From:	Killion, Mark
То:	Jennifer Altier
Sent:	7/10/2012 12:18:26 PM
Subject:	fourth e-mail
Attachments:	Objection Handling Messaging 071311.pptx; October 2011 Kadian Promotional Training Slides.pptx

Mark Killion Midwest Region Business Director Actavis Kadian LLC mkillion@kadian.com (e-mail) 317-837-8345 (office) 317-501-0588 (cell)



ACTAVIS0264950 P-25267 \_ 00001



# New Patient Start Messaging



ACTAVIS0264951 P-25267 \_ 00002

# Initial Question



- How does KADIAN<sup>®</sup> fit in to your prescribing habits?
  - If 1<sup>st</sup> line: Thank the HCP for their business and remind them of the key features and benefits of KADIAN<sup>®</sup>
  - If not 1<sup>st</sup> line: Why don't you use KADIAN<sup>®</sup> first line?
    - » Side effects
    - » Efficacy
    - » Older product



## Side Effects



#### What side effects do you see with KADIAN®?

#### Management of Excessive Drowsiness

- Most patients receiving KADIAN<sup>®</sup> will experience initial drowsiness. This usually disappears within 3-5 days and is not a cause of concern unless it is excessive, or accompanied by unsteadiness or confusion. Dizziness and unsteadiness may be associated with postural hypotension, particularly in elderly or debilitated patients, and has been associated with syncope and falls in non-tolerant patients started on opioids.
- Excessive or persistent sedation should be investigated. Factors to be considered should include: concurrent sedative medications, the presence of hepatic or renal insufficiency, hypoxia or hypercapnia due to exacerbated respiratory failure, intolerance to the dose used (especially in older patients), disease severity and the patient's general condition.
- The dosage should be adjusted according to individual needs, but additional care should be used in the selection of initial doses for the elderly patient, the cachectic or gravely ill patient, or in patients not already familiar with opioid analgesic medications to prevent excessive sedation at the onset of treatment.







#### What side effects do you see with KADIAN®?

#### Management of Nausea and Vomiting

 Nausea and vomiting are common after single doses of KADIAN<sup>®</sup> or as an early undesirable effect of chronic opioid therapy. The prescription of a suitable antiemetic should be considered, with the awareness that sedation may result (see Drug Interactions). The frequency of nausea and vomiting usually decreases within a week or so but may persist due to opioid-induced gastric stasis. Metoclopramide is often useful in such patients.

#### Management of Constipation

 Virtually all patients suffer from constipation while taking opioids, such as KADIAN<sup>®</sup>, on a chronic basis. Some patients, particularly elderly, debilitated or bedridden patients may become impacted. Tolerance does not usually develop for the constipating effects of opioids. Patients must be cautioned accordingly and laxatives, softeners and other appropriate treatments should be used prophylactically from the beginning of opioid therapy.



# Efficacy



- KADIAN<sup>®</sup> contains morphine as its active ingredient and has a long history of safety and efficacy when used as indicated
- KADIAN<sup>®</sup> has a well known side effect profile
- KADIAN<sup>®</sup> provides steady blood levels of morphine sulfate with few peaks and valleys
- KADIAN<sup>®</sup> is available in 8 different strengths and can be titrated in 10mg increments. The availability of these 8 doses provides flexibility in dose selection



# Efficacy (con't)



- KADIAN<sup>®</sup> provides convenience and flexibility with once or twice a day dosing.
- KADIAN<sup>®</sup> doses can be titrated up every other day.
- KADIAN<sup>®</sup> does not have a ceiling or recommended maximal dose, especially in patients with chronic pain of malignancy. In such cases the total dose of KADIAN should be advanced until the desired therapeutic endpoint is reached or clinicallysignificant opioid-related adverse reactions intervene.
- KADIAN<sup>®</sup> has no significant food effect and can be administered without regard to meals for dosing convenience.
- KADIAN<sup>®</sup> is available as an extended release capsule, but it has 3 modes of administration



### **Older Product**



#### Actavis is proud of KADIAN<sup>®</sup>'s 15 year history:

- KADIAN<sup>®</sup> contains morphine as its active ingredient and has a long history of safety and efficacy when used as indicated
- KADIAN<sup>®</sup> has a well known side effect profile
- KADIAN<sup>®</sup> is widely stocked in pharmacies nationwide
- Continue with other features and benefits of KADIAN<sup>®</sup>



## Question #2



- What LAO do you use 1<sup>st</sup> line?
  - Generic Morphine Sulfate
  - Avinza®
  - Other branded LAOs
- Do not make comparative product claims
  - Do not say or imply that KADIAN<sup>®</sup> is safer or more effective than another drug
  - This has not been demonstrated by substantial evidence or clinical experience



### Generic Morphine Sulfate



- What has been your experience with KADIAN<sup>®</sup> and morphine sulfate with your patients?
- Is there a reason you prefer one product for your patients?
- Is BID dosing important for you and your patients?
- Are steady plasma levels important to your patients? If so, why is that important to you?
- Have you converted patients from morphine sulfate to KADIAN®?
- How much do you consider the patient's out of pocket cost? Does this impact your prescribing decision?

