

Alert	Esmolol should be used only on recommendation of a paediatric cardiologist.
Indication	Cardiac intra-and postoperative hypertension Supraventricular tachycardia Hypercyanotic spells
Action	A cardio selective Beta ₁ adrenergic receptor blocking agent. At high doses it also inhibits beta ₂ receptors mainly in the bronchial and vascular musculature.
Drug type	Beta blocker
Trade name	Brevibloc
Presentation	100mg/10mL ampoule, 2.5gram vial (powder for reconstitution)
Dose	<p>Hypertension/Supraventricular tachycardia <u>Loading (Optional and may be omitted in unstable patients):</u> 100–500 microgram/kg over 1–2 minutes; repeat if required. <u>Maintenance:</u> Starting infusion rate: 25–100 microgram/kg/minute. Titrate to response in increments of 25–50 microgram/kg/minute, allowing at least 5 minutes between dose adjustments. Maximum infusion rate: 500–1000 microgram/kg/minute.</p> <p>Hypercyanotic spells <u>Bolus dose:</u> 100-200 microgram/kg/dose over 1–2 minutes.¹¹ Higher doses can be administered in consultation with cardiologists and/or intensivists.^{9,10} <u>Maintenance (if required):</u> 50-200 microgram/kg/minute.</p> <p>Hypertrophic cardiomyopathy with decreased cardiac output with or without hypotension (e.g. Twin-to-twin transfusion recipient, infant of diabetic mother, Pompe disease) Limited data. To be used only in consultation with a paediatric cardiologist. Start infusion rate: 15-25 microgram/kg/min. Increase dose to obtain desired response in heart rate and cardiac output in increments of 25 microgram/kg/minute every 1-2 hours to 75 microgram/kg/min. NOTE: Esmolol should NOT be used in hypertrophy resulting from valvar or arterial obstruction.</p>
Dose adjustment	Therapeutic hypothermia – Not applicable. ECMO – No information. Renal impairment – no dose adjustment required Hepatic impairment - no dose adjustment required
Maximum dose	1000 microgram/kg/minute has been used in treatment of hypertension. Dose greater than 200 microgram/kg/minute should only be used in consultation with paediatric cardiologist.
Route	IV (must only be administered via central line)
Preparation	<p>Using 100mg/10mL ampoule: <u>IV Bolus/Loading dose</u> Draw up 1 mL (10 000 microgram) of esmolol 10mg/mL and dilute with 9 mL sodium chloride 0.9% or glucose 5% to make a final volume of 10 mL with a final concentration of 1000 microgram/mL.</p> <p><u>Continuous infusion</u> 20mL Syringe Generally given undiluted: Draw up 20 mL of undiluted esmolol 10 mg/mL (10 000 microgram/mL) solution. 1 mL/kg/hour = 166.7 microgram/kg/min. 50mL Syringe Generally given undiluted: Draw up 50 mL of undiluted esmolol 10 mg/mL (10 000 microgram/mL) solution. 1 mL/kg/hour = 166.7 microgram/kg/min.</p>

