

<b>Alert</b>	Use only where cardiac monitoring and cardiorespiratory resuscitation equipment are available.																								
<b>Indication</b>	IV infusion for sedation and analgesia in mechanically ventilated neonates IV infusion for sedation and analgesia in therapeutic hypothermia. Intranasal therapy for procedures (e.g. Imaging) or premedication prior to general anaesthesia. Adjunct IV therapy with inhalational anaesthesia for both perioperative and postoperative procedures. Adjuvant IV therapy with nerve blocking agents for surgical procedures.																								
<b>Action</b>	Centrally acting $\alpha$ 2-agonist with sedative, anxiolytic, sympatholytic and analgesic properties with minimal depression of respiratory function. <sup>1</sup> It induces a state of condition similar to natural sleep, and patients remain rousable. <sup>1</sup>																								
<b>Drug type</b>	Central Nervous System - Sedative, hypnotic - centrally acting $\alpha$ 2-agonist																								
<b>Trade name</b>	Dexdor Concentrate for infusion dexMEDETOMIDine Accord Concentrate for infusion dexMEDETOMIDine Ever Pharma Concentrate for infusion dexMEDETOMIDine Medsurge Concentrate for infusion dexMEDETOMIDine Viatris Concentrate for infusion dexMEDETOMIDine-AFT Concentrate for infusion Precedex Concentrate for infusion Precedex Ready to Use Solution for infusion																								
<b>Presentation</b>	Dexdor Concentrate for infusion – 200 microgram/2 mL, 400 microgram /4 mL, 1000 microgram/10 mL dexMEDETOMIDine Accord Concentrate for infusion – 200 microgram /2 mL dexMEDETOMIDine Ever Pharma Concentrate for infusion – 200 microgram /2 mL, 400 microgram /4 mL dexMEDETOMIDine Medsurge Concentrate for infusion – 200 microgram /2 mL dexMEDETOMIDine Viatris Concentrate for infusion – 200 microgram /2 mL dexMEDETOMIDine-AFT Concentrate for infusion – 200 microgram /2 mL Precedex Concentrate for infusion – 200 microgram /2 mL Precedex Ready to Use Solution for infusion – 200 microgram /50 mL, 400 microgram /100 mL ( 4 microgram/mL)																								
<b>Dose</b>	<p><b>IV infusion</b></p> <table border="1"> <thead> <tr> <th>Current GA &amp; postnatal age in days<sup>2-4</sup></th> <th>Loading dose (if needed) over 15 minutes</th> <th>Infusion</th> <th>Titration frequency</th> <th>Maximum dose</th> </tr> </thead> <tbody> <tr> <td>&lt;37<sup>+0</sup> weeks gestation</td> <td>0.2 microgram/kg/dose</td> <td>0.2 microgram/kg/hour</td> <td>Every 30-60 minutes</td> <td>1 microgram/kg/hour</td> </tr> <tr> <td>≥37<sup>+0</sup> weeks, and ≤14 days of life</td> <td>0.35 microgram/kg/dose</td> <td>0.3 microgram/kg/hour</td> <td>Every 30-60 minutes</td> <td>1.2 microgram/kg/hour</td> </tr> <tr> <td>≥37<sup>+0</sup> weeks, and &gt;14 days of life</td> <td>0.5 microgram/kg/dose</td> <td>0.5 to 0.75 microgram/kg/hour</td> <td>Every 30-60 minutes</td> <td>1.5 microgram/kg/hour</td> </tr> </tbody> </table> <p><b>IV infusion - Incremental increase</b>                  Every 30-60 minutes, either increase the rate by 0.1-0.2 microgram/kg/hour increments to a maximum dose as per dosing table; and/or use a rescue dose of other sedative (midazolam) or analgesic (opioid) agent to achieve the desired effect.                  NOT FOR IV RESCUE BOLUS ADMINISTRATION.</p>					Current GA & postnatal age in days <sup>2-4</sup>	Loading dose (if needed) over 15 minutes	Infusion	Titration frequency	Maximum dose	<37 <sup>+0</sup> weeks gestation	0.2 microgram/kg/dose	0.2 microgram/kg/hour	Every 30-60 minutes	1 microgram/kg/hour	≥37 <sup>+0</sup> weeks, and ≤14 days of life	0.35 microgram/kg/dose	0.3 microgram/kg/hour	Every 30-60 minutes	1.2 microgram/kg/hour	≥37 <sup>+0</sup> weeks, and >14 days of life	0.5 microgram/kg/dose	0.5 to 0.75 microgram/kg/hour	Every 30-60 minutes	1.5 microgram/kg/hour
Current GA & postnatal age in days <sup>2-4</sup>	Loading dose (if needed) over 15 minutes	Infusion	Titration frequency	Maximum dose																					
<37 <sup>+0</sup> weeks gestation	0.2 microgram/kg/dose	0.2 microgram/kg/hour	Every 30-60 minutes	1 microgram/kg/hour																					
≥37 <sup>+0</sup> weeks, and ≤14 days of life	0.35 microgram/kg/dose	0.3 microgram/kg/hour	Every 30-60 minutes	1.2 microgram/kg/hour																					
≥37 <sup>+0</sup> weeks, and >14 days of life	0.5 microgram/kg/dose	0.5 to 0.75 microgram/kg/hour	Every 30-60 minutes	1.5 microgram/kg/hour																					

	<p><b>IV infusion - Cessation/weaning (ANMF consensus)</b></p> <table border="1" data-bbox="344 327 1465 920"> <thead> <tr> <th>Duration of DEX infusion</th> <th>Weaning</th> </tr> </thead> <tbody> <tr> <td>&lt;24 hours</td> <td>Cease abruptly</td> </tr> <tr> <td>24-72 hours</td> <td>Halve the infusion and then if haemodynamically stable after 2 hours, wean by 0.1 microgram/kg/hour every 6 hours</td> </tr> <tr> <td>&gt;72 hours</td> <td>Wean by 0.1 microgram/kg/hour every 12 hours until ceased. May also consider adding clonidine IV/ORAL</td> </tr> <tr> <td>Clonidine transition protocol</td> <td>                     Day 1 of weaning:                     <ul style="list-style-type: none"> <li>• Start clonidine at 2 microgram/kg every 6 hours</li> <li>• Reduce dexMEDETOMIDine dose by 50%, 30 minutes after the 2nd dose of clonidine.</li> <li>• Discontinue dexMEDETOMIDine, 30 minutes after the 3rd dose of clonidine.</li> </ul>                     Day 2 of weaning:                      Clonidine 2 microgram/kg every 8 hours                      Day 3 of weaning                      Clonidine 2 microgram/kg every 12 hours                      Day 4 of weaning                      Clonidine 2 microgram/kg one DOSE and STOP.                 </td> </tr> </tbody> </table> <p><b>INTRANASAL (ANMF consensus)</b>                      2 microgram/kg (0.5-4 microgram/kg) 30-45 minutes prior to procedure<sup>(5-13)</sup>                      If there is an inadequate response within 30 minutes of first dose, repeat once.</p>	Duration of DEX infusion	Weaning	<24 hours	Cease abruptly	24-72 hours	Halve the infusion and then if haemodynamically stable after 2 hours, wean by 0.1 microgram/kg/hour every 6 hours	>72 hours	Wean by 0.1 microgram/kg/hour every 12 hours until ceased. May also consider adding clonidine IV/ORAL	Clonidine transition protocol	Day 1 of weaning: <ul style="list-style-type: none"> <li>• Start clonidine at 2 microgram/kg every 6 hours</li> <li>• Reduce dexMEDETOMIDine dose by 50%, 30 minutes after the 2nd dose of clonidine.</li> <li>• Discontinue dexMEDETOMIDine, 30 minutes after the 3rd dose of clonidine.</li> </ul> Day 2 of weaning: Clonidine 2 microgram/kg every 8 hours Day 3 of weaning Clonidine 2 microgram/kg every 12 hours Day 4 of weaning Clonidine 2 microgram/kg one DOSE and STOP.		
Duration of DEX infusion	Weaning												
<24 hours	Cease abruptly												
24-72 hours	Halve the infusion and then if haemodynamically stable after 2 hours, wean by 0.1 microgram/kg/hour every 6 hours												
>72 hours	Wean by 0.1 microgram/kg/hour every 12 hours until ceased. May also consider adding clonidine IV/ORAL												
Clonidine transition protocol	Day 1 of weaning: <ul style="list-style-type: none"> <li>• Start clonidine at 2 microgram/kg every 6 hours</li> <li>• Reduce dexMEDETOMIDine dose by 50%, 30 minutes after the 2nd dose of clonidine.</li> <li>• Discontinue dexMEDETOMIDine, 30 minutes after the 3rd dose of clonidine.</li> </ul> Day 2 of weaning: Clonidine 2 microgram/kg every 8 hours Day 3 of weaning Clonidine 2 microgram/kg every 12 hours Day 4 of weaning Clonidine 2 microgram/kg one DOSE and STOP.												
<b>Dose adjustment</b>	Therapeutic hypothermia: No information. ECMO: Beyond the scope of the guideline. Renal impairment: No dose adjustment. Hepatic impairment: Clearance decreases in impairment; consider reducing the dose and titrating carefully.												
<b>Maximum dose</b>	Refer to dosing table.												
<b>Route</b>	IV Intranasal												
<b>Preparation</b>	<p><b>IV infusion</b>  <b>Note: Refer to <a href="#">Appendix</a> for tables to assist with concentration selection.</b></p> <p><b>Weight suggestions for infusion concentrations below are a guide only. Clinicians may choose infusion concentration different to the suggested based on expected dose and the corresponding 24 hour fluid volumes.</b></p> <table border="1" data-bbox="320 1543 1485 1742"> <thead> <tr> <th>Infant weight</th> <th>&lt;1 kg</th> <th>1 to &lt;3 kg</th> <th>≥3 kg</th> </tr> </thead> <tbody> <tr> <td><b>Suggested dexMEDETOMIDine concentration</b></td> <td><b>1 microgram/mL</b></td> <td><b>2 microgram/mL</b></td> <td><b>4 microgram/mL</b></td> </tr> <tr> <td><b>0.2 microgram/kg/hour is equal to</b></td> <td><b>0.2 mL/kg/hour</b></td> <td><b>0.1 mL/kg/hour</b></td> <td><b>0.05 mL/kg/hour</b></td> </tr> </tbody> </table>	Infant weight	<1 kg	1 to <3 kg	≥3 kg	<b>Suggested dexMEDETOMIDine concentration</b>	<b>1 microgram/mL</b>	<b>2 microgram/mL</b>	<b>4 microgram/mL</b>	<b>0.2 microgram/kg/hour is equal to</b>	<b>0.2 mL/kg/hour</b>	<b>0.1 mL/kg/hour</b>	<b>0.05 mL/kg/hour</b>
Infant weight	<1 kg	1 to <3 kg	≥3 kg										
<b>Suggested dexMEDETOMIDine concentration</b>	<b>1 microgram/mL</b>	<b>2 microgram/mL</b>	<b>4 microgram/mL</b>										
<b>0.2 microgram/kg/hour is equal to</b>	<b>0.2 mL/kg/hour</b>	<b>0.1 mL/kg/hour</b>	<b>0.05 mL/kg/hour</b>										