#### <u>Tactics</u>

- PK charts in Detail Aids
- Mini-conversion guide
- Form Trak
  - Co-Pay Cards







- Is there a reason you prefer one product for your patients?
- What dose do you prefer to start your new patients on? Is having a 10mg and 20mg option important for you and your patients?
- Is having a co-pay card program an important benefit to you and your patients?

 Have you converted patients from Avinza<sup>®</sup> to KADIAN<sup>®</sup>? <u>Tactics</u>

• Dosing Guide

•

- Co-Pay Cards
- Conversion guide
- Form Trak



#### **Other Branded Products**



- Is there a reason you prefer one product for your patients?
- Does having a product with a long history of safety and efficacy important for you?
- Is top tier formulary coverage an important factor for you when prescribing an LAO?

#### <u>Tactics</u>

- Detail Aid
- Co-Pay Cards
- Form Trak



### KADIAN<sup>®</sup> Boxed Warning

- KADIAN® is associated with a number of serious risks, many of which are potentially fatal
- The PI includes the following boxed warning concerning potentially fatal overdosing if KADIAN® capsules are chewed, crushed, or dissolved, and other serious 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.

# KADIAN<sup>®</sup> Bolded Warnings

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

### KADIAN<sup>®</sup> Indications and Usage

- KADIAN<sup>®</sup> 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<sup>®</sup> Capsules are NOT intended for use as a prn analgesic
- KADIAN<sup>®</sup> 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<sup>®</sup> 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.)

#### **KADIAN®** Contraindications

- KADIAN<sup>®</sup> 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<sup>®</sup> is contraindicated in any patient who has or is suspected of having paralytic ileus.

#### **Important**

- Do communicate the full product indication
  - Failing to do so implies that KADIAN is indicated for use in a broader range of conditions or patients than has been demonstrated
- Do discuss safety considerations with prescribers during each call
  - KADIAN<sup>®</sup> is associated with a number of serious risks, many of which are potentially fatal

#### <u>Important</u>

- Do discuss KADIAN<sup>®</sup> product features described in the PI, including:
  - KADIAN<sup>®</sup> contains morphine as its active ingredient and has a long history of safety and efficacy when used as indicated
  - KADIAN<sup>®</sup> has a well known side effect profile
  - KADIAN<sup>®</sup> provides steady blood levels of morphine sulfate with few peaks and valleys
  - KADIAN<sup>®</sup> is available in 8 different strengths and can be titrated in 10mg increments. The availability of these 8 doses provides flexibility in dose selection.

#### <u>Important</u>

- Do discuss KADIAN<sup>®</sup> product features described in the PI, including:
  - KADIAN<sup>®</sup> provides convenience and flexibility with once or twice a day dosing.
  - KADIAN<sup>®</sup> doses can be titrated up every other day.
  - KADIAN<sup>®</sup> does not have a ceiling or recommended maximal dose, especially in patients with chronic pain of malignancy. In such cases the total dose of KADIAN should be advanced until the desired therapeutic endpoint is reached or clinically-significant opioid-related adverse reactions intervene.
  - KADIAN<sup>®</sup> has no significant food effect and can be administered without regard to meals for dosing convenience.
  - KADIAN<sup>®</sup> is available as an extended release capsule, but it has 3 modes of administration

#### Important

- Do discuss marketing and patient support programs
  - Co-pay Assistance Program
  - Patient Assistance Program

#### <u>Important</u>

- Do not make comparative product claims
  - Do not say or imply that KADIAN<sup>®</sup> is safer or more effective than another drug
  - This has not been demonstrated by substantial evidence or clinical experience

#### Important

- Do not compare information from other LAO Pl's to the KADIAN<sup>®</sup> PI
- Do not engage in a discussion of any product other than KADIAN<sup>®</sup>



# KADIAN<sup>®</sup> Marketing Overview

Sales Representative Training

October, 2011



ACTAVIS0264972 P-25267 \_ 00023

#### Agenda



- Key Promotional Messages
- Tactics
- New Patient Start Messaging

# Indications – What are the approved uses for KADIAN®



- KADIAN<sup>®</sup> 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<sup>®</sup> Capsules are NOT intended for use as a prn analgesic.
- KADIAN<sup>®</sup> 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<sup>®</sup> 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.)

