Midazolam

5mg/5mL injection, 5mg/1mL injection, 1mg/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

Short Term Sedation

Oral

250 microgram/kg as a single dose

Conscious Sedation in Ventilated Neonates

Intravenous

50 to 150 microgram/kg. Repeat as required, usually every 2 to 4 hourly

Intravenous Infusion

10 to 60 microgram/kg/hour

Use with extreme caution in preterm neonates given risk of adverse neurological effects

Seizure Control

Intranasal

200 to 300 microgram/kg

Intravenous Bolus

200 microgram/kg as a loading dose followed by a continuous intravenous infusion

Intravenous Infusion

60 microgram/kg/hour increasing dose every 15 minutes as required, up to a maximum rate of 420 microgram/kg/hour.

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End of life symptomatic management (e.g., agitation, dyspnoea, seizures)

Consider seeking specialist advice from Palliative Care Service

Intranasal/buccal

300 microgram/kg

Intravenous/subcutaneous

50-200 microgram/kg/dose. Repeat as required every 2 to 4 hourly

Continuous subcutaneous infusion

10 to 60 microgram/kg/hour, adjusted according to clinical need

Preparation and Administration

Oral

- 1 mg/mL (1000 microgram/mL) oral solution: not commercially available however is manufactured by Women's and Children's Hospital and available at most public hospitals

  OR
- 5 mg in 1 mL (5000 microgram/mL) ampoule: injection solution may be used for oral administration

Oral absorption is rapid, although erratic. Maximum effect within 30 to 60 minutes and duration up to 2 hours.

Intranasal/buccal

- 5 mg in 1 mL (5000 microgram/mL) ampoule: injection solution may be used for intranasal/buccal administration. Concentrated strength reduces the volume to administer

Use undiluted. This contains 5 mg/mL **(5000 microgram/mL)**:

Dose	250microgram	500microgram	750microgram	1000microgram	1250microgram
Volume	0.05 mL	0.1 mL	0.15 mL	0.2 mL	0.25 mL

Administration technique for intranasal administration is important. Drop dose into alternating nostrils over 15 seconds. Absorption is rapid; maximum effect in 10 minutes and duration up to 2 hours. May be irritating and should only be used if a rapid effect is required.

Subcutaneous

- 5 mg in 5 mL (1000 microgram/mL) ampoule

Can be used undiluted (1000 microgram/mL) and is suitable for intermittent and continuous subcutaneous infusion.

Intravenous Bolus

- 5 mg in 5 mL (1000 microgram/mL) ampoule

Use undiluted. This contains 1 mg/mL **(1000 microgram/mL)**:

Dose	100microgram	200microgram	300microgram	400microgram	500microgram
Volume	0.1 mL	0.2 mL	0.3 mL	0.4 mL	0.5 mL

Administer as a push over at least 2 minutes

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Intravenous Infusion

Select the strength required based on the weight of the infant in the context of any fluid restrictions. Midazolam 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.

Dilute the appropriate volume of the 5 mg/5mL (1 mg/mL) midazolam injection using compatible fluid and administer by continuous infusion. Diluted preparation is stable for 24 hours at room temperature.

The three standard concentrations to select from are:

- Midazolam 50 microgram/mL (0.05 mg/mL)
- Midazolam 100 microgram/mL (0.1 mg/mL)
- Midazolam 200 microgram/mL (0.2 mg/mL)
- Midazolam 400 microgram/mL (0.4 mg/mL)

Formulae

To calculate infusion rate (mL/hr):

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

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

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

Midazolam Concentration Selection Table

Midazolam 50 microgram/mL

To make 25 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule, dilute 1.25 mL (1.25 mg) midazolam with 23.75 mL of compatible fluid (total of 25 mL).

To make 50 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule dilute 2.5 mL (2.5 mg) midazolam with 47.5 mL of compatible fluid (total of 50 mL).

