DEXMEDETOMIDINE

Newborn use only

2021

<table>
<tr><td>Alert</td><td>Use only where cardiac monitoring and cardiorespiratory resuscitation equipment are available.
Dexmedetomidine is not FDA or TGA approved for use in children.
There are insufficient trial data evaluating the use of dexmedetomidine in newborn infants.</td></tr>
<tr><td>Indication</td><td>Sedation for agitated ventilated patients.
Adjunct therapy with inhalational anaesthesia for both perioperative and postoperative procedures.
Sedation with nerve blocking agents for surgical procedures.</td></tr>
<tr><td>Action</td><td>Centrally acting α2-agonist with sedative, anxiolytic, sympatholytic and analgo-sedative properties. Haemodynamic effects including transient hypertension, bradycardia and hypotension resulting from the drug's peripheral vasoconstrictive and sympatholytic properties. Dexmedetomidine exerts its hypnotic action through activation of central pre- and postsynaptic α2-receptors in the locus coeruleus, inducing a state of unconsciousness similar to natural sleep, except patients remain rousable.[1, 2]</td></tr>
<tr><td>Drug type</td><td>Central Nervous System - Sedative, hypnotic - centrally acting α2-agonist</td></tr>
<tr><td>Trade name</td><td>Dexmedetomidine Mylan Concentrate for infusion
Dexmedetomidine Ever Pharma Concentrate for infusion
Dexmedetomidine Sandoz Concentrate for infusion
Dexmedetomidine-Teva Concentrate for infusion
Precedex Concentrate for infusion
Precedex Ready to Use Solution for infusion</td></tr>
<tr><td>Presentation</td><td>Dexmedetomidine Mylan Concentrate for infusion – 100 microgram/mL 2 mL vial.
Dexmedetomidine Ever Pharma Concentrate for infusion – 100 microgram/mL 2 mL, 4 mL, 10 mL vials; 50 microgram/mL 2 mL ampoule.
Dexmedetomidine Sandoz Concentrate for infusion – 100 microgram/mL 2 mL vial.
Dexmedetomidine-Teva Concentrate for infusion – 100 microgram/mL 2 mL vial.
Precedex Concentrate for infusion – 100 microgram/mL; 2 mL vial.
Precedex Ready to Use Solution for infusion – 4 microgram/mL; 20 mL vial; 4 microgram/mL 50 mL and 100 mL glass bottles.</td></tr>
<tr><td>Dose</td><td>IV
<table>
<tr><th>Refs: [3-5]</th><th>Loading dose [if needed] over 15 minutes</th><th>Infusion</th><th>Maximum dose</th></tr>
<tr><td>Preterm < 37 weeks gestation</td><td>0.2 microgram/kg/dose</td><td>0.2 microgram/kg/hour</td><td>1 microgram/kg/hour</td></tr>
<tr><td>Term infants ≤ 14 days</td><td>0.35 microgram/kg/dose</td><td>0.3 microgram/kg/hour</td><td>1.2 microgram/kg/hour</td></tr>
<tr><td>Term infants > 14 days</td><td>0.5 microgram/kg/dose</td><td>0.5 to 0.75 microgram/kg/hour</td><td>1.5 microgram/kg/hour</td></tr>
</table>
Incremental increase
Every 30 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.
Incremental decrease
Infusion should usually be weaned rather than discontinued abruptly, especially if used for greater than 72 hours.
Either:
Decrease the dose by 0.1 microgram/kg/hour every 30 minutes, OR
Decrease the infusion rate by 0.2 microgram/kg/hour every 8 hours.

It is not necessary to discontinue dexmedetomidine prior to extubation especially in postoperative patients.</td></tr>
<tr><td>Dose adjustment</td><td>Therapeutic hypothermia: No information.</td></tr>
</table>

