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October 20, 2009

UPS OVERNIGHT COURIER

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

**RE: NDA # 20-616 KADIAN® (morphine sulfate extended-release) Capsules,
10 mg, 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg, and 200 mg**

Dear Sir/Madam:

Actavis Elizabeth LLC is hereby submitting, in duplicate, the following promotional material(s), for KADIAN® (morphine sulfate extended-release) Capsules:

KADIAN - Conversion Guide
Material Code: KAD17D0179

If you have any questions relating to this submission, please do not hesitate to contact the undersigned at (908) 659-3017.

Sincerely,

ACTAVIS ELIZABETH LLC

Lucy Gary
Manager, Regulatory Affairs,
Labeling & Graphics

/cg
Enclosures



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

1. DATE SUBMITTED 10/20/2009	3 NDA/ANDA/AADA OR BLA/PLA/PMA Number: Single product <input checked="" type="checkbox"/> Multiple products <input type="checkbox"/> 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.
2. LABEL REVIEW NO. (Biologics)	

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. February 2009 Part# 40-9101	7. MANUFACTURER NAME License No. (Biologics)

FDA/CBER USE ONLY

REVIEWED BY	DATE	RETURNED BY	DATE
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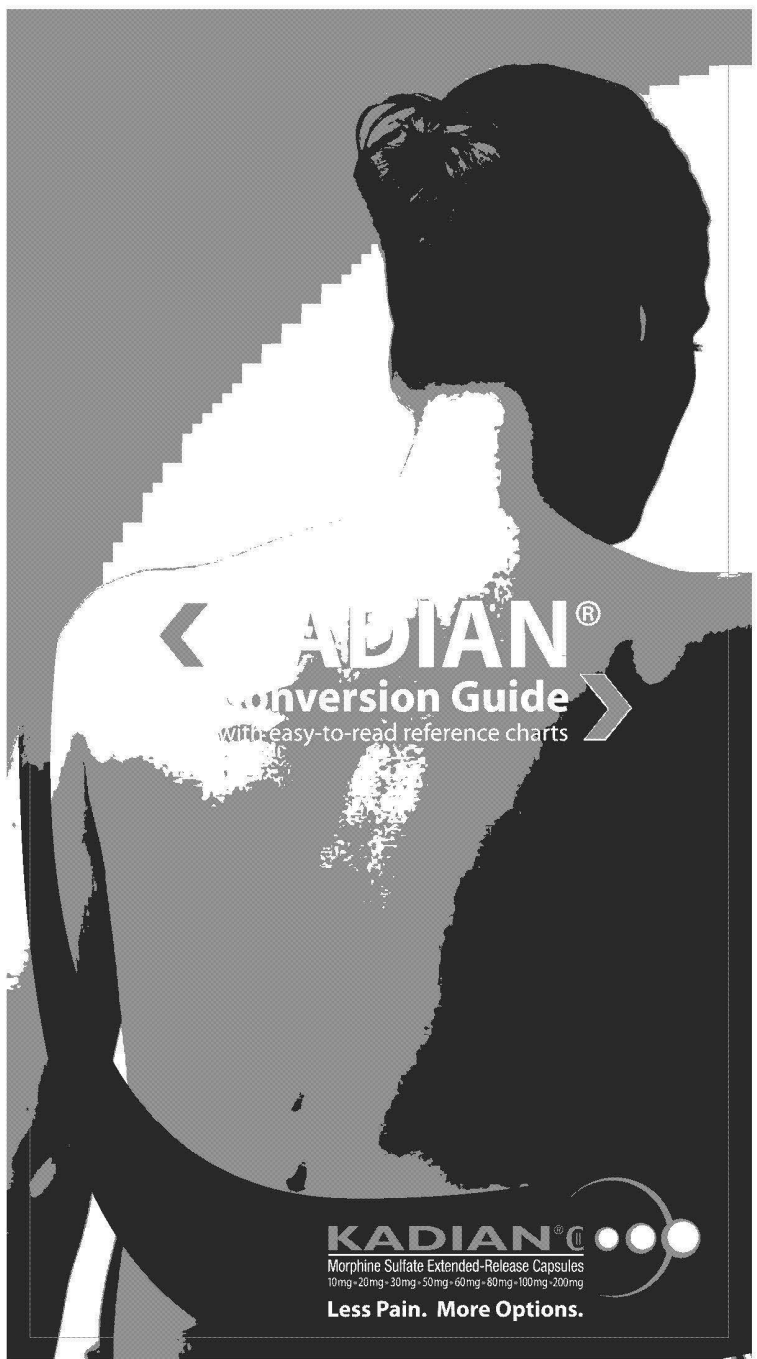
8. ADVERTISEMENT / PROMOTIONAL LABELING MATERIALS

