

**WHAT TO CONSIDER WHEN
PRESCRIBING EMBEDA™
(morphine sulfate and
naltrexone hydrochloride)
EXTENDED RELEASE CAPSULES**

A Guide for Healthcare Professionals

**Please see Important Safety Information on pages 14 and 15 and accompanying full
Prescribing Information, including boxed warning and Medication Guide.**

August 2009

EMBEDA™ (morphine sulfate and naltrexone hydrochloride) Extended Release Capsule CII is approved for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time. EMBEDA™ contains pellets of morphine sulfate, an opioid receptor agonist, with a sequestered core of naltrexone hydrochloride. EMBEDA™ is intended for oral use only.

In order to ensure that the benefits of EMBEDA™ outweigh the potential risks of EMBEDA™, a Risk Evaluation and Mitigation Strategy (REMS) has been implemented in response to a requirement of the Food and Drug Administration (FDA). The goals of this REMS are:

- To inform patients and providers about the potential for abuse, misuse, overdose, and addiction with EMBEDA™
- To inform patients and providers about the safe use of EMBEDA™

Please see the attached full Prescribing Information, including the boxed warning, and Medication Guide for important safety information for EMBEDA™.

FDA requires that a Medication Guide be dispensed with each EMBEDA™ prescription.

EMBEDA™ Capsules contain morphine, an opioid agonist and a Schedule II controlled substance with an abuse liability similar to other opioid agonists. EMBEDA™ can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing EMBEDA™ in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

Selection of patients for treatment with morphine sulfate should be governed by the same principles that apply to the use of similar opioid analgesics. Healthcare professionals (HCPs) should individualize treatment in every case, using non-opioid analgesics, opioids on an as-needed basis and/or combination products, and chronic opioid therapy in a progressive plan of pain management such as that outlined by the World Health Organization and Federation of State Medical Boards Model Guidelines.

It is important that you discuss the risks of EMBEDA™ with your patients and their caregivers and encourage them to read the Medication Guide (see attached copy). The Medication Guide provides important information on the safe and effective use of EMBEDA™ and will be provided to patients with each prescription. Patients should be counseled on the need to store EMBEDA™ safely out of the reach of children and household acquaintances.

Please take the time to review the “What to Consider When Prescribing EMBEDA™” guide, as well as the enclosed full Prescribing Information and Medication Guide. If you have any questions or concerns, you may contact our Professional Information Services Department at 800-776-3637 or visit www.EMBEDA.com.

Sincerely,

Eric Carter, PhD, MD
Chief Science Officer
King Pharmaceuticals®, Inc.

Please see Important Safety Information on pages 14 and 15 and accompanying full Prescribing Information, including boxed warning and Medication Guide.

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SELECTING APPROPRIATE PATIENTS FOR EMBEDA™

EMBEDA™ (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules are an extended-release oral formulation of morphine sulfate and naltrexone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.¹

EMBEDA™ is NOT intended for use as a prn analgesic.¹

EMBEDA™ is not indicated for acute/postoperative pain or if the pain is mild or not expected to persist for an extended period of time. EMBEDA™ is only indicated for postoperative use if the patient is already receiving chronic opioid therapy prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. HCPs should individualize treatment, moving from parenteral to oral analgesics, as appropriate.¹

Administer EMBEDA™ with caution and in reduced dosages in older or debilitated patients, as well as in patients with severe renal or hepatic insufficiency.

Selection of patients for treatment with morphine sulfate should be governed by the same principles that apply to the use of similar opioid analgesics. HCPs should individualize treatment in every case, using non-opioid analgesics, opioids on an as-needed basis and/or combination products, and chronic opioid therapy in a progressive plan of pain management, such as that outlined by the World Health Organization and Federation of State Medical Boards Model Guidelines.¹

Before starting long-term opioid therapy with any patient, thorough risk assessment and stratification should include²:

- Patient and family history, including an assessment of psychosocial factors
- Physical examination
- Other appropriate tests, including those for potential risk of substance misuse, abuse, or addiction

See pages 11 and 12 for additional monitoring methods.

