### Alert
High risk medication - may cause significant patient harm when used in error.

### Indication
**Analgesia/sedation:**
1. During assisted ventilation
2. Post-surgery
3. Pre-medication prior to intubation or other procedure

### Action
Narcotic analgesic – stimulates brain opioid receptors.

### Drug Type
Narcotic analgesic.

### Trade Name
DBL Morphine Sulfate

### Presentation
Morphine 10 mg/mL (10,000 microgram/mL) vial

### Dosage/Interval

<table>
<thead>
<tr>
<th>Infusion Type</th>
<th>Infusion Rate</th>
<th>Prescribed Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONTINUOUS IV INFUSION</td>
<td>5–40 microgram/kg/hour</td>
<td>1 mg/kg morphine and make up to 50 mL</td>
</tr>
<tr>
<td>IV BOLUS</td>
<td>50 microgram/kg every 4 hours</td>
<td></td>
</tr>
<tr>
<td>PRE-MEDICATION FOR INTUBATION</td>
<td>100 microgram/kg as a single dose</td>
<td></td>
</tr>
</tbody>
</table>

### Maximum Daily Dose
No extra benefit noted using doses higher than 20 microgram/kg/hour. Doses up to 100 microgram/kg/hour have been used in newborns; however this was associated with an increase in the duration of mechanical ventilation.

### Route
IV

### Preparation/Dilution

<p>| SINGLE STRENGTH continuous IV infusion |</p>
<table>
<thead>
<tr>
<th>Infusion rate</th>
<th>Prescribed amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mL/hour = 20 microgram/kg/hour</td>
<td>1 mg/kg morphine and make up to 50 mL</td>
</tr>
</tbody>
</table>

Draw up 1 mL (10 mg morphine sulfate) and add 9 mL sodium chloride 0.9% to make a volume of 10 mL with a concentration of 1 mg/mL.

**FURTHER DILUTE** 1 mg/kg (1 mL/kg) of the above solution with glucose 5% or glucose 10% to make a final volume of 50 mL with a concentration of 1 mL/hour = 20 microgram/kg/hour.

<p>| DOUBLE STRENGTH continuous IV infusion |</p>
<table>
<thead>
<tr>
<th>Infusion rate</th>
<th>Prescribed amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mL/hour = 40 microgram/kg/hour</td>
<td>2 mg/kg morphine and make up to 50 mL</td>
</tr>
</tbody>
</table>

Draw up 1 mL (10 mg morphine sulfate) and add 9 mL sodium chloride 0.9% to make a volume of 10 mL with a concentration of 1 mg/mL.

**FURTHER DILUTE** 2 mg/kg (2 mL/kg) of the above solution with glucose 5% or glucose 10% to make a final volume of 50 mL with a concentration of 1 mL/hour = 40 microgram/kg/hour.

<table>
<thead>
<tr>
<th>IV BOLUS</th>
<th></th>
</tr>
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<tr>
<td>Draw up 1 mL (10 mg morphine sulfate) and add 9 mL sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 1 mg/mL.</td>
<td></td>
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</tbody>
</table>

**PRE-MEDICATION FOR INTUBATION**
As above for IV bolus.

### Administration
**CONTINUOUS IV INFUSION:** Via syringe driver.

**IV BOLUS:** Administer over 5 minutes. Flush with 1 mL sodium chloride 0.9% before and after injection. Rapid IV administration may increase adverse effects.

**PRE-MEDICATION FOR INTUBATION:** As above for IV bolus. Wait a minimum of 5 minutes for onset of action; however for maximum effect wait 15 minutes after giving the dose.