	ECMO: Reduce dose to 0.24 microgram/kg/hour for neonates and 0.29 microgram/kg/hour for infants aged ≥3 months. [4, 5,27] Renal: Not applicable. Hepatic: Clearance decreases in impairment; consider reducing the dose and titrating carefully.
Maximum dose	Refer to dosing table.
Total cumulative dose	
Route	IV infusion. NOT FOR IV BOLUS ADMINISTRATION.
Preparation	Low concentration (consider for loading dose and initial infusion rate) Add 25 microgram/kg dexmedetomidine to sodium chloride 0.9% or glucose 5% to make a final volume of 50 mL with a concentration of 0.5 microgram/kg/mL. Gently mix the solution. 1 mL/hour = 0.5 microgram/kg/hour. **Consider higher concentrations if fluid restriction is required:** High concentration (consider this for an infusion dose higher than 0.5 microgram/kg/hour) Add 50 microgram/kg dexmedetomidine to sodium chloride 0.9% or glucose 5% to make a final volume of 50 mL with a concentration of 1.0 microgram/kg/mL. Gently mix the solution. 1 mL/hour = 1 microgram/kg/hour. Very high concentration (consider this for an infusion dose of 1 microgram/kg/hour or in fluid restricted infants) Add 100 microgram/kg dexmedetomidine to sodium chloride 0.9% or glucose 5% to make a final volume of 50 mL with a concentration of 2.0 microgram/kg/mL. Gently mix the solution. 1 mL/hour = 2 microgram/kg/hour. Precedex Ready to Use® solution (4 microgram/mL) can be diluted if required (as per consensus).
Administration	IV infusion using a syringe infusion pump. Infusion should not be placed on any infusion line where boluses may be given.
Monitoring	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.
Contraindications	1. Hypersensitivity to the medication or any of the excipients. 2. Heart block or severe ventricular dysfunction.
Precautions	1. 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. 2. Hypovolaemia. 3. Bradycardia. 4. Dosage reductions should be considered in patients with hepatic impairment or with concomitant use of other sedatives and analgesics. 5. 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.
Drug interactions	Enhances the effects of anaesthetics, sedatives, hypnotics and opioids.
Adverse reactions	• Severe bradycardia, arrhythmias and cardiac arrest. • 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. • Bradycardia and hypotension may be potentiated when dexmedetomidine is used concurrently with propofol or midazolam.

	• Nausea, fever, vomiting, hypoxia and anaemia. • Hypothermia. • Seizures.
Compatibility	Fluids: Glucose 5% and sodium chloride 0.9%. Y site: Giving other drugs via Y-site may change the infusion rate of dexmedetomidine. Adrenaline (epinephrine), alfentanil, amikacin, aminophylline, amiodarone, amphotericin B liposome, ampicillin, azithromycin, aztreonam, calcium gluconate, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, cisatracurium, clindamycin, dexamethasone, digoxin, dobutamine, dolasetron, dopamine, droperidol, ephedrine sulfate, erythromycin, esmolol, fentanyl, fluconazole, furosemide (frusemide), gentamicin, glyceryl trinitrate, glycopyrronium bromide (glycopyrrolate), heparin, hydromorphone, ketamine, lidocaine (lignocaine), linezolid, magnesium sulfate, methylprednisolone sodium succinate, metoclopramide, metronidazole, midazolam, milrinone, morphine, naloxone, noradrenaline (norepinephrine), pancuronium, paracetamol, piperacillin-tazobactam (EDTA-free), phenobarbital (phenobarbitone0, potassium chloride, promethazine, propofol, ranitidine, remifentanil, rocuronium, sodium bicarbonate, sodium nitroprusside, suxamethonium, thiopental sodium, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, vecuronium, verapamil.
Incompatibility	Amphotericin B conventional colloidal, amphotericin B lipid complex, diazepam, pantoprazole, phenytoin.
Stability	Reconstituted dexmedetomidine infusion is stable for 24 hours.
Storage	Store below 25°C in the original container.
Excipients	Sodium chloride 9 mg/mL, water for injections.
Special comments	
Evidence	Dexmedetomidine is approved for sedation in adult intensive care patients, and is increasingly used off-label in paediatric patients to prevent agitation: as premedication in the form of intranasal, buccal and oral solution, as an adjunct for elective surgery; as a sedative for magnetic resonance imaging; as intraoperative analgesia; for extracorporeal shock wave lithotripsy; as an adjuvant for nerve blocks; and intravenously in intensive care units with the purpose of sedation of children. [6] Compared with clonidine (an α2-agonist that has been used for several decades), dexmedetomidine has a greater selectivity for α2-receptors (α2: α1 ratio of 1620:1 vs. 220:1). As central α1-adrenoceptor activation counteracts the sedative α2 effects, dexmedetomidine is a more potent sedative than clonidine. **Efficacy** **Sedation for agitated ventilated patients:** A Cochrane systematic review including seven studies covering 1624 participants found that compared with other sedatives, long-term sedation using dexmedetomidine in critically ill adults reduced the duration of mechanical ventilation and ICU length of stay. Dexmedetomidine 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. There was no evidence that dexmedetomidine changed the overall death rate. [LOE I in adults] Children, infants and newborns were not included. [7] A systematic review published in abstract form only reported 31 studies of prolonged dexmedetomidine sedation in paediatric patients involving a total of 3342 patients with nearly all being case series (94%) and retrospective (87%). No randomised trials were found. [8] A RCT of dexmedetomidine use in term neonates with moderate to severe hypoxic ischaemic encephalopathy is awaiting publication. [9] A dose escalation study [10] 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 dexmedetomidine: 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 analgaesia (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 dexmedetomidine: 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 dexmedetomidine alone, although doses up to 0.2 microgram/kg/hour were not sufficient in most term neonates.