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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.	COMMENTS:
PSA	May 2009	KADIAN - Conversion Guide Sales Aid (KAD17D0179)	N/A	

Add Continuation Page

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KADIAN[®]
Conversion Guide
with easy-to-read reference charts

KADIAN[®]

Morphine Sulfate Extended-Release Capsules
10mg • 20mg • 30mg • 50mg • 60mg • 80mg • 100mg • 200mg

Less Pain. More Options.

About this conversion guide

This conversion guide was developed to assist physicians and other healthcare providers when converting patients with moderate to severe chronic pain to an approximate daily starting dose of KADIAN® (morphine sulfate extended-release) Capsules.

The tables included in this booklet should be considered for guidance only, and the actual dose of any opioid drug product should be determined and adjusted on an individual basis. (See page 7 for additional important information about this guide.)

Chronic pain facts

- Nearly 86 million people in the United States are affected by chronic pain¹
- 76% of Americans with chronic pain experience pain daily, including 48% who say it is constant²
- Chronic pain is responsible for the loss of approximately \$90 billion annually in reduced work productivity, sick time, and direct medical costs, among others¹

Chronic pain management with KADIAN®

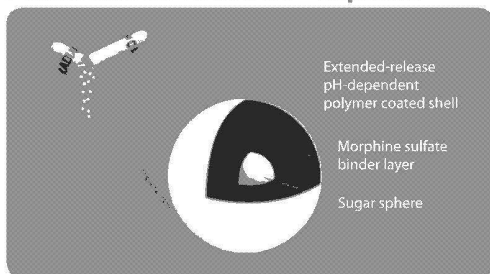
- KADIAN® capsules are an extended-release oral formulation of morphine sulfate indicated for the management of moderate to severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time
- KADIAN® capsules are not for use as a prn analgesic
- KADIAN® is an opioid agonist. Opioids are natural or synthetic analgesics derived from the opium plant, which work by binding to receptors in the spinal cord, brain, and other tissues, effectively alleviating pain in the body

Please see accompanying complete Prescribing Information.

How is KADIAN® different?

- Flexibility to dose once or twice daily
- No immediate-release (IR) component
- KADIAN® (morphine sulfate extended-release) Capsules meet your patients' needs in treating moderate to severe chronic pain by offering:
 - Flexible titration (10 mg increments)
 - Multiple dosing strengths
 - Flexible modes of administration
 - Taken as a capsule
 - Sprinkled on apple sauce
 - Through a 16 French or larger gastrostomy tube (G-tube)

Pellet inside KADIAN® capsule



Pellets are not shown at actual size.

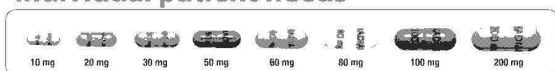
- Studies have shown that KADIAN® offers demonstrated efficacy and quality of life (QOL) improvements
 - Improvements in both malignant and nonmalignant pain³
 - Improvements in both QOL and sleep scores³⁻⁶

KADIAN® 
Morphine Sulfate Extended-Release Capsules
10mg • 20mg • 30mg • 50mg • 60mg • 80mg • 100mg • 200mg
Less Pain. More Options.

How is KADIAN® taken?

- KADIAN® (morphine sulfate extended-release) Capsules allow healthcare providers to fine-tune the dosing for their patients. KADIAN® provides the flexibility of different dosing strengths (8), frequencies, and modes of administration—for individualized pain relief

Flexible dosing strengths to meet individual patient needs

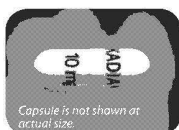


Capsules are not shown at actual size.

- Available in 10 mg, 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg, and 200 mg capsules

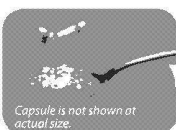
Flexible administration options⁷

- As a capsule
- Sprinkle dosing
- G-tube dosing



Capsule is not shown at actual size.

Capsule can be swallowed whole.



Capsule is not shown at actual size.

Capsule can be opened and the contents sprinkled on apple sauce for patients who have difficulty swallowing.