**20mL Syringe**

It is a 2 step dilution.

**Step 1:** Draw up dexMEDETOMIDine and add compatible fluid\* to make a diluted solution as per table below:

dexMEDETOMIDine concentration	1 microgram/mL	2 microgram/mL	4 microgram/mL
Volume of dexMEDETOMIDine (100 microgram/mL)	1 mL (100 microgram)	1 mL (100 microgram)	1 mL (100 microgram)
Volume of compatible fluid*	9 mL	9 mL	9 mL
<b>Total volume</b>	<b>10 mL</b> <b>(10 microgram/mL)</b>	<b>10 mL</b> <b>(10 microgram/mL)</b>	<b>10 mL</b> <b>(10 microgram/mL)</b>

**Step 2:** Draw up diluted dexMEDETOMIDine and add the same compatible fluid\* as per table below to make a final volume of 20 mL

dexMEDETOMIDine concentration	1 microgram/mL	2 microgram/mL	4 microgram/mL
Volume of diluted dexMEDETOMIDine from step 1	2 mL (20 microgram)	4 mL (40 microgram)	8 mL (80 microgram)
Volume of compatible fluid*	18 mL	16 mL	12 mL
<b>Total volume</b>	<b>20 mL</b>	<b>20 mL</b>	<b>20 mL</b>

\*Compatible fluid: glucose 5%, glucose 10% or sodium chloride 0.9%

**50mL Syringe**

It is a 2 step dilution.

**Step 1:** Draw up dexMEDETOMIDine and add compatible fluid\* to make a diluted solution as per table below:

dexMEDETOMIDine concentration	1 microgram/mL	2 microgram/mL	4 microgram/mL
Volume of dexMEDETOMIDine (100 microgram/mL)	1 mL (100 microgram)	1 mL (100 microgram)	Nil
Volume of compatible fluid*	9 mL	9 mL	Nil
<b>Total volume</b>	<b>10 mL</b> <b>(10 microgram/mL)</b>	<b>10 mL</b> <b>(10 microgram/mL)</b>	<b>10 mL</b> <b>(100 microgram/mL)</b>

**Step 2:** Draw up diluted dexMEDETOMIDine and add the same compatible fluid\* as per table below to make a final volume of 50 mL

dexMEDETOMIDine concentration	1 microgram/mL	2 microgram/mL	4 microgram/mL
Volume of diluted dexMEDETOMIDine from step 1	5 mL (50 microgram)	10 mL (100 microgram)	2 mL (200 microgram)
Volume of compatible fluid*	45 mL	40 mL	48 mL
<b>Total volume</b>	<b>50 mL</b>	<b>50 mL</b>	<b>50 mL</b>

\*Compatible fluid: glucose 5%, glucose 10% or sodium chloride 0.9%

Precedex Ready to Use® solution (4 microgram/mL) can be diluted if required (as per consensus).

	<p><b>INTRANASAL</b>  <u>Using 200 microgram in 2 mL vial (100 microgram/mL vial)</u></p> <p>Draw up 0.2 mL (20 microgram of dexMEDETOMIDine) and make up with 0.9% sodium chloride to a final volume of 1 mL with a concentration of 20 microgram/mL</p> <p>Recommended maximum volume in each nostril: 0.3 mL. Larger volumes may end up in the nasopharynx.</p>
<b>Administration</b>	<p><b>IV</b>  IV infusion using a syringe infusion pump.  Infusion should not be placed on any infusion line where boluses may be given.</p> <p><b>INTRANASAL</b>  Dose should be given 30-45 minutes before the procedure.  Divide dose between both nostrils (maximum 0.3 mL per nostril) to optimise absorption, reduce mucosal surface saturation and runoff down the throat.</p> <p><b>Direct administration</b>  Drop solution into alternating nostrils over 15 seconds</p> <p><b>Mucosal atomisation device (MAD)</b>  Attach MAD to the end of a 1 mL Luer- lock syringe and prime the device with the solution to the prescribed dose.  Insert the MAD loosely into the nostril to form a seal, preventing expulsion of fluid.  Briskly compress the syringe plunger to allow for maximal coverage of nasal mucosa with atomised particles.</p> <div style="display: flex; justify-content: space-around; align-items: center;">   </div>
<b>Monitoring</b>	<p>Continuous electrocardiogram (ECG), blood pressure and oxygen saturation monitoring.  Continuous or frequent temperature monitoring.  Monitor infant pain and comfort when used for sedation in ventilated patients.</p>
<b>Contraindications</b>	<p>Hypersensitivity to the medication or any of the excipients.  Heart block or severe ventricular dysfunction.</p>
<b>Precautions</b>	<p>If a patient is on vasodilators, haemodynamics must be monitored closely. If the patient becomes hypotensive, it may be necessary to decrease and/or stop dexMEDETOMIDine or use vasopressors as needed to increase blood pressure.  Hypovolaemia.  Bradycardia.  Dosage reductions should be considered in patients with hepatic impairment or with concomitant use of other sedatives and analgesics.  To prevent inadvertent bolus of residual medication, sodium chloride 0.9% or glucose 5% should be infused at the same rate as the discontinued dexMEDETOMIDine infusion until the volume of the IV line has been cleared.</p>
<b>Drug interactions</b>	<p>Enhances the effects of anaesthetics, sedatives, hypnotics and opioids.</p>
<b>Adverse reactions</b>	<p>Bradycardia, arrhythmias.  Transient hypertension or hypotension  Patients who are hypovolaemic may become hypotensive.  In situations where other vasodilators or negative chronotropic agents are administered, co-administration of dexMEDETOMIDine could have an additive pharmacodynamic effect causing hypotension and bradycardia.</p>

