Morphine

10 mg/mL injection
1 mg/mL oral solution

Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

This is a High Risk Medication ⚠
An overdose can be rapidly fatal.

Dose and Indications

1 mg = 1000 microgram

Use the same dose for sulfate and hydrochloride trihydrate salts of morphine.

Analgesia and Sedation

Consider the risk of respiratory depression and hypotension with use of morphine. Use only where there are facilities for respiratory support and cardiorespiratory monitoring.

Intravenous, Intramuscular & Subcutaneous Bolus

50 microgram to 100 microgram/kg/dose (0.05 mg to 0.1 mg/kg/dose)

Repeat doses as necessary.

Intravenous Infusion

10 to 20 microgram/kg/hour

Commence at the lowest infusion rate and titrate to effect; higher doses may be required.

A loading dose of 100 microgram/kg (0.1 mg/kg) may be given prior to commencement of infusion.

After prolonged use, titrate dose to discontinue.

Oral

0.1 mg to 0.2 mg/kg/dose. Repeat every four hours if necessary.

Morphine

10 mg/mL injection, 1 mg/mL oral solution

Neonatal Abstinence Syndrome

Oral

This guideline MUST be used in conjunction with the South Australian Perinatal Practice Guidelines – Neonatal Abstinence Syndrome (NAS)

Morphine treatment usually commenced if the Finnegan score is ≥ 8 for three assessments or ≥ 12 for one assessment.

Please note that all doses for the entire period of withdrawal management are calculated on the basis of birth weight and not current weight.

Modified Finnegan Neonatal Abstinence Severity (MFNASS) scoring	**Dosage and frequency (Oral)** **Calculate to the closest 0.05 mg/dose**
≥ 8	Non-pharmacological treatment and medical review
≥ 8 for three consecutive scores OR ≥ 12 for one score	Prescribe stat doses of morphine 0.1 mg/kg/dose as needed (minimum interval of 4 hourly, up to 3 doses in 24 hours). Continue non-pharmacological intervention (observe in the nursey for 24 hours)
Score ≥ 8 despite three stat doses in 24 hours	Commence morphine 0.1 mg/kg/dose, 6 hourly
Score ≥ 8 despite 0.1 mg/kg/dose, 6 hourly	Commence morphine 0.125 mg/kg/dose, 6 hourly
Score ≥ 8 despite 0.125 mg/kg/dose, 6 hourly	Commence morphine 0.175 mg/kg/dose, 6 hourly
Score ≥ 8 despite 0.175 mg/kg/dose, 6 hourly	Commence morphine 0.225 mg/kg/dose, 6 hourly

Where control is difficult, give the total daily dose in 6 divided doses (every 4 hours).

Inpatient morphine treatment for greater than 14 days requires government approval. Consult pharmacist or download form from DASSA.

Conversion of Intravenous to Oral Morphine, and Intravenous fentanyl to Intravenous or Oral morphine

The below conversions between opiates and formulations should only serve as a general guide. Multiple factors like inter- and intra-individual difference in opioid pharmacology may influence the accuracy of dose calculations. Clinical judgement should be used and individual patient characteristics considered when applying these calculations.

Conversion: Continuous IV Morphine infusion to Oral Morphine

1. Calculate the total dose of IV morphine received over the previous 24 hours
2. Convert to oral morphine by multiplying total dose by 2 (morphine IV:morphine oral, 1:2)
3. Administer oral total daily dose as 4 divided doses (i.e. every 6 hourly)

Example: *IV morphine continuous infusion at 10 microgram/kg/hour in a 1.5 kg patient*

- *Total dose of IV morphine received over the previous 24 hours = 360 microgram IV*
- *Convert to oral morphine: 360 microgram IV **x 2** = 720 microgram PO*
- *Total oral daily dose = 720 microgram PO*
- *Administer in 4 divided doses = approx. 180 microgram (0.18 mg) PO every 6 hours*

Conversion: Continuous IV Fentanyl infusion to Continuous IV Morphine infusion

The 1:10 conversion used below is a conservative estimate. Higher conversions of 1:13 to 1:20 have been mentioned in neonatal literature.

1. Convert IV fentanyl to IV morphine by multiplying rate of IV fentanyl (microgram/kg/hour) by 10 (fentanyl IV:morphine IV, 1:10). This provides the approximate equivalent rate of IV morphine (microgram/kg/hour)

Example: *IV fentanyl continuous infusion at 2 microgram/kg/hour*

*Convert to IV morphine: 2 microgram/kg/hour IV fentanyl **x 10***

= approx. 20 microgram/kg/hour IV morphine

Conversion: Continuous IV Fentanyl infusion to Oral Morphine

Step **ONE** Convert IV fentanyl to IV morphine

1. Calculate the total dose of IV fentanyl received over the previous 24 hours
2. Convert to IV morphine by multiplying total dose of IV fentanyl by 10 (fentanyl IV:morphine IV, 1:10). This provides the approximate equivalent dose of IV morphine over 24 hours

