not to crush or chew extended-release products; transdermal patches and buccal films should not be cut, torn, or damaged before use; how to properly measure oral solution doses; and when appropriate to sprinkle the contents of a capsule
  - h. How to safely taper dose and not abruptly discontinue
  - i. Safe storage and disposal, risks of theft by family members and household visitors
  - j. Never to share any opioid analgesic with another person
  - k. How and when to use naloxone products
  - l. Seek emergency medical treatment if an opioid overdose occurs
  - m. How to report adverse events to the FDA (1-800-fda-1088 or via <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>)
5. HCPs should have training on how to begin the process of intervention should an HCP suspect abuse (how to begin the conversation and get substance abuse treatment for patients).

## V. ADDICTION MEDICINE PRIMER

HCPs should be knowledgeable about the basic elements of addiction medicine and be familiar with opioid use disorders as well as neurobiology and pharmacotherapy.

1. Overview of the neurobiology of opioid use disorder (addictive cycle)
2. Use of screening tools to identify patients at risk, based on known risk factors, and to identify patients developing a problem as early as possible
3. Management of opioid use disorder – HCPs should know the types of pharmacologic and nonpharmacologic treatments available and when to refer to an addiction medicine specialist.
4. Concurrent pain and opioid use disorder – HCPs should know when to refer to a pain medicine and/or addiction medicine specialist.