	Bradycardia and hypotension may be potentiated when dexMEDETOMIDine is used concurrently with propofol or midazolam. Nausea, fever, vomiting, hypoxia and anaemia. Hypothermia. Seizures.
<b>Overdose</b>	AUSTRALIA: Contact the Poisons Information Centre on <b>13 11 26</b> for management  NEW ZEALAND: Contact the National Poisons Centre on <b>0800 764 766</b> for management
<b>Compatibility</b>	Fluids: Glucose 5% and sodium chloride 0.9%. TPN (Y-site): <sup>14</sup> Amino acid solutions, fat emulsions. Y site: <sup>14</sup> aciclovir, adrenaline (epinephrine), alfentanil, amikacin, amiNOPHYLLine, amiODAROne, amphotericin B liposome, ampicillin, atenolol, atracurium, atropine, aziTHROMYCIN, aztreonam, caffeine citrate, calcium chloride, calcium gluconate, cefaZOLin, cefEPIIME, cefoperazone, cefOTAXIME, cefOXITIN, cefTAZIDIME, cefTRIAXONE, ciPROFLOXAcin, cisatracurium, clindamycin, dexaMETHASOne, digoxin, dobutamine, dolasetron, dopamine, doxycycline, droperidol, enalaprilat, ephedrine sulfate, ERYthromycin, esmolol, fentanyl, flucONAZOLe, fluorouracil, foscarnet, fosfomycin, furosemide, ganciclovir, gentamicin, glycopyrrolate, glyceryl trinitrate, heparin, hydrocortisone, HYDROmorphone, insulin regular, isoproterenol, labetalol, levetiracetam, lidocaine, linEZOLID, LORazepam, magnesium sulfate, meropenem, methylprednisolone sodium succinate, metoclopramide, metoprolol, metronidazole, midazolam, milrinone, morphine, naloxone, nicardipine, nitroglycerine, noradrenaline (norepinephrine), octreotide, ondansetron, pamidronate, pancuronium, paracetamol (acetaminophen), pentoxifylline, phenobarbital, phenylephrine, phenytoin, piperacillin, piperacillin-tazobactam (EDTA-free), potassium chloride, potassium phosphate, proMETHazine, propOFol, proPRANOLol, ranitidine, remifentanil, rocuronium (dexMEDETOMIDine 4 microgram/mL in sodium chloride 0.9% and rocuronium 1 mg/mL in sodium chloride 0.9%), sildenafil, sodium acetate, sodium bicarbonate, sodium nitroprusside, suxamethonium, sufentanil, TACrolimus, thiopental sodium, ticarcillin, tobramycin, trimETHOPRIM-sulfamethoxazole, vancomycin, vasopressin, vecuronium, verapamil, zidovudine.
<b>Incompatibility</b>	Fluids: N/A PN at Y-site: N/A Y-site: amphotericin B conventional colloidal, amphotericin B lipid complex, DIAzepam, ketamine, pantoprazole, phenytoin.
<b>Stability</b>	Continuous IV infusion should be used within 24 hours
<b>Storage</b>	Store below 25°C in the original container.
<b>Excipients</b>	Dexdor Concentrate for infusion – sodium chloride, water for injections dexMEDETOMIDine Accord Concentrate for infusion – sodium chloride, water for injections dexMEDETOMIDine Ever Pharma Concentrate for infusion - Sodium chloride 9 mg/mL, water for injections. dexMEDETOMIDine Medsurge Concentrate for infusion - Sodium chloride, water for injections. dexMEDETOMIDine Viatris Concentrate for infusion - Sodium chloride, water for injection, nitrogen. dexMEDETOMIDine-AFT Concentrate for infusion - Sodium chloride, hydrochloric acid, sodium hydroxide, water for injections. Precedex Concentrate for infusion - Sodium chloride, water for injections. Precedex Ready to Use Solution for infusion - Sodium chloride, water for injections.
<b>Evidence</b>	<b>Overview</b> Current neonatal drugs to achieve sedation and analgesia consist of opioids and benzodiazepines, but these drugs have been associated with significant side effects, including tolerance, physical dependency, paradoxical agitation, withdrawal, inconsistent sedation, and respiratory depression. <sup>15</sup> The efficacy of these drugs in reducing pain is also uncertain. <sup>16-20</sup> Midazolam and morphine have also been shown to cause neuroapoptosis and neurodevelopmental abnormalities in neonatal animals. <sup>21,22</sup> Alpha-2 agonists can be used to provide sedation, analgesia and antianxiety. They sedate, but do not cause respiratory depression. They are now considered attractive alternatives for long-term sedation during mechanical ventilation in critically ill patients. dexMEDETOMIDine (DEX) and clonidine are the two commonly used alpha-2 agonists. <sup>23</sup> Whereas DEX has been shown to be neuroprotective including prevention of neuroapoptosis induced by other agents in animal studies. <sup>24</sup>

DEX is a selective alpha-2 agonist with minimal impact on respiratory function. It is structurally similar to clonidine but has more than 800 times greater affinity for alpha-2 receptors over alpha-1 receptors. It has both sedative and analgesic effects. The sedative effects result primarily from stimulation of alpha-2 adrenergic receptors in the locus coeruleus of the brainstem, leading to a reduction of central sympathetic output and thus greater firing of inhibitory neurons. The analgesic effects result from stimulation of alpha-2 adrenergic receptors in the dorsal horn of the spinal cord. Alpha-2 adrenergic receptor stimulation (1) reduces the release of substance P that transmits pain messages, and (2) inhibits nociceptive neurons.<sup>1,25</sup> DEX is thought to be safer than morphine or other stronger opioids. DEX attenuates stress responses, thereby creating a more stable hemodynamic profile during stressful events such as surgery or anaesthetic induction.(1) Unlike sedative drugs such as propofol and the benzodiazepines, DEX does not act at gamma-aminobutyric acid (GABA) receptors.<sup>25</sup>

DEX can be used alone or in conjunction with other agents to provide adequate sedation and analgesia.<sup>2,26</sup>

**Trends in the use of DEX in neonates:** A multicentre, observational cohort study included 395122 neonates born between 22weeks and 36 weeks gestation at 1 of 383 Pediatrix Medical Group NICUs across the US between calendar years 2010 and 2020. Median gestational age was 34 (IQR, 32-35) weeks, and median birth weight was 2040 (IQR, 1606-2440) g. There were 384 infants (0.1%of total; 58.9%male) who received DEX. Infants who received DEX were born more immature, had lower birth weight, longer length of hospitalization, more opioid exposure, and more days of mechanical ventilation. DEX use increased from 0.003%in 2010 to 0.185%in 2020 (P < .001 for trend), while overall opioid exposure decreased from 8.5%in 2010 to 7.2%in 2020 (P < .001 for trend). The median postmenstrual age at first DEX exposure was 31 (IQR, 27-36) weeks, and the median postnatal age at first DEX exposure was 3 (IQR, 1-35) days. The median duration of DEX was 6 (IQR, 2-14) days. The findings of this study suggest that DEX use in preterm infants increased significantly between 2010 and 2020, while the opioid exposure decreased.<sup>27</sup>

#### **Efficacy**

##### **Sedation and analgesia in mechanically ventilated (MV) neonates**

A 2024 Cochrane review did not identify any randomised controlled trials in neonates.<sup>25</sup>

A 2024 systematic review and meta-analysis included 6 studies involving 252 neonates.<sup>28</sup> This comprised 1 randomized controlled trial, 1 case-control study, 2 retrospective cohort studies, and 2 pharmacokinetic studies. Four studies compared DEX to a control (fentanyl, morphine, or placebo) for the purpose of sedation and possible analgesia while receiving mechanical ventilation (MV) or during therapeutic hypothermia (TH) for hypoxic ischaemic encephalopathy (HIE). All studies administered DEX intravenously (IV). A loading dose of DEX was used in 4 studies ranging from 0.05 to 0.5 microgram/kg given over 10 to 60 min and the mean maintenance infusion rate ranged from 0.05 to 1.2 microgram/kg/h. The total duration of infusion varied from 6 h to 12 days. One study evaluated DEX in term infants with HIE undergoing TH to mitigate shivering. One study compared DEX pharmacokinetics, safety, and efficacy in term versus preterm infants requiring MV. The review concluded that DEX **may be** effective in (1) achieving sedation and analgesia, (2) reducing the need for adjunctive sedation or analgesia, (3) shortening the time to extubate, (4) decreasing the duration of mechanical ventilation, and (5) accelerating the attainment of full enteral feeds. No significant adverse effects associated with DEX were reported in this review.<sup>28</sup> This review identified that DEX can be administered safely, at specific dosage ranges in neonates without leading to significant adverse events requiring its abrupt discontinuation. However, the evidence in this review stems mainly from non-randomized and retrospective studies which are associated with risks of bias. However, the results of this study were comparable to similar reviews in adult and paediatric population.<sup>23,29</sup>

**DEX infusion as prolonged sedation in adults:** 2019 Cochrane review in critically ill adults identified 7 studies, covering 1624 participants, and compared DEX with traditional sedatives, including propofol, midazolam and lorazepam. The review found long-term sedation using DEX reduced the duration of mechanical ventilation and ICU length of stay. DEX doubled the incidence of bradycardia, which was the most commonly reported adverse event. Effect on other adverse event rates compared to other sedatives

was heterogeneous including hypotension; hypertension; tachycardia; first degree heart block; hyperglycaemia; and hypoglycaemia. The general quality of evidence ranged from very low to low, due to high risks of bias, serious inconsistency and imprecision, and strongly suspected publication bias.<sup>23</sup>

**DEX infusion as prolonged sedation in children:** A 2020 systematic review analysed DEX for prolonged sedation in children. The review identified 32 studies, including a total of 3,267 patients.<sup>29</sup> Most of the studies were monocentric (91%) and retrospective (88%); one was a randomized trial. Minimum and maximum infusion dosages varied from 0.1–0.5 microgram/kg/hr to 0.3–2.5 microgram/kg/hr, respectively. The mean/median duration range was 25–540 hours. The use of a loading bolus was reported in eight studies (25%) (range, 0.5–1 microgram/kg), the mode of weaning in 11 (34%), and the weaning time in six of 11 (55%; range, 9–96 hr). The pooled prevalence of bradycardia was 2.6% (n = 10 studies; 14/387 patients; 95% CI, 0.3–7.3; I2 = 75%), the pooled prevalence incidence of bradycardia was 2.6% (n = 10 studies; 14/387 patients; 95% CI, 0.3–7.3; I2 = 75%), the pooled incidence of hypotension was 6.1% (n = 8 studies; 19/304 patients; 95% CI, 0.8–15.9; I2 = 84%). Three studies (9%) reported side effects' onset time which in all cases was within 12 hours of the infusion starting. Review concluded that DEX infusion can be considered relatively safe in children even when longer than 24 hours.

