Alprostadil

**Brand names**
Prostin VR Pediatric, generic (Prostaglandin E1, PGE1)

**Medication error potential**
Look-alike, sound-alike drug names. Alprostadil may be confused with ALPRAZolam.

**Contraindications and warnings**

- **U.S. boxed warning:** Apnea may occur in 10% to 12% of neonates with congenital heart defects and is seen most often in those weighing <2 kg at birth.\(^{(1)}\) Signs and symptoms generally appear during the first hour of drug infusion.\(^{(1)}\) The medication should only be used in facilities where ventilator support is available and respiratory status can be monitored.

- **Other warnings:** May cause gastric outlet obstruction in neonates secondary to antral hyperplasia. The effect appears to be related to the duration of therapy (i.e., >120 hr) and cumulative dose.\(^{(1,3)}\) Because alprostadil inhibits platelet aggregation, it should be used cautiously in neonates with bleeding tendencies.\(^{(1)}\) Infuse alprostadil at lowest effective dose and for shortest period of time while weighing the risks of long-term effects versus benefits.

**Infusion-related cautions**

Studies have shown that intra-aortic or intra-arterial infusion is no more effective than peripheral IV infusion in the management of patent ductus arteriosus (PDA); hence, infusion via a large peripheral vein is preferred.\(^{(1)}\)

If fever or hypotension develops, the infusion rate should be slowed until resolution.\(^{(1)}\) If apnea or bradycardia occur during the infusion, alprostadil should be discontinued and supportive therapy should be provided.\(^{(1)}\)

Cutaneous flushing is generally due to improper catheter placement and rapidly reverses with repositioning of the intra-arterial catheter.\(^{(1)}\)

Extravasation of concentrated solution may cause tissue sloughing and necrosis.\(^{(4)}\)

**Dosage**

- **Hepatic veno-occlusive disease:** 0.075 mcg/kg/hr increased q 12 hr until the maximum tolerated dose of 0.5 mcg/kg/hr has been reached.\(^{(5)}\) Used in conjunction with 100 units/kg/day of heparin as a continuous infusion.\(^{(5)}\)

- **PDA:** Short-term maintenance of PDA in neonates with ductal-dependent cyanotic and acyanotic congenital heart disease until surgery can be performed. 0.05–0.1 mcg/kg/min.\(^{(6-11)}\) Although larger doses (0.4 mcg/kg/min) have been given, exceeding 0.1 mcg/kg/min generally does not provide additional benefit.\(^{(12)}\) Some have suggested that smaller doses (0.01 mcg/kg/min)\(^{(36)}\) or very small doses (0.003–0.005 mcg/kg/min)\(^{(38)}\) adequately controlled PDA with fewer adverse effects. Early discontinuation of alprostadil following balloon atrial septostomy has been associated with an increased risk of rebound hypoxemia that necessitates reinstitution of alprostadil; hence, a graded approach to discontinuation that is based on illness severity and magnitude and duration of hypoxemia is suggested.\(^{(13)}\)

- **Peripheral gangrene secondary to ischemia:** 0.05 mcg/kg/min reversed acrocyanosis of the hands and feet within 4 days.\(^{(14,15)}\)

- **Pulmonary hypertension**
  - **Heart transplant:** 0.05 mcg/kg/min during extracorporeal membrane oxygenation (ECMO). After releasing aortic cross clamps, increase to 0.1–0.15 mcg/kg/min.\(^{(16,17)}\)
  - **Liver transplant:** Prior to unclamping, infuse 0.0125 mcg/kg/min. If hypotension occurs, double infusion to 0.025 mcg/kg/min.\(^{(18-22)}\)

**Dosage adjustment in organ dysfunction**

No dosage adjustment required in renal dysfunction.\(^{(23)}\) One case report noted markedly larger dosage requirements (0.8 mcg/kg/min) in a newborn with ductal-dependent congenital heart disease who was receiving ECMO.\(^{(24)}\)

