KADIAN®

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

Conversion Guide

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information.

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 are intended for guidance only. The prescriber should determine and adjust the actual dose of KADIAN® on a patient-specific basis.

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

Due to incomplete cross-tolerance when converting from a non-morphine analgesic to KADIAN® and individuals' variability, the following equianalgesic conversion tables should be used with 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.

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information.

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

KADIAN®

Morphine Sulfate Extended-Release Capsules

CII

KADIAN® 10 mg Capsules
KADIAN® 20 mg Capsules
KADIAN® 30 mg Capsules
KADIAN® 50 mg Capsules
KADIAN® 60 mg Capsules
KADIAN® 80 mg Capsules
KADIAN® 100 mg Capsules
KADIAN® 200 mg Capsules

℞ 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.

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.

Please see Boxed WARNING on this spread, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information.

Important Safety Information *(continued)*

KADIAN® (morphine sulfate extended-release) Capsules 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 intracraniallesions, 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.**)

continued

KADIAN® (morphine sulfate extended-release) Capsules 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.

Please see Boxed WARNING on this spread, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information.

Important Safety Information *(continued)*

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

Chronic pain management with KADIAN®

INDICATIONS AND USAGE

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 section of Full Prescribing Information**).

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

KADIAN® is not indicated for pain in the immediate post-operative 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 post-operative use if the patient is already receiving the drug prior to surgery or if the post-operative 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.)

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.

- Flexible titration (10 mg increments)
- Multiple dosing strengths
- Flexible modes of administration
  - Taken as a capsule
  - Sprinkled on apple sauce*
  - Through a 16 French gastrostomy tube (G-tube)**

*Apple sauce must be room temperature or cooler and used immediately.
**The administration of KADIAN® pellets through a nasogastric tube should not be attempted.

Pellets are not shown at actual size.

KADIAN®
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How is KADIAN® taken?

- KADIAN® 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

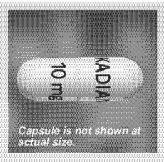
10 mg 20 mg 30 mg 50 mg 60 mg 80 mg 100 mg 200 mg

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 options

As a capsule



Capsule is not shown at actual size.

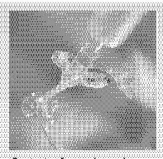
Capsule can be swallowed whole.

Sprinkle dosing

Capsule is not shown at actual size.

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

G-tube dosing



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

*Apple sauce must be room temperature or cooler and used immediately.
**The administration of KADIAN® pellets through a nasogastric tube should not be attempted.

Safety considerations:
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.

Cessation of Therapy:
When the patient no longer requires therapy with KADIAN® capsules, doses should be tapered gradually to prevent signs and symptoms of withdrawal in the physically dependent patient.

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.

- KADIAN® 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

KADIAN®

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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 equally divided doses q12h

- Consider giving an immediate-release opioid until the KADIAN® dose is titrated to the needed daily dose

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.

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 equally 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 28.

Important information about this guide

Due to incomplete cross-tolerance when converting from a non-morphine analgesic to KADIAN® and individuals' variability, the following equianalgesic conversion tables should be used with 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.

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Transdermal Fentanyl products

- Duragesic® (fentanyl transdermal system) CII Patch
  12 mcg/hr, 25 mcg/hr, 50 mcg/hr, 75 mcg/hr, 100 mcg/hr
- Generic equivalent

How to convert from Transdermal 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**[2]
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 60-134 mg of oral morphine per day. Many clinicians use a 1:2 ratio between transdermal fentanyl and oral morphine[2]
4. Administer this amount in the most convenient KADIAN® capsule dose strength, either as a single dose q24h or in equally divided doses q12h

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.

Converting from Transdermal Fentanyl to KADIAN®[2-6]

Transdermal Fentanyl daily dose (mcg/hr)[a]	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN® dose (mg) administered q24h or in divided doses q12h[b]
25	60-134	50
50	135-224	100
75	225-314	150
100	315-404	200

[a] Calculate the total daily transdermal fentanyl dose.

[b] It 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.[6]

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.[2]

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 equally divided doses, 50 mg q12h

KADIAN® (C II)
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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**[7]
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 equally divided doses q12h

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.

Converting from Hydrocodone to KADIAN®[2,4,7,8]

Hydrocodone[a] daily dose (mg)	Equianalgesic[b] morphine dose (mg)	Suggested total daily KADIAN® 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

[a]Calculate 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.[9] 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.