PROSDEx multicentre prospective observation study from 9 tertiary PICUs from Italy reported outcomes on 163 children.<sup>30</sup> The main indication for DEX use was as an adjuvant for drug-sparing (42%). Twenty-three patients (14%) received dexMEDETOMIDine as monotherapy. Only 7% received a loading dose. The median infusion duration was 108 hours (interquartile range (IQR), 60–168 hr), with dosages between 0.4 (IQR, 0.3–0.5) and 0.8 microgram/kg/hr (IQR, 0.6–1.2 microgram/kg/hr). At 24 hours of infusion, values of COMFORT-B Scale (n = 114), Withdrawal Assessment Tool-1 (n = 43) and Cornell Assessment of Pediatric Delirium (n = 6) were significantly decreased compared with values registered immediately pre-DEX (p < 0.001, p < 0.001, p = 0.027). Dosages/kg/hr of benzodiazepines, opioids, propofol, and ketamine were also significantly decreased (p < 0.001, p < 0.001, p = 0.001, p = 0.027). The infusion was weaned off in 85% of patients, over a median time of 36 hours (IQR, 12–48 hr), and abruptly discontinued in 15% of them. Thirty-seven percent showed hemodynamic changes, and 9% displayed hemodynamic adverse events that required intervention (dose reduction in 79% of cases). A multivariate logistic regression model showed that a loading dose (odds ratio, 4.8; CI, 1.2–18.7) and dosages greater than 1.2 microgram/kg/hr (odds ratio, 5.4; CI, 1.9–15.2) were independent risk factors for hemodynamic adverse events. Adverse events were reversible following dose reduction.<sup>30</sup>

A dose escalation study<sup>2</sup> in preterm (28-36 weeks gestation, n=18) and full-term (36-44 weeks, n=24) mechanically ventilated infants assessed the effects of 3 dosage levels of DEX: Level 1: loading dose (LD) 0.05 microgram/kg; maintenance dose (MD) 0.05 microgram/kg/hour; Level 2: LD 0.1 microgram/kg; MD 0.1 microgram/kg/hour; Level 3: LD 0.2 microgram/kg; MD 0.2 microgram/kg/hour. Rescue sedation (midazolam) was given in 1 (7%) at level 1, 1 (7%) at level 2, and 2 (14%) at level 3. Rescue sedation was required in 4 (17%) preterm infants and 4 (10%) term infants. Rescue analgesia (opioid) was given in 5 (36%) at level 1, and 5 (36%) at level 2; and 7 (50%) at level 3. Rescue sedation was required in 3 (17%) preterm infants and 14 (58%) term infants. Three adverse events were assessed as definitely related to DEX: diastolic hypotension in a preterm infant at dose level 2; hypertension in a term infant at dose level 1; and significant agitation in a term infant at dose level 3. They concluded premature neonates were adequately sedated with DEX alone, although doses up to 0.2 microgram/kg/hour were not sufficient in most term neonates.

O'Mara et al<sup>31</sup> reported a case control study of 48 preterm neonates requiring mechanical ventilation who received fentanyl (n=24) or DEX (n=24) for pain or sedation. DEX was administered as a 0.5 microgram/kg bolus, followed by a maintenance infusion 0.3 microgram/kg/hour, increased by 0.1 microgram/kg/hour up to twice daily if there were elevated sedation scores with a need for >3 doses of adjunctive sedation during a 12-hour period. Patients in the DEX group required less adjunctive sedation (54.1% vs. 16.5%, p<0.0001), shorter duration of mechanical ventilation, reduced time to meconium passage and reduced time to achievement of full enteral feeds. There were no differences in haemodynamic parameters between the 2 groups.

**Sedation and analgesia in therapeutic hypothermia**

An open label RCT of DEX use in 205 term neonates with moderate to severe HIE receiving therapeutic hypothermia in a NICU in Ukraine found dexMEDETOMIDine is a safe sedative agent with a stable haemodynamic profile, no adverse cerebral influence and possible neuroprotective effects in term infants with HIE, additional to standard therapeutic hypothermia.<sup>32</sup> A significant difference between groups in days of tracheal extubation ( $p=0.022$ ) was found; the chance for babies to be extubated before 7 days of treatment was significantly higher in the dexMEDETOMIDine group 68% versus 33% in the control group ( $p=0.018$ ) with HR 0.48 (95% CI 0.27-0.86,  $p=0.011$ ). Also, the NIRS index rScO<sub>2</sub> differed significantly between the studied and control groups on the 1st day of treatment (65% versus 79%,  $p=0.012$ ) and on the 2nd day of treatment (74% versus 81%,  $p=0.035$ ). Mean arterial pressure was higher in the dexMEDETOMIDine group compared to the control group (58 [51-65] mm Hg versus 53 [46-60] mm Hg,  $p<0.001$ ), with a lower dose of dobutamine (EV -1.87, 95% CI from -3.25 to -0.48,  $p=0.009$ ). In the dexMEDETOMIDine group, the rate of seizures was significantly lower on the 1st day of observation (4.3% versus 48.3%,  $p<0.001$ ); the incidence of unfavourable outcome as cerebral leukomalacia was also 7 times lower in the dexMEDETOMIDine group compared to the control group (2.2% versus 15.1%,  $p=0.018$ ).<sup>32</sup>

A 2022 single-centre retrospective study compared outcomes in neonates with HIE undergoing therapeutic hypothermia who received fentanyl to those who received dexMEDETOMIDine (DEX). A total of 45 neonates were included (fentanyl,  $n=19$ ; DEX,  $n=26$ ). The DEX group had a decreased the need for sedative bolus doses during therapeutic hypothermia compared with the fentanyl group; however, there was no difference in number of uncontrolled agitation scores or need for additional sedatives. The DEX group had a shorter time to discontinuation of sedatives after rewarming compared with the fentanyl group (0.52 versus 5 days, respectively;  $p=0.001$ ), shorter time to extubation after birth (3.1 versus 11.3 days, respectively;  $p=0.004$ ), and earlier time to resumption of feeds (8.5 versus 13 days, respectively;  $p=0.03$ ). A non-statistically significant reduction in seizures was noted (3 versus 7 subjects, respectively;  $p=0.07$ ). In summary, DEX during therapeutic hypothermia for HIE appeared to provide comparable control of agitation to fentanyl with a reduced need for additional sedatives and may lead to an earlier time to extubation and discontinuation of sedatives.<sup>33</sup>

**Sedation and analgesia for postoperative pain in newborns**

A retrospective cohort study was conducted evaluating the use/addition of DEX for treatment of pain or sedation in neonates after a surgical procedure. Patients in DEX group experienced more episodes of bradycardia (12.8% vs 5.1%;  $p=0.01$ ). There was no difference between groups in episodes of hypotension or respiratory depression. The addition of DEX to opioid infusions resulted in a significant decrease in the cumulative dose of opioids but was associated with more episodes of bradycardia than opioids alone.<sup>34</sup>

**Intranasal(IN) DEX for procedures (Imaging, premedication)**

The intranasal route of administration can be useful for sedation and premedication in paediatric subjects.<sup>1</sup> Bioavailability was found to be up to 82%.<sup>35,36</sup> IN dex in children is found to be useful especially for short procedures (e.g. imaging studies) that require the child to be sedated.<sup>13</sup> It is odorless and tasteless, and no published study on this drug reported neither nausea nor vomiting. Dex induces sleep similar to natural sleep. Thus, even with high dose IN dexMEDETOMIDine, external stimuli may easily awake patients. Dex can be used in varying doses, from 0.5 to 4 microgram/kg, depending on the level of sedation required.<sup>13</sup> A higher dose produces a deeper level of sedation, which may improve procedural success. Dex has minimal respiratory depression and acceptable cardiovascular effects. Patel et al. demonstrated IN dex 2-2.5 microgram/kg/dose may perform safe and effective sedation in children, and the IN route is far superior to the oral administration.<sup>12</sup> Talon et al, demonstrated IN Dex (2 microgram/kg) is superior to oral midazolam when administered 30 to 45 minutes before the reconstructive surgery in burn children.<sup>11</sup> IN DEX is more rapidly absorbed in blood compared to the oral form, and it preserves the airway reflexes and respiratory drive.<sup>11</sup>

A prospective observational pilot study evaluated the aerosolized intranasal route for DEX as a safe, effective, and efficient option for infant and paediatric sedation (aged 1 month to 5 years) for computed tomography imaging. The study used initial dose of 2.5 microgram/kg with subsequent doses of 1

microgram/kg if required. The mean time to sedation was 13.4 minutes, with excellent image quality, no failed sedations, or significant adverse events.<sup>8</sup> In a RCT, Yuen et al compared sedation levels in 116 children aged 1-8 years following administration of intranasal dexMEDETOMIDine. Children were assigned to receive either intranasal dexMEDETOMIDine 1 microgram/kg or 2 microgram/kg. Both doses produced a similar level of satisfactory sedation in children aged 1–4 years, whereas 2 microgram/kg/dose resulted in a higher proportion of satisfactory sedation in children aged 5–8 years.<sup>10</sup> In another RCT, Tug et al studied intranasal DEX in children 1-8 years of age scheduled for Magnetic Resonance Imaging (MRI) study. Intranasal DEX was administered at doses of 3 microgram/kg (Group 1) and 4 microgram/kg (Group 2) before imaging. Imaging studies were completed successfully in all patients. Intranasal DEX 4 microgram/kg was more efficient than intranasal DEX 3 microgram/kg.<sup>9</sup> Li et al. compared 3 microgram/kg intranasal DEX, administered by atomizer or drops in 279 children under 3 years of age undergoing echocardiogram. Both were equally effective.<sup>7</sup>

