DEXMEDETOMIDINE HYDROCHLORIDE

Indication	• Sedation for ventilated and non-ventilated infants[1] • For neonates with HIE, provides sedation and prevents shivering and does not suppress ventilation[2,3] • Intranasal for procedural sedation[4]

INTRAVENOUS

Presentation

- Vial 200 microgram in 2 mL (100 microgram in 1 mL)

Dosage[1]

- Starting dose: 0.2 microgram/kg/hour

*Current gest age (weeks)	Dose range	Titration frequency
Less than 30+0	at SMO discretion	
30+0–36+6	0.2–0.8 microgram/kg/hour	every 60 minutes
37+0 or more	0.2–1.2 microgram/kg/hour	every 30 minutes
HIE (any gestation)	0.2–0.8 microgram/kg/hour	every 60 minutes

**Current gestational age is the same as post menstrual age (PMA)*

Preparation (single strength)

- Single strength (suitable for most neonates)
  - o Draw up 25 microgram/kg and make up to 50 mL total volume with 0.9% sodium chloride
  - o *Concentration now equal to 0.5 microgram/kg/mL*
- Refer to Quick guides below for double or quad strength examples

Administration

- IV infusion
  - o Prime the infusion line and infuse via syringe driver at desired rate
- A 0.5 microgram/kg/mL solution:
  - o Infused at 0.4 mL/hour is equal to 0.2 microgram/kg/hour
  - o Infused at 1 mL/hour is equal to 0.5 microgram/kg/hour

NASAL

Presentation

- Vial 200 microgram in 2 mL (100 microgram in 1 mL)

Dosage[4-6]

- 1 microgram/kg 30 minutes prior to procedure
- If inadequate response within 30 minutes of first dose, repeat once[7]

Preparation

- Draw up 20 microgram (0.2 mL) and make up to total volume of 1 mL with 0.9% sodium chloride
  - o *Concentration now equal to 20 microgram/mL*
- Use a mucosal atomisation device (MAD)[8]
  - o Detach the 1 mL syringe from MAD
  - o Draw up prescribed dose from the 20 microgram/mL solution, plus 0.2 mL extra (for priming the MAD)
  - o Re-attach the syringe to MAD
  - o Reduce syringe volume to prescribed dose
- If more than 0.25 mL total dose volume, two MAD may be required (half dose each nostril)

Administration

- Position supine, support head and arms to limit movement during instillation
- Place MAD at entrance of nostril (creating a sealed nasal passage)
- Squirt dose into nasal passage and massage side of nose (to facilitate absorption[7])
- If two half doses required, repeat via other nostril

Special considerations

- Nasal route
  - Contraindicated if choanal atresia
  - Caution if known difficult airway or deformity of the nasal cavity[5]; discuss with SMO
- Infusion
  - Can be reconstituted as single, double or quad strength solutions[9]
  - Prolonged continuous infusion not recommended[10]
  - Maximum concentration 8 microgram/mL[4]
  - IV bolus injection not recommended[11]: do not infuse via an IV line used for bolus administration of medicines
- If hepatic impairment, consider dose adjustment[10,12]
- Effects brown adipose tissue and reduces shivering, resulting in lower cerebral temperatures with therapeutic cooling[2]

Monitoring

- Continuous cardiorespiratory monitoring[10]
- Blood pressure and heart rate[10], particularly when co-administered with other sedative and analgesic agents
- Continue monitoring during weaning (e.g. for side effects, symptoms of withdrawal and haemodynamic stability)
- Pain and comfort

Weaning[13]

- Withdrawal (agitation, tremor, sleeplessness) associated with prolonged use[10,14]
- If administered more than 24 hours
  - Do not cease abruptly–gradually taper[10]
  - Consider weaning regimen or transition to enteral medicines (e.g. clonidine) if sedation requirements persist beyond 3–7 days[7]

Duration of administration	Weaning
Less than 24 hours	• Can cease without weaning
24–72 hours	• Halve the infusion, *then* • If haemodynamically stable after 2 hours, wean by 0.1 microgram/kg/hour every 4–6 hours
More than 72 hours	• Wean by 0.1 microgram/kg/hour every 12–24 hours until ceased

Conversion to oral clonidine during weaning (if required)[7]	
Start clonidine	• 2 microgram/kg every 6 hours
30 minutes after second dose	• Reduce dexmedetomidine by 50%
30 minutes after third dose	• Cease dexmedetomidine

