Form Approved: OMB No. 0910-0001, Expiration Date: May 31, 2011; see OMB Statement on Page 3.

TRANSMITTAL OF ADVERTISEMENTS AND PROMOTIONAL LABELING FOR DRUGS AND BIOLOGICS FOR HUMAN USE

1. DATE SUBMITTED: 12/12/2011

2. LABEL REVIEW NO. (Biologics):

3. NDA/ANDA/AADA OR BLA/PLA/PMA
Number: 20-616
Single product ☒ Multiple products ☐
For multiple products, submit completed form and specimen of advertising/promotional materials to one application of choice, and attach separate sheet addressing items 3-5 for remainder of products. Refer to No. 3 on instruction sheet.

NOTE: Form 2253 is required by law. Reports are required for approved NDAs and ANDAs (21 CFR 314.81)

4. PROPRIETARY NAME: KADIAN

5. ESTABLISHED NAME: Morphine Sulfate Extended-Release Capsules
Prod. Code No. N/A

6. PACKAGE INSERT DATE and ID NO. (Latest final printed labeling)
Rev. Feb 2010 Part# 40-9101 Rev. Dec 2009 Part# 40-9120

7. MANUFACTURER NAME:
License No. (Biologics)

FDA/CBER USE ONLY

REVIEWED BY	DATE	RETURNED BY	DATE

8. **ADVERTISEMENT / PROMOTIONAL LABELING MATERIALS**

Please check only one: ☒ Professional ☐ Consumer

Material Type (use FDA codes) a.	Dissemination/ Publication Date b.	Applicant's Material ID Code and/or description c.	Previous review No. if applicable / date (PLA Submissions) d.
PSA	12/13/11	Pharmacy Flyer Material Code: KADI1194	N/A

COMMENTS:

Add Continuation Page

9. TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT
Charlene Salmorin
Director of Labeling, Regulatory Affairs

10. SIGNATURE OF RESPONSIBLE OFFICIAL
Charlene Salmorin

11. APPLICANT'S RETURN ADDRESS
200 Elmora Avenue
Elizabeth, NJ 07207 USA

12. RESPONSIBLE OFFICIAL'S
a. PHONE NO.
(908) 659-3017
b. FAX NO.
(908) 659-2250

13. FOR CBER PRODUCTS ONLY: *(Check one)*
☐ Part I/Draft ☐ Part II/Final

Now Available...

KADIAN®
Morphine Sulfate
Extended-Release Capsules
20mg • 30mg • 50mg • 60mg • 80mg • 100mg

Generic KADIAN®

(morphine sulfate extended-release)
Capsules CII from Actavis.

- **Produced and Packaged in the same facilities as the brand.**
- **Same Size, Color and Shape that existing KADIAN® patients are familiar with.**

20 mg 30 mg 50 mg 60 mg 80 mg 100 mg

Capsules are not shown at actual size.

Available Immediately at:

- CVS
- Rite Aid
- Walmart
- Kroger
- SuperValu
- Target
- A&P
- Albertsons
- Balls Food
- Bartell Drug
- Bi-Lo/Bruno
- CARE
- Discount Drug Mart
- Express Scripts Mail Order
- Kmart
- Longs
- Medicine Shoppe
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- OSCO
- Price Chopper
- Publix
- Sam's Club
- Sav-On
- Scott and White
- Southern Family Market
- Stop & Shop
- Thrifty White
- Wegman

℞ only

WARNING:

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

KADIAN® capsules are an extended-release oral formulation of morphine sulfate 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.

KADIAN® Capsules are NOT for use as a prn analgesic.

KADIAN® 100 mg and 200 mg Capsules ARE 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.

KADIAN® CAPSULES ARE TO BE SWALLOWED WHOLE OR THE CONTENTS OF THE CAPSULES SPRINKLED ON APPLE SAUCE. THE PELLETS IN THE CAPSULES ARE NOT TO BE CHEWED, CRUSHED, OR DISSOLVED DUE TO THE RISK OF RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF MORPHINE.

For further information, please visit www.KADIAN.com or call 1-888-496-3082.

Please see accompanying Full Prescribing Information and Important Safety Information.

KADIAN® is a registered trademark of Actavis Elizabeth LLC.