**Premedication prior to anaesthesia in children**

A 2014 systematic review compared DEX premedication with midazolam or ketamine premedication or placebo in children. Thirteen randomized controlled trials involving 1190 patients were included. The main parameters investigated included satisfactory separation from parents, satisfactory mask induction, postoperative rescue analgesia, emergence agitation and postoperative nausea and vomiting. Procedures included dental rehabilitation and tooth extraction, lymph node excision, herniorrhaphy, circumcision, bone marrow biopsy and aspiration, adenotonsillectomy and others. The children ranged in age from 2 to 10 years old and most were 4 to 6 years old. Eleven trials compared DEX with midazolam premedication, 2 compared DEX with ketamine and 3 compared DEX with a placebo. All trials administered premedication through non-invasive routes, including oral and transmucosal (intranasal, sublingual and buccal) administration, at 30-75 min before commencement of surgery. The dosing scheme for DEX was 1-2 microgram/kg for transmucosal premedication or 2.5-4 microgram/kg for oral premedication. Ten trials used inhalational general anaesthesia, and one trial provided sedation with propofol. When compared with midazolam, premedication with DEX resulted in an increase in satisfactory separation from parents (RD = 0.18, 95% CI: 0.06 to 0.30, p = 0.003) and a decrease in the use of postoperative rescue analgesia (RD = -0.19, 95% CI: -0.29 to -0.09, p = 0.0003). Children treated with DEX had a lower heart rate before induction. The incidence of satisfactory mask induction, emergence agitation and PONV did not differ between the groups. DEX was superior in providing satisfactory intravenous cannulation compared to placebo. This meta-analysis suggests that DEX is superior to midazolam premedication because it resulted in enhanced preoperative sedation and decreased postoperative pain. Review recommended further studies to evaluate the dosing schemes and long-term outcomes of DEX premedication in paediatric anaesthesia.<sup>37</sup>

**Adjunct with inhalational anaesthesia for procedures**

A systematic review<sup>38</sup> of RCTs in paediatric patients undergoing inhalational anaesthesia using sevoflurane included 14 RCTs involving painful procedures in children and infants of whom 777 received DEX and 693 received placebo. No trial enrolled newborns. Bolus DEX dose ranged from 0.3 to 2 microgram/kg and maintenance dose 0.1 to 0.7 microgram/kg/hour. Intraoperative DEX was associated with reduced postoperative opioid use in the post-anaesthesia care unit [RR 0.31 (0.17, 0.59), I<sup>2</sup> = 76%, p<0.0001], decreased post-operative pain intensity [SMD -1.18 (-1.88, -0.48), I<sup>2</sup> = 91%, p<0.0001] but had no effect upon postoperative nausea and vomiting incidence [RR = 0.67 (0.41, 1.08), I<sup>2</sup> = 0%, p = 0.48]. Subgroup analyses found administration during adeno-tonsillectomy and using a bolus <0.5 microgram/kg irrespective of continuous administration was associated with no effect. This supports the findings of a previous systematic review<sup>(39)</sup> of use of intraoperative dexMEDETOMIDine compared to opioids or placebo for acute postoperative pain in children which included 11 RCTs with 874 children. A lower risk for postoperative pain and need for postoperative opioids following intraoperative dexMEDETOMIDine compared with placebo or opioids in children undergoing surgery was reported. Five trials including 240 patients reported bradycardia or hypotension, with one episode of bradycardia treated with atropine and two episodes of hypotension treated with saline bolus. Newborns were not included in the trials.

A network meta-analysis of RCTs<sup>40</sup> assessing the effects of different auxiliary drugs in paediatric sevoflurane anaesthesia found dexMEDETOMIDine reduced likelihood of emergent agitation, reduced post-operative

nausea and vomiting, decreased sedative use and reduced paediatric anaesthesia emergence delirium compared to placebo, but was associated with a longer extubation time compared to those who were given placebo. Compared to other agents, fentanyl was more effective than dexMEDETOMIDine in reducing risk of emergence agitation and paediatric anaesthesia emergence delirium, but patients were more likely to experience postoperative nausea and vomiting and require additional analgesia compared to those in the dexMEDETOMIDine group. The network meta-analysis concluded dexMEDETOMIDine should be considered as the most appropriate prophylactic treatment that can be introduced into sevoflurane anaesthesia. Newborns were not included in the trials. [LOE I in infants and children].

Three case series have reported use of dexMEDETOMIDine as an adjunct to anaesthetic in infants undergoing surgical procedures.<sup>34,41,42</sup> Ozcengiz et al<sup>41</sup> reported 16 newborns aged 2-28 days who underwent general anaesthesia using dexMEDETOMIDine and sevoflurane for abdominal surgical procedures. Anaesthesia was induced with 1 microgram/kg ketamine intravenously, then dexMEDETOMIDine 1 microgram/kg infused over 10 minutes. Maintenance infusion was started as 0.5-0.8 microgram/kg/hour until the end of surgery. No significant differences were observed in haemodynamic parameters from baseline values. No patient had hypotension, bradycardia, hypertension, hypoxia or respiratory depression. Patients had mild to moderate hypothermia during the postoperative period. Lam et al<sup>42</sup> reported a case series of 50 neonates and infants with heart disease. Use of a dexMEDETOMIDine infusion during and/or after heart surgery was safe from a haemodynamic standpoint. Sellas et al<sup>34</sup> reported a retrospective case control study comparing postoperative infusion of dexMEDETOMIDine with opioid infusion (n=39 each group), of which 31 out of 35 newborns were mechanically ventilated. Average dose of dexMEDETOMIDine was 0.36 microgram/kg/hour. DexMEDETOMIDine reduced the cumulative dose of opioids but not the number of doses, and was associated with an increase in bradycardia episodes (12.8 versus 5.1%), but not hypotension or respiratory depression. Average dose associated with bradycardia was 0.3 microgram/kg/hour.

**DEX sedation with nerve blocks for surgical procedures**

In a RCT<sup>43</sup> in 104 infants (75% born preterm), with mean post-menstrual age of 41 weeks and mean weight of 3.5 kg at the time of surgery, were allocated to dexMEDETOMIDine sedation with caudal block (n=51) versus general sevoflurane anaesthesia with tracheal intubation and caudal block (n=46) for elective bilateral inguinal hernia surgery. DexMEDETOMIDine was given at a bolus dose of 2 microgram/kg over the first 10 min, followed by 1 microgram/kg over the next 10 min to achieve a Ramsay score of 3-4. Sedation was maintained with dexMEDETOMIDine infusion at 0.2 microgram/kg/hour to maintain a Ramsay score of 3-4. In the dexMEDETOMIDine group, 46 infants (90.2%) had their operations completed solely under this technique, two (3.9%) were converted to general anaesthesia with intubation, and three (5.9%) required brief administration of nitrous oxide or low-dose sevoflurane. Overall, 96.1% of infants in the dexMEDETOMIDine group did not require intubation. Conclusion: DexMEDETOMIDine sedation with loading dose of 2-3 microgram/kg and maintenance dose of 0.2 microgram/kg/hour with caudal block provides a feasible alternative to general anaesthesia in infants undergoing hernia surgery although supplemental methods were required in 9.8%.<sup>43</sup>

**DEX for awake intubation in adults with difficult airways**

A 2016 meta-analysis compared the efficacy and safety of IV loading dose +/- infusion of DEX with other alternative sedative agents used for performing awake intubation.<sup>44</sup> The efficacy (level of sedation, success rate for intubation at the first attempt, intubation time, intubation conditions, and patient satisfaction) and safety (incidence of hypertension, hypotension, tachycardia, bradycardia, hypoxia, postsurgical memory, hoarseness, and sore throat) were assessed. Thirteen RCTs with a combined subject population of 591 patients were included. Use of DEX was associated with a higher Ramsay sedation scale score [mean difference (MD): 1.02, 95% confidence interval (CI), 0.77–1.28, P < 0.00001], vocal cord movement score (MD = 0.72, 95% CI, 0.20–1.24, P = 0.007), coughing scores (MD = 0.66, 95% CI, 0.10–1.22, P = 0.02), limb movement scores (MD = 0.69, 95% CI, 0.47–0.91, P < 0.00001); increased risk of bradycardia [relative risk (RR): 3.03, 95% CI, 1.38–6.68, P = 0.006] and hypotension (RR: 2.87, 95% CI, 1.44–5.75, P = 0.003); and lower risk of hypoxia (RR: 0.32, 95% CI, 0.15–0.70; P = 0.004) and postsurgical memory (RR: 0.50, 95% CI, 0.35–0.72, P = 0.0002). In this meta-analysis, DEX appeared to be an effective and well-tolerated agent for

performing awake intubation. Its use was associated with better intubation conditions, preservation of airway patency, and reduced recall of intubation, as compared with the traditional sedative agents. The risk of bradycardia and hypotension was significantly higher with dexMEDETOMIDine as compared with that with other sedatives. However, these were easily managed with atropine and vasoactive agents.<sup>44</sup>

**DEX for opiate withdrawal**

Reports on dexMEDETOMIDine use for opioid withdrawal are limited to case studies and retrospective reviews involving a total of 20 paediatric patients.<sup>45</sup> When bolus doses are used, strategies described in published reports entail a loading dose of 0.5–1.0 microgram/kg administered over 5–10 minutes, followed by a continuous infusion at 0.1–1.4 microgram/kg/hour for a period of 1–16 days. Reported adverse effects include hypotension and bradycardia. (LOE IV)

**Prevention of postoperative junctional ectopic tachycardia in children after congenital heart surgery**

In an RCT<sup>46</sup> in 90 children who underwent elective cardiac surgery for congenital heart diseases randomised to dexMEDETOMIDine 0.5 microgram/kg intravenously over 20 minutes completed 10 minutes before induction, followed by 0.5 microgram/kg/hour infusion for 48 hours postoperatively versus placebo group. The incidence of junctional ectopic tachycardia was significantly reduced in the dexMEDETOMIDine group (3.3%) compared with placebo (16.7%) with  $P < 0.005$ . Heart rate while coming off cardiopulmonary bypass was significantly lower in the dexMEDETOMIDine group, and ventilation time, mean duration of intensive care unit and hospital stay (days) were significantly shorter. There was no difference between the 2 groups with regards to mortality, bradycardia, or hypotension. Conclusion: Prophylactic use of dexMEDETOMIDine is associated with significantly decreased incidence of postoperative junctional ectopic tachycardia in children after congenital heart surgery without significant side effects.