O'Mara et al [11] reported a case control study of 48 preterm neonates requiring mechanical ventilation who received fentanyl (n=24) or dexmedetomidine (n=24) for pain or sedation. Dexmedetomidine 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 dexmedetomidine 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.

Conclusion: There are no data from RCTs supporting the use of dexmedetomidine for sedation of ventilated children, infants or newborns. RCTs are required to determine the effectiveness and safety of dexmedetomidine in ventilated newborn infants. [LOE IV newborn infants]

Adjunct with inhalational anaesthesia for procedures: A systematic review [12] of RCTs in paediatric patients undergoing inhalational anaesthesia using sevoflurane included 14 RCTs involving painful procedures in children and infants of whom 777 received dexmedetomidine and 693 received placebo. No trial enrolled newborns. Bolus dexmedetomidine dose ranged from 0.3 to 2 microgram/kg and maintenance dose 0.1 to 0.7 microgram/kg/hour. Intraoperative dexmedetomidine was associated with reduced postoperative opioid use in the post-anaesthesia care unit [RR 0.31 (0.17, 0.59), I^2= 76%, p<0.0001], decreased post-operative pain intensity [SMD -1.18 (-1.88, -0.48), I^2 = 91%, p<0.0001] but had no effect upon postoperative nausea and vomiting incidence [RR = 0.67 (0.41, 1.08), I^2 = 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 [13] 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. [LOE I in infants and children]

A network meta-analysis of RCTs [14] 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 analgaesia 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. [15-17] Ozcengiz et al [16] reported 16 newborns aged 2-28 days who underwent general anaesthesia using dexmedetomidine and sevoflurane for abdominal surgical procedures. Excluded from the report were 4 infants who experienced bradycardia treated with atropine which led to a change in the induction protocol. Anaesthesia was induced with 1 microgram/kg ketamine intravenously, then dexmedetomidine 1 µg/kg infused over 10 minutes. Maintenance infusion was started as 0.5-0.8 µg/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 [15] 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 [17] 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. [LOE IV newborns]

Dexmedetomidine sedation with nerve blocks for surgical procedures: In a RCT [18] 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%. [18] [LOE II neonates]

Acute withdrawal from opioids: Reports on dexmedetomidine use for opioid withdrawal are limited to case studies and retrospective reviews involving a total of 20 paediatric patients.[19] 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 [20] 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. [LOE II GOR B]

Safety

When used for long-term sedation during mechanical ventilation in critically ill patients, dexmedetomidine doubled the incidence of bradycardia, with heterogeneous other effects compared to other agents including hypotension, hypertension, tachycardia, first degree heart block, hyperglycaemia and hypoglycaemia. [7]

In animal studies, there was no histological neurological injury associated with dexmedetomidine when administered by itself, and 13 of 16 studies reported beneficial neuroprotective effects of dexmedetomidine when administrated with other anaesthetics. [1] However, studies are lacking about the long-term neurobehavioral effects when administered in children for sedation or anaesthesia. A RCT to determine the long-term neurobehavioral effects of dexmedetomidine in children (compared to currently used neurotoxic anaesthetics), with the ultimate aim to find a safer alternative to the currently used neurotoxic anaesthetics in children is needed. [1]

Limited observational studies in newborn infants have reported dexmedetomidine to be generally well-tolerated and safe, although not without side effects particularly with use of bolus doses. [3, 11, 15, 17] In a dose escalation study in 42 newborns receiving mechanical ventilation, inadequate analgaesia was reported in 17 (40%) and inadequate sedation in 4 (10%), with 3 (5%) adverse events attributed to dexmedetomidine. [3] A report of use of dexmedetomidine for induction of anaesthesia in newborns reported 4 infants experiencing bradycardia which responded to atropine, resulting in a change in the induction protocol. [16] In postoperative neonatal surgical patients receiving prolonged infusion, dexmedetomidine resulted in a significant decrease in the cumulative dose of opioid but was associated with more episodes of bradycardia (12.8% versus 5.1%) than opioids alone. Hypothermia has been reported in newborns receiving dexmedetomidine for perioperative sedation. [16, 21] There is a case report of a newborn infant with electrical seizures during administration of dexmedetomidine which ceased following discontinuation. [22] In a RCT in 104 infants (75% born premature), allocated to dexmedetomidine sedation with caudal block versus general sevoflurane anaesthesia with tracheal intubation and caudal block for elective bilateral inguinal hernia surgery, infants in the dexmedetomidine group had significantly lower heart rates and higher mean arterial pressures intraoperatively, and 9.8% required additional anaesthetic agents or conversion to general anaesthesia. [18]

