

**NDA 22-321**  
**EMBEDA™ (morphine sulfate and naltrexone HCl) Extended-Release Capsules**

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

**I. GOALS**

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

**II. REMS ELEMENTS**

**A. Medication Guide**

In compliance with 21 CFR 208.24, the following measures will be instituted:

- A [Medication Guide](#) (see Section 1.14.1 of the NDA) will be dispensed with each EMBEDA™ prescription.
- Medication Guides will be included in the primary and secondary packaging of the commercial product.
- Two (2) Medication Guides will be included as an insert within each bottle of EMBEDA™.
- Additional Medication Guides (24) will be provided with each carton containing 12 bottles of EMBEDA™, partial cases will include two additional Medication Guides per bottle.
- The Medication Guide also will be available on the company website or through our toll-free medical information line.

**B. Communication Plan**

A communication plan will be implemented to healthcare providers and relevant institutions to support the implementation of this REMS:

1. Letters will be sent to the following audiences:
  - Physicians (pain specialists and primary care physicians)
  - Pharmacists
  - Information to medical associations
  - Information to pharmacy associations
  - Information to state medical and pharmacy boards

These communications will emphasize the key safety messages for EMBEDA™ and highlight the risks and the associated goals of the REMS. The Dear Healthcare Professional letter will include instructions to discuss the risks of EMBEDA™ with their patients and encourage them to read the Medication Guide. The Dear Pharmacist letter will include instructions to provide the Medication Guide with each prescription.

The following materials will be attached to each letter:

- [Full Prescribing Information](#)
- [Medication Guide](#)

Please see the following appended letters:

- [Dear Healthcare Professional Letter to Physicians](#)
- [Dear Pharmacist Letter](#)
- [Dear \[Medical or Pharmacy Board or Association\]](#)

2. King Pharmaceuticals, Inc. (King) will provide prescribers with the brochure, [What to Consider when Prescribing EMBEDA™](#) that describes the following:
  - a. Proper patient selection
  - b. Appropriate product dosing and administration
  - c. General opioid use including information about opioid abuse and how to identify patients who are at risk for addiction
  - d. The risks of abuse, misuse, overdose and addiction from exposure to opioids, including EMBEDA™
  - e. The risks of EMBEDA™ including:
    - i. The risk of overdose caused by exposure to an essentially immediate-release form of morphine that results from breaking, chewing, crushing or dissolving EMBEDA™
    - ii. The risk of overdose due to prescribing EMBEDA™ at doses of 100 mg/4 mg or greater to opioid non-tolerant patients
  - f. Information to counsel patients on the need to store opioid analgesics safely out of reach of children and household acquaintances
  - g. The importance of providing each patient a Medication Guide with each prescription, instructing the patient to read it and assisting the patient to understand the content.

Please see the appended brochure entitled "[What to Consider when Prescribing EMBEDA™](#)."

3. Distribution of materials:
  - a. At the time of EMBEDA™ availability, a Dear Healthcare Professional (HCP) letter ([Appendix A](#)) will be mailed to pain specialists and primary care physicians designed to convey and reinforce the risks of abuse, misuse, overdose and addiction of EMBEDA™. This letter will highlight important safety risks for EMBEDA™ and reinforce the importance of discussing this information with patients when prescribing EMBEDA™. The mailing will include a copy of the Prescribing Information (PI), the Medication Guide, and [What to Consider when Prescribing EMBEDA™](#). Extra materials will be

available via the product website or through the Sponsor toll-free medical information line.

- b. At the time of EMBEDA™ availability, a Dear Pharmacist letter ([Appendix B](#)) will be mailed to pharmacists designed to convey and reinforce the risks of abuse, misuse, overdose and addiction of EMBEDA™. This letter will highlight important safety risks for EMBEDA™ and reinforce the importance of discussing this information with patients when dispensing EMBEDA™. The letter will also inform them of the FDA requirement to distribute a Medication Guide to each patient to whom EMBEDA™ is dispensed. The mailing will include a copy of the PI and the Medication Guide. Extra materials will be available via the product website or through the Sponsor toll-free medical information line.
- c. At the time of EMBEDA™ availability, letters ([Appendix C](#)) will be mailed to the applicable associations (see [Section II.B.1.](#)) designed to convey and reinforce the risks of abuse, misuse, overdose and addiction of EMBEDA™. Information applicable to the associations will be included in each letter. All mailings will include a copy of the PI and the Medication Guide. Extra materials will be available via the product website or through the Sponsor toll-free medical information line.

### **C. Elements to Assure Safe Use**

EMBEDA™ has been shown to be effective, but is associated with risks including abuse, misuse, overdose, and addiction. EMBEDA™ can be approved without any elements to assure safe use at this time.

### **D. Implementation System**

Because EMBEDA™ can be approved without any elements to assure safe use at this time, an implementation system is not required.

### **E. Timetable for Submission of Assessments**

King Pharmaceuticals, Inc. will submit assessments of the REMS Program for EMBEDA™ 6 months and 1 year after the approval date of the NDA and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment time interval. The assessment is to be received by the FDA on the due date.