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	20	30	40	50	60	70	80	90	100	0.5
1	10	15	20	25	30	35	40	45	50	1
1.5	7	10	13	17	20	23	27	30	33	1.5
2	5	8	10	13	15	18	20	23	25	2
2.5	4	6	8	10	12	14	16	18	20	2.5
3	3	5	7	8	10	12	13	15	17	3
3.5	3	4	6	7	9	10	11	13	14	3.5
4	3	4	5	6	8	9	10	11	13	4

Discard remaining solution

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Midazolam 100 microgram/mL

To make 25 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule, dilute 2.5 mL (2.5 mg) midazolam with 22.5 mL of compatible fluid (total of 25 mL).

To make 50 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule, dilute 5 mL (5 mg) midazolam with 45 mL of compatible fluid (total of 50 mL).

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 micrograms/kg/hour									Weight (kg)
0.5	40	60	80	100	120	140	160	180	200	0.5
1	20	30	40	50	60	70	80	90	100	1
1.5	13	20	27	33	40	47	53	60	67	1.5
2	10	15	20	25	30	35	40	45	50	2
2.5	8	12	16	20	24	28	32	36	40	2.5
3	7	10	13	17	20	23	27	30	33	3
3.5	6	9	11	14	17	20	23	26	29	3.5
4	5	8	10	13	15	18	20	23	25	4

Discard remaining solution

Midazolam 200 microgram/mL

To make 25 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule, dilute 5 mL (5 mg) midazolam with 20 mL of compatible fluid (total of 25 mL).

To make 50 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule, dilute 10 mL (10 mg) midazolam with 40 mL of compatible fluid (total of 50 mL).

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)
1.5	27	40	53	67	80	93	107	120	133	1.5
2	20	30	40	50	60	70	80	90	100	2
2.5	16	24	32	40	48	56	64	72	80	2.5
3	13	20	27	33	40	47	53	60	67	3
3.5	11	17	23	29	34	40	46	51	57	3.5
4	10	15	20	25	30	35	40	45	50	4
4.5	9	13	18	22	27	31	36	40	44	4.5
5	8	12	16	20	24	28	32	36	40	5

Discard remaining solution

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Midazolam 400 microgram/mL

To make 25 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule, dilute 10 mL (10 mg) midazolam with 15 mL of compatible fluid (total of 25 mL).

To make 50 mL syringe:

Using the 5 mg in 5 mL (1 mg/mL) ampoule, dilute 20 mL (20 mg) midazolam with 30 mL of compatible fluid (total of 50 mL).

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	27	40	53	67	80	93	107	120	133	3
3.5	23	34	46	57	69	80	91	103	114	3.5
4	20	30	40	50	60	70	80	90	100	4
4.5	18	27	36	44	53	62	71	80	89	4.5
5	16	24	32	40	48	56	64	72	80	5

Discard remaining solution

Compatible Fluids

Glucose 5%, glucose 10%, glucose and sodium chloride containing solutions, sodium chloride 0.9%

Adverse Effects

Common

Drowsiness, over sedation, hypersalivation, nasal discomfort (with intranasal use), seizure-like myoclonus (premature neonates receiving via intravenous route with fast administration), hypotension

Infrequent

Paradoxical excitation, respiratory depression

Intravenous route: thrombophlebitis, severe hypotension, arrhythmias, respiratory arrest

Rare

Blood disorders (including leucopenia and leucocytosis), jaundice, transient elevated liver function tests, allergic reactions (including rash and anaphylaxis)

Monitoring

- Oximetry
- Cardiac Monitoring
- Sedation

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Practice Points

- Withdraw use slowly after chronic administration. Seizures may occur following abrupt discontinuation of chronic treatment.
- Midazolam interacts with other central nervous system depressants e.g., opioids and may increase the risk of drowsiness, respiratory depression, and hypotension
- Midazolam has been associated with respiratory depression and arrest when used for conscious sedation. Only use in non-critical care settings if respiratory and cardiac function can be monitored, and resuscitation equipment is available.
- Increased sensitivity to central nervous system (CNS) effects in renal and hepatic impairment; use doses at lower end of range.

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