#### Boxed Warning/ Important Safety Informatio

- When speaking to Healthcare Professionals about KADIAN<sup>®</sup>, it is important to remind them of the box warning and the Important Safety Information, which can be found on the first spread of each of the promotional tactics (Detail Aid, Dosing Guide and Conversion Guide)
- KADIAN<sup>®</sup> contains morphine sulfate, an opioid agonist and a Schedule II controlled substance

Key Product Attributes Kapian's of the start of the start

- 8 Dosing Strengths Flexibility in Dosing Strengths
- Polymer-coated pellet technology
- BID/QD Dosing Frequency Flexibility

### 8 Dosing Strengths/ Flexibility in Dosing Strength<sup>Strength</sup>

- KADIAN<sup>®</sup> capsules are supplied in 8 strengths: 10mg, 20mg, 30mg, 50mg, 60mg, 80mg, 100mg, and 200mg strengths – the most of any extended-release morphine
- The 8 strengths can be titrated in 10mg increments. The availability of these 8 doses provides flexibility in dose selection.
  - KADIAN<sup>®</sup> 100mg and 200mg 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<sup>®</sup> doses can be titrated up every other day

#### Polymer-Coated Pellet Technology



- KADIAN<sup>®</sup> utilizes polymer-coated pellet technology for reliable morphine delivery
- The distinctive pellet composition releases morphine steadily into the bloodstream for up to 24 hours
  - 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.

#### BID/QD Dosing Frequency Flexibility



- KADIAN<sup>®</sup> provides convenience and flexibility with once or twice a day dosing
  - KADIAN<sup>®</sup> Capsules are NOT for use as a prn analgesic



