

Alert	Hypertension may recur after cessation. Neonatal abstinence syndrome may recur after cessation. Evidence is insufficient to assess the efficacy and safety of clonidine for sedation and analgesia in term and preterm newborn infants receiving mechanical ventilation.
Indication	Sedation Hypertension Neonatal abstinence syndrome
Action	A central α_2 -adrenergic agonist with inhibitory effects on the release of noradrenaline in the locus coeruleus. This produces reduced sympathetic nervous activity with analgesia, and a decrease in arousability, blood pressure and heart rate. ^{1,2} Compared with dexmedetomidine, clonidine has a lower selectivity for α_2 -receptors (α_1 : α_2 ratio of 1:1620 for dexmedetomidine versus 1:220 for clonidine). As central α_2 effects are sedative, clonidine is less sedating than dexmedetomidine.
Drug type	Sedative, hypnotic. Centrally acting α_2 -agonist.
Trade name	IV: Catapres Ampoules, MZ Clonidine HCl Injection Oral: APO-Clonidine Tablets, Catapres 100 Tablets, Catapres 150 Tablets, Clonidine Lupin Tablets, solution or suspension compounded by pharmacy in-house (check which strength is stocked with Pharmacy Department).
Presentation	IV preparations: 150 microgram/mL ampoule Oral preparations: 100 microgram/tablet, 150 microgram/tablet Solution or suspension compounded by pharmacy in-house (check which strength is stocked with Pharmacy Department). (Preferred) IV clonidine (ampoule) may be given orally either neat or diluted with water prior to administration to give a suitable dose volume.
Dose	Sedation: IV continuous infusion: Loading dose of 0.5 to 1 microgram/kg over 15 minutes followed by a continuous infusion of 0.2 microgram/kg/hour and titrate up to a maximum of 1 microgram/kg/hour in hemodynamically stable neonates. ^{2,3,4} ORAL OR IV intermittent dosing: 1 microgram/kg/dose 8 hourly and titrate it up to a maximum 2 micrograms/kg/dose 6 hourly. ^{1,5-8} (Group consensus) Chronic hypertension: Oral: 0.5 to 2.5 microgram/kg/dose 6 to 8 hourly. ^{9,10} Neonatal abstinence syndrome (ANMF consensus): ^{1,5,6,16,28,29} Oral starting dose: 0.5 – 1 microgram/kg/dose 4 to 6 hourly and titrate the dose as per the need. Increase dose by 25% every 24 hours to a maximum 12 microgram/kg/day according to neonatal abstinence syndrome scores. ^{1,6} Weaning/ceasing clonidine: If a neonate has received regular clonidine for >5 days, the dose should be weaned by about 50% each day for 2 to 3 days (reflecting an average half-life of 17 hours in neonates) before ceasing the drug. Watch for tachycardia, hypertension, sweating, agitation, but remember these may also be opioid withdrawal symptoms. ⁶ Intravenous clonidine can be converted to oral/nasogastric route when requirements are less than 0.75 microgram/kg/hour. The same daily dose is divided into 3 doses for 8 hourly administration (i.e. 4 to 6 microgram/kg orally every 8 hours). [Group consensus]