	<p>Using 2.5gram powder vial: Reconstitute the 2.5gram vial with 50 mL of sodium chloride 0.9% or glucose 5% to make 50 mg/mL (50 000 microgram/mL) solution.</p> <p><u>IV Bolus/Loading dose</u> Draw up 0.2 mL of the reconstituted solution (10 000 microgram of esmolol) and dilute with 9.8 mL sodium chloride 0.9% or glucose 5% to make a final volume of 10 mL with a final concentration of 1000 microgram/mL.</p> <p><u>Continuous infusion</u></p> <p><u>20mL Syringe</u> Draw up 4 mL of the reconstituted solution (200 000 microgram of Esmolol) and add to 16 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 20 mL with a final concentration of 10 mg/mL (10 000 microgram/mL). 1 mL/kg/hour = 166.7 microgram/kg/min.</p> <p><u>50mL Syringe</u> Draw up 10 mL of the reconstituted solution (500 000 microgram of Esmolol) and add to 40 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 50 mL with a final concentration of 10 mg/mL (10 000 microgram/mL). 1 mL/kg/hour = 166.7 microgram/kg/min.</p>
Administration	<p>Bolus: Administer over 1-2 minutes. Maintenance: Continuous intravenous infusion</p>
Monitoring	Continuous blood pressure, ECG and heart rate
Contraindications	Hypotension, bradycardia, sick sinus syndrome or heart failure
Precautions	Asthma
Drug interactions	Adrenaline, alprostadil, amiodarone, diazoxide, dobutamine, lacosamide, morphine, nifedipine,
Adverse reactions	Hypotension – reversible with dose reduction or discontinuation, Bradycardia, bronchospasm, drowsiness, infusion site reaction, heart block, hypokalaemia, hyperkalaemia, renal tubular acidosis (hyperkalaemic)
Compatibility	<p>Fluid: glucose 5%, sodium chloride 0.9%, glucose 5% +0.45% sodium chloride, glucose 5% + 0.9% sodium chloride</p> <p>Medications: Adrenaline, amiodarone, benzylpenicillin, dopamine, dobutamine, fluconazole, gentamicin, heparin, hydrocortisone, insulin, metronidazole, midazolam, morphine, noradrenaline, sodium bicarbonate, vancomycin, vecuronium</p>
Incompatibility	<p>Fluid: glucose 10%, Amino acid solutions and lipid emulsion.</p> <p>Medications: Amphotericin, esomeprazole, furosemide, milrinone, omeprazole, thiopental sodium</p>
Stability	Diluted solution is stable for 24 hours at <25°C
Storage	Keep at room temperature below 25°. Do not refrigerate or freeze.
Excipients	Sodium acetate trihydrate, glacial acetic acid, hydrochloric acid and water for injections
Special comments	
Evidence	<p>Efficacy</p> <p>Cardiac intra- and post-operative hypertension: Tabbutt et al used Esmolol as the first line for management of intra- and post-operative hypertension in a cohort of 118 children who had coarctation of aorta. There were 30 neonates, and hypertension was defined as systolic blood pressure > 80 mmHg within 30 minutes of cross-clamp release. A bolus dose of 125 to 500 microgram/kg was administered immediately followed by an infusion at 125 to 500 microgram/kg/min for a minimum of 15 minutes. The median duration of Esmolol use was 19 hours (0.5 -100) and maximum dose was 521 microgram/kg/min (125 to 9333 microgram/kg/min). Eight (27%) neonates needed sodium nitroprusside in addition to control hypertension in the first 24 hours after surgery and 5 (17%) needed oral anti-hypertensive medication at discharge.¹</p> <p>In a prospective cohort study of 20 children with a congenital heart defect aged 1 month to 12 years, intravenous continuous infusion of Esmolol was used for management of post-operative hypertension. Ten patients had aortic coarctation. A blood pressure (BP) ≤90th centile for age was considered normal. In this study, esmolol was started administered based on the patient's age (50 to 150 microgram/kg/min), and then titrated until either BP normalised or a maximum dose of 1000 microgram/kg/min was reached.</p>

Mean esmolol dose required to normalise BP was 700 microgram/kg/min (range 300 to 1000 microgram/kg/min) and the mean time to normalise BP was 1.65 hours. In one participant, BP control could not be achieved.² Vincent et al used Esmolol as an adjunct to sodium nitroprusside in 7 children with repair of coarctation of aorta who continued to have hypertension despite IV sodium nitroprusside at a dose of 2 to 5 microgram/kg/min. The participants received a bolus of 500 microgram/kg/min over one minute followed by a continuous infusion to normalise the BP. In this study, the maximal dosage of esmolol ranged from 50 to 250 microgram/kg/min. After commencement of Esmolol, a significant decrease in heart rate, systolic, diastolic and mean arterial pressures was noted in all participants.³

Supraventricular Tachycardia: Esmolol can be used successfully to treat recurrent or adenosine unresponsive SVT, as a monotherapy or in combination with digoxin and or amiodarone in neonates.^{4,5} Adamson et al used Esmolol as the first-line for termination of supraventricular tachycardia (SVT) induced as a part of diagnostic electrophysiology or a catheter ablation procedure in 25 children aged 1 to 16 years. The participants received a 1,000 microgram/kg bolus followed by continuous infusion at 300 microgram/kg/min if the episode of SVT did not convert within 10 min. In 63% participants, termination of SVT was achieved and the mean time to conversion was 2 min (0 to 5 min) following the start of Esmolol.⁶ Esmolol has also been used to treat tachycardia associated with infections.⁷