### **New Tactics**

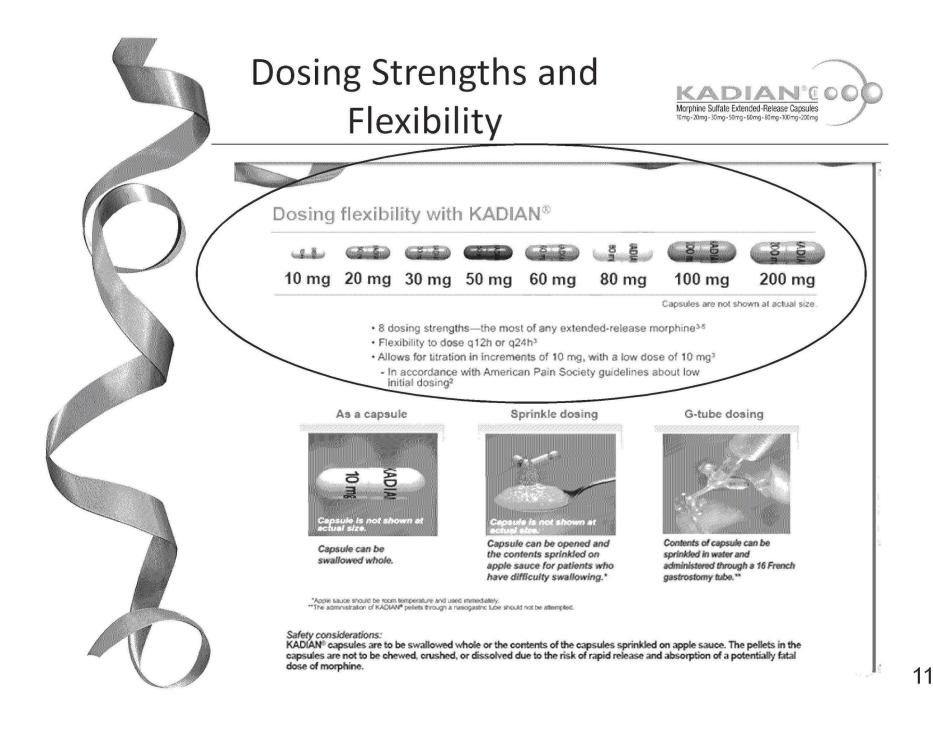


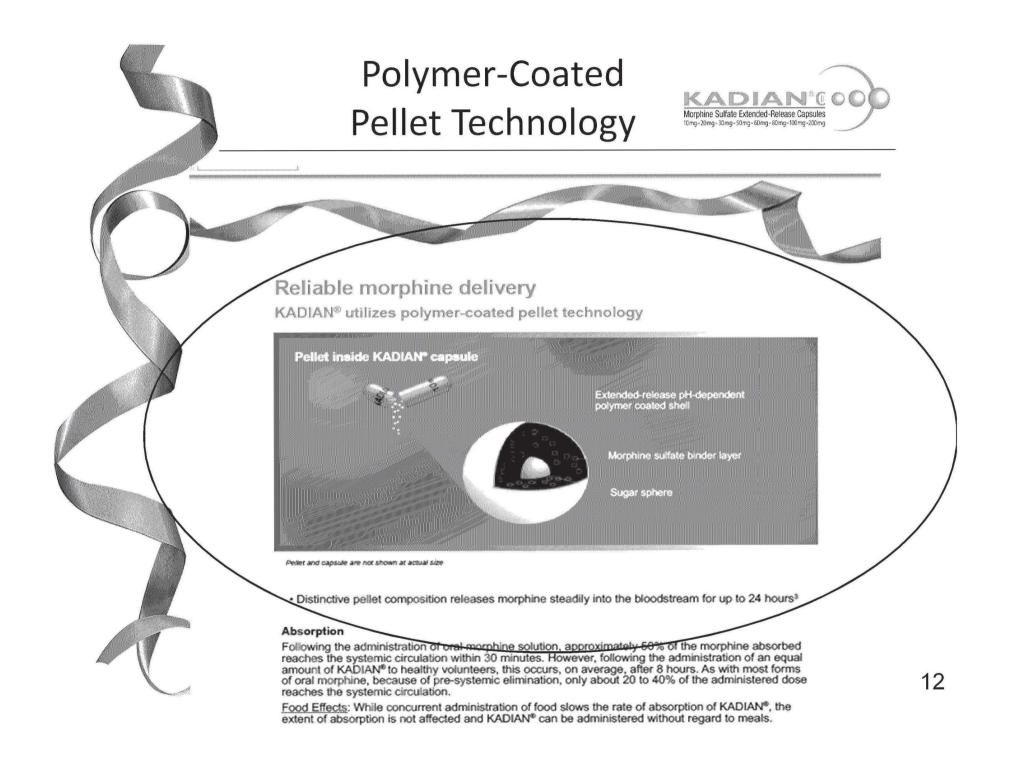
ACTAVIS0264980 P-25267 \_ 00031





- All 3 core pieces (Detail Aid, Dosing Guide and Conversion Guide) provide the same information to highlight the product attributes, as seen on the following slides
- All core pieces included PI, boxed warning and Important Safety Information





#### Detail Aid



- 8 Page booklet designed to provide healthcare professionals with an overview of the KADIAN<sup>®</sup> product attributes
- Includes information on:
  - Boxed Warning/Important Safety Information
  - World Health Organization (WHO) guidelines for pain management
  - Indications and Usage
  - Polymer-coated pellet technology
  - Pharmacokinetic data
  - Dosing flexibility
- This tactic allows you to provide healthcare professionals with important information about the key product attributes of KADIAN<sup>®</sup>

#### Dosing Guide



12 page pocket guide with a more detailed focus on dosing issues, including:

- Initiating Therapy with KADIAN<sup>®</sup> Capsules
- Individualization of Dosage
- Initiating in Patients without Proven Opioid Tolerance
- Considerations in the Adjustment of Dosing Regimens
- Alternative Methods of Administration
- This tactic provides additional details on how healthcare professionals can take advantage of the dosing flexibility of KADIAN<sup>®</sup> to better meet the needs of their patients in pain

## Conversion Guide



- 30 page spiral bound booklet that includes:
  - The core promotional messages for KADIAN®
  - How patients on other pain medications can be safely converted to KADIAN<sup>®</sup>
- Healthcare professionals need to assess each patient's treatment plan individually especially when considering changes in therapy. When a HCP determines that KADIAN<sup>®</sup> is the appropriate medication to treat their patient's pain, the information in the Conversion Guide can help the HCP determine how to transition the patient to KADIAN<sup>®</sup> therapy