Step **TWO** Convert IV morphine to Oral morphine

1. Convert IV morphine to oral morphine by multiplying total dose by 2 (morphine IV:morphine oral, 1:2)
2. Administer oral total daily dose as 4 divided doses (i.e. every 6 hourly)

Example: *IV fentanyl continuous infusion at 2 microgram/kg/hour in a 1kg patient*

- *Total dose of intravenous fentanyl received over the previous 24 hours = 48 microgram IV fentanyl*
- *Convert to IV morphine: 48 microgram IV fentanyl **x 10** = 480 microgram IV morphine*
- *Convert to oral morphine: 480 microgram IV morphine **x 2** = 960 microgram PO morphine*
- *Total oral daily dose = 960 microgram PO morphine*
- *Administer in 4 divided doses = 240 microgram (0.24 mg) PO every 6 hours*

Preparation and Administration

Oral:

For the oral solution containing 1 mg/mL morphine:

Dose	0.1 mg	0.2 mg	0.2 mg	0.3 mg	0.4 mg	0.5 mg
Volume	0.1 mL	0.2 mL	0.2 mL	0.3 mL	0.4 mL	0.5 mL

Intravenous Bolus

Dilute 1 mL of the 10 mg/mL morphine injection with 9 mL of compatible fluid (to a total volume of 10 mL). The resulting solution contains 1 mg/mL morphine.

Dose	50 microgram (0.05 mg)	100 microgram (0.1 mg)	200 microgram (0.2 mg)	300 microgram (0.3 mg)	400 microgram (0.4 mg)
Volume	0.05 mL	0.1 mL	0.2 mL	0.3 mL	0.4 mL

Shake well to ensure thorough mixing.

It may be administered undiluted or diluted to a suitable volume with compatible fluid for ease of administration.

Administered as a push over at least 5 minutes. Discard remaining solution in compliance with local policy requirements for destruction of controlled medications.

Intravenous Infusion

Select the strength required based on the weight of the infant in the context of any fluid restrictions. Morphine Concentration Selection Tables can be found on the following pages of this guideline to assist prescribers to gauge which strength is best for the patient.

Preparation requires a **TWO STEP** dilution process (see preparation steps below). Diluted preparations below are stable for 24 hours at room temperature. Discard remaining solution.

The three standard concentrations to select from are:

- Morphine 40 microgram/mL
- Morphine 80 microgram/mL
- Morphine 160 microgram/mL

Formulae

To calculate infusion rate (mL/hr):

$$\text{Rate (mL/hr)} = \frac{\text{dose (microgram/kg/hour) x weight (kg)}}{\text{Strength (microgram/mL)}}$$

To calculate the dose (microgram/kg/hour):

$$\text{Dose (microgram/kg/hour)} = \frac{\text{Rate (mL/hr) x Strength (microgram/mL)}}{\text{Weight (kg)}}$$

Morphine Concentration Selection Tables

Morphine 40 microgram/mL

Double dilution to make 25 mL syringe:

STEP ONE: Dilute 1 mL (10 mg/mL) of morphine injection with 9 mL of 0.9% sodium chloride (to a total of 10 mL). This makes a 1 mg/mL solution.

STEP TWO: Add 1 mL morphine (1 mg/mL) to 24 mL of compatible fluid (to a total of 25 mL). This makes a 40 microgram/mL (0.04 mg/mL) solution.

Double dilution to make 50 mL syringe:

STEP ONE: Dilute 1 mL (10 mg/mL) of morphine injection with 9 mL of 0.9% sodium chloride (to a total of 10 mL). This makes a 1 mg/mL solution.

STEP TWO: Add 2 mL morphine (1 mg/mL) to 48 mL of compatible fluid (to a total of 50 mL). This makes a 40 microgram/mL (0.04 mg/mL) solution.

Table 1: Concentration selection table for morphine 40 microgram/mL

Recommended for neonates weighing less than 1 kg

Rate (mL/hr)	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1	Rate (mL/hr)
Weight (kg)	Approximate microgram/kg/hour									Weight (kg)
0.5	16	24	32	40						0.5
1	8	12	16	20	24	28	32	36	40	1
1.5	5	8	11	13	16	19	21	24	27	1.5
2	4	6	8	10	12	14	16	18	20	2

Morphine 80 microgram/mL

Double dilution to make 25 mL syringe:

STEP ONE: Dilute 1 mL (10 mg/mL) of morphine injection with 9 mL of 0.9% sodium chloride (to a total of 10 mL). This makes a 1 mg/mL solution.

STEP TWO: Add 2 mL morphine (1 mg/mL) to 23 mL of compatible fluid (total of 25 mL). This makes an 80 microgram/mL (0.08 mg/mL) solution.