Hypercyanotic spells in tetralogy of Fallot: Beta blockers (e.g., propranolol and Esmolol) are recommended as adjuvant therapy for hypercyanotic spells. Published reports on Esmolol for this indication are limited to single case reports.^{9,10} Nussbaum et al reported 2 cases: First case was a 14-week old 3.0 kg infant who was born at 30 weeks gestation. Esmolol at a dose of 100 microgram/kg/minute was used. Second case was a 6-month old infant in whom a bolus dose of 750 microgram/kg/dose followed by 75 microgram/kg/minute was used.⁹ Geary et al used 200 microgram/kg/minute infusion of Esmolol in a 9-month old, 10-kg baby to treat hypercyanotic spell as an adjuvant therapy and achieved good outcome.¹⁰ Esmolol IV infusion between 50 and 200 microgram/kg/min has been suggested.¹¹

Hypertrophic cardiomyopathy (HCM) with left ventricular outflow tract (LVOT) obstruction (e.g. recipient of Twin-to-twin transfusion syndrome, infant of diabetic mother, Pompe disease)
Data is very limited. Gruendler et al reported 2 cases of twin-to-twin transfusion syndrome (TTTS) recipients treated with esmolol infusion for persistent hypotension despite other inotropic support. One was born at 26 weeks with left ventricular outflow tract obstruction. Esmolol was started with 10 microgram/kg/min and titrated to 60 microgram/kg/minute until replaced by oral metoprolol. Second case of TTS recipient was born at 25 weeks gestation. Cardiac echo confirmed biventricular hypertrophy with left ventricular outflow tract obstruction with progressively reduced left ventricular filling. This infant was treated for persistent hypotension with esmolol at 10 microgram/kg/minute and increased to a maximum of 50 microgram/kg/minute until replaced by oral metoprolol. Codazzi et al reported a neonate with HCM and LVOT obstruction resulting from insulin dependent type 2 diabetes in mother. Infant was treated with esmolol 50 microgram/kg/minute and increased to 100 microgram/kg/minute with improvement in cardiac function. Therapy was subsequently shifted to oral propranolol.¹³ Noori et al reported a neonate with Pompe disease and severe HCM that was treated with an esmolol infusion starting at 50 microgram/kg/minute and increased up to 225 microgram/kg/minute.¹⁴

ANMF - paediatric cardiology expert consensus: Paediatric cardiologist should always be consulted prior to using esmolol for these particular indications. Esmolol is not recommended in severe valvar or arterial obstruction resulting in secondary HCM.

Safety
In a cohort of 107 children with a mean age of 18 months who received esmolol at a dose of 125 to 500 microg/kg/min there were no deaths and no serious adverse events. Systemic hypotension in 8%, bradycardia 1%, wheezing in 3% and reaction at the injection site were reported in 1% participants. Seven subjects discontinued the study because of adverse events.⁸

Pharmacokinetics
In children, plasma concentration of esmolol appears to increase in proportion to the dose. The time to steady state is reported to be 21 minutes with a volume of distribution is 0.53 L/kg. The reported mean terminal elimination half-life is 2.7 to 4.8 min and total body clearance is 126 mL/kg/min. Esmolol clearance in the newborns and infants (281mL/kg/min) is higher compared with older children (126