Withdrawal from prolonged dexmedetomidine infusion (>72 hours) was reported to result in increased heart rate and blood pressure, reduced COMFORT scores, and 30%, whether weaned or abruptly stopped, had withdrawal symptoms including agitation, tremor and decreased sleep. [23]

Dexmedetomidine has been reported to be safe in paediatric patients with congenital heart disease and is not associated with any significant ECG interval abnormalities other than a trend towards lower heart rate. [24] The therapeutic use of dexmedetomidine has been reported for acute termination of re-entrant supraventricular tachycardia (SVT) in 15 infants aged 6 to 16 days. Twenty seven doses of dexmedetomidine (mean dose 0.7 +/- 0.3 microgram/kg) for a total of 27 episodes of SVT. [25]

Pharmacokinetics

Dexmedetomidine is an α2-adrenoceptor agonist with sedative, anxiolytic, sympatholytic, and analgesic sparing effects, and minimal depression of respiratory function. It is potent and highly selective for α2-receptors with an α2: α1 ratio of 1620:1. Dexmedetomidine exerts its hypnotic action through activation of central pre- and postsynaptic α2-receptors in the locus coeruleus. Hemodynamic effects include transient hypertension, bradycardia, and hypotension resulting from the drug's peripheral vasoconstrictive and sympatholytic properties. Dexmedetomidine is rapidly distributed and is mainly hepatically metabolised into inactive metabolites by glucuronidation and hydroxylation (cytochrome P450 enzymes). 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. Dexmedetomidine is eliminated mainly through biotransformation by the liver with an extraction ratio of 0.7 reported. Less than 1% is excreted unchanged with metabolites being excreted renally (95%) and faecally (4%). Direct N-glucuronidation accounts for about 34% of dexmedetomidine metabolism. An elimination half-life of 2.1–3.1 hours is reported in healthy volunteers, and 2.2 to 3.7 hours in ICU patients. The sedative effect of dexmedetomidine is concentration dependent, with plasma concentrations between 0.2 and

	0.3 ng/mL resulting in significant and rousable sedation in adults, and unarousable deep sedation at plasma concentrations above 1.9 ng/mL. [2] 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 µg/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.[26] 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.[3] In a pharmacokinetic study [4, 5] 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 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 µg/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. [4, 5] 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 µg/kg/hour in neonates and 0.75 µg/kg/hour in infants was well tolerated after open heart surgery. [27] Conclusion: Dexmedetomidine has reduced clearance and a longer half-life in preterm compared to term infants, and term infants compared to older infants. [3-5] 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 [4, 5] and with concomitant use of other sedatives or analgesics.
Practice points	**Sedation for agitated ventilated patients:** There is insufficient trial data evaluating the use of dexmedetomidine in newborn infants. (LOE IV, dose escalation study) **For sedation with nerve blocks for surgical procedures:** Dexmedetomidine sedation loading dose 2-3 microgram/kg with maintenance dose 0.2 microgram/kg/hour with caudal block provides a feasible alternative to general anaesthesia in infants undergoing hernia surgery although supplemental anaesthesia was required in 9.8%. [18] [LOE II neonates] **Acute withdrawal from opioids:** There are insufficient data of the use of Dexmedetomidine for treatment of NAS so its use is not recommended for this indication. Clonidine may be preferred with its reduced sedative properties.
References	1. 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. Paediatr Anaesth. 2019;29:125-36. 2. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine. Clinical Pharmacokinetics. 2017;56:893-913.

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Authors Contribution

Original author/s	Srinivas Bolisetty, David Osborn
Evidence Review	David Osborn
Expert review	Dr Hari Ravindranathan, Dr Donald Hannah, Dr David Schell
Nursing Review	Ms Eszter Jozsa
Pharmacy Review	Ms Michelle Jenkins, Ms Cindy Chen, Ms Carmen Burman
ANMF Group contributors	Dr Himanshu Popat, Dr Nilkant Phad, Ms Carmen Burman, Ms Thao Tran, Ms Chantelle Smith, Mr James Marceau, Ms Emily Do, Ms Wendy Huynh
Final editing and review of the original	Dr Ian Whyte, Dr Srinivas Bolisetty, Assoc Prof David Osborn, Ms Wendy Huynh, Ms Thao Tran,
Electronic version	Dr Ian Callander, Ms Cindy Chen
Facilitator	Dr Srinivas Bolisetty