Contents of capsule can be sprinkled in water and administered through a 16 French or larger gastrostomy tube.*

Avoids limitations of other opioid therapies

- Can be taken with or without food⁷
- No ceiling dose—contains no fumaric acid, acetaminophen, or ibuprofen⁷
- Multiple dosing strengths allow for titration 10 mg at a time
- Frequency of adverse events (AEs) may be minimized by careful individualization of therapy⁷

*The administration of KADIAN® pellets through a nasogastric tube should not be attempted.

Please see accompanying complete Prescribing Information.

Does KADIAN® have side effects?

- KADIAN® has a side effect profile similar to other opioids. The most commonly reported side effects include drowsiness, constipation, nausea, dizziness, and anxiety⁷

What should be considered when prescribing KADIAN®?

- KADIAN® (morphine sulfate extended-release) Capsules contain 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
- Serious adverse reactions that may be associated with KADIAN® therapy in clinical use are those observed with other oral opioid analgesics and include: respiratory depression, respiratory arrest, circulatory depression, cardiac arrest, hypotension, and/or shock
- 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
- KADIAN® capsules are not for use as a prn analgesic



How should opioid-naive patients be started on KADIAN®?

- There has been no evaluation of KADIAN® as an initial opioid analgesic in the management of pain. Because it may be more difficult to titrate a patient to adequate analgesia using an extended-release morphine, it is advisable to begin treatment using an immediate-release morphine formulation
- Patients who do not have a proven tolerance to opioids should be started on the 10 mg or 20 mg strength, and usually increased at a rate not greater than 20 mg every other day

How should other oral morphine formulations be converted to KADIAN®?

1. Determine the total daily dose of the current opioid therapy being used. (If both parenteral and oral doses of the same opioid are being given, calculate a separate KADIAN® capsule dose for each and combine)
 2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio
 3. Refer to specific analgesic tables on the following pages to find an equianalgesic KADIAN® capsule dose
 4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h
- Consider giving an immediate-release opioid until the KADIAN® dose is titrated to the needed daily dose

Please see accompanying complete Prescribing Information.

How should other parenteral or oral opioid formulations be converted to KADIAN®?

1. Determine the total daily dose of the current opioid therapy being used. (If both parenteral and oral doses of the same opioid are being given, calculate a separate KADIAN® capsule dose for each and combine)
 2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio
 3. Refer to specific analgesic tables on the following pages to find an equianalgesic KADIAN® capsule dose
 4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h
- Consider giving an immediate-release opioid until the KADIAN® dose is titrated to the needed daily dose

For additional information about parenteral opioid conversion, please see page 22.

Important information about this guide

Due to incomplete cross-tolerance when converting from a non-morphine analgesic to KADIAN® and individuals' genetic variability, the following equianalgesic conversion tables should be used with some degree of caution. For these reasons, it is better to underestimate the patient's 24-hour oral morphine requirement and provide rescue medication, than to overestimate and manage an adverse event.⁷



Fentanyl products

- Actiq® 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, 1600 mcg
- Fentora® 100 mcg, 200 mcg, 300 mcg, 400 mcg, 600 mcg, 800 mcg
- Duragesic® Patch 12 mcg/hr, 25 mcg/hr, 50 mcg/hr, 75 mcg/hr, 100 mcg/hr
- Generic equivalent and other immediate-release products

How to convert from Fentanyl to KADIAN®

1. Determine the total daily dose of fentanyl (include immediate-release fentanyl), which is **approximately 50-150 times more potent than morphine on a mg-to-mg basis**⁸
2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio (1:2 ratio)
3. Refer to analgesic table on the facing page to find the equianalgesic KADIAN® capsule dose
 - Package inserts list the recommended conversion for 25 mcg/hr of transdermal fentanyl at 45-134 mg of oral morphine per day. Many clinicians use a 1:2 ratio between transdermal fentanyl and oral morphine⁸
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Please see accompanying complete Prescribing Information.

Converting from Fentanyl to KADIAN®⁸⁻¹²

Fentanyl daily dose (mcg/hr) ^a	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN® starting dose (mg) administered q24h or in divided doses q12h ^b
25	45-134	50
50	135-224	100
75	225-314	150
100	315-404	200

^aCalculate the total daily fentanyl dose.