**IV bolus during general anaesthesia**

There are no studies in neonates. There were trials in children. Jooste EH et al, had observed that rapid IV bolus administration of DEX (0.25 or 0.5 microgram/kg over 5 seconds) in 12 children who underwent heart transplants was clinically well-tolerated, although its use resulted in a transient but significant increase in systemic and pulmonary blood pressure and a decrease in heart rate (HR).<sup>56</sup> In addition, Hauber JA et al, documented that fast IV bolus administration of 0.5 microgram/kg DEX improved paediatric patients' recuperation profile by lowering the occurrence of EA. Although a statistically significant change in haemodynamics was observed, no patient required intervention for hemodynamic changes.<sup>57</sup> Dawes et al determined the DEX dose that can be given as a rapid 5 seconds bolus to healthy children during total intravenous anaesthesia without causing significant hemodynamic effects. The ED50 of dexMEDETOMIDine administered over 5 seconds without significant hemodynamic compromise is 0.49 microgram/kg.<sup>58</sup> Chen et al, in their RCT, studied different bolus doses of DEX to prevent and treat emergence agitation in children who underwent hernia repair.<sup>59</sup> The doses of 0.75 and 1 microgram/kg improved recovery.

**Safety**

A 2024 systematic review identified that DEX can be administered safely, at specific dosage ranges in neonates without leading to significant adverse events. However, the evidence stems mainly from non-randomized and retrospective studies which are associated with risks of bias.<sup>28</sup>

**Long term neuroprotection:** A 2019 systematic review evaluated preclinical (n=661) and clinical (n=240) studies on the histological and neurobehavioural long term effects of DEX and found that DEX did not induce histologic injury and showed a beneficial effect when administered with another anaesthetic. A total of 20 preclinical studies were included in this review. None of the clinical studies met the predefined eligibility criteria. Histologic injury by dexMEDETOMIDine was evaluated in 11 studies, and was confirmed in three of these studies (caspase-3 activation or apoptosis). Decrease of injury caused by another anaesthetic was evaluated in 16 studies and confirmed in 13 of these. Neurobehavioral tests were performed in seven out of the 20 studies. Of these seven rodent studies, three studies tested the effects of DEX alone on neurobehavioral outcome in animals. All three studies found no negative effect of DEX on the outcome. In 6 studies, outcome was evaluated when DEX was administered following another anaesthetic. DEX was found to lessen the negative effects of the anaesthetic.<sup>47</sup>

**Haemodynamic effects:** DEX increases the incidence of bradycardia.<sup>28,41,43</sup> with heterogeneous other effects compared to other agents including hypotension, hypertension and tachycardia. Haemodynamic effects appear to be predictable and dose dependent and reversible with cessation/weaning of dose.<sup>2</sup> Bradycardia responded to atropine in a small case series.<sup>41</sup> Loading dose and higher infusion dose are independent risk factors for haemodynamic effects.<sup>30</sup>

**Hypothermia** has been reported in newborns receiving DEX for perioperative sedation.<sup>41,48</sup>

**Electrical seizures:** There is a case report of a newborn infant with electrical seizures during administration of DEX which ceased following discontinuation.<sup>49</sup>

**Withdrawal after cessation of DEX:** Prolonged administration of DEX is associated with withdrawal symptoms when it is discontinued abruptly or weaned expeditiously. This withdrawal effect, characterized by agitation, hypertension, and tachycardia,<sup>50-53</sup> Burbano et al observed that 27% of patients experienced agitation and tachycardia and 35% experienced hypertension; these withdrawal signs occurred at more than twice the rate among those for whom DEX was discontinued abruptly.<sup>50</sup> Haenecour et al found a 35% incidence of DEX withdrawal in children after receiving infusions longer than 48 hours.<sup>53</sup> Similarly, Whalen et al described a 30% incidence of DEX withdrawal after prolonged infusion (>48 hours) in children.<sup>52</sup> Liu et al reported a clonidine transition protocol in 22 infants and children to facilitate weaning of DEX. Median age was 3.5 months (IQR, 2–28.5) in this study. Clonidine was initiated if the duration of DEX was  $\geq 72$  hours or earlier at the discretion of the treating physician. The dose of clonidine was 2 mcg/kg every 6 hours for patients <6 months of age and 4 mcg/kg every 6 hours for patients  $\geq 6$  months of age. DEX dose rate was decreased by 50%, 30 minutes after the 2nd dose of clonidine, and DEX was discontinued 30 minutes after the 3rd dose of clonidine. While weaning regimen was not detailed for different age groups in the report, it can be inferred that, weaning of clonidine was commenced 24 hours after the cessation of DEX and clonidine weaning occurred over 4 days by dropping frequency (6 hourly day 1, 8 hourly day 2, 12 hourly day 3 and one dose day 4).<sup>51</sup> The population in this study were predominantly infants and children beyond neonatal age group and there were no preterm infants. DEX has reduced clearance and a longer half-life in preterm compared to term infants.<sup>1</sup>

ANMF consensus: DEX infusion of  $\leq 24$  hours can be ceased abruptly; DEX infusion  $>24 \leq 72$  hours: Halve the infusion and then reduce by 0.1 mcg/kg/hour every 12 hours; DEX infusion  $>72$  hours: Start clonidine transition protocol as per the dose section.

#### **Pharmacokinetics**

DEX is rapidly distributed and is mainly hepatically metabolised into inactive metabolites by glucuronidation and hydroxylation (cytochrome P450 enzymes). Renal impairment does not influence the pharmacokinetics of dexMEDETOMIDine to any significant extent.<sup>1</sup> dexMEDETOMIDine A high inter-individual variability in dexMEDETOMIDine pharmacokinetics has been described. Body size, hepatic impairment, and presumably plasma albumin and cardiac output have a significant impact on dexMEDETOMIDine pharmacokinetics. Less than 1% is excreted unchanged with metabolites being excreted renally (95%) and faecally (4%).

In neonatal pharmacokinetic studies, where 20 ventilated infants with a median PMA of 44 weeks (range, 33-61) on a median maximum dexMEDETOMIDine infusion dose during the study period of 1.8 microgram/kg/hour, younger PMA was a significant predictor of lower clearance. Infants with a history of cardiac surgery had ~40% lower clearance, and infants with PMA of 33 to 61 weeks and body weight of 2 to 6 kg, the estimated clearance and volume of distribution were 0.87 to 2.65 L/kg/hour and 1.5 L/kg, respectively. (54) Preterm neonates had lower weight-adjusted plasma clearance (0.3 vs. 0.9 L/hour/kg) and an increased elimination half-life (7.6 vs. 3.2 hours) than term neonates. Premature neonates were reported to be adequately sedated with dexMEDETOMIDine alone, although doses up to 0.2 microgram/kg/hour were not sufficient in most term neonates.<sup>2</sup> In a pharmacokinetic study<sup>3,4</sup> in 95 children aged 1 week to 14 years and weight 3.1 to 58.9 kg, clearance maturation increases from 18.2 L/hour/70 kg at birth in a term neonate to reach 84.5% of the mature value by 1 year of age. Children given an infusion after cardiac surgery had 27% reduced clearance compared to a population given a bolus dose. Simulation of published infusion rates

