REMS High Alert

morphine (mor-feen)

Astramorph PF, AVINza, Doloral, Duramorph PF, Embeda, Epimorph, Infumorph, Kadian, M-Eslon, Morphine H.P, M.O.S, M.O.S.-S.R, MS Contin, Statex

Classification

Therapeutic: opioid analgesics
Pharmacologic: opioid agonists

Schedule II

Pregnancy Category C

Indications

Severe pain (the 20 mg/mL oral solution concentration should only be used in opioid-tolerant patients). Management of moderate to severe chronic pain in patients requiring use of a continuous around-the-clock opioid analgesic for an extended period of time (extended/sustained-release). Pulmonary edema. Pain associated with MI.

Action

Binds to opiate receptors in the CNS. Alters the perception of and response to painful stimuli while producing generalized CNS depression. **Therapeutic Effects:** Decrease in severity of pain. Addition of naltrexone in *Embeda* product is designed to prevent abuse or misuse by altering the formulation. Naltrexone has no effect unless the capsule is crushed or chewed.

Pharmacokinetics

Absorption: Variably absorbed (about 30%) following oral administration. More reliably absorbed from rectal, subcut, and IM sites. Following epidural administration, systemic absorption and absorption into the intrathecal space via the meninges occurs.

Distribution: Widely distributed. Crosses the placenta; enters breast milk in small amounts.

Protein Binding: Premature infants: <20%; Adults: 35%.

Metabolism and Excretion: Mostly metabolized by the liver. Active metabolites excreted renally.

Half-life: Premature neonates: 10–20 hr; Neonates: 7.6 hr; Infants 1–3 mo: 6.2 hr; Children 6 mo–2.5 yr: 2.9 hr; Children 3–6 yr: 1–2 hr; Children 6–19 yr with sickle cell disease: 1.3 hr; Adults: 2–4 hr.

TIME/ACTION PROFILE (analgesia)

ROUTE	ONSET	PEAK	DURATION
PO	unknown	60 min	4–5 hr
PO-ER	unknown	3–4 hr	8–24 hr
IM	10–30 min	30–60 min	4–5 hr
Subcut	20 min	50–90 min	4–5 hr
Rect	unknown	20–60 min	3–7 hr
IV	rapid	20 min	4–5 hr
Epidural	6–30 min	1 hr	up to 24 hr
IT	rapid (min)	unknown	up to 24 hr

Contraindications/Precautions

Contraindicated in: Hypersensitivity; Some products contain tartrazine, bisulfites, or alcohol and should be avoided in patients with known hypersensitivity; Acute, mild, intermittent, or postoperative pain (extended/sustained-release); Significant respiratory depression (extended/sustained-release); Acute or severe bronchial asthma (extended/sustained-release); Paralytic ileus (extended/sustained-release).

Use Cautiously in: Head trauma; ↑ intracranial pressure; Severe renal, hepatic, or pulmonary disease; Hypothyroidism; Seizure disorder; Adrenal insufficiency; History of substance abuse; Undiagnosed abdominal pain; Prostatic hyperplasia; Patients undergoing procedures that rapidly ↓ pain (cordotomy, radiation); long-acting agents should be discontinued 24 hr before and replaced with short-acting agents; ***Geri:*** Geriatric or debilitated patients (dose ↓ suggested); ***OB, Lactation:*** Avoid chronic use; has been used during labor but may cause respiratory depression in the newborn; ***Pedi:*** Neonates and infants <3 mo (more susceptible to respiratory depression); ***Pedi:*** Neonates (oral solution contains sodium benzoate which can cause potentially fatal gasping syndrome).

Adverse Reactions/Side Effects

CNS: confusion, sedation, dizziness, dysphoria, euphoria, floating feeling, hallucinations, headache, unusual dreams. **EENT:** blurred vision, diplopia, miosis. **Resp:** RESPIRATORY DEPRESSION. **CV:** hypotension, bradycardia. **GI:** constipation, nausea, vomiting. **GU:** urinary retention. **Derm:** flushing, itching, sweating. **Misc:** physical dependence, psychological dependence, tolerance.

Interactions

Drug-Drug: Use with extreme caution in patients receiving **MAO inhibitors** within 14 days prior (may result in unpredictable, severe reactions—↓ initial dose of morphine to 25% of usual dose). ↑ CNS depression with **alcohol**, **sedative/hypnotics**, **clomipramine**, **barbiturates**, **tricyclic antidepressants**, and **antihistamines**. Administration of **partial-antagonist opioid analgesics** may precipitate opioid withdrawal in physically dependent patients. **Buprenorphine**, **nalbuphine**, **butorphanol**, or **pentazocine** may ↓ analgesia. May ↑ the anticoagulant effect of **warfarin**. **Cimetidine** ↓ metabolism and may ↑ effects.