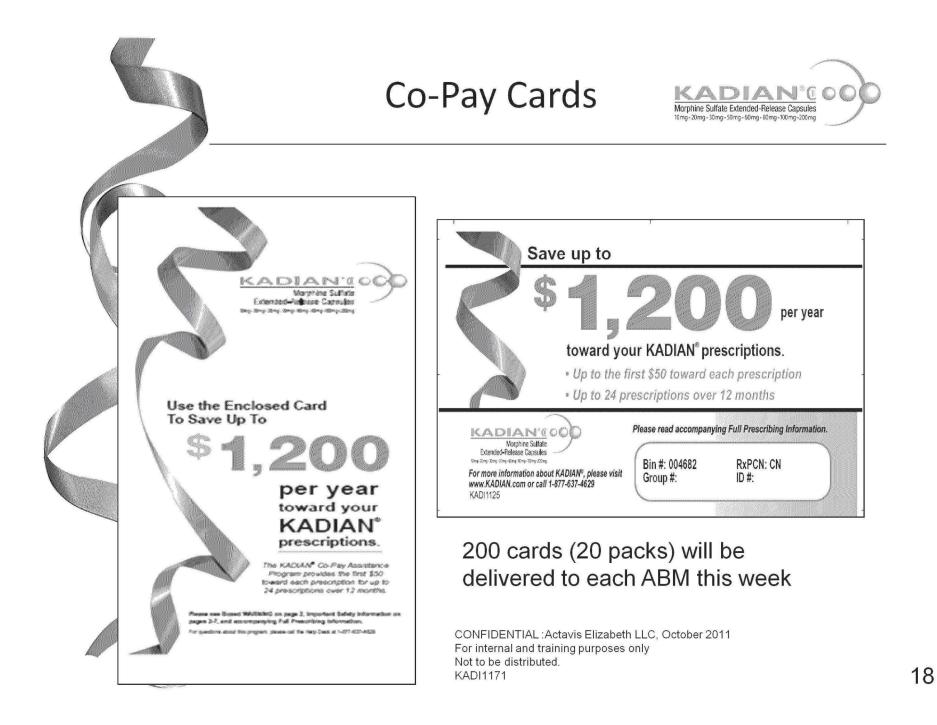
- Additional tactics provide healthcare professionals with reminders of the key benefits of KADIAN<sup>®</sup>, along with important benefits for their patients:
  - KADIAN<sup>®</sup> has a generous Co-Pay Assistance Program. The \$50 co-pay card can significantly reduce a patient's out-of-pocket expenses
  - KADIAN<sup>®</sup> has excellent managed care coverage with most plans at second or third tier
  - KADIAN<sup>®</sup> is in a preferred position on many state public aid programs
  - KADIAN<sup>®</sup> is stocked in pharmacies nationwide

## Additional Tactics



- Co-Pay Cards
- Practitioner Request Form (Co-Pay Cards)
- Form Trak Templates
- Shelf-Talkers

CONFIDENTIAL :Actavis Elizabeth LLC, October 2011 For internal and training purposes only Not to be distributed. KADI1171



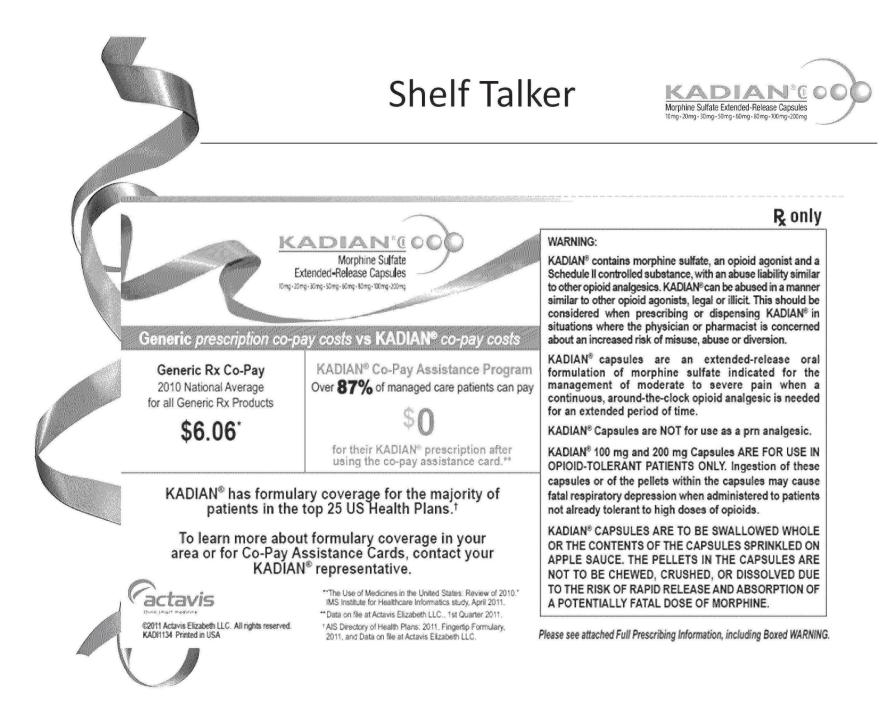
Practitioner Request Form
PRACTITIONER REQUEST FORM
Name Address City Stale ZP
Co-Pay Assistance Cards
Signature Data
Cactavis radius also in Alexandraticati Normal
CONFIDENTIAL :Actavis Elizabeth LLC, October 2011 For internal and training purposes only Not to be distributed. KADI1171