[b]Consider giving the patient 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

1. 60 mg total daily dose of hydrocodone
2. 60 mg daily dose of hydrocodone x 1 (using a 1:1 ratio) = 60 mg daily dose of equianalgesic morphine
3. Suggested total daily dose of KADIAN® = 60 mg
4. Administer KADIAN® capsules as a single dose, 60 mg q24h, or equally divided doses, 30 mg q12h

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Hydromorphone products

- Dilaudid® (hydromorphone hydrochloride) Oral Liquid Solution 5 mg/mL
- Dilaudid® (hydromorphone hydrochloride) Rectal Suppositories 3 mg
- Dilaudid® (hydromorphone hydrochloride) Tablets 2 mg, 4 mg, 8 mg
- Generic equivalent and other immediate-release products
- Exalgo® CII (hydromorphone HCl) 8 mg, 12 mg, 16 mg

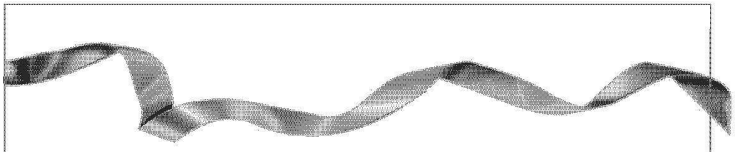
How to convert from hydromorphone to KADIAN®

1. Determine the total daily dose of hydromorphone, which is **approximately 4 times more potent than morphine**[7]
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 equally divided doses q12h

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.



Converting from Hydromorphone to KADIAN®[7,10]

Do not use this chart for conversion from parenteral (IM/IV) opioid analgesics to KADIAN®. Refer to parenteral conversion factors on pages 28-29.

Hydromorphone daily dose (mg)[a]	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN® 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

[a]Calculate the total daily hydromorphone dose (including any rectal dosing). Remember that the equianalgesic conversion is an estimated figure.

[b]Consider giving the patients 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

1. 16 mg total daily dose of hydromorphone
2. 16 mg daily dose of hydromorphone x 4 (using a 1:4 ratio) = 64 mg daily dose of equianalgesic morphine
3. Suggested total daily dose of KADIAN® = 60 mg
4. Administer KADIAN® capsules as a single dose, 60 mg q24h, or equally divided doses, 30 mg q12h

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Methadone products

- Dolophine® Hydrochloride CII (methodone hydrochloride) Tablets 5 mg, 10 mg
- Methadose® Dispersible Tablets 40 mg
- Methadose® CII (methadone hydrochloride oral concentrate USP) Oral Concentrate 10 mg/mL
- Methadose® CII (methodone hydrochloride) 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 morphine**[2]
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 equally divided doses q12h

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

Converting from Methadone to KADIAN®[2,4,5,7,11-16]

Do not use this chart for conversion from parenteral (IM/IV) opioid analgesics to KADIAN®. Refer to parenteral conversion factors on pages 28-29.

Methadone daily dose (mg)[a]	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN® 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

[a]Calculate the total daily methadone dose. Remember that the equianalgesic conversion is an estimated figure.

[b]Consider giving the patient 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.

Ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure.[2] Methadone has a long half-life and tends to accumulate in the plasma.[15]

Sample conversion calculation

1. 20 mg total daily dose of methadone
2. 20 mg daily dose of methadone x 3 (using a 1:3 ratio) = 60 mg daily dose of equianalgesic morphine
3. Suggested daily dose of KADIAN® = 60 mg
4. Administer KADIAN® capsules as a single dose, 60 mg q24h, or equally divided doses, 30 mg q12h

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

Morphine products

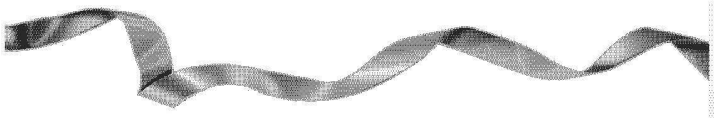
- AVINZA® CII (morphine sulfate extended-release capsules) Capsules 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, 120 mg
- Embeda® CII (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg
- KADIAN® CII (morphine sulfate extended-release) Capsules 10 mg, 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg, 200 mg
- MS Contin® CII (morphine sulfate) Tablets 15 mg, 30 mg, 60 mg, 100 mg, 200 mg
- Oramorph® SR CII (morphine sulfate) 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 equally divided doses q12h

Patients on other oral morphine formulations may be converted to KADIAN® by administering one-half of the patient's total daily oral morphine dose as KADIAN® capsules every 12 hours (twice-a-day) or by administering the total daily oral morphine dose as KADIAN® capsules every 24 hours (once-a-day). KADIAN® should not be given more frequently than every 12 hours.