	<p>that provide adequate sedation for intensive care patients found a target therapeutic concentration of between 0.4 and 0.8 microgram/L. A recommended dose regimen based on the target concentration range of 0.4–0.8 microgram/L was considered safe and efficacious, and consisted of a standard loading dose 0.6 microgram/kg = 2.9 microgram/kg/hour over 10 minutes, a maintenance dose for general sedation 0.33 microgram/kg/hour for neonates and 0.4 microgram/kg/hour for 3 month infants, and a maintenance dose for postoperative cardiac infusion of 0.24 microgram/kg/hour and 0.29 microgram/kg/hour for 3 month infants.<sup>3,4</sup></p> <p>In a dose escalation study in full-term neonates and infants requiring mechanical ventilation after open heart surgery, dexMEDETOMIDine clearance was significantly diminished in full-term newborns and increased rapidly in the first few weeks of life. Typical clearance post cardiac surgery increased from 10 mL/min/kg (34 mL/min) for a full term newborn, 18.2 mL/min/kg (69 mL/min) at 2 weeks, to 18.4 mL/min/kg (77 mL/min) at 1 month. A continuous infusion of up to 0.3 microgram/kg/hour in neonates and 0.75 microgram/kg/hour in infants was well tolerated after open heart surgery.<sup>55</sup></p> <p>In summary, Dex has reduced clearance and a longer half-life in preterm compared to term infants, and term infants compared to older infants.<sup>2-4</sup> Whereas doses up to 0.2 microgram/kg/hour may be sufficient in most preterm neonates, infusion rates of 0.33 microgram/kg/hour for neonates and 0.4 microgram/kg/hour for 3 month infants are recommended. Lower infusion rates are recommended for infants undergoing cardiac surgery<sup>3,4</sup> and with concomitant use of other sedatives or analgesics.</p>
<p><b>References</b></p>	<ol style="list-style-type: none"> <li>1. Weerink MA, Struys MM, Hannivoort LN, Barends CR, Absalom AR, Colin P. Clinical pharmacokinetics and pharmacodynamics of dexMEDETOMIDine. <i>Clinical pharmacokinetics</i>. 2017;56(8):893-913.</li> <li>2. Chrysostomou C, Schulman SR, Castellanos MH, Cofer BE, Mitra S, da Rocha MG, et al. A phase II/III, multicenter, safety, efficacy, and pharmacokinetic study of dexMEDETOMIDine in preterm and term neonates. <i>The Journal of pediatrics</i>. 2014;164(2):276-82. e3.</li> <li>3. Potts AL, Anderson BJ, Warman GR, Lerman J, Diaz SM, Vilo S. DexMEDETOMIDine pharmacokinetics in pediatric intensive care—a pooled analysis. <i>Pediatric Anesthesia</i>. 2009;19(11):1119-29.</li> <li>4. Potts AL, Warman GR, Anderson BJ. DexMEDETOMIDine disposition in children: a population analysis. <i>Pediatric Anesthesia</i>. 2008;18(8):722-30.</li> <li>5. Cimen ZS, Hanci A, Sivrikaya GU, Kilinc LT, Erol MK. Comparison of buccal and nasal dexMEDETOMIDine premedication for pediatric patients. <i>Pediatric Anesthesia</i>. 2013;23(2):134-8.</li> <li>6. Yuen VM, Hui TW, Irwin M, Yao TJ, Wong G, Yuen M. Optimal timing for the administration of intranasal dexMEDETOMIDine for premedication in children. <i>Anaesthesia</i>. 2010;65(9):922-9.</li> <li>7. Li B, Zhang N, Huang J, Qiu Q, Tian H, Ni J, et al. A comparison of intranasal dexMEDETOMIDine for sedation in children administered either by atomiser or by drops. <i>Anaesthesia</i>. 2016;71(5):522-8.</li> <li>8. Mekitarian Filho E, Robinson F, de Carvalho WB, Gilio AE, Mason KP. Intranasal dexMEDETOMIDine for sedation for pediatric computed tomography imaging. <i>The Journal of pediatrics</i>. 2015;166(5):1313-5. e1.</li> <li>9. Tug A, Hanci A, Turk HS, Aybey F, Isil CT, Sayin P, et al. Comparison of two different intranasal doses of dexMEDETOMIDine in children for magnetic resonance imaging sedation. <i>Pediatric Drugs</i>. 2015;17:479-85.</li> <li>10. Yuen VM, Hui T, Irwin M, Yao T, Chan L, Wong G, et al. A randomised comparison of two intranasal dexMEDETOMIDine doses for premedication in children. <i>Anaesthesia</i>. 2012;67(11):1210-6.</li> <li>11. Talon MD, Woodson LC, Sherwood ER, Aarsland A, McRae L, Benham T. Intranasal dexMEDETOMIDine premedication is comparable with midazolam in burn children undergoing reconstructive surgery. <i>Journal of burn care &amp; research</i>. 2009;30(4):599-605.</li> <li>12. Patel V, Singh N, Saksena AK, Singh S, Sonkar S, Jolly SM. A comparative assessment of intranasal and oral dexMEDETOMIDine for procedural sedation in pediatric dental patients. <i>Journal of Indian Society of Pedodontics and Preventive Dentistry</i>. 2018;36(4):370-5.</li> <li>13. Pansini V, Curatola A, Gatto A, Lazzareschi I, Ruggiero A, Chiaretti A. Intranasal drugs for analgesia and sedation in children admitted to pediatric emergency department: a narrative review. <i>Ann Transl Med</i>. 2021;9(2):189.</li> </ol>

14. Merative™ Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: <https://www.micromedexsolutions.com/> (cited: Feb/26/2026).
15. Tobias JD. Tolerance, withdrawal, and physical dependency after long-term sedation and analgesia of children in the pediatric intensive care unit. *Critical care medicine*. 2000;28(6):2122-32.
16. Ng E, Taddio A, Ohlsson A. Intravenous midazolam infusion for sedation of infants in the neonatal intensive care unit. *Cochrane Database of Systematic Reviews*. 2017(1).
17. Kinoshita M, Stempel KS, Borges do Nascimento IJ, Bruschetti M. Systemic opioids versus other analgesics and sedatives for postoperative pain in neonates. *Cochrane Database of Systematic Reviews*. 2023(3).
18. Kinoshita M, Olsson E, Borys F, Bruschetti M. Opioids for procedural pain in neonates. *Cochrane Database of Systematic Reviews*. 2023(6).
19. Kinoshita M, Borges do Nascimento IJ, Styrismisdóttir L, Bruschetti M. Systemic opioid regimens for postoperative pain in neonates. *Cochrane Database of Systematic Reviews*. 2023(4).
20. Bellù R, Romantsik O, Nava C, de Waal KA, Zanini R, Bruschetti M. Opioids for newborn infants receiving mechanical ventilation. *Cochrane Database of Systematic Reviews*. 2021(3).
21. Bajic D, Commons KG, Soriano SG. Morphine-enhanced apoptosis in selective brain regions of neonatal rats. *International Journal of Developmental Neuroscience*. 2013;31(4):258-66.
22. Young C, Jevtovic-Todorovic V, Qin YQ, Tenkova T, Wang H, Labruyere J, et al. Potential of ketamine and midazolam, individually or in combination, to induce apoptotic neurodegeneration in the infant mouse brain. *British journal of pharmacology*. 2005;146(2):189-97.
23. Chen K, Lu Z, Xin YC, Cai Y, Chen Y, Pan SM. Alpha-2 agonists for long-term sedation during mechanical ventilation in critically ill patients. *Cochrane Database of Systematic Reviews*. 2015;1:CD010269.
24. Sanders R, Sun P, Patel S, Li M, Maze M, Ma D. DexMEDETOMIDine provides cortical neuroprotection: impact on anaesthetic-induced neuroapoptosis in the rat developing brain. *Acta Anaesthesiol Scand*. 2010;54(6):710-6.
25. Lim JY, Ker CJ, Lai NM, Romantsik O, Fiander M, Tan K. DexMEDETOMIDine for analgesia and sedation in newborn infants receiving mechanical ventilation. *Cochrane Database of Systematic Reviews*. 2024;5:CD012361.
26. Chrysostomou C, De Toledo JS, Avolio T, Mota MV, Berry D, Morell VO, et al. DexMEDETOMIDine use in a pediatric cardiac intensive care unit: can we use it in infants after cardiac surgery? *Pediatric critical care medicine*. 2009;10(6):654-60.
27. Curtis S, Kilpatrick R, Billimoria ZC, Zimmerman K, Tolia V, Clark R, et al. Use of dexMEDETOMIDine and opioids in hospitalized preterm infants. *JAMA Network Open*. 2023;6(11):e2341033-e.
28. Portelli K, Kandraju H, Ryu M, Shah PS. Efficacy and safety of dexMEDETOMIDine for analgesia and sedation in neonates: A systematic review. *Journal of Perinatology*. 2024;44(2):164-72.
29. Daverio M, Sperotto F, Zanetto L, Coscini N, Frigo AC, Mondardini MC, et al. DexMEDETOMIDine for prolonged sedation in the PICU: a systematic review and meta-analysis. *Pediatric Critical Care Medicine*. 2020;21(7):e467-e74.
30. Sperotto F, Mondardini MC, Dell'Oste C, Vitale F, Ferrario S, Lapi M, et al. Efficacy and safety of dexMEDETOMIDine for prolonged sedation in the PICU: a prospective multicenter study (PROSDEx). *Pediatric Critical Care Medicine*. 2020;21(7):625-36.
31. O'Mara K, Gal P, Wimmer J, Ransom JL, Carlos RQ, Dimaguila MAV, et al. DexMEDETOMIDine versus standard therapy with fentanyl for sedation in mechanically ventilated premature neonates. *The Journal of Pediatric Pharmacology and Therapeutics*. 2012;17(3):252-62.
32. Surkov D. Is dexMEDETOMIDine a potential neuroprotective agent for term neonates with hypoxic-ischemic encephalopathy? *Pediatric Anesthesia & Critical Care Journal (PACCJ)*. 2019;7(1).
33. Naveed M, Bondi DS, Shah PA. DexMEDETOMIDine versus fentanyl for neonates with hypoxic ischemic encephalopathy undergoing therapeutic hypothermia. *The journal of pediatric pharmacology and therapeutics*. 2022;27(4):352-7.