^bIt is likely that some immediate-release (IR) opioids may be needed for breakthrough pain until the KADIAN® dose can be titrated upward to the needed daily dose, thus ensuring a smooth transition. **It is recommended that the fentanyl patch be removed and the first KADIAN® dose not to be started until 12-18 hours have passed to allow fentanyl to be completely washed out of the lipid system.**

The Duragesic® package insert recommends a conversion of 25 mcg/hr fentanyl per 60-134 mg of oral morphine per day.¹²

In the case of fentanyl, equianalgesic conversion is based on its transdermal administration, which is predicated on the agent's lipid solubility and an absorption rate-controlling membrane.⁸

Sample conversion calculation

1. 50 mcg/hr total daily dose of fentanyl
2. 50 mcg/hr daily dose of fentanyl x 2 (using a 1:2 ratio) = 100 mg daily dose of equianalgesic morphine
3. Suggested total daily dose of KADIAN® = 100 mg
4. Administer KADIAN® capsules as a single dose, 100 mg q24h, or divided doses, 50 mg q12h



Hydrocodone products

- Lorcet® 5 mg (hydrocodone/acetaminophen 500 mg), 7.5 mg, 10 mg (hydrocodone/acetaminophen 650 mg)
- Lortab® 2.5 mg, 5 mg, 7.5 mg, 10 mg (hydrocodone/acetaminophen 500 mg)
- Lortab® Elixir 2.5 mg/5 mL (hydrocodone/acetaminophen 167 mg and alcohol 7% by volume)
- Maxidone® 10 mg (hydrocodone/acetaminophen 750 mg)
- Norco® 5 mg, 7.5 mg, 10 mg (hydrocodone/acetaminophen 325 mg)
- Vicodin® 5 mg (hydrocodone/acetaminophen 500 mg)
- Vicodin® ES 7.5 mg (hydrocodone/acetaminophen 750 mg)
- Vicodin® HP 10 mg (hydrocodone/acetaminophen 660 mg)
- Vicoprofen® 7.5 mg (hydrocodone/ibuprofen 200 mg)
- Zydone® 5 mg, 7.5 mg, 10 mg (hydrocodone/acetaminophen 400 mg)
- Generic equivalent and other immediate-release products

How to convert from hydrocodone to KADIAN®

1. Determine the total daily dose of hydrocodone, which is **slightly less potent than or equivalent to morphine**¹³
2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio (1:1 ratio)
3. Refer to analgesic table on the facing page to find the equianalgesic KADIAN® capsule dose
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Please see accompanying complete Prescribing Information.

Converting from Hydrocodone to KADIAN[®] 8,10,13,14

Hydrocodone daily dose (mg) ^a	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN [®] starting dose (mg) administered q24h or in divided doses q12h ^b
10	10	10
20	20	20
30	30	30
40	40	40
60	60	60
80	80	80

Hydrocodone

^aCalculate the total daily hydrocodone dose. For combination products (eg, hydrocodone/acetaminophen), note that the maximum daily dose for a particular product is dependent mostly on the recommended acetaminophen maximum daily dose of 4000 mg.¹⁵ Also, remember that the equianalgesic conversion is an estimated figure. At lower hydrocodone doses, it may be necessary to start with the lowest KADIAN[®] capsule strength.

^bConsider giving the patient some immediate-release (IR) hydrocodone PRN to make up the difference (if the starting dose is less than an equianalgesic dose) until the KADIAN[®] dose is titrated upward to the needed daily dose.

Sample conversion calculation

- 60 mg total daily dose of hydrocodone
- 60 mg daily dose of hydrocodone x 1 (using a 1:1 ratio) = 60 mg daily dose of equianalgesic morphine
- Suggested total daily dose of KADIAN[®] = 60 mg
- Administer KADIAN[®] capsules as a single dose, 60 mg q24h, or divided doses, 30 mg q12h



Hydromorphone products

- Dilaudid® Oral Liquid Solution 5 mg/mL
- Dilaudid® Rectal Suppositories 3 mg
- Dilaudid® Tablets 2 mg, 4 mg, 8 mg
- Generic equivalent and other immediate-release products

How to convert from hydromorphone to KADIAN®

1. Determine the total daily dose of hydromorphone, which is **approximately 4 times more potent than morphine**¹³
2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio (1:4 ratio)
3. Refer to analgesic table on the facing page to find the equianalgesic KADIAN® capsule dose
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Please see accompanying complete Prescribing Information.