Drug-Natural Products: Concomitant use of **kava-kava**, **valerian**, or **chamomile** can ↑ CNS depression.

Route/Dosage

Larger doses may be required during chronic therapy.

PO, Rect (Adults ≥50 kg): *Usual starting dose for moderate to severe pain in opioid-naive patients*—30 mg q 3–4 hr initially *or* once 24-hr opioid requirement is determined, convert to controlled-, extended-, *or* sustained-release morphine by administering total daily oral morphine dose every 24 hr (as *Kadian* or *Avinza*), 50% of the total daily oral morphine dose every 12 hr (as *Kadian, MS Contin*), or 33% of the total daily oral morphine dose every 8 hr (as *MS Contin*). See equianalgesic chart, Appendix B. *Avinza* dose should not exceed 1600 mg/day because of fumaric acid in formulation.

PO, Rect (Adults and Children <50 kg): *Usual starting dose for moderate to severe pain in opioid-naive patients*—0.3 mg/kg q 3–4 hr initially.

PO (Children >1 mo): *Prompt-release tablets and solution*—0.2–0.5 mg/kg/dose q 4–6 hr as needed. *Controlled-release tablet*—0.3–0.6 mg/kg/dose q 12 hr.

IM, IV, Subcut (Adults ≥50 kg): *Usual starting dose for moderate to severe pain in opioid-naive patients*—4–10 mg q 3–4 hr. *MI*—8–15 mg, for very severe pain additional smaller doses may be given every 3–4 hr.

IM, IV, Subcut (Adults and Children <50 kg): *Usual starting dose for moderate to severe pain in opioid-naive patients*—0.05–0.2 mg/kg q 3–4 hr, maximum: 15 mg/dose.

IM, IV, Subcut (Neonates): 0.05 mg/kg q 4–8 hr, maximum dose: 0.1 mg/kg. Use preservative-free formulation.

IV, Subcut (Adults): *Continuous infusion*—0.8–10 mg/hr; may be preceded by a bolus of 15 mg (infusion rates vary greatly; up to 400 mg/hr have been used).

IV, Subcut (Children >1 mo): *Continuous infusion, postoperative pain*—0.01–0.04 mg/kg/hr. *Continuous infusion, sickle cell or cancer pain*—0.02–2.6 mg/kg/hr.

IV (Neonates): *Continuous infusion*—0.01–0.03 mg/kg/hr.

Epidural (Adults): *Intermittent injection*—5 mg/day (initially); if relief is not obtained at 60 min, 1–2 mg increments may be made; (total dose not to exceed 10 mg/day. *Continuous infusion*—2–4 mg/24 hr; may ↑ by 1–2 mg/day (up to 30 mg/day).

Epidural (Children >1 mo): 0.03–0.05 mg/kg, maximum dose: 0.1 mg/kg or 5 mg/24 hr. Use preservative-free formulation.

IT (Adults): 0.2–1 mg. Use preservative-free formulation.

NURSING IMPLICATIONS

Assessment

- Assess type, location, and intensity of pain prior to and 1 hr following PO, subcut, IM, and 20 min (peak) following IV administration. When titrating opioid doses, increases of 25–50% should be administered until there is either a 50% reduction in the patient's pain rating on a numerical or visual analogue scale or the patient reports satisfactory pain relief. When titrating doses of short-acting morphine, a repeat dose can be safely administered at the time of the peak if previous dose is ineffective and side effects are minimal.
- Patients on a continuous infusion should have additional bolus doses provided every 15–30 min, as needed, for breakthrough pain. The bolus dose is usually set to the amount of drug infused each hour by continuous infusion.
- Patients taking sustained-release morphine may require additional short-acting opioid doses for breakthrough pain. Doses of short-acting opioids should be equivalent to 10–20% of 24 hr total and given every 2 hr as needed.
- An equianalgesic chart (see Appendix B) should be used when changing routes or when changing from one opioid to another.
- ***High Alert:*** Assess level of consciousness, BP, pulse, and respirations before and periodically during administration. If respiratory rate is <10/min, assess level of sedation. Physical stimulation may be sufficient to prevent significant hypoventilation. Subsequent doses may need to be decreased by 25–50%. Initial drowsiness will diminish with continued use. ***Geri:*** Assess geriatric patients frequently; older adults are more sensitive to the effects of opioid analgesics and may experience

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side effects and respiratory complications more frequently. ***Pedi:*** Assess pediatric patient frequently; children are more sensitive to the effects of opioid analgesics and may experience respiratory complications, excitability and restlessness more frequently.

