Midazolam

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

1 mg = 1000 microgram

Dose and Indications

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.

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 to 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	250 microgram	500 microgram	750 microgram	1000 microgram	1250 microgram
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 mins and duration up to 2 hrs. May be irritating and should only be used if a rapid effect is required.

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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

Use extreme caution when preparing IV bolus doses for extremely low birth weight infants (less than 1000 g):

> **Volumes administered in low-birth-weight infants may be less than 0.1 mL**
> **Check carefully to avoid a ten-fold dosing error**

> 5 mg in 5 mL (1000 microgram/mL) ampoule:

Dose	50 microg	100 microg	200 microg	300 microg	400 microg	500 microg
Volume	0.05 mL	0.1 mL	0.2 mL	0.3 mL	0.4 mL	0.5 mL

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

Administer as a push over at least 2 minutes.

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

The four 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):

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

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Midazolam Concentration Selection Tables

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

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 25mL).

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 microgram/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

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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

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

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.
- Flumazenil is a specific benzodiazepine antagonist. Flumazenil administration is not generally recommended due to potential for severe adverse effects. Standard treatment for overdose/unwanted effects associated with midazolam is supportive care. There is very little evidence for use of this drug in neonates. Should it be required to be administered after careful consideration of side effects.

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Document Ownership & History

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Approval Date	Version	Who approved New/Revised Version	Reason for Change
12/12/2024	V3.1	Clinical Guideline Domain Custodian	Addition of warning for IV doses given in extremely low birth weight infants. Addition of flumazenil for reversal.
12/12/2022	V3.0	Domain Custodian, Clinical Governance, Safety and Quality	Formal review in line with 5 year scheduled timeline review
28/04/2012	V2.0	SA Health Safety and Quality Strategic Governance Committee	Full review
11/2012	V1.0	SA Maternal & Neonatal Clinical Network	Original SA Maternal & Neonatal Clinical Network approved version.