Converting from Hydromorphone to KADIAN[®]13,16

Hydromorphone daily dose (mg) ^a	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN [®] starting dose (mg) administered q24h or in divided doses q12h ^b
6	24	20
8	32	30
12	48	50
16	64	60
20	80	80
24	96	100

^aCalculate the total daily hydromorphone dose (including any rectal dosing). Remember that the equianalgesic conversion is an estimated figure.

^bConsider giving the patients small doses of hydromorphone PRN to make up the difference (if the starting dose is less than an equianalgesic dose) until the KADIAN[®] dose is titrated upward to the needed daily dose.

Sample conversion calculation

- 16 mg total daily dose of hydromorphone
- 16 mg daily dose of hydromorphone x 4 (using a 1:4 ratio) = 64 mg daily dose of equianalgesic morphine
- Suggested total daily dose of KADIAN[®] = 60 mg
- Administer KADIAN[®] capsules as a single dose, 60 mg q24h, or divided doses, 30 mg q12h

Hydromorphone



13

Methadone products

- Dolophine® Hydrochloride Tablets 5 mg, 10 mg
- Methadose® Dispersible Tablets 40 mg
- Methadose® Oral Concentrate 10 mg/mL
- Methadose® Oral Tablets 5 mg, 10 mg
- Generic equivalent and other immediate-release products

How to convert from methadone to KADIAN®

1. Determine the total daily dose of methadone, which is **approximately 3 times more potent than morphine⁸**
2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio (1:3 ratio)
3. Refer to analgesic table on the facing page to find the equianalgesic KADIAN® capsule dose
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Please see accompanying complete Prescribing Information.

Converting from Methadone to KADIAN®^{8,10,11,13,17-22}

Methadone daily dose (mg) ^a	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN® starting dose (mg) administered q24h or in divided doses q12h ^b
20	60	60
30	90	90
40	120	120
50	150	150
60	180	180
80	240	240
100	300	300

^aCalculate the total daily methadone dose. Remember that the equianalgesic conversion is an estimated figure.

^bConsider giving the patient small doses of methadone PRN to make up the difference (if the starting dose is less than an equianalgesic dose) until the KADIAN® dose is titrated upward to the needed daily dose.

Ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure.⁸ Methadone has a long half-life and tends to accumulate in the plasma. Plasma accumulations of methadone are more likely to occur in older patients and those with hepatic or renal dysfunction and should not be used in these patient populations.²¹

Sample conversion calculation

- 20 mg total daily dose of methadone
- 20 mg daily dose of methadone x 3 (using a 1:3 ratio) = 60 mg daily dose of equianalgesic morphine
- Suggested daily dose of KADIAN® = 60 mg
- Administer KADIAN® capsules as a single dose, 60 mg q24h, or divided doses, 30 mg q12h



› Methadone
‹

Morphine products

- AVINZA® Capsules 30 mg, 60 mg, 90 mg, 120 mg
- KADIAN® (morphine sulfate extended-release) Capsules 10 mg, 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg, 200 mg
- MS Contin® Tablets 15 mg, 30 mg, 60 mg, 100 mg, 200 mg
- Oramorph® SR Sustained Release Tablets 15 mg, 30 mg, 60 mg, 100 mg
- Generic equivalent and other immediate-release products

How to convert from other morphine products to KADIAN®

- 1.** Determine the total daily dose of the current opioid therapy being used. (If both parenteral and oral doses of the same opioid are being given, calculate a separate KADIAN® capsule dose for each and combine)
- 2.** Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio (1:1 ratio)
- 3.** Refer to specific analgesic tables on the following pages to find an equianalgesic KADIAN® capsule dose
- 4.** Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Please see accompanying complete Prescribing Information.

Converting from other morphine products to KADIAN® (conversion factor is 1:1)

Morphine daily dose (mg) ^a	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN® starting dose (mg) administered q24h or in divided doses q12h ^b
30	30	30
60	60	60
90	90	90
100	100	100
200	200	200

^aCalculate the total daily morphine dose. This amount can be given as KADIAN® capsules in a single daily q24h dose or in divided doses q12h.

^bConsider giving patients small doses of immediate-release (IR) morphine PRN to make up the difference (if the starting dose is less than an equianalgesic dose) until the KADIAN® dose is titrated upward to the needed daily dose.