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Compatibility

- Fluids
  - 5% glucose[11], 0.9% sodium chloride[11]
- Via Y-site
  - Amikacin[11], amiodarone[11], ampicillin[11], atropine sulfate[10], azithromycin[11], calcium gluconate[11], cefazolin[11], cefepime[11], cefotaxime[11], cefoxitin[11], ceftazidime[11], ceftriaxone[11], ciprofloxacin[11], cisatracurium[11], clindamycin[11], dexamethasone[11], digoxin[11], dopamine[10], dobutamine[10], droperiodol[11], erythromycin[11], esmolol[11], fentanyl[11], fluconazole[11], furosemide[11], gentamicin[11], glyceryl trinitrate[11], glycopyrrolate[10], heparin sodium[11], hydrocortisone sodium succinate[10], lidocaine[11], magnesium sulfate[11], methylprednisolone sodium succinate[11], metronidazole[11], midazolam[11], milrinone[11], morphine sulfate[11], noradrenaline (norepinephrine)[11], piperacillin-tazobactam[11], potassium chloride[11], sodium bicarbonate[11], sodium nitroprusside[11], tobramycin[11], trimethoprim-sulfamethoxazole[11] vancomycin[11], vecuronium[11]

Incompatibility

- No information[11]

Interactions

- CNS depressants: may compound effects on sedation, respiratory depression, bradycardia and hypotension[4]
- Beta-blocker: co-administration may increase hypotensive and bradycardic effects[4]
- Amiodarone: case reports of cardiac arrest with co-infusion[15]

Stability	• Vials o Store at 25 °C[12] • Infusion solution o Stable for 24 hours at 2–8 °C[11]
Side effects	• Circulatory: bradyarrhythmia[10] (particularly vagally mediated bradycardia, often transient with treatment initiation), tachyarrhythmia[10], hypotension[10], hypertension on discontinuation[10] • Metabolic: hyperthermia (may not respond to cooling)[10] o Discontinue if sustained unexplained fever o Not recommended in malignant hyperthermia-sensitive patients
Actions	• α2-adrenoceptor agonist with sedative, anxiolytic, sympatholytic, and analgesic-sparing effects, and minimal depression of respiratory function[16] • Highly selective and centrally acting with approximately seven (7) times the α2 selectivity compared to clonidine, making dexmedetomidine a more powerful sedative[8,17] • Peripheral activity on the spinal dorsal horn leads to analgesic effects[16,17] • At recommended dose range has neuroprotective properties[16-18]
Abbreviations	*Current gestational age is the same as *postmenstrual age* (PMA) CNS: central nervous system, HIE: hypoxic ischaemic encephalopathy, IV: intravenous, MAD: mucosal atomisation device, SMO: most senior medical officer
Keywords	sedation, analgesic, anxiolytic, sympatholytic, alpha 2 agonist, procedural sedation, HIE, hypoxic ischaemic encephalopathy

The Queensland Clinical Guideline *Neonatal Medicines* is integral to and should be read in conjunction with this monograph. Refer to the disclaimer. Destroy all printed copies of this monograph after use.

Quick guide: 50 microgram/kg (DOUBLE strength preparation *example*)

Weight example	Draw up dose for weight	Make up to total volume:	Concentration equal to:	Infused at (mL/hour)	Delivers (microgram/kg/hour)
1 kg	50 microgram	50 mL with 0.9% sodium chloride	1 microgram/kg/mL	0.2 mL/hour	0.2 microgram/kg/hour
3 kg	150 microgram				
6 kg	300 microgram			0.5 mL/hour	0.5 microgram/kg/hour
For 6 kg neonate, infusion is less than maximum solution concentration at 6 microgram/mL					

Quick guide: 100 microgram/kg (QUAD strength preparation *example*)

Weight example	Draw up dose for weight	Make up to total volume:	Concentration equal to:	Infused at (mL/hour)	Delivers (microgram/kg/hour)
1 kg	100 microgram	50 mL with 0.9% sodium chloride	2 microgram/kg/mL	0.1 mL/hour	0.2 microgram/kg/hour
2.5 kg	250 microgram				
4 kg	400 microgram			0.25 mL/hour	0.5 microgram/kg/hour
For 4 kg neonate, infusion reaches maximum solution concentration of 8 microgram/mL *If greater than 4 kg up to 6 kg, use single of double strength*					

Dosage rationale

Aspect	Consideration
Dose	• In this monograph dosing derived from multiple evidence sources (e.g. literature and neonatal formularies, clinical experience in paediatric and neonatal settings)
Duration	• Consensus: based on clinical experience of usage (5–7 days)
Gestation limits	• Lower limit in studied neonates was 30 weeks[1] • A case report describes successful use (infusion for 19 days) in a 24-week neonate on high frequency ventilation, who developed agitation refractory to other sedating medications[19] • At lower gestational ages o Consider individual circumstances and risk and benefit o Seek expert advice
HIE	• The peak dose for premature or HIE affected neonates is based on the increased half-life in these neonates o Whilst volume of distribution is higher in term infants due to increased lean body mass, HIE affected neonates are more likely to have a pre-existing bradycardia secondary to cooling o Bradycardia is an effect of the medication; therefore upper limit of infusion dose reduced • Reference half-lives o Term neonates: 3.2 hours[1,2] o Preterm neonates: 7.6 hours[1] o Hypoxic ischemic encephalopathy: 7.3 hours[2]
Long term impact	No data regarding long term developmental impact[18]

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