- Prolonged use may lead to physical and psychological dependence and tolerance. This should not prevent patient from receiving adequate analgesia. Most patients who receive morphine for pain do not develop psychological dependence. Progressively higher doses may be required to relieve pain with long-term therapy.
- Assess bowel function routinely. Institute prevention of constipation with increased intake of fluids and bulk and with laxatives to minimize constipating effects. Administer stimulant laxatives routinely if opioid use exceeds 2–3 days, unless contraindicated.
- ***Lab Test Considerations:*** May ↑ plasma amylase and lipase levels.
- ***Toxicity and Overdose:*** If an opioid antagonist is required to reverse respiratory depression or coma, naloxone is the antidote. Dilute the 0.4-mg ampule of naloxone in 10 mL of 0.9% NaCl and administer 0.5 mL (0.02 mg) by direct IV push every 2 min. For children and adults weighing <40 kg, dilute 0.1 mg of naloxone in 10 mL of 0.9% NaCl for a concentration of 10 mcg/mL and administer 0.5 mcg/kg every 2 min. Titrate dose to avoid withdrawal, seizures, and severe pain.

Potential Nursing Diagnoses

Acute pain (Indications)
Chronic pain (Indications)
Risk for injury (Side Effects)

Implementation

- ***High Alert:*** Do not confuse Avinza (morphine sulfate) with Invanz (ertapenem) or Evista (raloxifene). Do not confuse MS Contin (morphine sulfate) with Oxycontin (oxycodone). Do not confuse morphine (non-concentrated oral liquid) with morphine (concentrated oral liquid).
- ***High Alert:*** Do not confuse morphine with hydromorphone — errors have resulted in death. Other errors associated with morphine include overdose and infusion pump miscalculations, especially in children. Consider patients' previous analgesic use and current requirements, but clarify doses that greatly exceed normal range. Have second practitioner independently check original order, dose calculations, and infusion pump settings. Use only preservative-free formulations for neonates, and for epidural and intrathecal routes in all patients.
- Explain therapeutic value of medication prior to administration to enhance the analgesic effect.
- Regularly administered doses may be more effective than prn administration. Analgesic is more effective if given before pain becomes severe.
- Coadministration with nonopioid analgesics may have additive analgesic effects and may permit lower doses.
- When transferring from other opioids or other forms of morphine to extended-release tablets, administer a total daily dose of oral morphine equivalent to previous daily dose (see Appendix B) and divided every 8 hr (MS Contin), every 12 hr (Embeda, Kadian, MS Contin), every 24 hr (Kadian or Avinza).
- Morphine should be discontinued gradually to prevent withdrawal symptoms after long-term use.
- **PO:** Doses may be administered with food or milk to minimize GI irritation.
- Administer oral solution with properly calibrated measuring device; may be diluted in a glass of fruit juice just prior to administration to improve taste. Verify correct dose (mg) and correct volume (mL) prior to administration. Use an oral syringe when using 20 mg/mL concentration of oral solution.
- Swallow extended-release tablets whole; do not break, crush, dissolve, or chew (could result in rapid release and absorption of a potentially toxic dose).
- *Embeda, Kadian, and Avinza* capsules may be opened and the pellets sprinkled onto applesauce immediately prior to administration. Patients should rinse mouth and swallow to assure ingestion of entire dose. Pellets should not be chewed, crushed, or dissolved. *Kadian* capsules may also be opened and sprinkled on approximately 10 mL of water and flushed while swirling through a pre-wetted 16 French gastrostomy tube fitted with a funnel at the port end. Additional water should be used to transfer and flush any remaining pellets. *Kadian* should not be administered via a nasogastric tube.
- **Rect:** *MS Contin* and *Oramorph SR* have been administered rectally.
- **IM**, **Subcut:** Use IM route for repeated doses, because morphine is irritating to subcut tissues.

IV Administration

- **IV:** Solution is colorless; do not administer discolored solution.
- **Direct IV:** ***Diluent:*** Dilute with at least 5 mL of sterile water or 0.9% NaCl for injection. ***Concentration:*** 0.5–5 mg/mL. ***Rate: High Alert:*** Administer 2.5–

15 mg over 5 min. Rapid administration may lead to increased respiratory depression, hypotension, and circulatory collapse.