Sample conversion calculation

- 60 mg total daily dose of morphine
- 60 mg daily dose of morphine x 1 (using a 1:1 ratio) = 60 mg daily dose of equianalgesic morphine
- Suggested total daily dose of KADIAN® = 60 mg
- Administer KADIAN® capsules as a single dose, 60 mg q24h, or divided doses, 30 mg q12h



Oxycodone products

- Combunox® (Oxycodone HCl and Ibuprofen) Tablets 5 mg/400 mg
- OxyContin® Tablets 10 mg, 20 mg, 40 mg, 80 mg, 160 mg
- OxyFast® Oral Concentrate Solution 20 mg/mL
- OxylR® Immediate-Release Oral Capsules 5 mg
- Percocet® Tablets 2.5 mg, 5 mg, 7.5 mg, or 10 mg oxycodone/325 mg acetaminophen
- Percodan® Tablets approximately 4.5 mg (as hydrochloride and terephthalate) oxycodone/325 mg aspirin
- Tylox® Capsules 5 mg oxycodone/500 mg acetaminophen
- Generic equivalent and other immediate-release products

How to convert from oxycodone to KADIAN®

1. Determine the total daily dose of oxycodone, which is **approximately 1.5 times more potent than morphine¹³**
2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio (1:1.5 ratio)
3. Refer to analgesic table on the facing page to find the equianalgesic KADIAN® capsule dose
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Please see accompanying complete Prescribing Information.

Converting from Oxycodone to KADIAN[®] 13,23

Oxycodone daily dose (mg) ^a	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN [®] starting dose (mg) administered q24h or in divided doses q12h ^b
20	30	30
30	45	40
40	60	60
60	90	90
80	120	120
100	150	150

^aCalculate the total daily oxycodone dose (including sustained-release and immediate-release [IR] tablets, capsules, or solution). Remember that the equianalgesic conversion is an estimated figure, and that, on average, 38% of the oxycodone daily dose is in an IR form.²⁴ Product prescribing information suggests an equivalency ratio of 1:1.5 for oral oxycodone to oral morphine, which is considered conservative by some investigators.⁹ Other authors reference ratios of 1:1 and 1:2 oxycodone to oral morphine.

^bConsider giving patients small doses of IR morphine PRN to make up the difference (if the starting dose is less than an equianalgesic dose) until the KADIAN[®] dose is titrated upward to the needed daily dose.

Sample conversion calculation

- 40 mg total daily dose of oxycodone
- 40 mg daily dose of oxycodone x 1.5 (using a 1:1.5 ratio) = 60 mg daily dose of equianalgesic morphine
- Suggested total daily dose of KADIAN[®] = 60 mg
- Administer KADIAN[®] capsules as a single dose, 60 mg q24h, or divided doses, 30 mg q12h



Oxymorphone products

- Opana® (Oxymorphone Hydrochloride) Tablets 5 mg, 10 mg
- Opana® ER (Oxymorphone Hydrochloride) extended-release tablets 5 mg, 10 mg, 20 mg, 40 mg

How to convert from oxymorphone to KADIAN®

1. Determine the total daily dose of oxymorphone, which is **approximately 3 times more potent than morphine**²⁵
2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic morphine dose, using the appropriate ratio (1:3 ratio)
3. Refer to analgesic table on the facing page to find the equianalgesic KADIAN® capsule dose
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Please see accompanying complete Prescribing Information.

Converting from Oxymorphone to KADIAN^{®25}

Oxymorphone daily dose (mg) ^a	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN [®] starting dose (mg) administered q24h or in divided doses q12h ^b
5	15	20
10	30	30
20	60	60
40	120	120

^aCalculate the daily oxymorphone dose. Remember that the equianalgesic conversion is an estimated figure.

^bConsider giving the patient some immediate-release (IR) oxymorphone PRN to make up the difference (if the starting dose is less than an equianalgesic dose) until the KADIAN[®] dose is titrated upward to the needed daily dose.

Sample conversion calculation

- 20 mg total daily dose of oxymorphone
- 20 mg daily dose of oxymorphone x 3 (using a 1:3 ratio) = 60 mg daily dose of equianalgesic morphine
- Suggested total daily dose of KADIAN[®] = 60 mg
- Administer KADIAN[®] capsules as a single dose, 60 mg q24h, or divided doses, 30 mg q12h

› Oxymorphone
‹



Step down from parenteral opioids

In the hospital setting, parenteral administration of morphine may be necessary when patients are unable to take oral medications, when patients have frequent episodes of incident pain, and in those patients with acute or severe pain who require parenteral analgesia to facilitate dosage escalations.⁹

Eventually, patients receiving parenteral opioid analgesia may need to be switched to a more convenient oral form, especially when they leave the hospital. This step-down analgesia is easily accomplished with KADIAN® (morphine sulfate extended-release) Capsules. The following conversion factors will help the clinician when changing from parenteral opioid analgesia and other opioid agents to KADIAN®.

