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Confidential -- Not For Public Disclosure

March 4, 2010

VIA OVERNIGHT MAIL DELIVERY

Thomas Abrams, RPh, MBA
Director
Division of Drug Marketing, Advertising, and Communications
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: NDA 20-616
Kadian® (morphine sulfate extended-release) Capsules, CII
MACMIS #18148

Dear Mr. Abrams,

Actavis US ("Actavis") acknowledges receipt of a Warning Letter dated February 18, 2010, from the Division of Drug Marketing, Advertising, and Communications ("DDMAC") to Actavis Chief Executive Officer Doug Boothe, which concerns two promotional materials disseminated by Actavis. The two promotional materials are: (1) KAD18D0231 (the "Comparison Detailer" as referred to in the letter); and (2) KAD200901 (the "Co-Pay Assistance Program Brochure" as referred to in the letter which was distributed to consumers attached to a Co-Pay Assistance Program Card). In the Warning Letter, DDMAC states that these promotional materials are false or misleading because they: (1) omit and minimize serious risks associated with Kadian; (2) broaden Kadian's indication and fail to present limitations to its approved indication; and (3) present unsubstantiated superiority and effectiveness claims.

Actavis has carefully reviewed the issues addressed in the February 12, 2010 Warning Letter, and hereby provides the following response.

I. Ceasing Use and Distribution of Certain Kadian Promotional Materials

Actavis has already instructed its sales force to cease use and distribution of the two promotional materials identified in the Warning Letter. Any employees in possession of these materials have been instructed to return the materials to the Digital Direct warehouse in Honey Brook, Pennsylvania, at which time they will be destroyed.

In addition, after receiving the Warning Letter, Actavis has reviewed all Kadian promotional materials (as well as the Kadian website) to identify representations and claims similar to those that DDMAC identified as violative. Based on this review, Actavis has

determined that each of the Kadian hard-copy promotional materials that are currently in use incorporate claims of concern to DDMAC. Thus, Actavis has made the decision to cease use and distribution of each of these hard-copy promotional materials,[1] and Actavis has already instructed its sales force of this decision. As with the two pieces identified in the Warning Letter, Actavis has instructed employees in possession of these materials to return the materials to the Digital Direct warehouse for destruction. In addition, the field sales force has been instructed to retrieve any affected Kadian promotional materials remaining in the field by removing the materials from a physician's office whenever possible and returning those materials to the warehouse for destruction.

With respect to the Kadian website, Actavis has carefully reviewed the website's content and format, and is in the process of revising the website to address the issues raised in the Warning Letter. As of March 2, 2010, those visiting the Kadian website receive the message "The KADIAN® site is under construction. Please check back soon." In addition, this page provides a link to the full Prescribing Information for Kadian. Actavis will submit the revised website content to FDA for review at the time a revised website is launched.

In addition, Actavis commits that, going forward, any new Kadian promotional materials will incorporate changes addressing the issues raised in DDMAC's Warning Letter and all applicable FDA regulations.

In light of the above actions, the remaining Kadian material that will be disseminated consists solely of the Co-Pay Assistance Program Card (accompanied by the full Prescribing Information), without the accompanying Co-Pay Assistance Program Brochure. Specifically, upon relaunch of the website, the card and full Prescribing Information will be distributed solely to healthcare professionals through registration on the site, for distribution to their patients as appropriate. If, at a later date, Actavis decides to offer the Co-Pay Assistance Program Card directly to consumers, it will provide a full disclosure of the risks in a manner that the consumer can readily comprehend.

II. Corrective Letters

As discussed below, Actavis proposes to disseminate corrective letters to the audiences that may have received the two promotional materials addressed in the Warning Letter (KAD18D0231 and KAD200901). The proposed corrective letters are found at Attachments A and B, respectively.

A. KAD18D0231

Actavis has confirmed that this material was distributed to physicians between June 2009 and February 2010 through office visits by the sales force. Actavis has also confirmed that approximately 3,940 of these materials were distributed to physicians during this time period.

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[1] Please refer to Attachment C for a list of the Kadian promotional materials for which Actavis has ceased further use and distribution.