- **Continuous Infusion:** ***Diluent:*** May be added to D5W, D10W, 0.9% NaCl, 0.45% NaCl, Ringer's or LR, dextrose/saline solution, or dextrose/Ringer's or LR. ***Concentration:*** 0.1–1 mg/mL or greater for continuous infusion. ***Rate:*** Administer via infusion pump to control the rate. Dose should be titrated to ensure adequate pain relief without excessive sedation, respiratory depression, or hypotension. May be administered via patient-controlled analgesia (PCA) pump.
- **Y-Site Compatibility:** acetaminophen, aldesleukin, alfentanil, allopurinol, amifostine, amikacin, aminocaproic acid, aminophylline, amiodarone, amsacrine, anikinra, anidulafungin, argatroban, ascorbic acid, atropine, aztreonam, benztropine, bivalirudin, bleomycin, bumetanide, buprenorphine, butorphanol, calcium chloride, calcium gluconate, carboplatin, carmustine, caspofungin, cefazolin, cefotaxime, cefotetan, cefoxitin, ceftaroline, ceftazidime, ceftriaxone, cefuroxime, chloramphenicol, chlorpromazine, cisatracurium, cladribine, clindamycin, cyanocobalamin, cyclophosphamide, cyclosporine, cytarabine, dactinomycin, daptomycin, dexamethasone, dexmedetomidine, dexrazoxane, digoxin, diltiazem, diphenhydramine, dobutamine, docetaxel, dolasetron, dopamine, doripemen, doxorubicin, doxycycline, droperidol, enalaprilat, ephedrine, epinephrine, epirubicin, epoetin alfa, eptifibatide, ertapenem, erythromycin, esmolol, etomidate, etoposide, etoposide phosphate, famotidine, fenoldopam, fentanyl, filgrastim, fluconazole, fludarabine, fluorouracil, foscarnet, gemcitabine, gentamicin, glycopyrrolate, granisetron, heparin, hydrocortisone, hydromorphone, idarubicin, ifosfamide, imipenem/cilastatin, irinotecan, isoproterenol, ketorolac, labetalol, leucovorin calcium, lidocaine, linezolid, lorazepam, magnesium sulfate, mannitol, mechlorethamine, melphalan, meperidine, meropenem, methotrexate, methyldopate, methylprednisolone, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, mitoxantrone, multivitamins, mycophenolate, nafcillin, nalbuphine, naloxone, nicardipine, nitroglycerin, nitroprusside, norepinephrine, octreotide, ondansetron, oxacillin, oxaliplatin, oxytocin, paclitaxel, palonosetron, pamidronate, pancuronium, papaverine, pemetrexed, penicillin G, phenobarbital, phentolamine, phenylephrine, phytonadione, piperacillin/tazobactam, potassium acetate, potassium chloride, procainamide, prochlorperazine, promethazine, propranolol, protamine, pyridoxime, quniupristin/dalfopristin, ranitidine, remifentanil, rituximab, rocuronium, scopolamine, sodium acetate, sodium bicarbonate, streptokinase, succinylcholine, sufentanil, tacrolimus, teniposide, theophylline, thiamine, thiotepa, ticarcillin/clavulanate, tigecycline, tirofiban, tobramycin, tolazoline, vancomycin, vasopressin, vecuronium, verapamil, vinblastine, vincristine, vinorelbine, vitamin B complex with C, voriconazole, warfarin, zidovudine, zoledronic acid.
- **Y-Site Incompatibility:** alemtuzumab, amphotericin B cholesteryl, amphotericin B colloidal, amphotericin B lipid complex, amphotericin B liposome, azathioprine, dantrolene, diazoxide, doxorubicin liposome, folic acid, ganciclovir, indomethacin, micafungin, pentamidine, pentobarbital, phenytoin, sargramostim, trastuzumab.
- **Epidural:** Administer undiluted. If a lidocaine test dose is administered, flush catheter with 0.9% NaCl and wait 15 min before administration of *DepoDur* Do not use an in-line filter. Do not admix or administer other medications in epidural space for 48 hr after administration. Administer within 4 hr after removing from vial. Store in refrigerator; do not freeze.

Patient/Family Teaching

- Instruct patient how and when to ask for pain medication.
- May cause drowsiness or dizziness. Caution patient to call for assistance when ambulating or smoking and to avoid driving or other activities requiring alertness until response to medication is known.
- Advise patient to change positions slowly to minimize orthostatic hypotension.
- Caution patient to avoid concurrent use of alcohol or other CNS depressants with this medication.
- Encourage patients who are immobilized or on prolonged bedrest to turn, cough, and breathe deeply every 2 hr to prevent atelectasis.
- **Home Care Issues:** ***High Alert:*** Explain to patient and family how and when to administer morphine and how to care for infusion equipment properly. ***Pedi:*** Teach parents or caregivers how to accurately measure liquid medication and to use only the measuring device dispensed with the medication.
- Emphasize the importance of aggressive prevention of constipation with the use of morphine.

Evaluation/Desired Outcomes

- Decrease in severity of pain without a significant alteration in level of consciousness or respiratory status.
- Decrease in symptoms of pulmonary edema.

Why was this drug prescribed for your patient?