APPROPRIATE DOSING AND ADMINISTRATION

EMBEDA™ may be administered once or twice a day and is available in 6 dosage strengths: 20 mg/0.8 mg, 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, and 100 mg/4 mg (morphine sulfate/naltrexone hydrochloride).¹

EMBEDA™ should not be given more frequently than every 12 hours.¹



Capsules shown are not the actual size.

THE 100 MG/4 MG CAPSULES ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY.¹

Care should be taken to use low initial doses of EMBEDA™ in patients who are not already opioid tolerant, especially those who are receiving concurrent treatment with muscle relaxants, sedatives, or other CNS-active medications.¹

Initiating Therapy With EMBEDA™

It is critical to adjust the dosing regimen for each patient individually, taking into account the patient's prior analgesic treatment experience. When selecting the initial dose of EMBEDA™, particular attention should be paid to¹:

1. the total daily dose, potency, and kind of opioid the patient has been taking previously;
2. the reliability of the relative potency estimate used to calculate the equivalent dose of morphine needed (*note*: potency estimates may vary with the route of administration);
3. the patient's degree of opioid experience and opioid tolerance;
4. the general condition and medical status of the patient;
5. concurrent medication; and
6. the type and severity of the patient's pain.

The first dose of EMBEDA™ may be taken with the last dose of any immediate-release or short-acting opioid medication due to the extended-release characteristics of EMBEDA™.¹

The following dosing recommendations can be considered approaches to what is actually a series of clinical decisions over time in the management of the pain of an individual patient.¹

See the full Prescribing Information for details on conversion.

Individualizing the Dosage

For every patient, it is important to weigh the following when choosing an opioid and individualizing initial dosing and titration²:

- Health status
- Previous exposure to opioids
- Attainment of therapeutic goals
- Predicted or observed harms

Patients may develop some degree of tolerance, which will require dosage adjustment until they have achieved their individual balance between effective analgesia and opioid side effects, such as confusion, sedation, and constipation.¹

- EMBEDA™ (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules should be titrated no more frequently than every other day to allow patients to stabilize before escalating the dose
- If breakthrough pain occurs, the dose may be supplemented with a small dose (less than 20% of the total daily dose) of a short-acting analgesic
- Patients who exhibit signs of excessive opioid side effects, such as sedation, should have their dose reduced
- Patients who experience inadequate analgesia on once-daily dosing should be switched to twice-daily dosing
- EMBEDA™ should not be dosed more frequently than every 12 hours

During periods of changing analgesic requirements, including initial titration, frequent communication is recommended between physician, other members of the healthcare team, the patient, and the caregiver/family.¹

Alternative Methods of Administration

Patients who have difficulty swallowing whole capsules or tablets may benefit from an alternative method of administration. EMBEDA™ pellets may be sprinkled over applesauce. Other foods have not been tested and should not be substituted for applesauce.¹

1. Sprinkle the pellets onto a small amount of applesauce and use immediately.
2. The patient must be cautioned not to chew the pellets.
3. Rinse mouth to ensure all pellets have been swallowed.
4. Patients should consume entire portion and should not divide applesauce into separate doses.

Do not administer EMBEDA™ pellets through a nasogastric or gastric tube.¹

Maintenance of Therapy

Continual reevaluation of the patient receiving morphine sulfate is important, with special attention given to the maintenance of pain control and the relative incidence of side effects associated with therapy. If the level of pain increases, effort should be made to identify the source of increased pain, while adjusting the dose as described above to decrease the level of pain.¹

During chronic therapy, especially for non-cancer-related pain (or pain associated with other terminal illnesses), the continued need for the use of opioid analgesics should be reassessed, as appropriate.¹ Outcomes to consider include²:

- Progress toward meeting therapeutic goals
- Presence of opioid-related adverse effects
- Changes in the underlying pain condition
- Changes in psychiatric or medical comorbidities
- Evidence of aberrant drug-related behaviors, addiction, or diversion

Cessation of Therapy

In general, EMBEDA™ should not be abruptly discontinued. However, EMBEDA™, like other opioids, can be safely discontinued without the development of withdrawal symptoms, by slowly tapering the daily dose.¹

The American Pain Society and the American Academy of Pain Management issued recommendations for discontinuing opioid therapy as part of new treatment guidelines published in 2009.²

PATIENT COUNSELING INFORMATION

Patients receiving EMBEDA™ should be given the following instructions by their HCP¹:

- Patients should be advised that EMBEDA™ contains morphine and naltrexone and should be taken only as directed
- The dose of morphine sulfate should not be adjusted without consulting with an HCP. EMBEDA™ should be swallowed whole (not crushed, dissolved, or chewed) due to a risk of fatal morphine overdose or naltrexone-precipitated withdrawal symptoms. Alternately, EMBEDA™ capsules may be opened and the entire contents sprinkled on a small amount of applesauce immediately prior to ingestion
- Patients should not consume alcoholic beverages while on EMBEDA™ therapy. Additionally, patients must not use prescription or nonprescription medications containing alcohol while on EMBEDA™ therapy. The coingestion of alcohol with EMBEDA™ may result in an increase of plasma levels and potentially fatal overdose of morphine

- Patients should be advised of the most common adverse reactions that may occur while taking EMBEDA™ (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules: constipation, nausea, somnolence, vomiting, dizziness, pruritus, and headache
- Patients should be advised that EMBEDA™ may cause drowsiness, dizziness, or light-headedness and may impair mental and/or physical ability required for the performance of potentially hazardous tasks (eg, driving, operating machinery). Patients started on EMBEDA™ or patients whose dose has been adjusted should refrain from any potentially dangerous activity until it is established that they are not adversely affected
- Patients should not combine EMBEDA™ with central nervous system depressants (sleep aids, tranquilizers) except by the orders of the prescribing HCP because dangerous additive effects may occur resulting in serious injury or death
- Patients should be advised that EMBEDA™ is a potential drug of abuse. They should protect it from theft
- Special care must be taken to avoid accidental ingestion or use by individuals (including children) other than the patient for whom it was originally prescribed, as such unsupervised use may have severe, even fatal, consequences
- Patients should be advised that EMBEDA™ 100 mg/4 mg is for use only in opioid-tolerant patients
- Women of childbearing potential who become or are planning to become pregnant should consult an HCP prior to initiating or continuing therapy with EMBEDA™
- Safe use in pregnancy has not been established. Prolonged use of opioid analgesics during pregnancy may cause fetal neonatal physical dependence, and neonatal withdrawal may occur
- As with other opioids, patients taking EMBEDA™ should be advised of the potential for severe constipation; appropriate laxatives and/or stool softeners, as well as other appropriate treatments, should be initiated from the onset of opioid therapy
- Patients should be advised to seek medical attention immediately if signs of a serious allergic reaction occur, such as swelling of the face, throat, or tongue, trouble breathing, feeling dizzy or faint, pounding heartbeat, chest pain, or a feeling of doom

COUNSELING PATIENTS ON PROPER STORAGE AND DISPOSAL

Before prescribing EMBEDA™, advise patients about the following guidelines for storing their medication^{1,2}:

- Keep EMBEDA™ in a safe or locked location away from children and household acquaintances. Accidental use by a child is a medical emergency and can result in death. If a child accidentally takes EMBEDA™, seek emergency help right away

Please see Important Safety Information on pages 14 and 15 and accompanying full Prescribing Information, including boxed warning and Medication Guide.