KADI1194 November 2011 Printed in USA

actavis
think smart medicine

Important Safety Information

- KADIAN® is contraindicated in patients with a known hypersensitivity to morphine, morphine salts or any of the capsule components, or in any situation where opioids are contraindicated. This includes in patients with respiratory depression (in the absence of resuscitative equipment or in unmonitored settings), and in patients with acute or severe bronchial asthma or hypercarbia.

  KADIAN® is contraindicated in any patient who has or is suspected of having paralytic ileus.

  Care should be taken in the prescribing of the 100 mg and 200 mg capsule strengths. Patients should be instructed against use by individuals other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

- KADIAN® may be expected to have additive effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression because respiratory depression, hypotension, and profound sedation or coma may result.

- Respiratory depression is the chief hazard of all morphine preparations. Respiratory depression occurs more frequently in elderly and debilitated patients, and those suffering from conditions accompanied by hypoxia, hypercapnia, or upper airway obstruction (when even moderate therapeutic doses may significantly decrease pulmonary ventilation).

  KADIAN® should be used with extreme caution in patients with chronic obstructive pulmonary disease or corpulmonale, and in patients having a substantially decreased respiratory reserve (e.g. severe kyphoscoliosis), hypoxia, hypercapnia, or pre-existing respiratory depression. In such patients, even usual therapeutic doses of morphine may increase airway resistance and decrease respiratory drive to the point of apnea. In these patients, alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose.

- The respiratory depressant effects of morphine with carbon dioxide retention and secondary elevation of cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure. KADIAN® produces effects which may obscure neurologic signs of further increases in pressure in patients with head injuries. Morphine should only be administered under such circumstances when considered essential and then with extreme care.

- KADIAN® may cause severe hypotension. There is an added risk to individuals whose ability to maintain blood pressure has already been compromised by a reduced blood volume, or a concurrent administration of drugs such as phenothiazines or general anesthetics. (see **PRECAUTIONS - Drug Interactions section of Full Prescribing Information.**) KADIAN® may produce orthostatic hypotension and syncope in ambulatory patients.

  KADIAN®, like all opioid analgesics, should be administered with caution to patients in circulatory shock, as vasodilation produced by the drug may further reduce cardiac output and blood pressure.

- KADIAN® should be used with great caution and in reduced dosage in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, other tranquilizers, and alcohol because respiratory depression, hypotension, and profound sedation or coma may result.

- KADIAN® should not be given to patients with gastrointestinal obstruction, particularly paralytic ileus, as there is a risk of the product remaining in the stomach for an extended period and the subsequent release of a bolus of morphine when normal gut motility is restored. As with other solid morphine formulations diarrhea may reduce morphine absorption.

- Opioid analgesics have a narrow therapeutic index in certain patient populations, especially when combined with CNS depressant drugs, and should be reserved for cases where the benefits of opioid analgesia outweigh the known risks of respiratory depression, altered mental state, and postural hypotension.

- The administration of KADIAN® may obscure the diagnosis or clinical course in patients with acute abdominal conditions.

- KADIAN® may aggravate pre-existing convulsions in patients with convulsive disorders.

- Patients taking KADIAN® who are scheduled for cordotomy or other interruption of pain transmission pathways should have KADIAN® ceased 24 hours prior to the procedure and the pain controlled by parenteral short-acting opioids. In addition, the post-procedure titration of analgesics for such patients should be individualized to avoid either oversedation or withdrawal syndromes.

- KADIAN® may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatitis. Opioids may cause increases in the serum amylase level.

- 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.

- KADIAN® should be administered with caution, and in reduced dosages in elderly or debilitated patients; patients with severe renal or hepatic insufficiency; patients with Addison's disease; myxedema; hypothyroidism; prostatic hypertrophy or urethral stricture.

  Caution should also be exercised in the administration of KADIAN® to patients with CNS depression, toxic psychosis, acute alcoholism and delirium tremens, and convulsive disorders.

  KADIAN® may impair the mental and/or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Patients must be cautioned accordingly. Patients should also be warned about the potential combined effects of KADIAN® with other CNS depressants, including other opioids, phenothiazines, sedative/hypnotics and alcohol (see **Drug Interactions section of Full Prescribing Information**).