Experience has shown that it is often better to slightly underestimate the 24-hour requirement of oral morphine than to overestimate it. Various authors have recommended convenient but slightly different conversion ratios.^{8,10,13,17,18,21,22,23}

Conversions provided in the following table use the conservative parenteral-to-oral morphine equianalgesic dosage ratio of 1:3 for tolerant patients.¹⁷

KADIAN® can be administered to patients previously receiving treatment with parenteral morphine or other opioids. While there are useful tables of oral and parenteral equivalents in cancer analgesia, there is substantial interpatient variation in the relative potency of different opioid drugs and formulations. For these reasons, it is better to underestimate the patient's 24-hour oral morphine requirement and provide rescue medication, than to overestimate and manage an adverse event.⁷

Please see accompanying complete Prescribing Information.

How to calculate the KADIAN® dose

1. Determine the daily dose of the parenteral opioid analgesic being used
2. Calculate the conversion of the total daily dose of the current opioid therapy into the equianalgesic oral morphine dose, using the appropriate ratio
3. Refer to specific analgesic tables to find an equianalgesic KADIAN® capsule dose
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in divided doses q12h

Conversion factors from commonly prescribed parenteral (IM/IV) opioid analgesics to KADIAN®¹⁷

Prior Parenteral Opioid (IM/IV)	Conversion factor to KADIAN®
Morphine	3
Hydromorphone	20
Methadone	6
Meperidine	0.4

These conversion factors are derived from well-controlled relative analgesic potency studies and conservatively assume that 10 mg of morphine administered intramuscularly is equianalgesic to 30 mg of orally administered morphine. These conversion factors apply only to the conversion of parenteral opioid preparations to oral controlled-release morphine sulfate and not to the reverse conversion.



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Parenteral opioids

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.

Safety considerations:

KADIAN® (morphine sulfate extended-release) Capsules contain 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.

Serious adverse reactions that may be associated with KADIAN® therapy in clinical use are those observed with other oral opioid analgesics and include: respiratory depression, respiratory arrest, circulatory depression, cardiac arrest, hypotension, and/or shock.

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.

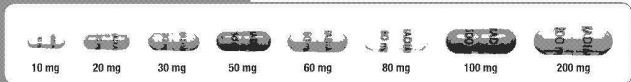
KADIAN® capsules are to be swallowed whole or the contents of the capsules sprinkled on apple sauce. The pellets in the capsules are not to be chewed, crushed, or dissolved due to the risk of rapid release and absorption of a potentially fatal dose of morphine.

Please see accompanying complete Prescribing Information.

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**opioid (extended-release) Capsules offer
the flexibility to individualize therapy⁷**



Capsules are not shown at actual size.

- Flexibility to dose once or twice daily
- Flexible dosing modes of administration (capsule, sprinkle, G-tube)
- No immediate-release (IR) component
- Innovative polymer-coated pellet technology allows for smooth, consistent plasma concentrations

KADIAN® offers demonstrated efficacy and QOL improvements³⁻⁶

KADIAN® can be individualized for well-tolerated pain relief⁷

- No ceiling dose—contains no fumaric acid, acetaminophen, or ibuprofen⁷
- Multiple dosing strengths allow for titration 10 mg at a time
- Frequency of AEs may be minimized by careful individualization of therapy⁷

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

Please see accompanying complete Prescribing Information.



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10mg, 20mg, 30mg, 50mg, 60mg, 80mg, 100mg, 200mg

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KADIAN[®] (morphine sulfate extended-release) Capsules

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

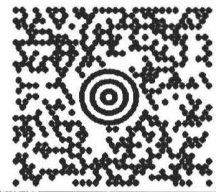
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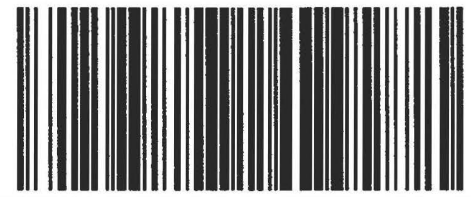
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