- Prevent theft, misuse, or abuse. Keep EMBEDA™ in a safe or locked location to protect it from being stolen. EMBEDA™ can be a target for people who misuse or abuse prescription medicines or street drugs
- Never give EMBEDA™ to anyone else, even if they have the same symptoms you have. It may harm them or even cause death. Selling or giving away this medicine is against the law

OPIOID USE AND THE RISK OF MISUSE, ABUSE, AND ADDICTION

EMBEDA™ contains morphine, a mu-opioid agonist, and is a Schedule II controlled substance. EMBEDA™ can be abused and is subject to criminal diversion.¹

Abuse

Drug addiction is characterized by compulsive use, use for nonmedical purposes, and continued use despite harm or risk of harm. Drug addiction is a treatable disease, utilizing a multidisciplinary approach, but relapse is common.¹

“Drug-seeking” behavior and attempts at wrongful procurement of prescription medicines are very common in addicts and drug abusers. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing or referral, repeated “loss” of prescriptions, tampering with prescriptions, and reluctance to provide prior medical records or contact information for other treating HCPs. “Doctor shopping” to obtain additional prescriptions is common among drug abusers. However, it is important to note that “drug-seeking behavior” may also be exhibited by patients who are experiencing undertreatment for their moderate to severe chronic pain.¹

Abuse and addiction are separate and distinct from physical dependence and tolerance. HCPs should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction and is characterized by misuse for nonmedical purposes, often in combination with other psychoactive substances. EMBEDA™, like other opioids, can be diverted for nonmedical use into illicit channels of distribution. Careful record keeping of prescribing information, including quantity, frequency, and renewal requests, is strongly advised.¹

Proper assessment of the patient, proper prescribing practices, periodic reevaluation of therapy, and proper dispensing and storage are appropriate measures that help to reduce abuse of opioid drugs.¹

EMBEDA™ (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules are intended for oral use only. Misuse or abuse of EMBEDA™ by crushing or chewing the pellets will result in the uncontrolled release of both morphine and naltrexone, posing the risk of overdose and death. In opioid-tolerant individuals, the absorption of naltrexone may increase the risk of precipitating withdrawal. The risk of overdose and death is increased with concurrent abuse of alcohol and other central nervous system depressants. The sequestered naltrexone is intended to have no clinical effect when EMBEDA™ is taken as directed; however, if crushed or chewed, up to 100% of the sequestered naltrexone dose could be released, bioequivalent to an immediate-release naltrexone oral solution of the same dose.

Due to the presence of talc as one of the excipients in capsules, parenteral abuse can be expected to result in local tissue necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valvular heart injury. Parenteral drug abuse is commonly associated with transmission of infectious diseases, such as hepatitis and HIV.¹

Dependence

Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia in the absence of disease progression or other external factors. Physical dependence is manifested by withdrawal symptoms after abrupt discontinuation of a drug or upon administration of an antagonist. Physical dependence and tolerance are not unusual during chronic opioid therapy.¹

The opioid abstinence or withdrawal syndrome is characterized by some or all of the following: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other symptoms also may develop, including irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.¹

In general, opioids should not be abruptly discontinued.¹

Opioid use requires a balanced approach, acknowledging both the need to treat legitimate pain and the public health concern of abuse. Thorough screening and assessment tools—including examinations of patient and family history, physical and psychosocial health, and risks for misuse, abuse, and addiction—can help identify patients for whom opioid therapy is appropriate and those at higher risk for addiction or aberrant drug-related behavior.²

Risk stratification

Using the results of an initial evaluation, patients can be categorized as low, moderate, or high risk, as shown in the following chart. This stratification assists the HCP in selecting the appropriate intensity of monitoring when starting patients on long-term opioid therapy.³

Levels of risk for opioid misuse in patients with chronic pain³

Characteristic	Low risk	Moderate risk	High risk
Substance abuse	Never	Past	Current
Smoking (nicotine)	Never	Past	Current
Family history of addiction	None	Significant	Significant
Psychosocial factors	No major diagnoses; minor diagnoses treated or stable	Past major diagnoses; current issues with minor diagnosis	Current major diagnoses untreated or unstable
Age	Older	N/A	Younger
History of sexual abuse	No	N/A	Yes
Controlled prescriptions lost or stolen	No	N/A	Yes
Unauthorized substances in urine drug screens	Consistently negative	Initially positive	Consistently positive
Recommendations based on risk stratification			
Appropriate healthcare setting for each group	Primary care	Primary care with specialist support	Specialty pain management

Recommended healthcare settings vary by level of assessed risk.

