South Australian Neonatal Medication Guidelines

midazolam

1mg/mL & 5mg/mL injection, 1mg/mL oral mixture*

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

1mg = 1000micrograms

Short Term Sedation

Oral

0.25mg/kg as a single dose

Conscious Sedation in Ventilated Neonates

Intravenous Infusion

10 to 60 micrograms/kg/hour

A loading dose of 100micrograms/kg (0.1mg/kg) may be used prior to the infusion commencing

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Seizure Control

Intranasal

0.2 to 0.4 mg/kg using the 5mg/mL (plastic) ampoule

Intravenous Bolus

200micrograms/kg (0.2mg/kg) as a loading dose followed by a continuous intravenous infusion

Intravenous infusion

60microgram/kg/hour increasing dose every 15 minutes up to a maximum rate of 300microgram/kg/hour

Preparation and Administration

Oral

The 1mg/mL solution contains:

Dose	0.5mg	1mg	1.5mg	2mg	2.5mg	3mg
Volume	0.5mL	1mL	1.5mL	2mL	2.5mL	3mL

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

* 1mg/mL solution is not commercially available however is manufactured by WCH

Intranasal

Always use the 5mg/mL PLASTIC ampoule for this indication to reduce the volume to administer. The 5mg/mL (plastic) ampoule contains:

Dose	0.25mg	0.5mg	0.75mg	1mg	1.25mg
Volume	0.05mL	0.1mL	0.15mL	0.2mL	0.25mL

Administration technique 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.

Intravenous Bolus

The 1mg/mL midazolam injection contains:

Dose	100micrograms (0.1mg)	200micrograms (0.2mg)	300micrograms (0.3mg)	400micrograms (0.4mg)	500micrograms (0.5mg)
Volume	0.1mL	0.2mL	0.3mL	0.4mL	0.5mL

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 the following pages of this guideline to assist prescribers to gauge which strength is best for the patient.

Dilute the appropriate volume of the 1mg/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 50micrograms/mL (0.05mg/mL)
- Midazolam 100micrograms/mL (0.1mg/mL)
- Midazolam 200micrograms/mL (0.2mg/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):

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

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Midazolam Concentration Selection Table for 25mL syringes

Dilution for Midazolam 50microgram/mL

Dilute 1.25mL midazolam (1mg/mL) with 23.75mL of compatible fluid (total of 25mL). This makes a 50microgram/mL midazolam solution.

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	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

Dilution for Midazolam 100microgram/mL

Dilute 2.5mL midazolam (1mg/mL) with 22.5mL of compatible fluid (total of 25mL). This makes a 100microgram/mL midazolam solution.

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								0.5
1	20	30	40	50	60	70				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		10	13	17	20	23	27	30	33	3
3.5		9	11	14	17	20	23	26	29	3.5
4			10	13	15	18	20	23	25	4

Discard remaining solution

Dilution for Midazolam 200microgram/mL

Dilute 5mL midazolam (1mg/mL) with 20mL of compatible fluid (total of 25mL). This makes a 200microgram/mL midazolam solution.

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)
1.5	27	40	53							1.5
2	20	30	40	50	60					2
2.5	16	24	32	40	48	56	64			2.5
3	13	20	27	33	40	47	53	60		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		13	18	22	27	31	36	40	44	4.5
5		12	16	20	24	28	32	36	40	5

Discard remaining solution

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Midazolam Concentration Selection Table for 50mL syringes

Dilution for Midazolam 50microgram/mL

Dilute 2.5mL midazolam (1mg/mL) with 47.5mL of compatible fluid (total of 50mL). This makes a 50microgram/mL midazolam solution.

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	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

Dilution for Midazolam 100microgram/mL

Dilute 5mL midazolam (1mg/mL) with 45mL of compatible fluid (total of 50mL). This makes a 100microgram/mL midazolam solution

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								0.5
1	20	30	40	50	60	70				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		10	13	17	20	23	27	30	33	3
3.5		9	11	14	17	20	23	26	29	3.5
4			10	13	15	18	20	23	25	4

Discard remaining solution

Dilution for Midazolam 200microgram/mL

Dilute 10mL midazolam (1mg/mL) with 40mL of compatible fluid (total of 50mL). This makes a 200microgram/mL midazolam solution

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)
1.5	27	40	53							1.5
2	20	30	40	50	60					2
2.5	16	24	32	40	48	56	64			2.5
3	13	20	27	33	40	47	53	60		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		13	18	22	27	31	36	40	44	4.5
5		12	16	20	24	28	32	36	40	5

Discard remaining solution

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Compatible Fluids

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

Adverse Effects

Common

Drowsiness, oversedation, hypersalivation, nasal discomfort (with intranasal), seizure-like myoclonus (premature neonates receiving via intravenous route)

Infrequent

Paradoxical excitation, respiratory depression, hypotension

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
- 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.
- Midazolam has a relatively short duration of action compared to some other benzodiazepines
- Flumazenil is a specific benzodiazepine antagonist and may be used to rapidly reverse respiratory depression.
- Increased sensitivity to central nervous system (CNS) effects in renal and hepatic impairment; use doses at lower end of range.

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1.0	November 2012	current	Original version

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