	KADIAN <sup>®</sup> Commercial	<b>Competitive Commercial</b>
μ.	KADIAN <sup>®</sup> Medicare Part D	Competitive Medicare Part D

- In-depth Form Trak training will take place tomorrow
- The templates must be handed out with the safety information and PI

CONFIDENTIAL :Actavis Elizabeth LLC, October 2011 For internal and training purposes only Not to be distributed. KADI1171



P-25267 00043

21

ACTAVIS0264992

## Mini Conversion Guide





Converting from other oral morphine products to KADIAN<sup>®</sup> (morphine sulfate extended-release) Capsules.

(conversion factor is 1:1)

#### Do not use this chart for conversion from parenteral (IM/IV) opioid analgesics to KADIAN<sup>6</sup>.

30	30	30
60	60	аласаниялания колосон пологоли и колосон и колосон и колосон колосон колосон колосон колосон колосон колосон к бор
90	90	9¢
100	100	100
2:00	2000	206

"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. "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 medied daily dose.

#### Sample conversion calculation

- 1.60 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
- 3. Suggested total daily dose of KADIAN<sup>4</sup> = 60 mg
- Administer KADIAN\* capsules as a single dose, 60 mg q24h, or equally divided doses, 30 mg q12h

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

#### KADIAN\*C Morphine Sulfate

#### Extended-Release Capsules Regiong-long-long-long-long-long-long-

#### Morphine products

- aVINZA<sup>#</sup> CII (morphine sulfate extended-release capsules) Capsules 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, 120 mg
- Embeda<sup>#</sup> CII (morphine sulfate and naltrexone hydrochloride) Extended Release Capsules 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg
- KADIAN<sup>®</sup> Cli (morphine sulfate extended-release) Capsules 10 mg, 20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg, 200 mg.
- MS Contin<sup>®</sup> Cll (morphine sulfate) Tablets 15 mg, 30 mg, 60 mg, 100 mg, 200 mg
- Oramorph<sup>®</sup> SR Cll (morphine sulfate) Sustained Release Tablets 15 mg, 30 mg, 60 mg, 100 mg
- <sup>©</sup> Generic equivalent and other immediate-release products

How to convert from other morphine products to KADIAN®

- 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<sup>®</sup> capsule dose for each and combine)
- 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)
- Refer to specific analgesic tables on the previous page to find an equianalgesic KADIAN<sup>®</sup> capsule dose
- Administer this amount in the most convenient KADIAN<sup>®</sup> 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.



## Tactical Summary



Opportunity	Message	Tactics
Generic Morphine Sulfate	Financial Comparison Message	<ul> <li>Shelf Talkers</li> <li>Detail Aid (PK Charts)</li> <li>Dosing Guide</li> <li>Form Trak (KADIAN only)</li> <li>New Co-Pay Cards/Request Form</li> <li>Mini conversion guide/Conversion guide</li> </ul>

CONFIDENTIAL :Actavis Elizabeth LLC, October 2011 For internal and training purposes only Not to be distributed. KADI1171





- Online ordering: fulfill.digitaldirect.com
- Your user name and password will be sent to you via e-mail
- You can order the majority of promotional materials through this site
  - Work through your RBD to request additional co-pay cards





## Warehouse Ordering



Item Id:		KADI1006
Description	1:	Kadian Conversion Guide
Order Limi		5
Availability		97
(as of t	10/16/2011	8:58:56 PM)
Shipped in	packs of 1	0
	1	Add All Selected
Order 🗸	Qty: -	Items to Cart
Item Id:		KADI1007
Description Order Limi		Kadian Dosing Guide S
Availability		5 64
		8:58:56 PM)
	packages	The second s
mmann		Add All Selected
Order 🔽	Qty: 1	Items to Cart
	Illesse .	
Item Id:		KADI1014
Description		Shelf Talker
Order Limi		100
Availability		192 8:58:56 PM)
(as or ,	10/10/2011	8:58:50 PM)
Order 🔽	ope 1	Add All Selected
order j.	~~~y .  -	Items to Cart
Item Id: Description		KADI1107 Mini Conversion Guide
Availability		877
		8:58:56 PM)
Innoversity		
Order 🔽	Oty: 1	Add All Selected
TTTT I MARKAN		Items to Cart