Actavis proposes to send this corrective letter addressing the KAD18D0231 material via first class mail to this group of 1,900 physicians identified in the Actavis database of target physicians for the sales force. Note that this physician database remains unchanged from the date of initial dissemination of the promotional pieces.

Please also note that the proposed corrective letter for the KAD18D0231 material also references the additional Kadian promotional materials that these doctors may have seen during this same time period (identified in Attachment C).

B. KAD200901

Actavis has confirmed that this material was distributed to consumers between January 2009 and February 2010 through the following means: telephone registration, web site registration, and through physician distribution. Actavis has also confirmed that approximately 170,000 of these materials were distributed to consumers during this time period. Approximately 6.5% of these cards were redeemed.

Actavis proposes to mail this corrective letter addressing the KAD200901 material via first class mail to the following: (1) consumers who received the material as a mailer through website registration, telephone registration, and (2) consumers who used the Co-Pay Assistance Card but do not fall into the first category.

Actavis believes that consumers who fall into the above second category, but not the first category, most likely received the KAD200901 material at a physician's office. Therefore, Actavis also proposes to distribute the corrective letter to these same offices and request that physicians provide this corrective letter to any patients who may have received the KAD200901 material and place the corrective letter in their office waiting rooms.

III. Changes to Actavis Policies, Procedures and Training

As a further corrective measure, Actavis is revising its Standard Operating Procedure for reviewing and approving promotional labeling and advertising. The SOP will require that a committee comprising personnel from the Regulatory Affairs, Medical Affairs, Legal, and Marketing Departments review all promotional labeling and advertising before release of that material for dissemination. Previously, the SOP only required a more limited pre-clearance review. A committee review will provide a more rigorous and balanced review of materials.

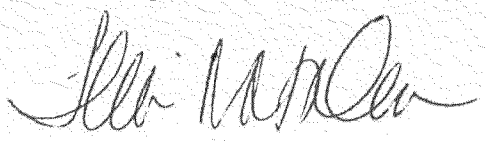
Finally, Actavis intends to conduct training of the Kadian sales force team to ensure that it understands the content of the corrective letters and can appropriately communicate that message to physicians during office visits.

NDA 20-616
Kadian® (morphine sulfate extended-release) Capsules, CII
MACMIS #18148

Actavis takes very seriously the issues raised in DDMAC's Warning Letter and is committed to working with FDA to resolve all outstanding issues concerning Kadian-related promotional activities.

Please do not hesitate to contact me at 908-659-2317 if you have questions.

Sincerely,



Terri Nataline
Vice President, Regulatory and Medical Affairs
Actavis US

Enclosures

cc: Elaine Hu Cunningham, Pharm. D., Senior Regulatory Review Officer
CDER, DDMAC Communications
(via facsimile: 301-847-8444)

Doug Boothe
Chief Executive Officer
Actavis US

ATTACHMENT A

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IMPORTANT:
Correction of Drug Information about
KADIAN® (morphine sulfate extended-release) Capsules, CII

March __, 2010

Dear Health Care Professional,

Between March 2009 and December 2010, Actavis US ("Actavis") sales representatives, during office visits with physicians, distributed a certain material to promote Kadian that was the subject of a Warning Letter (dated February 18, 2010) issued by the U.S. Food and Drug Administration ("FDA"). The cover page of this material read: "Why settle for generic MS Contin® tablets…"

In the Warning Letter, FDA raised the following concerns regarding the material: (1) it omitted and minimized serious risks associated with Kadian; (2) it broadened Kadian's indication and failed to present limitations to its approved indication; and (3) it presented unsubstantiated superiority claims. Upon receiving this letter, Actavis immediately ceased using or distributing this material.

Actavis would like to take the opportunity to correct and clarify the statements and representations made in this specific promotional material. Please note that the issues discussed below apply to other Kadian promotional materials distributed during this time period, including: (1) the Kadian Visual Aid; (2) a Kadian Conversion Guide; and (3) a material titled "Behind the Scenes, the KADIAN Capsules Story." Actavis has also ceased using or distributing these materials.