**Maximum dosage**

0.4–0.8 mcg/kg/min has been used without adverse effects, but doses of >0.1 mcg/kg/min have not improved efficacy in PDA.\(^{(1,6,24,25)}\)

**Additives**
None
Alprostadil

**Suitable diluents**
Must be diluted before administration in D5W, D10W, or NS.\(^{(26)}\)

**Maximum concentration**
20 mcg/mL\(^{(26)}\)

**Preparation and delivery**
*Parenteral products should be visually inspected for particulate matter and discoloration before use. Refer to appropriate references for more information on compatibility with other drugs and solutions, compatibility following Y-site delivery, and suggested storage and extended stability.*\(^{(26)}\)

**Delivery system issues:** Direct contact of the concentrated alprostadil solution with the wall of the plastic volumetric infusion chamber should be avoided because the drug may interact with the plastic to produce a hazy solution. If this occurs, the chamber and solution should be discarded. The infusion solution should be added to the plastic volumetric chamber first. Various concentrations (i.e., 500 mcg/mL, 250 mcg/mL, 125 mcg/mL) were stable for 30 days when stored in 1-mL polypropylene syringes.\(^{(1,26)}\)

**Stability:** Concentrated solution should be refrigerated.\(^{(26)}\) Prepare fresh solution every 24 hours.\(^{(26)}\)

**IV push**
Not recommended because of short half-life\(^{(1)}\)

**Intermittent infusion**
Not recommended because of short half-life\(^{(1)}\)

**Continuous infusion**
The manufacturer suggests the following dilutions and infusion rates to provide a dose of 0.1 mcg/kg/min.\(^{(1)}\)

<table>
<thead>
<tr>
<th>Add 1 Ampul (500 mcg) to</th>
<th>Approximate Concentration of Resulting Solution</th>
<th>Infusion Rate (mL/kg/min)</th>
<th>Infusion Rate (mL/kg/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250 mL</td>
<td>2 mcg/mL</td>
<td>0.05</td>
<td>3</td>
</tr>
<tr>
<td>100 mL</td>
<td>5 mcg/mL</td>
<td>0.02</td>
<td>1.2</td>
</tr>
<tr>
<td>50 mL</td>
<td>10 mcg/mL</td>
<td>0.01</td>
<td>0.6</td>
</tr>
<tr>
<td>25 mL</td>
<td>20 mcg/mL</td>
<td>0.005</td>
<td>0.3</td>
</tr>
</tbody>
</table>

**Other routes of administration**
None

**Comments**

**Rare adverse effects:** Reports of an urticarial rash\(^{(27)}\) and “harlequin color change”\(^{(28)}\) have been documented during alprostadil infusion in neonates with cardiac heart defects. The rash is erythematous, migratory, primarily limited to the upper torso, self-limiting, and resolve upon drug discontinuation.\(^{(25,27)}\)

Ectopic calcifications in the deep tissues of the axillae, thoracic inlet, and neck were noted on the chest x-ray of an infant who had received a cumulative alprostadil dose of 5654 mcg/kg for documented transposition. Brown fat necrosis was confirmed on autopsy.\(^{(29)}\)

A “pseudo-Barter syndrome” has been reported during infusions and is characterized by severe hyponatremia and polyuria, which resolves upon drug discontinuation.\(^{(1,30)}\)

Leukocytosis has been reported and resolves with discontinuation of therapy.\(^{(21)}\)

Cortical proliferation may develop as early as 9 days into therapy (usually 4–6 weeks) and may present as soft tissue swelling (e.g., periorbital, upper and lower extremities), peripheral hard edema, and cortical hyperostosis.\(^{(1,32-35,37,38)}\) The changes are reversible upon alprostadil discontinuation but have taken up to 38 weeks to resolve completely.\(^{(32)}\) It is believed that the effects are dose and duration dependent.\(^{(32-35,37,38)}\)