## Alprostadil (Prostaglandin E₁)

**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 E₁ or PGE₁.

**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 ductal-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]

<table>
<thead>
<tr>
<th>Infusion strength</th>
<th>Prescribed amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mL/hour = 10 nanogram/kg/minute</td>
<td>30 microgram/kg alprostadil (Prostin VR, PGE₁) and make up to 50 mL</td>
</tr>
</tbody>
</table>

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]

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<tbody>
<tr>
<td>1 mL/hour = 50 nanogram/kg/minute</td>
<td>150 microgram/kg alprostadil (Prostin VR, PGE₁) and make up to 50 mL</td>
</tr>
</tbody>
</table>

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 | 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. |
| Precautions | Concomitant administration with heparin may result in an increased risk of bleeding. |
| Drug Interactions | Apnoea is frequent. Commencement of alprostadil ≤ 20 nanogram/kg/min and low maintenance dose reduces apnoea 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. |
| Adverse Reactions | 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. |
| Compatibility | Y-site: Levofloxacin |
| Incompatibility | Diluted solution stable for up to 24 hours. |
| Stability | Ampoule: Store at 2 to 8°C. Do not freeze. |
| Storage | 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. |
| Special Comments | 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 defects. |
Alprostadil (Prostaglandin E\textsubscript{1})

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\textsubscript{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.

**References**