Morphine

Class: Analgesic, opioid

Indications: Relief of moderate-to-severe acute and chronic pain; relief of pain of myocardial infarction; relief of dyspnea of acute left ventricular failure and pulmonary edema; preanesthetic medication

Infumorph: Used in continuous microinfusion devices for intrathecal or epidural administration in treatment of intractable chronic pain

Extended release products: Moderate-to-severe pain when continuous, around-the-clock opioid analgesia is needed for an extended period of time

Note: Opioid tolerance: Use of morphine sulfate extended release tablets/capsules ≥90 mg, and/or the oral solution 100 mg/5 mL (20 mg/mL) should be reserved for opioid-tolerant patients (ie, already taking at least 60 mg daily of oral morphine equivalent for at least 1 week).

Available dosage form in the hospital: MORPHINE SULPHATE 10 MG, 30MG, 60 MG TAB

MORPHINE SULPHATE 10MG/ML AMP

Trade Names:

Dosage: These are guidelines and do not represent the doses that may be required in all patients. Doses and dosage intervals should be titrated to pain relief/prevention.

Acute pain (moderate-to-severe):

Oral (immediate release formulations): Opioid-naive: Initial: **Note:** Usual dosage range: 10-30 mg every 4 hours as needed. Patients with prior opioid exposure may require higher initial doses.

Solution: 10-20 mg every 4 hours as needed

Tablet: 15-30 mg every 4 hours as needed

I.M., SubQ: **Note:** Repeated SubQ administration causes local tissue irritation, pain, and induration. The use of I.M. injections is no longer recommended especially for repeated administration due to painful administration, variable absorption and lag time to peak effect; other routes are more reliable and less painful (APS, 2008).

Initial: Opioid-naive: 5-10 mg every 4 hours as needed; usual dosage range: 5-15 mg every 4 hours as needed. Patients with prior opioid exposure may require higher initial doses.

I.V.: Initial: Opioid-naive: 2.5-5 mg every 3-4 hours; patients with prior opioid exposure may require higher initial doses. **Note:** Administration of 2-3 mg every 5 minutes until pain relief or if associated sedation, oxygen saturation <95%, or serious adverse event occurs may be appropriate in treating acute moderate-to-severe pain

in settings such as the immediate postoperative period or the emergency department (Aubrun, 2012; Lvovschi, 2008); dose reduction in the immediate postoperative period (postanesthesia care unit) in the elderly is usually not necessary (Aubrun, 2002). A maximum cumulative dose (eg, 10 mg) prompting reevaluation of continued morphine use and/or dose should be included as part of any medication order intended for short-term use (eg, PACU orders). Refer to institution-specific protocols as appropriate.

Acute myocardial infarction, analgesia (unlabeled use): Initial management: 4-8 mg (lower doses in the elderly); subsequently may give 2-8 mg every 5-15 minutes as needed (O'Gara, 2012)

Critically-ill patients, analgesia (unlabeled dose): 2-4 mg every 1-2 hours **or** 4-8 mg every 3-4 hours as needed (Barr, 2013)

I.V., SubQ continuous infusion: 0.8-10 mg/hour; usual range: Up to 80 mg/hour. **Note:** May administer a loading dose (amount administered should depend on severity of pain) prior to initiating the infusion. A continuous (basal) infusion is not recommended in an opioid-naive patient (ISMP, 2009)

Continuous infusion for critically-ill patients: Usual dosage range: 2-30 mg/hour (Barr, 2013)

Patient-controlled analgesia (PCA) (APS, 2008): **Note:** In opioid-naive patients, consider lower end of dosing range:

Usual concentration: 1 mg/mL

Demand dose: Usual: 1 mg; range: 0.5-2.5 mg

Lockout interval: 5-10 minutes

Epidural: Pain management: **Note: Must be preservative-free.** Administer with extreme caution and in reduced dosage to geriatric or debilitated patients. Vigilant monitoring is particularly important in these patients.

Single-dose: **Lumbar region:** Astramorph/PF™, Duramorph: 30-100 mcg/kg (optimal range: 2.5-3.75 mg; may depend upon patient comorbidities; Bujedo, 2012; Sultan, 2011)

Continuous infusion (may be combined with bupivacaine): 0.2-0.4 mg/hour (Bujedo, 2012)

Continuous microinfusion (Infumorph):

Opioid-naive: Initial: 3.5-7.5 mg over 24 hours

Opioid-tolerant: Initial: 4.5-10 mg over 24 hours, titrate to effect; usual maximum is ~30 mg per 24 hours

Intrathecal (I.T.): **Note: Must be preservative-free.** Administer with extreme caution and in reduced dosage to geriatric or debilitated patients. I.T. dose is usually $^{1}/_{10}$ (one-tenth) that of epidural dosage.