Please see Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.



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

Do not use this chart for conversion from parenteral (IM/IV) opioid analgesics to KADIAN®. Refer to parenteral conversion factors on pages 28-29.

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

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

[b]Consider giving patients 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

1. 60 mg total daily dose of morphine
2. 60 mg daily dose of morphine x 1 (using a 1:1 ratio) = 60 mg daily dose of equianalgesic morphine
3. Suggested total daily dose of KADIAN® = 60 mg
4. Administer KADIAN® capsules as a single dose, 60 mg q24h, or equally divided doses, 30 mg q12h

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Oxycodone products

- Combunox® (oxycodone HCl and ibuprofen) Tablets 5 mg/400 mg
- OxyContin® (oxycodone HCl) Controlled-Release Tablets 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 160 mg
- OxyFast® (oxycodone hydrochlride) Oral Concentrate Solution 20 mg/mL
- OxyIR® (oxycodone hydrochlride) Immediate-Release Oral Capsules 5 mg
- Percocet® CII (oxycodone and acetaminophen tablets, USP) 2.5 mg, 5 mg, 7.5 mg, or 10 mg oxycodone/325 mg acetaminophen
- Percodan® CII (oxycodone and aspirin tablets, USP) approximately 4.5 mg (as hydrochloride and terephthalate) oxycodone/325 mg aspirin
- Tylox® CII (oxycodone and acetaminophen capsules, USP) 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 morphine**[7]
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 equally divided doses q12h

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

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Converting from Oxycodone to KADIAN®[7,17]

Oxycodone daily dose (mg)[a]	Equianalgesic morphine dose (mg)	Suggested total daily KADIAN® 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

[a]Calculate 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.[18] Product prescribing information suggests an equivalency ratio of 1:1.5 for oral oxycodone to oral morphine, which is considered conservative by some investigators.[2] Other authors reference ratios of 1:1 and 1:2 oxycodone to oral morphine.

[b]Consider giving patients 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

1. 40 mg total daily dose of oxycodone
2. 40 mg daily dose of oxycodone x 1.5 (using a 1:1.5 ratio) = 60 mg daily dose of equianalgesic morphine
3. Suggested total daily dose of KADIAN® = 60 mg
4. Administer KADIAN® capsules as a single dose, 60 mg q24h, or equally divided doses, 30 mg q12h

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Oxymorphone products

- Opana® CII (oxymorphone hydrochloride) Tablets 5 mg, 10 mg
- Opana® ER CII (oxymorphone hydrochloride) extended-release tablets 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30mg, 40mg

How to convert from oxymorphone to KADIAN®

1. Determine the total daily dose of oxymorphone, which is **approximately 3 times more potent than morphine**[19]
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 equally divided doses q12h

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

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Converting from Oxymorphone to KADIAN® [19]

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

[a]Calculate the daily oxymorphone dose. Remember that the equianalgesic conversion is an estimated figure.

[b]Consider giving the patient some 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

1. 20 mg total daily dose of oxymorphone
2. 20 mg daily dose of oxymorphone x 3 (using a 1:3 ratio) = 60 mg daily dose of equianalgesic morphine
3. Suggested total daily dose of KADIAN® = 60 mg
4. Administer KADIAN® capsules as a single dose, 60 mg q24h, or equally divided doses, 30 mg q12h

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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.[3]

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.[2,4,7,11,12,15-17]

Conversions provided in the following table use the conservative parenteral-to-oral morphine equianalgesic dosage ratio of 1:3 for tolerant patients.[11]

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.

There is a lack of systematic evidence about these types of analgesic substitutions. Therefore, specific recommendations are not possible. Healthcare professionals are advised to refer to published relative potency data, keeping in mind that such ratios are only approximate.

In general, it is safest to give half of the estimated total daily oral morphine dose as the initial dose and to manage inadequate analgesia by supplementation with IR morphine.

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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 equally divided doses q12h

Conversion factors from commonly prescribed parenteral (IM/IV) opioid analgesics to KADIAN® [11]

From 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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Indications and Usage

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 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.)

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 Boxed WARNING on page 4, Important Safety Information on pages 4-7, and accompanying Full Prescribing Information for KADIAN® (morphine sulfate extended-release) Capsules.

