# Esmolol

## Newborn use only

**2023**

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| **Alert** | Esmolol should be used only on recommendation of a paediatric cardiologist. |
| **Indication** | Cardiac intra-and postoperative hypertension<br>Supraventricular tachycardia<br>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** | 100 mg/10 mL ampoule, 2.5 gram vial (powder for reconstitution) |
| **Dose** | **Hypertension/Supraventricular tachycardia**<br>Loading (Optional and may be omitted in unstable patients):<br>100–500 microgram/kg over 1–2 minutes; repeat if required.<br>Maintenance:<br>Starting infusion rate: 25–100 microgram/kg/minute.<br>Titrate to response in increments of 25–50 microgram/kg/minute, allowing at least 5 minutes between dose adjustments.<br>Maximum infusion rate: 500–1000 microgram/kg/minute.<br><br>**Hypercyanotic spells**<br>Bolus dose:<br>100-200 microgram/kg/dose over 1–2 minutes. (11) Higher doses can be administered in consultation with cardiologists and/or intensivists. (9,10)<br>Maintenance (if required):<br>50-200 microgram/kg/minute.<br><br>**Hypertrophic cardiomyopathy with decreased cardiac output with or without hypotension (e.g. Twin-to-twin transfusion recipient, infant of diabetic mother, Pompe disease)**<br>Limited data. To be used only in consultation with a paediatric cardiologist.<br>Start infusion rate: 15-25 microgram/kg/min.<br>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.<br>NOTE: Esmolol should NOT be used in hypertrophy resulting from valvar or arterial obstruction. |
| **Dose adjustment** | Therapeutic hypothermia – Not applicable.<br>ECMO – No information.<br>Renal impairment – no dose adjustment required<br>Hepatic impairment - no dose adjustment required |
| **Maximum dose** | 1000 microgram/kg/minute has been used in treatment of hypertension.<br>Dose greater than 200 microgram/kg/minute should only be used in consultation with paediatric cardiologist. |
| **Total cumulative dose** | |
| **Route** | IV (must only be administered via central line) |
| **Preparation** | **Fixed concentration 10 mg/mL**<br>**Using 100 mg/10 mL ampoule**:<br>Draw up 50 mL of Esmolol 10 mg/mL (10 000 microgram/mL) solution and administer as a continuous infusion where 1 mL/**kg**/hour = 166.7 microgram/kg/min.<br>**FURTHER DILUTE for INITIAL BOLUS/LOADING ONLY:** Draw up 1 mL (10 000 microgram of Esmolol) 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 1 mg/mL (1000 microgram/mL).<br><br>**Using 2.5 gram powder vial**:<br>Reconstitute the 2.5 gram vial with 50 mL of sodium chloride 0.9% or glucose 5% to make 50 mg/mL (50 000 microgram/mL) solution. |

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| | **Further dilute:** Draw up 10 mL (500 000 microgram of Esmolol) of reconstituted solution 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).<br>1 mL/**kg**/hour = 166.7 microgram/kg/min<br>**FURTHER DILUTE for INITIAL BOLUS/LOADING ONLY**: From the above solution, draw up 1 mL (10 000 microgram) 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 1 mg/mL (1000 microgram/mL). |
| **Administration** | Bolus: Administer over 1-2 minutes.<br>Maintenance: Continuous intravenous infusion |
| **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,<br>Bradycardia, bronchospasm, drowsiness, infusion site reaction, heart block, hypokalaemia, hyperkalaemia, renal tubular acidosis (hyperkalaemic) |
| **Compatibility** | Fluid: glucose 5%, sodium chloride 0.9%, glucose 5% +0.45% sodium chloride, glucose 5% + 0.9% sodium chloride<br>Medications: Adrenaline, amiodarone, benzylpenicillin, dopamine, dobutamine, fluconazole, gentamicin, heparin, hydrocortisone, insulin, metronidazole, midazolam, morphine, noradrenaline, sodium bicarbonate, vancomycin, vecuronium |
| **Incompatibility** | Fluid: glucose 10%, Amino acid solutions and lipid emulsion.<br>Medications: Amphotericin, esomeprazole, furosemide, milrinone, omeprazole, thiopental sodium |
| **Stability** | Diluted solution is stable for 24 hours at <25 $^{o}$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** | **Efficacy**<br>**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)<br>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) ≤90$^{th}$ 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. 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)<br>**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) |

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| | 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)<br>**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 all 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)<br>**Hypertrophic cardiomyopathy (HCM) with left ventricular outflow tract (LVOT) obstruction (e.g. recipient of Twin-to-twin transfusion syndrome, infant of diabetic mother, Pompe disaease)**<br>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 tritrated 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]<br>**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.<br>**Safety**<br>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).<br>**Pharmacokinetics**<br>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** | • Correct hypovolaemia before starting esmolol where possible.<br>• 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.<br>• Esmolol is highly irritant and can cause extravasation injuries.<br>• Concentration above 10 mg/mL: MUST BE ADMINISTERED VIA CENTRAL LINE |
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