Dose adjustment	Therapeutic hypothermia: no information. ECMO: no information. Renal: commence on a low dose in infants with renal impairment and adjust according to response. Hepatic: not applicable.																																												
Maximum dose	IV infusion for sedation: 2 microgram/kg/hour has been reported. ^{4,11} Neonatal abstinence syndrome: 12 microgram/kg/day. ^{1,6} Hypertension: 25 microgram/kg/day has been reported. However, it is recommended to use in combination with other antihypertensive agents rather than at higher dose as a single agent. ¹⁰																																												
Route	IV Oral																																												
Preparation	<p>IV continuous infusion Note: Refer to Appendix for tables to assist with concentration selection.</p> <p>NOTE: Use the smallest volume syringe available/suitable for drawing up the drug for the preparation. (e.g. for <1 mL draw up – use 1 mL syringe). For 10 mL syringe - Recommend using syringe that has markings at 0.2mL increments.</p> <p>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</p> <table border="1" style="width: 100%; border-collapse: collapse; margin-bottom: 10px;"> <thead> <tr> <th style="text-align: left;">Infant weight</th> <th style="text-align: center;"><1.5 kg</th> <th style="text-align: center;">1.5 to 4 kg</th> <th style="text-align: center;">> 4 kg</th> </tr> </thead> <tbody> <tr> <td style="text-align: left;">Suggested clonidine concentration</td> <td style="text-align: center;">0.5 microgram/mL</td> <td style="text-align: center;">3 microgram/mL</td> <td style="text-align: center;">6 microgram/mL</td> </tr> <tr> <td style="text-align: left;">0.2 microgram/kg/hr is equal to</td> <td style="text-align: center;">0.4 mL/kg/hour</td> <td style="text-align: center;">0.067 mL/kg/hour</td> <td style="text-align: center;">0.033 mL/kg/hour</td> </tr> </tbody> </table> <p>20 mL Syringe It is a 2-step dilution. Step 1: Draw up clonidine and add compatible fluid* to make a diluted solution as per table below:</p> <table border="1" style="width: 100%; border-collapse: collapse; margin-bottom: 10px;"> <thead> <tr> <th style="text-align: left;">Clonidine concentration</th> <th style="text-align: center;">0.5 microgram/mL</th> <th style="text-align: center;">3 microgram/mL</th> <th style="text-align: center;">6 microgram/mL</th> </tr> </thead> <tbody> <tr> <td style="text-align: left;">Volume of clonidine (150 microgram/mL)</td> <td style="text-align: center;">1 mL (150 microgram)</td> <td style="text-align: center;">1 mL (150 microgram)</td> <td style="text-align: center;">1 mL (150 microgram)</td> </tr> <tr> <td style="text-align: left;">Volume of compatible fluid*</td> <td style="text-align: center;">14 mL</td> <td style="text-align: center;">14 mL</td> <td style="text-align: center;">14 mL</td> </tr> <tr> <td style="text-align: left;">Total volume</td> <td style="text-align: center;">15 mL (10 microgram/mL)</td> <td style="text-align: center;">15 mL (10 microgram/mL)</td> <td style="text-align: center;">15 mL (10 microgram/mL)</td> </tr> </tbody> </table> <p>Step 2: Draw up diluted clonidine and add compatible fluid* as per table below to make a final volume of 20 mL</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left;">Clonidine concentration</th> <th style="text-align: center;">0.5 microgram/mL</th> <th style="text-align: center;">3 microgram/mL</th> <th style="text-align: center;">6 microgram/mL</th> </tr> </thead> <tbody> <tr> <td style="text-align: left;">Volume of diluted clonidine from step 1</td> <td style="text-align: center;">1 mL (10 microgram)</td> <td style="text-align: center;">6 mL (60 microgram)</td> <td style="text-align: center;">12 mL (120 microgram)</td> </tr> <tr> <td style="text-align: left;">Volume of compatible fluid*</td> <td style="text-align: center;">19 mL</td> <td style="text-align: center;">14 mL</td> <td style="text-align: center;">8 mL</td> </tr> <tr> <td style="text-align: left;">Total volume</td> <td style="text-align: center;">20 mL</td> <td style="text-align: center;">20 mL</td> <td style="text-align: center;">20 mL</td> </tr> </tbody> </table> <p>* Compatible fluid: sodium chloride 0.9% only</p>	Infant weight	<1.5 kg	1.5 to 4 kg	> 4 kg	Suggested clonidine concentration	0.5 microgram/mL	3 microgram/mL	6 microgram/mL	0.2 microgram/kg/hr is equal to	0.4 mL/kg/hour	0.067 mL/kg/hour	0.033 mL/kg/hour	Clonidine concentration	0.5 microgram/mL	3 microgram/mL	6 microgram/mL	Volume of clonidine (150 microgram/mL)	1 mL (150 microgram)	1 mL (150 microgram)	1 mL (150 microgram)	Volume of compatible fluid*	14 mL	14 mL	14 mL	Total volume	15 mL (10 microgram/mL)	15 mL (10 microgram/mL)	15 mL (10 microgram/mL)	Clonidine concentration	0.5 microgram/mL	3 microgram/mL	6 microgram/mL	Volume of diluted clonidine from step 1	1 mL (10 microgram)	6 mL (60 microgram)	12 mL (120 microgram)	Volume of compatible fluid*	19 mL	14 mL	8 mL	Total volume	20 mL	20 mL	20 mL
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50 mL Syringe