Adapted from Weaver et al.³

A patient identified as high risk will require the most vigilance, such as urine drug screens at every visit initially, pill counts and urine screens on short notice between visits, and queries to prescription monitoring programs every 1 to 2 months.³

Assessment for all patients

A thorough assessment process should determine a treatment strategy that optimizes efficacy and minimizes the risk of side effects, misuse, abuse, and diversion. Subsequently, patients on chronic opioid therapy must be monitored and periodically reassessed because therapeutic risks and benefits can be affected by changes in the following²:

- Underlying pain condition
- Presence of coexisting disease
- Changes in psychological or social circumstances

With appropriate vigilance, chronic opioid therapy is possible for patients with non-cancer-related pain and a history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors. These cases require more frequent and stringent monitoring, and consultation with a mental health or addiction specialist is strongly encouraged.²

Any patient who is prescribed an opioid should be counseled that this medication may be only one part of a multimodal treatment plan. As treatment continues, it is important to monitor patients to assess risks and benefits and the need for ongoing opioid use, using these criteria²:

- Pain severity
- Functional ability
- Adverse events
- Signs of any aberrant drug-related behaviors, substance use, or psychological issues

Monitoring methods may extend beyond patient self-reports, including²:

- Pill counts
- Urine drug screens
- Caregiver or family interviews
- Prescription monitoring program data

To help ensure safe opioid use, patients should be advised to keep their medication locked and out of the reach of children and household acquaintances. Patients should follow applicable state regulations when disposing of unused medication.^{1,2}

It is also important to ensure that patients understand the following:

- Only an HCP can prescribe an opioid
- Only a patient who is prescribed an opioid should take this medication
- Always follow HCPs' directions when taking an opioid

RISKS OF INAPPROPRIATE OPIOID USE

Exposure to opioids, including EMBEDA™ (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules, carries the risks of misuse, abuse, overdose, and addiction. This should be considered when prescribing or dispensing EMBEDA™ in situations where there are concerns about an increased risk for aberrant drug-related behavior.¹

Special care must be taken to avoid accidental ingestion or use by individuals (including children) other than the patient for whom it was originally prescribed. Such unsupervised use may have severe, even fatal, consequences.¹

WARNINGS AND PRECAUTIONS

EMBEDA™ is to be swallowed whole or the contents of the capsules sprinkled on applesauce. The pellets in the capsules are not to be crushed, dissolved, or chewed. The resulting morphine dose may be fatal, particularly in opioid-naive individuals. In opioid-tolerant individuals, the absorption of naltrexone may increase the risk of precipitating withdrawal.¹

EMBEDA™ 100 mg/4 mg is for use in opioid-tolerant patients only. Ingestion of these capsules or of the pellets within the capsules may cause fatal respiratory depression when administered to patients not already tolerant to high doses of opioids.¹

PROVIDING ADDITIONAL INFORMATION TO PATIENTS

It is important that you discuss the risks of EMBEDA™ with your patients and their caregivers and instruct them to read through the Medication Guide (see attached copy).¹

Every patient who is prescribed EMBEDA™ should be given an EMBEDA™ Medication Guide. Patients should also share information from the guide with members of their households. While the Medication Guide does not take the place of discussing medical conditions and treatments with patients, it summarizes the most important information about EMBEDA™.¹

EMBEDA™: IMPORTANT SAFETY INFORMATION

Indication

- EMBEDA™ (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules are an extended-release oral formulation of morphine sulfate and naltrexone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time
- **EMBEDA™ is NOT intended for use as a prn analgesic**
- EMBEDA™ is not indicated for acute/postoperative pain or if the pain is mild or not expected to persist for an extended period of time