## New Patient Start Messaging

27

ACTAVIS0264998 P-25267 \_ 00049

# Initial Question KADIAN®

- How does KADIAN<sup>®</sup> fit in to your prescribing habits?
  - If 1<sup>st</sup> line: Thank the HCP for their business and remind them of the key features and benefits of KADIAN<sup>®</sup>
  - If not 1<sup>st</sup> line: Why don't you use KADIAN<sup>®</sup> first line?
    - » Side effects
    - » Efficacy
    - » Older product

28

# Side Effects



### What side effects do you see with KADIAN<sup>®</sup>?

#### Management of Excessive Drowsiness

- Most patients receiving KADIAN<sup>®</sup> will experience initial drowsiness. This usually disappears within 3-5 days and is not a cause of concern unless it is excessive, or accompanied by unsteadiness or confusion. Dizziness and unsteadiness may be associated with postural hypotension, particularly in elderly or debilitated patients, and has been associated with syncope and falls in non-tolerant patients started on opioids.
- Excessive or persistent sedation should be investigated. Factors to be considered should include: concurrent sedative medications, the presence of hepatic or renal insufficiency, hypoxia or hypercapnia due to exacerbated respiratory failure, intolerance to the dose used (especially in older patients), disease severity and the patient's general condition.
- The dosage should be adjusted according to individual needs, but additional care should be used in the selection of initial doses for the elderly patient, the cachectic or gravely ill patient, or in patients not already familiar with opioid analgesic medications to prevent excessive sedation at the onset of treatment.



## Side Effects (con't)



### What side effects do you see with KADIAN<sup>®</sup>?

#### Management of Nausea and Vomiting

 Nausea and vomiting are common after single doses of KADIAN<sup>®</sup> or as an early undesirable effect of chronic opioid therapy. The prescription of a suitable antiemetic should be considered, with the awareness that sedation may result (see Drug Interactions). The frequency of nausea and vomiting usually decreases within a week or so but may persist due to opioid-induced gastric stasis. Metoclopramide is often useful in such patients.

#### Management of Constipation

 Virtually all patients suffer from constipation while taking opioids, such as KADIAN<sup>®</sup>, on a chronic basis. Some patients, particularly elderly, debilitated or bedridden patients may become impacted. Tolerance does not usually develop for the constipating effects of opioids. Patients must be cautioned accordingly and laxatives, softeners and other appropriate treatments should be used prophylactically from the beginning of opioid therapy.



- KADIAN<sup>®</sup> contains morphine as its active ingredient and has a long history of safety and efficacy when used as indicated
- KADIAN<sup>®</sup> has a well known side effect profile

Efficacy

- KADIAN<sup>®</sup> provides steady blood levels of morphine sulfate with few peaks and valleys
- KADIAN<sup>®</sup> is available in 8 different strengths and can be titrated in 10mg increments. The availability of these 8 doses provides flexibility in dose selection

# Efficacy (con't)



- KADIAN<sup>®</sup> provides convenience and flexibility with once or twice a day dosing.
- KADIAN<sup>®</sup> doses can be titrated up every other day.
- KADIAN<sup>®</sup> does not have a ceiling or recommended maximal dose, especially in patients with chronic pain of malignancy. In such cases the total dose of KADIAN should be advanced until the desired therapeutic endpoint is reached or clinicallysignificant opioid-related adverse reactions intervene.
- KADIAN<sup>®</sup> has no significant food effect and can be administered without regard to meals for dosing convenience.
- KADIAN<sup>®</sup> is available as an extended release capsule, but it has 3 modes of administration

## **Older Product**



## Actavis is proud of KADIAN<sup>®</sup>'s 15 year history:

- KADIAN<sup>®</sup> contains morphine as its active ingredient and has a long history of safety and efficacy when used as indicated
- KADIAN<sup>®</sup> has a well known side effect profile
- KADIAN<sup>®</sup> is widely stocked in pharmacies nationwide
- Continue with other features and benefits of KADIAN<sup>®</sup>