I. Indication

FDA objected to certain representations in the material, stating that these representations suggested that Kadian is appropriate to treat broad types of chronic pain.

Please see below the full indication statement for Kadian, including limitations on use, as reflected in the Indications and Usage section of the full Prescribing Information:

> 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 (see **CLINICAL PHARMACOLOGY**).

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FOR REVIEW PURPOSES ONLY

60 Columbia Rd., Bldg. B
Morristown, NJ 07960 (973) 993-4501 www.actavis.com

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

KADIAN® is not indicated for pain in the immediate postoperative period (the first 12-24 hours following surgery), or if the pain is mild or not expected to persist for an extended period of time. KADIAN® is only indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines.)

II. Risks

FDA stated that while the material disclosed certain risks (including information on the boxed warning), the material failed to include other important and serious risk information.

Please see below the most important and serious risks associated with Kadian, and please refer the enclosed full Prescribing Information for additional discussion of these risks:

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.

Other important and serious risks associated with Kadian include:

Contraindictions:

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.

Warnings:

KADIAN® Capsules are to be swallowed whole and are not to be chewed, crushed, or dissolved. Taking chewed, crushed, or dissolved KADIAN® Capsules leads to rapid release and absorption of a potentially fatal dose of morphine.

KADIAN® 100 mg and 200 mg Capsules ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. This capsule strength may cause fatal respiratory depression when ingested or administered to patients who are not previously exposed to opioids.

Care should be taken in the prescribing of this capsule strength. 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.

Misuse, Abuse and Diversion of Opioids
KADIAN® contains morphine an opioid agonist and a Schedule II controlled substance. Opioid agonists have the potential for being abused and are sought by drug abusers and people with addiction disorders and are subject to criminal diversion.

Morphine 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.

Abuse of KADIAN® by crushing, chewing, snorting or injecting the dissolved product will result in the uncontrolled delivery of the opioid and pose a significant risk to the abuser that could result in overdose and death (see **WARNINGS** and **DRUG ABUSE AND DEPENDENCE** sections in the full Prescribing Information)

Concerns about abuse, addiction, and diversion should not prevent the proper management of pain. Healthcare professionals should contact their State Professional Licensing Board, or State Controlled Substances Authority for information on how to prevent and detect abuse or diversion of this product.

Interactions with Alcohol and Drugs of Abuse
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.

Impaired Respiration
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 cor pulmonale, 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.

Head Injury and Increased Intracranial Pressure
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.

Hypotensive Effect
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 also **PRECAUTIONS - Drug Interactions**.) 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.

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
KADIAN® 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 KADIAN® 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 KADIAN®, 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 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.

Selection of patients for treatment with KADIAN® should be governed by the same principles that apply to the use of any potent opioid analgesics. Specifically, the increased risks associated with its use in the following populations should be considered: the elderly or debilitated and those with severe impairment of hepatic, pulmonary, or renal function; hypothyroidism; adrenocortical insufficiency (e.g., Addison's Disease); CNS depression or coma; toxic psychosis; prostatic hypertrophy, or urethral stricture; acute alcoholism; delirium tremens; kyphoscoliosis, or inability to swallow.

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.

Cordotomy
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.

Use in Pancreatic/Biliary Tract Disease
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 and Physical 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.

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.

In general, opioids should not be abruptly discontinued (see **DOSAGE AND ADMINISTRATION: Cessation of Therapy** in the full Prescribing Information).

Special Risk Groups
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.

Driving and Operating Machinery
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** in the full Prescribing Information)

III. Unsubstantiated Superiority Claims

FDA objected to several claims in the material that reference MS Contin® (morphine sulfate controlled-release) Tablets, CII, Avinza® (morphine sulfate extended-release capsules), CII, and generic controlled-release morphine tablets. Specifically, the material:

- Stated "Why settle for generic MS Contin® tablets…When you can prescribe the benefits of KADIAN® capsules."
- Made claims regarding the pharmacokinetic properties of Kadian versus generic controlled-release morphine tablets.
- Made claims regarding "better pain control and improved sleep scores" versus generic controlled-release morphine tablets.
- Made claims about the dosing flexibility of Kadian versus MS Contin and Avinza.