It is a 2-step dilution.

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

Clonidine concentration	0.5 microgram/mL	3 microgram/mL	6 microgram/mL
Volume of clonidine (150 microgram/mL)	1 mL (150 microgram)	1 mL (150 microgram)	2 mL (300 microgram)
Volume of compatible fluid*	14 mL	14 mL	8 mL
Total volume	15 mL (10 microgram/mL)	15 mL (10 microgram/mL)	10 mL (30 microgram/mL)

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

Clonidine concentration	0.5 microgram/mL	3 microgram/mL	6 microgram/mL
Volume of diluted clonidine from step 1	2.5 mL (25 microgram)	15 mL (150 microgram)	10 mL (300 microgram)
Volume of compatible fluid*	47.5 mL	35 mL	40 mL
Total volume	50 mL	50 mL	50 mL

* Compatible fluid: sodium chloride 0.9% only

IV intermittent dose

Step 1:

Draw up 1 mL (150 microgram) of Clonidine and add to 5 mL of sodium chloride 0.9% to make a final volume of 6 mL with a concentration of **25 microgram/mL**.

Step 2:

FURTHER DILUTE

Draw up 0.8 mL (20 microgram) and add to sodium chloride 0.9% to make a final volume of 20 mL with a concentration of 1 microgram/mL.

Oral

Solution or suspension:

Compounded by pharmacy in-house (check which strength is stocked with Pharmacy Department).

Tablet:

100 microgram tablets

1. Disperse 100 microgram tablet in 20 mL of water for injections to make concentration of 5 microg/mL.
2. Shake or stir until an even dispersion is formed. Tablet will disperse within 2 minutes.
3. Administer the required dose immediately, discard any remaining solution.

150 microgram tablets

1. Disperse 150 microgram tablet in 30 mL of water for injections to make concentration of 5 microg/mL.
2. Shake or stir until an even dispersion is formed. Tablet will disperse within 2 minutes.
3. Administer the required dose immediately, discard any remaining solution.