IMPORTANT SAFETY INFORMATION

- **EMBEDA™ contains morphine, an opioid agonist and a Schedule II controlled substance with an abuse liability similar to other opioid agonists**
- **Morphine can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing EMBEDA™ in situations where the healthcare professional or pharmacist is concerned about an increased risk of misuse, abuse, or diversion**
- **EMBEDA™ contains pellets of an extended-release oral formulation of morphine sulfate, an opioid receptor agonist, surrounding an inner core of naltrexone hydrochloride, an opioid receptor antagonist, and is indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time**
- **Ingestion of these capsules or the pellets within the capsules may cause fatal respiratory depression when administered to patients not already tolerant to high doses of opioids**
- **Patients should not consume alcoholic beverages or use prescription or nonprescription medications containing alcohol while on EMBEDA™ therapy, due to the risk of an increase of plasma levels and potentially fatal overdose of morphine**
- **EMBEDA™ is to be swallowed whole or the contents of the capsules sprinkled on applesauce. The pellets in the capsules are not to be crushed, dissolved, or chewed due to the risk of rapid release and absorption of a potentially fatal dose of morphine**
- **Crushing, dissolving, or chewing EMBEDA™ will also result in the release of naltrexone, which may precipitate withdrawal in opioid-tolerant individuals**
- EMBEDA™ is contraindicated in patients with a known hypersensitivity to morphine, morphine salts, naltrexone, or in any situation where opioids are contraindicated, and in patients with significant respiratory depression, acute or severe bronchial asthma, and hypercapnia (in unmonitored settings or the absence of resuscitative equipment)

Please see accompanying full Prescribing Information, including boxed warning and Medication Guide.

- EMBEDA™ is contraindicated in any patient who has or is suspected of having paralytic ileus
- EMBEDA™ should be administered cautiously and in reduced dosages in patients with severe renal or hepatic insufficiency, Addison disease, myxedema, hypothyroidism, prostatic hypertrophy or urethral stricture, and in elderly or debilitated patients
- Caution should also be exercised in the administration of EMBEDA™ to patients with CNS depression, toxic psychosis, acute alcoholism, and delirium tremens
- All opioids may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings
- Consuming EMBEDA™ that has been tampered with by crushing, dissolving, or chewing the extended-release formulation can release sufficient naltrexone to precipitate withdrawal in opioid-dependent individuals. Symptoms of withdrawal usually appear within 5 minutes of ingestion of naltrexone and can last for up to 48 hours. Mental status changes can include confusion, somnolence, and visual hallucinations. Significant fluid losses from vomiting and diarrhea can require intravenous fluid administration. Patients should be closely monitored and therapy with non-opioid medications should be tailored to meet individual requirements
- Care should be taken to use low initial doses of EMBEDA™ in patients who are not already opioid tolerant, especially those who are receiving concurrent treatment with muscle relaxants, sedatives, or other CNS-active medications
- **EMBEDA™ 100 mg/4 mg Capsules ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY**
- EMBEDA™ should not be abruptly discontinued
- Common adverse events reported during initiation of therapy include drowsiness, dizziness, constipation, and nausea
- Additional common adverse events reported during clinical studies include constipation, nausea, and somnolence
- Serious adverse events associated with morphine in clinical use include respiratory depression, respiratory arrest, apnea, circulatory depression, cardiac arrest, hypotension, and/or shock

References: **1.** Embeda [package insert]. Bristol, TN: King Pharmaceuticals, Inc; 2009. **2.** Chou R, Fanciullo GJ, Fine PG, et al; for the American Pain Society–American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain.* 2009;10(2):113-130. **3.** Weaver MF, Schnoll SH. Risk assessment for opioid misuse in chronic pain treatment. *Adv Pain Manage.* 2008;2(2):68-75.

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