Please note that FDA objected to each of the above claims as misleading, and objected to any representation in the distributed material that Kadian is safer or more effective than these other products.

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Please see the enclosed full Prescribing Information for Kadian.

If you have any questions, please call 1-877-637-4629.

ATTACHMENT B

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IMPORTANT:
Correction of Drug Information about
KADIAN® (morphine sulfate extended-release) Capsules, CII

March __, 2010

Dear Valued Consumer,

You are receiving this letter because you may have received from Actavis US ("Actavis") a Co-Pay Assistance Program Card which was attached to a Co-Pay Assistance Program Brochure. This letter specifically concerns the Co-Pay Assistance Program Brochure, which was the subject of a Warning Letter issued by the U.S. Food and Drug Administration ("FDA") on February 18, 2010.

In the Warning Letter, FDA raised the following concerns about the Brochure: (1) it omitted and minimized serious risks associated with Kadian; (2) it broadened Kadian's indication and failed to present limitations to its approved indication; and (3) it presented unsubstantiated effectiveness claims.

Actavis would like to take the opportunity to correct and clarify the statements and representations about Kadian made in the Brochure.

I. Indication

FDA objected to the general discussion in the Brochure regarding "chronic pain" and "pain management," stating that this discussion suggested that Kadian is appropriate to treat all types of chronic pain.

Please note that Kadian is indicated to treat only certain types of pain. Specifically:

> KADIAN® capsules are an extended-release oral formulation of morphine sulfate that is used to manage moderate to severe pain that continues around-the-clock and is expected to last for an extended period of time.
>
> **KADIAN® is NOT for use to treat pain that occurs once in a while ("as needed").**
>
> KADIAN® is not indicated for pain in the immediate post-operative period (12-24 hours following surgery) for patients not previously taking opioids.
>
> KADIAN® is not indicated for pain in the post-operative period if the pain is mild or not expected to persist for an extended period of time.

Actavis Inc | 60 Columbia Rd., Bldg. B
Morristown, NJ 07960 | (973) 993-4501 | www.actavis.com

Please remember to consider the above information about the appropriate use of Kadian, including its limitations on use, and discuss these issues with your doctor.

II. Risks

FDA stated that while the Brochure disclosed certain risks associated with Kadian (including information on its boxed warning (see below)), the Brochure failed to include other important and serious risk information. Moreover, FDA objected to the Brochure's use of medically technical language to explain these risks because such information is not likely to be understood by consumers.

Please see below a discussion of the most important and serious risks associated with Kadian, and please refer to the enclosed full Prescribing Information for additional discussion of these risks:

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.

Most Important Information to Know About Kadian

- Kadian, which is a federally controlled substance (CII), can be abused by people who abuse prescription medicines or street drugs. To prevent theft, misuse, or abuse of KADIAN®, keep it in a safe place. Do not give Kadian to anyone else. It may harm them or even cause death. After you stop taking Kadian, flush any unused capsules down the toilet.

- Do not crush, dissolve, or chew Kadian capsules or the capsule contents before swallowing. Abuse of Kadian by crushing, chewing, snorting or injecting the dissolved product will result in the uncontrolled delivery of morphine and pose a significant risk to the abuser that could result in overdose or death.

- KADIAN® is **NOT** for use to treat pain that occurs once in a while ("as needed").

- Kadian 100 mg and 200 mg capsules are for use only in opioid tolerant patients. "Opioid tolerant" means that you regularly use another opioid medicine for constant pain and that your body is used to it. **Ingesting Kadian 100 mg and 200 mg capsules when you are not opioid tolerant may cause serious breathing problems and death.**

Do Not Take Kadian If:

- You have a known hypersensitivity (allergy) to morphine, morphine salts, or any of the ingredients in Kadian (See the accompanying Prescribing Information for a complete list of ingredients in Kadian).

- You are having an asthma attack or have severe asthma, trouble breathing, or lung problems.

- You have a bowel blockage called paralytic ileus.