	<p>IV clonidine (ampoule)</p> <p>May be given orally as either neat or diluted with water prior to administration to give a suitable dose volume.</p> <p>10 microgram/mL</p> <ol style="list-style-type: none"> 1. Draw up 1 mL (150 microgram) of clonidine 2. Make up to 15 mL using water for injections making a 10 microgram/mL solution 3. Administer required dose immediately, discard remaining solution <p>1 microgram/mL</p> <ol style="list-style-type: none"> 1. Draw up 1 mL (10 microgram) of above 10 microgram/mL clonidine solution 2. Make up to 10 mL using water injections making a 1 microg/mL solution 3. Administer required dose immediately, discard remaining solution
Administration	<p>Continuous IV infusion Use a dedicated infusion line to avoid boluses.</p> <p>IV intermittent Infuse over 10 minutes.</p>
Monitoring	<p>Neonatal abstinence syndrome: monitor Neonatal Abstinence Syndrome scores, cardiorespiratory observations and intermittent blood pressure. Sedation of infants on mechanical ventilation: continuous electrocardiogram (ECG) and/or oxygen saturation and continuous or intermittent blood pressure, pain and comfort scores.</p> <p>Hypertension: For initial treatment, continuous ECG and/or oxygen saturation, and continuous or intermittent blood pressure monitoring.</p>
Contraindications	<p>Hypersensitivity to the drug. Heart block or severe ventricular dysfunction.</p>
Precautions	<p>Rebound hypertension may occur after cessation. Rebound neonatal abstinence syndrome may occur after cessation. May need to reduce dose in infants with renal impairment.</p>
Drug interactions	<p>Clonidine will enhance the effects of anaesthetics, sedatives, hypnotics and opioids. Clonidine will interact with other hypertensives; NSAIDs; α2-adrenergic blockers eg phentolamine; β-blockers; digitalis glycosides; tricyclic antidepressants; and α-blocking neuroleptics.</p>
Adverse reactions	<p>Hypotension, bradycardia, rebound hypertension, somnolence, and xerostomia.</p>
Overdose	<p>AUSTRALIA: Contact the Poisons Information Centre on 13 11 26 for management</p> <p>NEW ZEALAND: Contact the National Poisons Centre on 0800 764 766 for management</p>
Compatibility	<p>Fluids: Sodium chloride 0.9%</p> <p>PN at Y-site: No information for PN solutions or fat emulsions.</p> <p>Y-site: amiNOPHYLLine, caffeine citrate, dobutamine hydrochloride, dopamine hydrochloride, esomeprazole sodium, fentanyl citrate, heparin sodium, insulin regular, isoprenaline, ketamine hydrochloride, labetalol hydrochloride, levosimendan, magnesium sulfate, methADONE hydrochloride, milrinone lactate, morphine hydrochloride, noradrenaline (norepinephrine) bitartrate, oxycodone hydrochloride, pantoprazole sodium, potassium chloride, sildenafil citrate.</p>
Incompatibility	<p>Fluids: No information</p> <p>PN at Y-site: No information for PN solutions or fat emulsions.</p> <p>Y-site: amiODAROne hydrochloride</p> <p>Variable Y-site: furosemide, midazolam hydrochloride</p>
Stability	<p>Tablet dispersed in water: make a fresh solution for each dose and use immediately. IV solution diluted make fresh for each dose and use immediately Check with Pharmacy Department for compounded oral suspension or solution.</p>