# Question #2



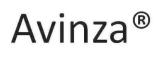
- What LAO do you use 1<sup>st</sup> line?
  - Generic Morphine Sulfate
  - Avinza®
  - Other branded LAOs
- Do not make comparative product claims
  - Do not say or imply that KADIAN<sup>®</sup> is safer or more effective than another drug
  - This has not been demonstrated by substantial evidence or clinical experience

## Generic Morphine Sulfate

- What has been your experience with KADIAN<sup>®</sup> and morphine sulfate with your patients?
- Is there a reason you prefer one product for your patients?
- Is BID dosing important for you and your patients?
- Are steady plasma levels important to your patients? If so, why is that important to you?
- Have you converted patients from morphine sulfate to KADIAN®?
- How much do you consider the patient's out of pocket cost? Does this impact your prescribing decision?

#### <u>Tactics</u>

- PK charts in Detail Aids
- Mini-conversion guide
- Form Trak
  - Co-Pay Cards





- Is there a reason you prefer one product for your patients?
- What dose do you prefer to start your new patients on? Is having a 10mg and 20mg option important for you and your patients?
- Is having a co-pay card program an important benefit to you and your patients?
- Have you converted patients from Avinza<sup>®</sup> to KADIAN<sup>®</sup>?
   <u>Tactics</u>
- Dosing Guide

۲

- Co-Pay Cards
- Conversion guide
- Form Trak





- Is there a reason you prefer one product for your patients?
- Does having a product with a long history of safety and efficacy important for you?
- Is top tier formulary coverage an important factor for you when prescribing an LAO?

### <u>Tactics</u>

- Detail Aid
- Co-Pay Cards
- Form Trak

37

### KADIAN<sup>®</sup> Boxed Warning



KADIAN® is associated with a number of serious risks, many of which are potentially fatal. The PI includes the following boxed warning concerning potentially fatal overdosing if KADIAN® capsules are chewed, crushed, or dissolved, and other serious 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.

# KADIAN<sup>®</sup> Bolded Warnings

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

- KADIAN<sup>®</sup> 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.

## KADIAN<sup>®</sup> Indications and Usage KADIAN<sup>®</sup> 000

KADIAN<sup>®</sup> 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<sup>®</sup> Capsules are NOT intended for use as a prn analgesic

 KADIAN<sup>®</sup> 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<sup>®</sup> 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.)

## KADIAN<sup>®</sup> Contraindications

- KADIAN<sup>®</sup> 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<sup>®</sup> is contraindicated in any patient who has or is suspected of having paralytic ileus.



- Do communicate the full product indication
  - Failing to do so could imply that KADIAN is indicated for use in a broader range of conditions or patients than has been demonstrated
- Do discuss safety considerations with prescribers during each call
  - KADIAN<sup>®</sup> is associated with a number of serious risks, many of which are potentially fatal



- Do discuss KADIAN<sup>®</sup> product features described in the PI, including:
  - KADIAN<sup>®</sup> contains morphine as its active ingredient and has a long history of safety and efficacy when used as indicated
  - KADIAN<sup>®</sup> has a well known side effect profile
  - KADIAN<sup>®</sup> provides steady blood levels of morphine sulfate with few peaks and valleys
  - KADIAN<sup>®</sup> is available in 8 different strengths and can be titrated in 10mg increments. The availability of these 8 doses provides flexibility in dose selection.



- Do discuss KADIAN<sup>®</sup> product features described in the PI, including:
  - KADIAN<sup>®</sup> provides convenience and flexibility with once or twice a day dosing.
  - KADIAN<sup>®</sup> doses can be titrated up every other day.
  - KADIAN<sup>®</sup> does not have a ceiling or recommended maximal dose, especially in patients with chronic pain of malignancy. In such cases the total dose of KADIAN should be advanced until the desired therapeutic endpoint is reached or clinically-significant opioid-related adverse reactions intervene.
  - KADIAN<sup>®</sup> has no significant food effect and can be administered without regard to meals for dosing convenience.
  - KADIAN<sup>®</sup> is available as an extended release capsule, but it has 3 modes of administration



- Do discuss marketing and patient support programs
  - Co-pay Assistance Program
  - Patient Assistance Program

45



- Do not make comparative product claims
  - Do not say or imply that KADIAN<sup>®</sup> is safer or more effective than another drug
  - This has not been demonstrated by substantial evidence or clinical experience



- Do not compare information from other LAO PI's to the KADIAN<sup>®</sup> PI
- Do not engage in a discussion of any product other than KADIAN<sup>®</sup>

47