- Do not take Kadian with alcohol, other opioids, or illicit drugs because dangerous additive effects may occur resulting in serious injury or death. In addition, alcohol can cause very high levels of morphine in your blood and you can die due to an overdose of morphine.

Possible Side Effects of Kadian

- Kadian can cause serious breathing problems that may be life-threatening, especially if Kadian is used in the wrong way. Call your healthcare provider or get medical help right away if your breathing slows down, you have shallow breathing, you feel faint, dizzy, confused, or have any unusual symptoms. These can be symptoms that you have taken too much Kadian or that the dose is too high for you. **These symptoms may lead to serious problems or death if not treated right away.**

- Kadian can cause physical dependence, which is not the same as drug addiction. Do not stop taking Kadian or any other opioid without talking to your doctor.

- There is a chance of abuse or addiction with Kadian.

- Serious allergic reactions, while extremely rare, have been reported with use of Kadian. Get medical help right away if you experience any symptoms of a severe allergic reactions, such as: feeling dizzy or faint, trouble breathing, chest pain, or swelling of the face, throat, or tongue.

- Do not drive or operate machinery or perform other potentially hazardous activities until you know how you react to this medicine or a change in the dose.

Please Remember

- These are not all the risks and side effects associated with Kadian. For more information, please contact your doctor.

- Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

III. Unsubstantiated Effectiveness Claims

FDA objected to the following statements in the Brochure regarding chronic pain:

- ". . . Many Americans suffer from chronic or ongoing pain. It can cause you to miss work and can even keep you from enjoying life. If left untreated, pain can place stress on your body and your mental health . . . ."

- " . . . Chronic pain . . . can be inconvenient and can keep you from your daily tasks."

FDA stated that the above representations suggested that use of Kadian results in a positive impact on a patient's work, physical and mental functioning, daily activities, or enjoyment of life. FDA stated that these representations were misleading because they suggested that Kadian is more effective than has been demonstrated.

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Please see the enclosed full Prescribing Information for Kadian. If you have any questions regarding Kadian or this letter, please consult with your doctor or call 1-877-637-4629.

ATTACHMENT C

ATTACHMENT C

Kadian Materials for Which Actavis Ceased Further Distribution and Use

2253 Submission Date	Piece	Number Printed	Dates of Distribution	Method of Distribution
02/16/09	Co-Pay Assistance Program (KAD200901)	177,000	March 2009-February 2010	Physician visits by sales team, website registration, telephone registration
06/24/09	Kadian "Behind the Scenes…" (KAD180229C)	15,000	June 2009 – February 2010	Physician visits by sales team
08/03/09	Kadian "When You Can Prescribe Benefits…" (KAD18D0231)	15,000	August 2009 – February 2010	Physician visits by sales team
10/20/09	Kadian Conversion Guide Sales Aid (KAD17D0179)	3,000	October 2009 – February 2010	Physician visits by sales team
10/29/09	Kadian Sales Aid (KAD18D0228)	1,000	October 2009 – February 2010	Physician visits by sales team
11/06/09	Kadian Reprint (KAD19ETOH)	2,000	November 2009 – February 2010	Physician visits by sales team

ATTACHMENT C

Kadian Materials for Which Actavis Ceased Further Distribution and Use

2253 Submission Date	Piece	Number Printed	Dates of Distribution	Method of Distribution
02/16/09	Co-Pay Assistance Program (KAD200901)	177,000	March 2009-February 2010	Physician visits by sales team, website registration, telephone registration
06/24/09	Kadian "Behind the Scenes…" (KAD180229C)	15,000	June 2009 – February 2010	Physician visits by sales team
08/03/09	Kadian "When You Can Prescribe Benefits…" (KAD18D0231)	15,000	August 2009 – February 2010	Physician visits by sales team
10/20/09	Kadian Conversion Guide Sales Aid (KAD17D0179)	3,000	October 2009 – February 2010	Physician visits by sales team
10/29/09	Kadian Sales Aid (KAD18D0228)	1,000	October 2009 – February 2010	Physician visits by sales team
11/06/09	Kadian Reprint (KAD19ETOH)	2,000	November 2009 – February 2010	Physician visits by sales team