Alprostadil (Prostaglandin E_1) 2016

Alert	1 microgram = 1000 nanogram.
Indication	For temporary maintenance of ductus arteriosus patency until corrective or palliative surgery can be performed in neonates with ductal-dependent congenital heart defects.
Action	Relaxes the ductus arteriosus in early postnatal life and supports its patency.
Drug Type	Prostaglandin E_1 or PGE_1
Trade Name	Prostin VR.
Presentation	Ampoules (sterile solution) 500 microgram/mL 1 mL
Dosage / Interval	**Starting Dose** Dose: 10 nanogram/kg/minute (range: 5 to 50 nanogram/kg/minute). For known congenital heart disease patients and prior to ductal closure: Start at 10 nanogram/kg/min. If there is no clinical or echocardiographic response to the maximum dose of 50 nanogram/kg/min, then consult a paediatric cardiologist. Very rarely they may suggest a very short trial of up to 100 nanogram/kg/min. **Maintenance Dose** 3-20 nanogram/kg/minute. Aim is to be on the lowest dose that safely maintains ductal patency.
Maximum dose	Higher doses ≥50 nanogram/kg/minute may be needed to resuscitate infants with poor perfusion and oxygenation ('grey baby') and with ductal closure in suspected duct-dependent congenital heart disease.
Route	Continuous IV infusion.
Preparation/Dilution	**LOW DOSE continuous IV infusion [use if attempting to avoid ventilation and keep ductus open]** **Infusion strength** | **Prescribed amount** 1 mL/hour = 10 nanogram/kg/minute | 30 microgram/kg alprostadil (Prostin VR, PGE_1) and make up to 50 mL First dilution: Draw up 1 mL (500 microgram) of alprostadil and add 9 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 10 mL with a concentration of 50 microgram/mL. Second dilution: From this, draw up 0.6 mL/kg (30 microgram/kg) and dilute to 50 mL with sodium chloride 0.9% or glucose 5%. Infuse at rate of **1 mL/h = 10 nanogram/kg/minute.** **HIGH DOSE continuous IV infusion [consider if ductus closed and/or mechanically ventilated]** **Infusion strength** | **Prescribed amount** 1 mL/hour = 50 nanogram/kg/minute | 150 microgram/kg alprostadil (Prostin VR, PGE1) and make up to 50 mL First dilution: Draw up 1 mL (500 microgram of alprostadil) and add 9 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 10 mL with a concentration of 50 microgram/mL. Second dilution: From this, draw up 3 mL/kg (150 microgram/kg) and dilute to 50 mL with sodium chloride 0.9% or glucose 5%. Infusing at rate of **1 mL/h = 50 nanogram/kg/minute.**

Administration	Continuous intravenous infusion. Ensure reliable intravenous access as short half-life.
Monitoring	Continuous pulse oximetry, heart rate, ECG and blood pressure monitoring. Assess urine output and peripheral perfusion frequently.
Contraindications	
Precautions	Ensure adequate cardiorespiratory monitoring and cardiorespiratory resuscitation equipment available for immediate use if necessary. Apnoea is frequent. Commencement of alprostadil ≤ 20 nanogram/kg/min and low maintenance dose reduces apnoea incidence. Titrate to infant's response (increased oxygenation, echo findings and side effects) - Aim is to be on the lowest dose that safely maintains the ductal patency. Hyperosmolar – infuse at concentrations < 20 microgram/mL. Neonates with total anomalous pulmonary venous return below the diaphragm – may precipitate pulmonary oedema because of increased pulmonary blood flow.
Drug Interactions	Concomitant administration with heparin may result in an increased risk of bleeding.
Adverse Reactions	Apnoea is frequent. Commencement of alprostadil ≤ 20 nanogram/kg/min and low maintenance dose reduces apnea incidence. Methylxanthines (caffeine or aminophylline) may be used to prevent or treat apnoea. [4] May lower blood pressure by relaxing the vascular smooth muscle causing vasodilatation and can elevate body temperature. Other reported effects include abdominal distension, bradycardia, enterocolitis, vomiting and skin rash. [5] With prolonged use, skeletal changes [10] and hypertrophic pyloric stenosis [11, 12] have been reported. Extravasation may cause tissue necrosis.
Compatibility	Fluids: Glucose 5%, sodium chloride 0.9%. Y-site: Amino acid solutions, ampicillin; cefazolin; cefotaxime; chlorothiazide; dobutamine; dopamine; fentanyl; gentamicin; methylprednisolone; nitroprusside; potassium chloride; tobramycin, vancomycin; vecuronium. Syringe: Caffeine; dobutamine; dopamine; adrenaline (epinephrine); fentanyl; midazolam; morphine.
Incompatibility	Y-site: Levofloxacin
Stability	Diluted solution stable for up to 24 hours.
Storage	Ampoule: Store at 2 to 8°C. Do not freeze.
Special Comments	Do not use if cloudy (crystallised). Undiluted solution (500 microgram/mL) is hyperosmolar. Dilute before administration to a concentration of 20 microgram/mL or less.
Evidence summary	**Efficacy:** **Infants with ductal-dependent congenital heart defects:** No randomised controlled trials. Level III-3 studies report maintenance of oxygenation and ductal patency with doses of alprostadil 3 to 20 nanogram/kg/minute. [1, 3, 5, 6] Level III-3 studies report lower rates of apnoea with alprostadil ≤ 20 nanogram/kg/minute [1, 3]. Use of methylxanthines reduced the incidence of apnoea in newborn infants with ductal-dependent congenital heart disease receiving alprostadil. [4] (LOE II, GOR B). Infants on alprostadil infusions who are intubated for transport have higher rates of complications compared to non-

	intubated infants. [7] (LOE III-3, GOR C) In infants undergoing balloon atrial septostomy, rapid withdrawal of alprostadil infusion may be associated with hypoxaemia. [8] **Pharmacokinetics:** Metabolism of PGE_1 is an oxygen-dependent process, occurring in the pulmonary vascular bed and reduced in patients with pulmonary hypertension. [9] There is an increased volume of distribution in patients on ECMO requiring increased infusion rates to maintain ductal patency. [10] (LOE IV, GOR C) **Safety:** Reported complications include apnoea (19%), abdominal distension (16%), bradycardia (13%), enterocolitis (6.5%), hypotension (6.5%), vomiting (5%), fever (1.6%) and skin rash (1.6%). [6] (LOE III-3) With prolonged use, skeletal changes [11] and hypertrophic pyloric stenosis [12, 13] have been reported.
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Original version Date: 23/06/2016	**Author: Neonatal Medicines Formulary Consensus Group**
Current Version number: 1	**Current Version Date:** 23/06/2016
Risk Rating: Medium	**Due for Review: 23/06/2019**
Approval by: As per Local policy	**Approval Date:**