References: 1. KADIAN® CII [prescribing information]. Morristown, NJ: Actavis Elizabeth LLC. 2010. **2.** Gordon DB, Stevenson KK, Griffie J, Muchka S, Rapp C, Ford-Roberts K. Opioid equianalgesic calculations. *J Palliat Med*. 1999;2(2):209-218. **3.** Levy MH. Pharmacologic treatment of cancer pain. *N Engl J Med*. 1996;335(15):1124-1132. **4.** Baumann TJ. Pain management. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 3rd ed. Stamford, CT: Appleton & Lange; 1997:1259-1278. **5.** Smith AP, Lee NM, Loh HH. Opioid analgesics and antagonists. In: Munson PL, Mueller RA, Breese GR, eds. *Principles of Pharmacology: Basic Concepts & Clinical Applications*. New York, NY: Chapman & Hall; 1995:402-416. **6.** Full Prescribing Information. Duragesic® CII (fentanyl transdermal system/Ortho-McNeil - Janssen Pharmaceuticals, Inc.). *Physicians' Desk Reference®*. 64th ed. Montvale, NJ: PDR Network, LLC; 2010:2604-2611. **7.** McCaffery M, Pasero C. Pain: Clinical Manual. 2nd ed. St. Louis, MO: Mosby; 1999:241-243. **8.** Full Prescribing Information. Vicodin HP® CIII (hydrocodone bitartrate/Abbott Laboratories). *Physicians' Desk Reference®*. 64th ed. Montvale, NJ: PDR Network, LLC; 2010:563-564. **9.** Full Prescribing Information. Extra Strength Tylenol® (acetaminophen/McNeil Consumer & Specialty Pharmaceuticals). *Physicians' Desk Reference®*. 64th ed. Montvale, NJ: PDR Network, LLC; 2010:2049-2052. **10.** Full Prescribing Information. Dilaudid® CII (hydromorphone HCl/Purdue Pharma L.P.). *Physicians' Desk Reference®*. 64th ed. Montvale, NJ: PDR Network, LLC; 2010:2797-2800. **11.** American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 5th ed. Glenview, IL: American Pain Society; 2003. **12.** Twycross RG. Opioids. In: Wall PD, Melzack R, eds. *Textbook of Pain*. London, England: Churchill Livingstone; 1994:943-962. **13.** Hanks G, Cherny N. Opioid analgesic therapy. In: Doyle D, Hanks GWC, MacDonald N, eds. *Oxford Textbook of Palliative Medicine*. 2nd ed. New York, NY: Oxford University Press; 1998:331-355. **14.** Miyoshi HR, Leckband SG. Systemic opioid analgesics. In: Loeser JD, Butler SH, Chapman CR, Turk DC, eds. *Bonica's Management of Pain*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001:1682-1709. **15.** Bonica JJ, Ventafridda V, Twycross RG. Cancer pain. In: Bonica JJ, ed. *The Management of Pain*. 2nd ed. Philadelphia, PA: Lea & Febiger; 1990:400-460. **16.** Supernaw RB. Pharmacotherapeutic management of selected pain phenomena. In: Weiner RS, ed. *Pain Management: A Practical Guide for Clinicians*. Boca Raton, FL: St. Lucie Press; 1998:137-150. **17.** Full Prescribing Information. Oxycontin® CII (oxycodone HCl/Purdue Pharma L.P.) *Physicians' Desk Reference®*. 64th ed. Montvale, NJ: PDR Network, LLC; 2010:2807-2813. **18.** Mandema JW, Kaiko RF, Oshlack B, Reder RF, Stanski DR. Characterization and validation of a pharmacokinetic model for controlled-release oxycodone. *Br J Clin Pharmacol*. 1996;42:747-756. **19.** Full Prescribing Information. Opana® CII (oxymorphone hydrochloride) Extended-Release Tablets/Endo Pharmaceuticals). *Physicians' Desk Reference®*. 64th ed. Montvale, NJ: PDR Network, LLC; 2010:1110-1114.

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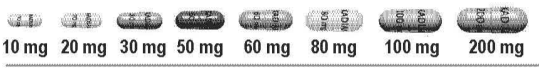
KADIAN® 10 mg Capsules	KADIAN® 60 mg Capsules
KADIAN® 20 mg Capsules	KADIAN® 80 mg Capsules
KADIAN® 30 mg Capsules	KADIAN® 100 mg Capsules
KADIAN® 50 mg Capsules	KADIAN® 200 mg Capsules



Capsules are not shown at actual size.

- Dose once or twice daily
- Flexible administration options (capsule, sprinkle, G-tube)
- Polymer-coated pellet technology allows for smooth, consistent plasma concentrations
- No ceiling or recommended maximal dose
- Multiple dosing strengths allow for titration 10 mg at a time
- Frequency of AEs may be minimized by careful individualization of therapy

℞ only

WARNING:

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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.
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