Storage	<p>Ampoule: Store below 25°C. Protect from light. Tablet: Store below 25°C. Check with Pharmacy Department for compounded oral suspension or solution.</p>
Excipients	<p>IV</p> <p>Catapres ampoules - sodium chloride, hydrochloric acid, water for injections. MZ Clonidine HCl Injection - 9 mg of sodium chloride, hydrochloric acid, water for injections</p> <p>Tablets</p> <p>APO-Clonidine - allura red AC, hypolose, microcrystalline cellulose, magnesium stearate, maize starch, lactose monohydrate, calcium hydrogen phosphate, colloidal anhydrous silica. Catapres 100 - maize starch, lactose monohydrate, calcium hydrogen phosphate, colloidal anhydrous silica, povidone, stearic acid. Catapres 150 - maize starch, lactose monohydrate, calcium hydrogen phosphate, colloidal anhydrous silica, povidone, stearic acid. Clonidine Lupin - allura red AC, hypolose, microcrystalline cellulose, magnesium stearate, maize starch, lactose monohydrate, calcium hydrogen phosphate, colloidal anhydrous silica.</p> <p>Solution or Suspension Check with Pharmacy Department for compounded oral solution or suspension.</p>
Evidence	<p>Clonidine is an α_2-agonist used to produce reductions in blood pressure and sedation that has been used for treatment of hypertension, sedation of ventilated infants and perioperative sedation. Compared with dexmedetomidine, clonidine has a lower selectivity for α_2-receptors (α_1: α_2ratio of 1: 1620 for dexmedetomidine versus 1: 220 for clonidine). As central α_2 effects are sedative, clonidine is less sedating than dexmedetomidine.¹</p> <p>Efficacy</p> <p>Neonates receiving mechanical ventilation: In a single RCT, clonidine infusion 1 microgram/kg/hour or placebo was administered to 112 mechanically ventilated term newborn infants who were on IV fentanyl and midazolam.² The median duration of clonidine infusion was 7 days starting from the fourth day of mechanical ventilation. In this study, no differences in mortality [RR 0.69, 95% CI 0.12 to 3.98], duration of mechanical ventilation (7.1 days versus 5.8 days, P = 0.07) or duration of stay in the intensive care unit were reported. Sedation scale values (COMFORT) and analgesia scores (Hartwig) during the first 72 hours of infusion were lower in the clonidine than the placebo group. Clonidine 1 microgram/kg/hour in ventilated newborns reduced fentanyl and midazolam demand with deeper levels of analgesia and sedation without substantial side effects. This was not demonstrated in older infants, possibly due to lower clonidine serum levels. Evidence is insufficient to show the efficacy and safety of clonidine for sedation and analgesia in term and preterm newborn infants receiving mechanical ventilation.¹² (LOE II GOR D)</p> <p>There are no trials comparing clonidine versus dexmedetomidine in paediatric patients. A systematic review of dexmedetomidine use in paediatric patients found dexmedetomidine was associated with similar sedation scores to midazolam, a reduction in opioid use with use of a higher dose dexmedetomidine 0.5 microgram/kg/hour but not 0.25 microgram/kg/hour infusion, and reduced duration of mechanical ventilation compared to paediatric patients treated with midazolam and fentanyl.¹³</p> <p>Perioperative sedation In addition to the RCT mentioned above, a retrospective study reported use of clonidine for sedation in 32 term born neonates who received a cardiac surgery at a median postnatal age of 22 days. Post operatively, IV clonidine bolus doses of 0.5–1 microgram/kg/dose were given initially up to a cumulative dose of 2 microgram/kg, after which an infusion was started at 0.5 microgram/kg/hr and increased to a maximum of 2 microgram/kg/hr to ensure infant’s COMFORT B score between 10–20. Thereafter, clonidine infusion was continued for up to 72 hours. Authors reported a favourable hemodynamic profile and shorter stay in the intensive care in infants who received clonidine in addition to morphine for sedation compared to midazolam and morphine.³</p>

A systematic review in paediatric patients almost all over 1 year of age, found clonidine premedication 4 microgram/kg may reduce postoperative pain in children. Side effects were minimal, but some of the studies used atropine prophylactically with the intention of preventing bradycardia and hypotension. (LOE I GOR C children) Infants enrolled in the trials were ≥ 1 year age.^{14,15}

Neonatal abstinence syndrome (NAS)

Network meta-analysis of pharmacological treatments for NAS included buprenorphine, clonidine, diluted tincture of opium and clonidine, diluted tincture of opium, morphine, methadone, and phenobarbital. In network meta-analysis, clonidine had non-significant change in length of treatment (mean difference versus morphine -10.52 days [-24.05 to 2.92]), median rank 2 (6 to 1) and length of stay (days: mean difference versus morphine, -6.09 (-12.93 to 0.79), median rank 2 (7 to 1). Rate of treatment failure was not reported.¹⁶