34. Sellas MN, Kyllonen KC, Lepak MR, Rodriguez RJ. DexMEDETOMIDine for the management of postoperative pain and sedation in newborns. *The Journal of Pediatric Pharmacology and Therapeutics*. 2019;24(3):227-33.
35. Iiro T, Vilo S, Manner T, Aantaa R, Lahtinen M, Scheinin M, et al. Bioavailability of dexMEDETOMIDine after intranasal administration. *European journal of clinical pharmacology*. 2011;67:825-31.
36. Yoo H, Iiro T, Vilo S, Manner T, Aantaa R, Lahtinen M, et al. Mechanism-based population pharmacokinetic and pharmacodynamic modeling of intravenous and intranasal dexMEDETOMIDine in healthy subjects. *European journal of clinical pharmacology*. 2015;71:1197-207.
37. Peng K, Wu S-r, Ji F-h, Li J. Premedication with dexMEDETOMIDine in pediatric patients: a systematic review and meta-analysis. *Clinics*. 2014;69(11):777-86.
38. Bellon M, Le Bot A, Michelet D, Hilly J, Maesani M, Brasher C, et al. Efficacy of intraoperative dexMEDETOMIDine compared with placebo for postoperative pain management: a meta-analysis of published studies. *Pain and therapy*. 2016;5:63-80.
39. Schnabel A, Reichl SU, Poepping DM, Kranke P, Pogatzki-Zahn EM, Zahn PK. Efficacy and safety of intraoperative dexMEDETOMIDine for acute postoperative pain in children: a meta-analysis of randomized controlled trials. *Pediatric Anesthesia*. 2013;23(2):170-9.
40. Wang W, Huang P, Gao W, Cao F, Yi M, Chen L, et al. Efficacy and acceptability of different auxiliary drugs in pediatric sevoflurane anesthesia: a network meta-analysis of mixed treatment comparisons. *Scientific Reports*. 2016;6(1):36553.
41. Dilek Ö, Yasemin G, Atci M. Preliminary experience with dexMEDETOMIDine in neonatal anesthesia. *Journal of Anaesthesiology Clinical Pharmacology*. 2011;27(1):17-22.
42. Lam F, Bhutta AT, Tobias JD, Gossett JM, Morales L, Gupta P. Hemodynamic effects of dexMEDETOMIDine in critically ill neonates and infants with heart disease. *Pediatric cardiology*. 2012;33:1069-77.
43. Bong CL, Tan J, Lim S, Low Y, Sim S-W, Rajadurai VS, et al. Randomised controlled trial of dexMEDETOMIDine sedation vs general anaesthesia for inguinal hernia surgery on perioperative outcomes in infants. *British journal of anaesthesia*. 2019;122(5):662-70.
44. Zhou L-J, Fang X-Z, Gao J, Zhangm Y, Tao L-J. Safety and efficacy of dexMEDETOMIDine as a sedative agent for performing awake intubation: a meta-analysis. *American journal of therapeutics*. 2016;23(6):e1788-e800.
45. Oschman A, McCabe T, Kuhn RJ. DexMEDETOMIDine for opioid and benzodiazepine withdrawal in pediatric patients. *American Journal of Health-System Pharmacy*. 2011;68(13):1233-8.
46. Chrysostomou C, Morell VO, Wearden P, Sanchez-de-Toledo J, Jooste EH, Beerman L. DexMEDETOMIDine: therapeutic use for the termination of reentrant supraventricular tachycardia. *Congenit*. 2013;8(1):48-56.
47. van Hoorn CE, Hoeks SE, Essink H, Tibboel D, de Graaff JC. A systematic review and narrative synthesis on the histological and neurobehavioral long-term effects of dexMEDETOMIDine. *Pediatric Anesthesia*. 2019;29(2):125-36.
48. Finkel JC, Quezado ZM. Hypothermia-induced bradycardia in a neonate receiving dexMEDETOMIDine. *Journal of clinical anesthesia*. 2007;19(4):290-2.
49. Kubota T, Fukasawa T, Kitamura E, Magota M, Kato Y, Natsume J, et al. Epileptic seizures induced by dexMEDETOMIDine in a neonate. *Brain and Development*. 2013;35(4):360-2.
50. Burbano NH, Otero AV, Berry DE, Orr RA, Munoz RA. Discontinuation of prolonged infusions of dexMEDETOMIDine in critically ill children with heart disease. *Intensive care medicine*. 2012;38:300-7.
51. Liu J, Miller J, Ferguson M, Bagwell S, Bourque J. The impact of a clonidine transition protocol on dexMEDETOMIDine withdrawal in critically ill pediatric patients. *The Journal of Pediatric Pharmacology and Therapeutics*. 2020;25(4):278-87.
52. Whalen LD, Di Gennaro JL, Irby GA, Yanay O, Zimmerman JJ. Long-term dexMEDETOMIDine use and safety profile among critically ill children and neonates. *Pediatric Critical Care Medicine*. 2014;15(8):706-14.

53. Haenecour AS, Seto W, Urbain CM, Stephens D, Laussen PC, Balit CR. Prolonged dexMEDETOMIDine infusion and drug withdrawal in critically ill children. *The Journal of Pediatric Pharmacology and Therapeutics*. 2017;22(6):453-60.
54. Greenberg RG, Wu H, Laughon M, Capparelli E, Rowe S, Zimmerman KO, et al. Population pharmacokinetics of dexMEDETOMIDine in infants. *The Journal of Clinical Pharmacology*. 2017;57(9):1174-82.
55. Su F, Gastonguay MR, Nicolson SC, DiLiberto M, Ocampo-Pelland A, Zuppa AF. DexMEDETOMIDine pharmacology in neonates and infants after open heart surgery. *Anesthesia & Analgesia*. 2016;122(5):1556-66.
56. Jooste E, Muhly W, Ibinson J, Suresh T, Damian D, Phadke A, et al. Acute hemodynamic changes after rapid intravenous bolus dosing of dexMEDETOMIDine in pediatric heart transplant patients undergoing routine cardiac catheterization. *Anesthesia & Analgesia*. 2010;111(6):1490-6.
57. Hauber JA, Davis PJ, Bendel LP, Martyn SV, McCarthy DL, Evans M-C, et al. DexMEDETOMIDine as a rapid bolus for treatment and prophylactic prevention of emergence agitation in anesthetized children. *Anesthesia & Analgesia*. 2015;121(5):1308-15.
58. Dawes J, Myers D, Görges M, Zhou G, Ansermino JM, Montgomery CJ. Identifying a rapid bolus dose of dexMEDETOMIDine (ED 50) with acceptable hemodynamic outcomes in children. *Pediatric Anesthesia*. 2014;24(12):1260-7.
59. Chen F, Wang C, Lu Y, Huang M, Fu Z. Efficacy of different doses of dexMEDETOMIDine as a rapid bolus for children: a double-blind, prospective, randomized study. *BMC anesthesiology*. 2018;18:1-7.

**Appendix**

**Infusion tables to assist concentration selection**

**Table 1:** Infusion rates when using dexMEDETOMIDine concentration **1 microgram/mL** (suggested for weight <1 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
1	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
1.5	0.07	0.13	0.2	0.27	0.33	0.4	0.47	0.53	0.6	0.67
2	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
2.5	0.04	0.08	0.12	0.16	0.2	0.24	0.28	0.32	0.36	0.4
3	0.03	0.07	0.1	0.13	0.17	0.2	0.23	0.27	0.3	0.33
3.5	0.03	0.06	0.09	0.11	0.14	0.17	0.2	0.23	0.26	0.29
4	0.03	0.05	0.08	0.1	0.13	0.15	0.18	0.2	0.23	0.25
4.5	0.02	0.04	0.07	0.09	0.11	0.13	0.16	0.18	0.2	0.22
5	0.02	0.04	0.06	0.08	0.1	0.12	0.14	0.16	0.18	0.2

**Table 2:** Infusion rates when using dexMEDETOMIDine concentration **2 microgram/mL**  
(suggested for weight 1 to <3 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	0.4	0.8	1.2	1.6	2	2.4	2.8	3.2	3.6	4
1	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
1.5	0.13	0.27	0.4	0.53	0.67	0.8	0.93	1.07	1.2	1.33
2	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
2.5	0.08	0.16	0.24	0.32	0.4	0.48	0.56	0.64	0.72	0.8
3	0.07	0.13	0.2	0.27	0.33	0.4	0.47	0.53	0.6	0.67
3.5	0.06	0.11	0.17	0.23	0.29	0.34	0.4	0.46	0.51	0.57
4	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
4.5	0.04	0.09	0.13	0.18	0.22	0.27	0.31	0.36	0.4	0.44
5	0.04	0.08	0.12	0.16	0.2	0.24	0.28	0.32	0.36	0.4

**Table 3:** Infusion rates when using dexMEDETOMIDine concentration **4 microgram/mL**  
(suggested for weight ≥3 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	Approximate micrograms/kg/hour									
0.5	0.8	1.6	2.4	3.2	4	4.8	5.6	6.4	7.2	8
1	0.4	0.8	1.2	1.6	2	2.4	2.8	3.2	3.6	4
1.5	0.3	0.5	0.8	1.1	1.3	1.6	1.9	2.1	2.4	2.7
2	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
2.5	0.16	0.32	0.48	0.64	0.8	0.96	1.12	1.28	1.4	1.6
3	0.13	0.27	0.4	0.53	0.67	0.8	0.93	1.07	1.2	1.3
3.5	0.11	0.23	0.34	0.46	0.57	0.69	0.8	0.91	1	1.1
4	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
4.5	0.09	0.18	0.27	0.36	0.44	0.53	0.62	0.71	0.8	0.9
5	0.08	0.16	0.24	0.32	0.4	0.48	0.56	0.64	0.7	0.8

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

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

VERSION/NUMBER	DATE
Original 1.0	16/06/2025
Version 1.1	27/02/2026
REVIEW	27/02/2031

This standard concentration formulary has been developed by the ANMF standard concentration working group. The working group (in alphabetical order): Mohammad Irfan Azeem, Susanah Brew, Cindy Chen, Michelle Jenkins, Kerrie Knox, Rebecca O’Grady

**Authors Contribution of the current version**

Author/s	Srinivas Bolisetty, Bhavesh Mehta
Evidence Review	Srinivas Bolisetty
Nursing Review	Celia Cunha Brites
Pharmacy Review	Kerrie Knox, Susannah Brew, Michelle Jenkins
ANMF Group contributors	Nilkant Phad, Rebecca Barzegar, Amber Seigel, Jutta van den Boom, Mohammed Irfan Azeem, Susannah Brew, Thao Tran, Cindy Chen, Michelle Jenkins, Kerrie Knox, Renae Gengaroli, Bryony Malloy, Samantha Hassall, Benjamin Emerson-Parker, Simarjit Kaur
Final editing	Rebecca O’Grady
Facilitator	Srinivas Bolisetty