### Monitoring
Observe for signs of respiratory and cardiac depression – continuous cardiorespiratory monitoring.
**Morphine (Parenteral)**

**Newborn Use Only**

<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Hypersensitivity to morphine sulfate or any component.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Interactions</td>
<td>Concomitant use with other CNS depressants potentiates effects of opioids, increasing risk of respiratory depression, profound sedation or coma.</td>
</tr>
<tr>
<td>Adverse Reactions</td>
<td>See Precautions.</td>
</tr>
<tr>
<td>Compatibility</td>
<td>Fluids: Glucose 5%, glucose 10%, Hartmann’s, sodium chloride 0.45% and sodium chloride 0.9%</td>
</tr>
</tbody>
</table>

Y site: Amino acid solutions, adrenaline hydrochloride, amifostine, amikacin, amiodarone, ampicillin, anidulafungin, atracurium, atropine, aztreonam, bivalirudin, caspofungin, cefotaxime, cefoxitin, ceftriaxone, ceftriaxone, cephalosporin, chloramphenicol, cisatracurium, clindamycin, dexmethasone, digoxin, dopamine, etoposide, erythromycin, esmolol, filgrastim, fluconazole, fosfamet, gentamicin, granisetron, haloperidol lactate, hycosine hydrobromide, insulin (short-acting), ketorolac, labetalol, levomepromazine, lignocaine, linezolid, magnesium sulfate, methylprednisolone sodium succinate, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, noradrenaline, palonosetron, pancuronium, piperacillin-tazobactam (EDTA-free), potassium chloride, remifentanil, sodium nitroprusside, tacrolimus, tigecycline, tirofiban, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, vencuronium, zidovudine. |

**Incompatibility**

Fluids: Morphine may precipitate out of solution when the final pH is greater than 6.4. |

Y-site: Aminophylline, azathioprine, azithromycin, flucloxacillin, folic acid, ganciclovir, indomethacin, pentamidine, pethidine, promethazine, sodium nitrite, thiopentone. |

**Stability**

Diluted solution for continuous IV infusion is stable for 48 hours. |

**Storage**


**Special Comments**

Prolonged use (>5–7 days) may be associated with dependence.
### Evidence summary

**Dosing:**
A dose of 10 microgram/kg/hour is recommended by a systematic review and meta-analysis of 13 studies of ventilated neonates, a retrospective review examining age and infusion rates and a 5 year outcome of a large RCT using low dose morphine. In addition, hypotension is not a side effect of morphine when low doses are used.

A prospective study of 68 neonates who underwent non-cardiac surgery measured morphine plasma concentrations and comfort scores during postoperative management. Doses of 5–7 micrograms/kg/hour for neonates 7 days or less and 10 micrograms/kg/hour for neonates over 7 days were recommended.

Although the pharmacokinetics of morphine differ in premature infants in regards to the ratio of morphine-3-glucuronide to morphine-6-glucuronide metabolite formation, there appears to be no clinical advantage in using higher dose regimen.

**Effectiveness:**
As there is no strong evidence for using morphine in ventilated neonates but it is recognised that ventilation is a painful procedure. It has been recommended that opioids should be used selectively with ventilated neonates based on clinical judgements and evaluation of pain indices (PIPP-R, PAT).

Several studies identified morphine was safer than midazolam for sedating ventilated neonates. In post-operative management, morphine is safer than either fentanyl or midazolam. When used with IV paracetamol the morphine clearance was higher over 48 hours.

Several studies indicated that continuous infusion of morphine does not alleviate procedural pain and they recommend an alternative such as sucrose be used for these procedures. In addition, morphine should be used with caution in non-intubated neonates.

The use of morphine for tracheal intubation is unclear. In a published review of 14 surveys of practice there were multiple groups of medications used for premedication for elective intubation. However, the author indicated that there was sufficient evidence for stress and pain to support some use of premedication.

### Level of evidence

Morphine should be used selectively based on clinical judgement and the use of a validated pain score (Level A, Grade A).
A dose of morphine 10 microgram/kg/hour is recommended for ventilated neonates (Level A, Grade A).
For postoperative management the recommended doses are 5–7 microgram/kg/hour for neonates 7 days or less and 10 microgram/kg/hour for neonates over 7 days (Level B, Grade B).
A premedication regimen can be used for all elective intubation (Level C, Grade C).

### References

7. Bellu, R., K. de Waal, and R. Zanini, Opioids for neonates receiving mechanical ventilation: a
17. Lexi-comp paediatric and neonatal dosage handbook, Version: 2.6.0, Hudson, OH, USA.