Three RCTs of clonidine in infants with NAS have used differing strategies.^{1,5,6} Bada et al in infants ≥ 35 weeks' gestation with NAS compared morphine 0.4 mg/kg/day versus clonidine 5 microgram/kg/day divided into 8 doses as initial treatment of NAS. A 25% dose escalation every 24 hours was possible per protocol (maximum of 1 mg/kg per day for morphine and 12 microgram/kg per day for clonidine).¹ After control of symptoms, the dose was tapered by 10% every other day. Infants treated with clonidine ($n = 16$) versus morphine ($n = 15$) had decreased duration of treatment (median 39 days versus 28 days; $P = .02$), improved NNNS scores and lower height of arousal and excitability ($P < .05$). One-year motor, cognitive, and language scores did not differ between groups. Surran et al in 64 infants compared morphine 0.32 to 0.8 mg/kg/day divided 3 hourly and clonidine 6 to 12 microgram/kg/day divided 6 hourly according to NAS Score versus morphine sulfate 0.32 to 0.8 mg/kg/day divided 3 hourly and phenobarbital 6 to 12 mg/kg/day divided 8 hourly.⁶ Clonidine dose was weaned by halving daily dose every 24 hours for 2 steps then ceasing. Phenobarbital reduced duration of treatment 4.6 days, (95% CI: 0.3, 8.9; $P=0.03$). Two clonidine treated infants failed NMS-weaning attempts and were switched to phenobarbital whereas there were no failures occurred in the phenobarbital group. However, 3 (8.8%) infants in the phenobarbital group, manifested over sedation signs (poor feeds and mild respiratory depression) and serum phenobarbital measures were supratherapeutic (>40 mg/dL) and required dosage adjustment. There were no arrhythmias or abnormal BPs observed (hypo- or hypertension) in the clonidine group, no inpatient mortality and no infant was re-admitted to the hospital within 1 week post discharge. Agthe et al in 80 infants with NAS treated with oral diluted tincture of opium, compared oral clonidine 1 microgram/kg every 4 hours versus placebo.⁵ Median length of therapy was reduced in the clonidine group (11 versus 15 days), although 7 infants in the clonidine group required restarting opium after initial discontinuation. Clonidine reduced opioid use and rate of treatment failures (0% versus 12.5%). Hypertension, hypotension, bradycardia, or desaturations did not occur in either group. Three infants in the clonidine group died because of myocarditis, sudden infant death syndrome, and homicide, all after hospital discharge and before 6 months of age. Leikin et al studied 14 neonates.²⁸ The mean gestational age was 30.1 weeks (range 24.4–40.7 weeks); three patients were full-term. Eleven had been on intravenous fentanyl for sedation; three were born to opioid-dependent mothers. All neonates were treated with clonidine, administered in doses of 0.5–1 microgram/kg orally every 6 hours. No neonate received opioids. Mean duration of treatment was 6.8 days (range 4–15). Mean abstinence scores were 6.4 pretreatment (range 0–20) and 1.9 post-treatment (range 0–5). No neonates suffered an adverse event (hypotension, bradycardia, excessive sedation, and oxygen desaturation) from clonidine administration, and no seizures were identified.²⁸

Conclusion: The optimal regimen to manage symptomatic NAS is unclear due to the low quality, small size and short-term outcomes considered in the published studies.¹⁷

Hypertension

For chronic hypertension, expert opinion suggested that drug therapy should be initiated mainly because sustained BP elevation may have renal, cardiac, and central nervous system effects.^{10,18,19} The ESCAPE Trial of 385 children 3 to 18 years with chronic kidney disease (GFR 15–80 mL/minute/1.73 m²), hypertension was treated with ramipril 6 mg/ m²/day and patients were randomly assigned to intensified blood-pressure control (target 24-hour mean arterial pressure below the 50th percentile) or conventional blood-pressure control (mean arterial pressure 50–95th percentile) achieved by the addition of antihypertensive therapy that does not target the renin–angiotensin system. Intensified blood-pressure control, with target 24-hour blood-pressure levels in the low range of normal, confers a substantial benefit with respect to renal function among children with chronic kidney disease.¹⁸ (LOE II GOR B)