- CNS Depressants: Morphine should be used with great caution and in reduced dosage in patients who are concurrently receiving other central nervous system (CNS) depressants including sedatives, hypnotics, general anesthetics, antiemetics, phenothiazines, other tranquilizers and alcohol because of the risk of respiratory depression, hypotension and profound sedation or coma.

- Muscle Relaxants: KADIAN® may enhance the neuromuscular blocking action of skeletal relaxants and produce an increased degree of respiratory depression.

- Mixed Agonist/Antagonist Opioid Analgesics: Agonist/antagonist analgesics (i.e., pentazocine, nalbuphine, and butorphanol) should be administered with caution to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic such as KADIAN®.

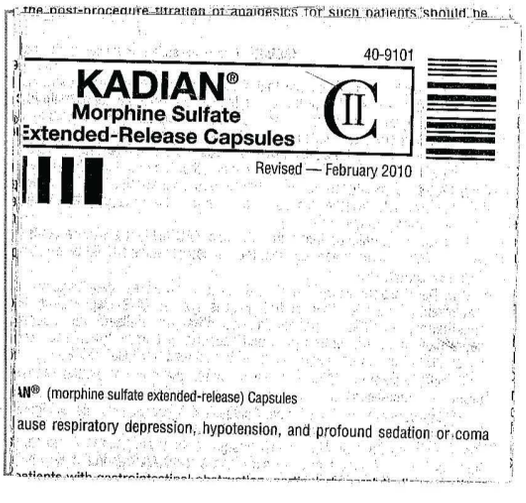
- Monoamine Oxidase Inhibitors (MAOIs): MAOIs have been reported to intensify the effects of at least one opioid drug causing anxiety, confusion and significant depression of respiration or coma. KADIAN® should not be used in patients taking MAOIs or within 14 days of stopping such treatment.

- There is an isolated report of confusion and severe respiratory depression when a hemodialysis patient was concurrently administered morphine and cimetidine.

- Morphine can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone. Morphine may also lead to acute retention of urine by causing spasm of the sphincter of the bladder, particularly in men with prostatism.

- The most serious adverse events associated with KADIAN® and other opioid analgesics are respiratory depression, respiratory arrest, apnea, circulatory depression, cardiac arrest, hypotension, and/or shock.

- The most frequent adverse events are drowsiness, dizziness, constipation, and nausea.


the post-procedure titration of analgesics for such patients should be

40-9101

KADIAN®
Morphine Sulfate
Extended-Release Capsules
CII

Revised — February 2010

IAN® (morphine sulfate extended-release) Capsules

ause respiratory depression, hypotension, and profound sedation or coma

KADIAN® (morphine sulfate extended-release) Capsules

Interactions with other CNS Depressants

KADIAN® should be used with great caution and in reduced dosage in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, other tranquilizers, and alcohol because respiratory depression, hypotension, and profound sedation or coma may result.

Gastrointestinal Obstruction

KADIAN® should not be given to patients with gastrointestinal obstruction, particularly paralytic ileus, as there is a risk of the product remaining in the stomach for an extended period and the subsequent release of a bolus of morphine when normal gut motility is restored. As with other solid morphine formulations diarrhea may reduce morphine absorption.

Other

Although extremely rare, cases of anaphylaxis have been reported.

PRECAUTIONS

General

40-9120

Morphine Sulfate Extended-Release Capsules, USP

CII

Revised — December 2009

Gastrointestinal Obstruction

Morphine sulfate extended-release should not be given to patients with gastrointestinal obstruction, particularly paralytic ileus, as there is a risk of the product remaining in the stomach for an extended period and the subsequent release of a bolus of morphine when normal gut motility is restored. As with other solid morphine formulations diarrhea may reduce morphine absorption.

Other

Although extremely rare, cases of anaphylaxis have been reported.

PRECAUTIONS

General

Morphine sulfate extended-release is intended for use in patients who require continuous, around-the-clock opioid analgesia for an extended period of time. As with any potent opioid, it is critical to adjust the dosing regimen for morphine sulfate extended-release for each patient, taking into account the patient's prior analgesic treatment experience. Although it is clearly impossible to enumerate every consideration that is important to the selection of the initial dose of morphine sulfate extended-release, attention should be given to the points under **DOSAGE AND ADMINISTRATION**.

Opioid analgesics have a narrow therapeutic index in certain patient populations, especially when combined

CARLA HEDRICK
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ELIZABETH NJ 072021106

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