	mL/kg/min). Similarly, in children with coarctation of aorta Esmolol clearance is higher than other congenital heart defects. ^{2,8}
Practice points	<ul style="list-style-type: none"> • Correct hypovolaemia before starting esmolol where possible. • Esmolol has rapid onset and short duration of action (Half-life: 9 mins) and usually used for short term, when stopping treatment taper the infusion gradually to avoid rebound effects. • Esmolol is highly irritant and can cause extravasation injuries. • Concentration above 10 mg/mL: MUST BE ADMINISTERED VIA CENTRAL LINE
References	<ol style="list-style-type: none"> 1. Tabbutt S, Nicolson SC, Dominguez TE et al. Perioperative course in 118 infants and children undergoing coarctation repair via a thoracotomy: a prospective, multicenter experience. <i>J Thorac Cardiovasc Surg.</i> 2008 Nov; 136(5):1229-36. 2. Wiest et al. Esmolol for the management of pediatric hypertension after cardiac operations, <i>J Thorac cardiovascular surgery</i>, 1998, 115:890-7. 3. Vincent RN, Click LA, Williams HM, et al. Esmolol as an adjunct in the treatment of systemic hypertension after operative repair of coarctation of the aorta. <i>Am J Cardiol.</i> 1990 Apr 1; 65(13):941-3. 4. Epcacan S. Management of Neonatal Supraventricular Tachycardia; a Single Center Experience. <i>EJMI</i> 2019; 3(1):46–53. 5. Sahin G, Ozturk E, Kasar T, et al. Sustained tachyarrhythmia in children younger than 1 year of age: Six year single-centre experience. <i>Pediatr Int.</i> 2018 Feb;60(2):115-121 6. Adamson PC, Rhodes LA, Saul JP, et al. The pharmacokinetics of esmolol in pediatric subjects with supraventricular arrhythmias. <i>Pediatr Cardiol.</i> 2006 Jul-Aug; 27(4):420-7. 7. Luyt D, Dance M, Litmanovitch M, et al. Esmolol in the treatment of severe tachycardia in neonatal tetanus. <i>Anaesth Intensive Care.</i> 1994 Jun; 22(3):303-4. 8. Tabbutt S, Nicolson SC, Adamson PC, et al. The safety, efficacy, and pharmacokinetics of esmolol for blood pressure control immediately after repair of coarctation of the aorta in infants and children: a multicenter, double-blind, randomized trial. <i>J Thorac Cardiovasc Surg.</i> 2008 Aug; 136(2):321-8. 9. Nussbaum J, Zane EA, Thys DM. Esmolol for the treatment of hypercyanotic spells in infants with tetralogy of Fallot. <i>Journal of cardiothoracic anesthesia.</i> 1989;3(2):200-2. 10. Geary V, Thaker U, Chalmers P, Sheikh F. Esmolol in tetralogy of Fallot. <i>J Cardiothorac Anesth</i> 1989;3(4):524-6. 11. Munoz R, Morell V, da Cruz EM, Vetterly C, da Silva JP, editors. Critical care of children with heart disease: Basic medical and surgical concepts. Tetralogy of Fallot p 199-206. Springer London; 2010 Jun 21. 12. Gruendler K, Schwarz CE, Lorenz L, Poets CF, Franz AR. Beta blocker therapy in recipients of twin-to-twin transfusion syndrome. <i>Archives of Disease in Childhood-Fetal and Neonatal Edition.</i> 2019 Sep 1;104(5):F541-3. 13. Codazzi AC, Ippolito R, Novara C, Tondina E, Cerbo RM, Tzialla C. Hypertrophic cardiomyopathy in infant newborns of diabetic mother: a heterogeneous condition, the importance of anamnesis, physical examination and follow-up. <i>Italian Journal of Pediatrics.</i> 2021 Dec;47:1-6. 14. Noori S, Acherman R, Siassi B, Luna C, Ebrahimi M, Pavlova Z, Ramanathan R. A rare presentation of Pompe disease with massive hypertrophic cardiomyopathy at birth. 15. Merative™ Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: July/25/2023).

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Authors Contribution of the current version

Author/s	Mohammad Irfan Azeem, Nilkant Phad, Bhavesh Mehta
Evidence Review	Nilkant Phad, Srinivas Bolisetty

Expert review	David Schell, Gary Sholler, Jonathan Skinner
Nursing Review	Benjamin Emerson-Parker, Renae Gengaroli
Pharmacy Review	Mohammad Irfan Azeem, Rebecca O'Grady
ANMF Group contributors	Amber Seigel, Rebecca Barzegar, Jutta Van Den Boom, Kerrie Knox, Cindy Chen, Thao Tran, Simarjit Kaur, Michelle Jenkins, Susannah Brew, Bryony Malloy, Celia Cunha Da Silva, Dianne Lee, Charles Tian, Trong Tran, Ian Callander, Emma Roylance
Final editing	Srinivas Bolisetty
Electronic version	Helen Huynh, Ian Callander
Facilitator	Nilkant Phad, Srinivas Bolisetty

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