Opioid-naive: Single dose: Lumbar region: Astramorph/PF™, Duramorph: 0.1-0.3 mg (may provide adequate relief for up to 24 hours; APS, 2008); repeat doses are **not** recommended. If pain recurs within 24 hours of administration, use of an alternate route of administration is recommended. **Note:** Although product labeling recommends doses up to 1 mg, an analgesic ceiling exists with doses >0.3 mg and the risk of respiratory depression is higher with doses >0.3 mg (Rathmell, 2005).

Continuous microinfusion (Infumorph): Lumbar region: After initial in-hospital evaluation of response to single-dose injections (Astramorph/PF™, Duramorph) the initial dose of Infumorph is 0.2-1 mg over 24 hours

Opioid-tolerant: Continuous microinfusion (Infumorph): Lumbar region: Dosage range: 1-10 mg over 24 hours, titrate to effect; usual maximum is ~20 mg over 24 hours

Rectal: 10-20 mg every 3-4 hours

Chronic pain: Note: Patients taking opioids chronically may become tolerant and require doses higher than the usual dosage range to maintain the desired effect. Tolerance can be managed by appropriate dose titration. There is no optimal or maximal dose for morphine in chronic pain. The appropriate dose is one that relieves pain throughout its dosing interval without causing unmanageable side effects. Consider total daily dose, potency, prior opioid use, degree of opioid experience and tolerance, conversion from previous opioid (including opioid formulation), patient's general condition, concurrent medications, and type and severity of pain during prescribing process.

Oral (extended release formulations): A patient's morphine requirement should be established using immediate release formulations. Conversion to long-acting products may be considered when chronic, continuous treatment is required. Higher dosages should be reserved for use only in opioid-tolerant patients.

Capsules, extended release (Avinza®): Daily dose administered once daily (for best results, administer at same time each day)

Opioid-naive: Initial: 30 mg once daily; adjust in increments ≤30 mg daily every 4 days

Conversion from other oral morphine formulations to Avinza®: Total daily morphine dose given as once daily. The first dose of Avinza® may be taken with the last dose of the immediate release morphine. Maximum: 1600 mg daily due to fumaric acid content.

Capsules, extended release (Kadian®): **Note:** Not intended for use as an initial opioid in the management of pain; use immediate release formulations before initiation. Total daily oral morphine dose may be either administered once daily or in 2 divided doses daily (every 12 hours). The first dose of Kadian® may be taken with the last dose of the immediate release morphine.

Tablets, extended release (MS Contin®): Daily dose divided and administered every 8 or every 12 hours

Conversion from parenteral morphine or other opioids to extended release formulations: Substantial interpatient variability exists in relative potency. Therefore, it is safer to underestimate a patient's daily oral morphine requirement and provide breakthrough pain relief with immediate release morphine than to overestimate requirements. Consider the parenteral to oral morphine ratio or other oral or parenteral opioids to oral morphine conversions.

Renal impairment:
Cl_{cr} 10-50 mL/minute: Children and Adults: Administer at 75% of normal dose.

Cl_{cr} <10 mL/minute: Children and Adults: Administer at 50% of normal dose.

Intermittent HD:

Children: Administer 50% of normal dose.

Adults: No dosage adjustment necessary.

Peritoneal dialysis: Children: Administer 50% of normal dose.

CRRT: Children and Adults: Administer 75% of normal dose, titrate.

Hepatic impairment: No dosage adjustment provided in manufacturer's labeling. Pharmacokinetics unchanged in mild liver disease; substantial extrahepatic metabolism may occur. In cirrhosis, increases in half-life and AUC suggest dosage adjustment required.

Common side effects: **Note:** Individual patient differences are unpredictable, and percentage may differ in acute pain (surgical) treatment. Reactions may be dose, formulation, and/or route dependent.

Frequency not defined:

Cardiovascular: Circulatory depression, flushing, shock

Central nervous system: Dysphonia, physical and psychological dependence, sedation

Endocrine & metabolic: Antidiuretic hormone release, hypogonadism

Neuromuscular & skeletal: Bone mineral density decreased

>10%:

Cardiovascular: Bradycardia, hypotension

Central nervous system: Drowsiness (9% to 48%; tolerance usually develops to drowsiness with regular dosing for 1-2 weeks), dizziness (6% to 20%), fever (<3% to >10%), confusion, headache (following epidural or intrathecal use)

Dermatologic: Pruritus (may be dose related)

Gastrointestinal: Xerostomia (78%), constipation (9% to 40%; tolerance develops very slowly if at all), nausea (7% to 28%; tolerance usually develops to nausea and vomiting with chronic use), vomiting

Genitourinary: Urinary retention (16%; may be prolonged, up to 20 hours, following epidural or intrathecal use)

Hematologic: Anemia (following intrathecal use)

Local: Pain at injection site

Neuromuscular & skeletal: Weakness

Respiratory: Oxygen saturation decreased

Miscellaneous: Histamine release

Pregnancy Risk Factor: C