KADIAN®
Morphine Sulfate Sustained Release Capsules

INDICATIONS AND USAGE
KADIAN® is indicated for the management of moderate to severe pain where treatment with an opioid analgesic is for more than a few days (see CLINICAL PHARMACOLOGY). KADIAN® was developed for use in patients with chronic pain who require repeated dosing every 8 to 12 hours. It is not indicated for patients with unstable, nonconvulsive severe respiratory conditions, for whom the rapidity of onset, the duration of action, the long half-life, and the cumulative effects of morphine may be hazardous. KADIAN® has not been tested as an analgesic for the treatment of mild pain.

WARNINGS (see also CLINICAL PHARMACOLOGY)

Impaired Respiratory Function
Respiratory depression is the chief hallmark of all opioid preparations. Respiratory depression is more likely to occur when patients are receiving parenteral administration of morphine as a single dose or multiple doses, when given concurrently or sequentially with other respiratory depressants, and when administered in the setting of renal or hepatic failure, hypoxemia, hypercarbia, sepsis, or other causes of respiratory depression. Morphine should be used with extreme caution in patients with chronic obstructive pulmonary disease or some form of pulmonary disease, and in patients having a significantly decreased respiratory reserve (including children, neonates, patients with recent head injury, recent surgery, severe hypothyroidism, or 24 hour postpartum). In such patients, even usual therapeutic doses of morphine may increase airway resistance and decrease respiratory drive to the point of apnea.

Hypertensive Crisis
In patients with significant underlying cardiovascular disease, hypotensive events have been observed. This is more likely in patients who are receiving other antihypertensive agents with an intrinsic hypotensive effect, including atenolol, labetalol, and clonidine. The concomitant use of morphine and atenolol has been associated with profound hypotension and death.

Drug Interactions

Antihypertensives

Hypotensive events have been observed in patients with hypertension when KADIAN has been discontinued abruptly or reduced too rapidly.

Hypotensive Effect

Hypotensive reactions are more likely to occur in patients with compromised cardiovascular status, e.g., impaired cardiac reserve, impaired cardiac function, and those with poor vascular tone. Hypotensive effects may be additive with other drugs such as monoamine oxidase inhibitors, clonidine, and opioids (e.g., oxycodone, oxycodeone). Elderly patients are particularly susceptible to hypotension due to a decrease in cardiac contractility and vascular smooth muscle tone.

Monitoring

Clinically significant hypotension is more likely in patients receiving KADIAN when blood pressure is measured using an automated device (e.g., automated tonometry) or while patients are sitting. Hypotensive effects may be additive with other drugs such as monoamine oxidase inhibitors, clonidine, and opioids (e.g., oxycodone, oxycodeone). Elderly patients are particularly susceptible to hypotension due to a decrease in cardiac contractility and vascular smooth muscle tone.

Laboratory Tests

KADIAN should not be used in patients with significant liver disease. KADIAN may cause significant changes in hepatic drug metabolizing enzymes. Therefore, it should be used cautiously in patients who have hepatic disease that is severe enough to cause changes in hepatic blood flow or drug disposition. If KADIAN is used in such patients, careful monitoring is necessary.

Hypotension

Hypotensive reactions are more likely to occur in patients with compromised cardiovascular status, e.g., impaired cardiac reserve, impaired cardiac function, and those with poor vascular tone. Hypotensive effects may be additive with other drugs such as monoamine oxidase inhibitors, clonidine, and opioids (e.g., oxycodone, oxycodeone). Elderly patients are particularly susceptible to hypotension due to a decrease in cardiac contractility and vascular smooth muscle tone.

Opioid Antagonist

Opioid antagonists should not be administered in the absence of clinically significant respiratory depression or in the absence of significant hypotension. Their use in the treatment of oxycodone or morphine overdose is not recommended.