Double dilution to make 50 mL syringe:

STEP ONE: Dilute 1 mL (10 mg/mL) of morphine injection with 9 mL of 0.9% sodium chloride (to a total of 10 mL). This makes a 1 mg/mL solution.

STEP TWO: Add 4 mL morphine (1 mg/mL) to 46 mL of compatible fluid (total of 50 mL). This makes an 80 microgram/mL (0.08 mg/mL) solution.

Table 2: Concentration selection table for morphine 80 microgram/mL

Recommended for neonates weighing 1 to 3 kg

Rate (mL/hr)	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1	Rate (mL/hr)
Weight (kg)	Approximate microgram/kg/hour									Weight (kg)
1	16	24	32	40						1
1.5	11	16	21	27	32	37				1.5
2	8	12	16	20	24	28	32	36	40	2
2.5	6	10	13	16	19	22	26	29	32	2.5
3	5	8	11	13	16	19	21	24	27	3

Morphine 160 microgram/mL

Double dilution to make 25 mL syringe:

STEP ONE: Dilute 1 mL (10 mg/mL) of morphine injection with 9 mL of 0.9% sodium chloride (to a total of 10 mL). This makes a 1 mg/mL solution.

STEP TWO: Add 4 mL morphine (1 mg/mL) to 21 mL of compatible fluid (total of 25 mL). This makes a 160 microgram/mL (0.16 mg/mL) solution.

Double dilution to make 50 mL syringe:

STEP ONE: Dilute 1 mL (10 mg/mL) of morphine injection with 9 mL of 0.9% sodium chloride (to a total of 10 mL). This makes a 1 mg/mL solution.

STEP TWO: Add 8 mL morphine (1 mg/mL) to 42 mL of compatible fluid (total of 50 mL). This makes a 160 microgram/mL (0.16 mg/mL) solution.

Table 2: Concentration selection table for morphine 160 microgram/mL

Recommended for neonates weighing greater than 3 kg

Rate (mL/hr)	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1	Rate (mL/hr)
Weight (kg)	Approximate microgram/kg/hour									Weight (kg)
3	11	16	21	27	32	37				3
3.5	9	14	18	23	27	32	37			3.5
4	8	12	16	20	24	28	32	36	40	4
4.5	7	11	14	18	21	25	28	32	36	4.5
5	6	10	13	16	19	22	26	29	32	5

Compatible Fluids

Glucose 5%, glucose 10%, sodium chloride 0.9%

Adverse Effects

Common

Vomiting (initial dose/s), drowsiness, miosis, constipation, urinary retention, hypotension, apnoea, respiratory depression (dose related)

Infrequent

Urticaria, hypothermia, bradycardia or tachycardia, increased intracranial pressure, ureteric or biliary spasm, rigidity, flushing,

Rare

Syndrome of inappropriate anti-diuretic hormone secretion (SIADH), tremor, muscle twitching and seizures

Monitoring

- If on morphine infusion, cardio-respiratory and blood pressure monitoring is mandatory
- Close observation for at least 30 minutes is required to assess for respiratory depression
- Observe for abdominal distention and loss of bowel sounds
- Sedation
- Urinary retention

Practice Points

- Naloxone should be available where morphine is administered
- Consider the place of paracetamol as an adjunct when using morphine as an analgesic
- Continuous morphine infusions should only be administered in a clinical environment where respiratory support is available
- Therapeutic doses can cause respiratory depression, bradycardia, hypotension and urinary retention. Respiratory Depression is a severe adverse effect of morphine and is best judged by degree of sedation, as respiratory rate is a late and unreliable indicator. When occurring as an acute overdose use naloxone as the antidote
- Chronic dependent use and Neonatal Narcotic Abstinence Syndrome should not be treated with naloxone due to potential for withdrawal
- Contraindicated in patients with a hypersensitivity to opiates
- Use cautiously in patients with shock, hypotension, increased intracranial pressure, convulsions, irregular breathing patterns, in patients with cardiac arrhythmias, in patients with hepatic or renal impairment and in patients with urinary retention.
- Use cautiously in HIE patients undergoing therapeutic hypothermia as clearance of morphine may be reduced, increasing risk of accumulation. Monitor renal function and patient for sedation
- Extended treatment with opioids, particularly continuous infusions, may induce drug tolerance and physiological dependence. Abrupt discontinuation or rapid weaning may result in symptoms of neonatal withdrawal syndrome

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04/07/2024	V4.4	Domain Custodian, Clinical Governance, Safety and Quality	Change in oral product to 1 mg/mL oral solution due to return in product availability
21/3/2024	V4.3	Domain Custodian, Clinical Governance, Safety and Quality	Change in oral product to 2 mg/mL oral solution due to product discontinuation
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3/6/2021	V4.1	Chair, SA Maternal, Neonatal & Gynaecology Community of Practice	Updated link to NAS Authority Application Form
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31/10/2018	V3.2	Chair Neonatal Medication Guidelines Work Group	Amendment to Administration Formulae
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