	<p>There are few case reports of clonidine use for neonatal hypertension.^{9,20,21} One study of 11 infants and children with severe arterial hypertension associated with renal failure reported a single dose of clonidine 10 microgram/kg infused over 4 hours, or an additional dose of 5 microgram/kg resulted in a satisfactory response in 9 patients.²²</p> <p>Doses of oral clonidine for treatment of chronic hypertension in neonates and paediatric patients in expert reviews vary from 2–10 microgram/kg/day in 3 or 4 divided doses, maximal 25 microgram/kg/day.^{9,10}</p> <p>Safety</p> <p>Clonidine may cause hypotension, bradycardia, rebound hypertension, somnolence, and xerostomia.³⁻⁸</p> <p>Pharmacokinetics</p> <p>Clonidine displays age-related changes in pharmacokinetics attributable to the maturation of clearance during infancy.^{23,24} It has a long elimination half-life (16.9 hours in neonates, 11.4 hours in infants and 7.4 hours in children). Clearance in neonates is approximately one-third of that in adults.²³</p> <p>Long half-lives necessitate the use of loading doses to reach therapeutic concentrations within a reasonable time. Without a loading dose, steady state would only have been achieved toward the end of the 72-hour study period for neonates.²¹ Bioavailability of orally administered clonidine formulations has been estimated to be approximately 55% in children.²⁶ A target plasma concentration of above 2 microgram/L has been proposed. Clonidine titrated infusions with a loading dose of 2 microgram/kg followed by a continuous infusion of up to 2 microgram/kg/hour are recommended in hemodynamically stable PICU patients to achieve adequate sedation. Clonidine titrated infusions with a loading dose of 1 microgram/kg followed by a continuous infusion of up to 1 microgram/kg/hour are recommended in hemodynamically stable neonates.^{2,4}</p>
<p>Practice points</p>	<p>Neonatal abstinence syndrome: The optimal regimen to manage symptomatic NAS is unclear.¹⁷ In infants with NAS secondary to opioid withdrawal, clonidine may reduce need for morphine treatment and duration of treatment.^{1,5,16} (LOE II, GOR C)</p> <p>Sedation: Evidence is insufficient to show the efficacy and safety of clonidine for sedation and analgesia in term and preterm newborn infants receiving mechanical ventilation.¹² (LOE II GOR D)</p> <p>Chronic hypertension: Recommend using at lower doses (2–10 microgram/kg/day) in 3 or 4 divided doses in combination with other antihypertensive agents rather than at higher dose as a single agent.</p>
<p>References</p>	<ol style="list-style-type: none"> 1. Bada HS, Sithisarn T, Gibson J, et al. Morphine versus clonidine for neonatal abstinence syndrome. <i>Pediatrics</i>. 2015;135: e383-91. 2. Hunseler C, Balling G, Rohlig C, et al. Continuous infusion of clonidine in ventilated newborns and infants: a randomized controlled trial. <i>Pediatr Crit Care Med</i>. 2014; 15:511-22. 3. Kleiber N, de Wildt SN, Cortina G, et al. Clonidine as a First-Line Sedative Agent After Neonatal Cardiac Surgery: Retrospective Cohort Study. <i>Pediatr Crit Care Med</i>. 2016 Apr;17(4):332-41. 4. Hayden JC, Bardol M, Doherty DR, et al. Optimizing clonidine dosage for sedation in mechanically ventilated children: A pharmacokinetic simulation study. <i>Paediatr Anaesth</i>. 2019 Oct;29:1002-1010. 5. Agthe AG, Kim GR, et al. Clonidine as an adjunct therapy to opioids for neonatal abstinence syndrome: a randomized, controlled trial. <i>Pediatrics</i>. 2009;123: e849-56. 6. Surran B, Visintainer P, Chamberlain S, et al. Efficacy of clonidine versus phenobarbital in reducing neonatal morphine sulfate therapy days for neonatal abstinence syndrome. A prospective randomized clinical trial. <i>J Perinatol</i>. 2013; 33:954-9. 7. Gauda EB, Chavez-Valdez R, Northington FJ, et al. Clonidine for sedation in infants during therapeutic hypothermia with neonatal encephalopathy: pilot study. <i>J Perinatol</i>. 2022;42:319-327. 8. Arenas-López S, Riphagen S, Tibby SM, et al. Use of oral clonidine for sedation in ventilated paediatric intensive care patients. <i>Intensive Care Med</i>. 2004 Aug;30(8):1625-9. 9. Batsky DL. Neonatal Hypertension. <i>Clinics in Perinatology</i>. 2014; 41:529-42. 10. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: Diagnosis, management, and outcome. <i>Pediatric Nephrology</i>. 2012; 27:17-32. 11. Neubert A, Baarslag MA, Dijk MV, et al. The CLOSED trial: CLONidine compared with midazolam for SEDation of paediatric patients in the intensive care unit: study protocol for a multicentre randomised controlled trial. <i>BMJ Open</i>. 2017 Jun 21;7(6): e016031. 12. Romantsik O, Calevo MG, Norman E, Bruschetti M. Clonidine for sedation and analgesia for neonates receiving mechanical ventilation. <i>Cochrane Database of Systematic Reviews</i>. 2017

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Appendix

Infusion tables to assist concentration selection

Table 1: Infusion rates when using clonidine concentration **0.5 microgram/mL**
(suggested for weight <1.5 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 microgram/kg/hour									
0.5	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
1	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
1.5	0.03	0.07	0.1	0.13	0.17	0.2	0.23	0.27	0.3	0.33
2	0.03	0.05	0.08	0.1	0.13	0.15	0.18	0.2	0.23	0.25
2.5	0.02	0.04	0.06	0.08	0.1	0.12	0.14	0.16	0.18	0.2
3	0.02	0.03	0.05	0.07	0.08	0.1	0.12	0.13	0.15	0.17
3.5	0.01	0.03	0.04	0.06	0.07	0.09	0.10	0.11	0.13	0.14
4	0.01	0.03	0.04	0.05	0.06	0.08	0.09	0.1	0.11	0.13
4.5	0.01	0.02	0.03	0.04	0.06	0.07	0.08	0.09	0.1	0.11
5	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09	0.1

Table 2: Infusion rates when using clonidine concentration **3 microgram/mL**
(suggested for weight 1.5 to 4 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 microgram/kg/hour									
0.5	0.6	1.2	1.8	2.4	3	3.6	4.2	4.8	5.4	6
1	0.3	0.6	0.9	1.2	1.5	1.8	2.1	2.4	2.7	3
1.5	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
2	0.15	0.3	0.45	0.6	0.75	0.9	1.05	1.2	1.35	1.5
2.5	0.12	0.24	0.36	0.48	0.6	0.72	0.84	0.96	1.08	1.2
3	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
3.5	0.09	0.17	0.26	0.34	0.43	0.51	0.6	0.69	0.77	0.86
4	0.08	0.15	0.23	0.3	0.38	0.45	0.53	0.6	0.68	0.75
4.5	0.07	0.13	0.2	0.27	0.33	0.40	0.47	0.53	0.6	0.67
5	0.06	0.12	0.18	0.24	0.3	0.36	0.42	0.48	0.54	0.6

Table 3: Infusion rates when using clonidine concentration **6 microgram/mL**
(suggested for weight >4 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 microgram/kg/hour									
0.5	1.2	2.4	3.6	4.8	6	7.2	8.4	9.6	10.8	12
1	0.6	1.2	1.8	2.4	3	3.6	4.2	4.8	5.4	6
1.5	0.4	0.8	1.2	1.6	2	2.4	2.8	3.2	3.6	4
2	0.3	0.6	0.9	1.2	1.5	1.8	2.1	2.4	2.7	3
2.5	0.24	0.48	0.72	0.96	1.2	1.44	1.68	1.92	2.16	2.4
3	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
3.5	0.17	0.34	0.51	0.69	0.86	1.03	1.2	1.37	1.54	1.71
4	0.15	0.3	0.45	0.6	0.75	0.9	1.05	1.2	1.35	1.5
4.5	0.13	0.27	0.4	0.53	0.67	0.8	0.93	1.07	1.2	1.33
5	0.12	0.24	0.36	0.48	0.6	0.72	0.84	0.96	1.08	1.2

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