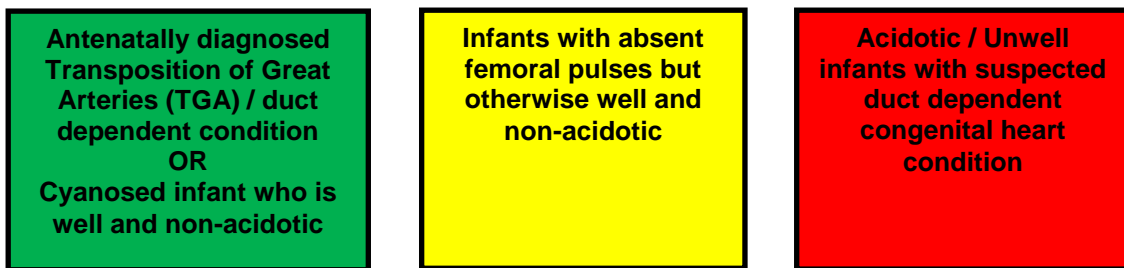


# Yorkshire & Humber Neonatal ODN and Yorkshire & Humber Paediatric CHD Network

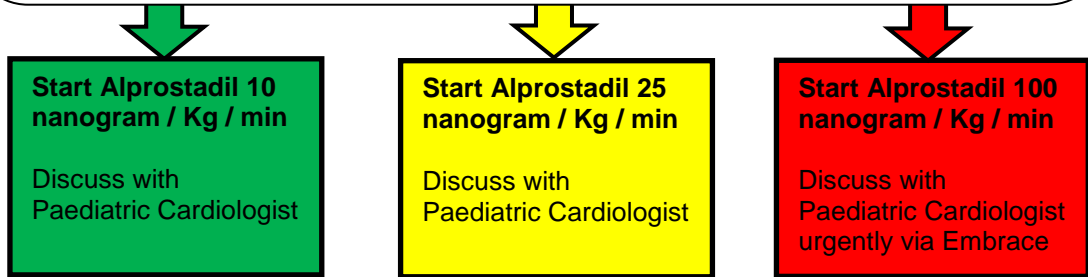
## Regional Guideline on use of Alprostadil in duct dependent congenital heart conditions in neonates

Ownership: Dr Sam Wallis, Consultant Neonatologist  
 Publication Date: Jan 2012, Reviewed September 2015.  
 Next Review Date: September 2018

### Summary: Use of Alprostadil in duct dependent congenital heart conditions



- Manage Airway, Breathing, Circulation as per NLS / APLS guideline for sick infant
- Sepsis, respiratory (incl. PPHN) or metabolic conditions can mimic or can be associated with duct dependent heart conditions – treat these if any clinical suspicion.
- Acidotic / unwell infants usually need mechanical ventilation for severe hypoxaemia, acidosis or cardio-respiratory failure
- **Do not delay in starting Alprostadil, which can be given peripherally or centrally**
- Priming your line and running alprostadil alongside a continuous dextrose infusion allows quicker delivery of alprostadil and may allow quicker recognition if the line tissues or is unintentionally clamped



Aim for oxygen saturations between 75-85% (if cyanosed) or palpable femoral pulses

Double the dose after every 20 min if no improvement in oxygen saturations or femoral pulses and discuss with paediatric cardiologist via Embrace

Aim for maximum achievable oxygen saturations (unless a non-cardiac cause is reliably excluded) / palpable femorals

Consider correcting metabolic acidosis

**Time Critical Emergency:** Consider time critical emergency if oxygen saturations do not increase above 70% or no improvement in acidosis or lactate levels despite 100nanograms/Kg/min of Alprostadil

**Calling Embrace on 0845 147 2472** at an early stage to allow discussion of transport options is strongly recommended.

# Alprostadil

<b>Indication</b>	<p>To maintain or restore patency of the ductus arteriosus <i>Only to be used in infants who are ventilated or where ventilation is immediately available</i></p> <p>Vasodilator with specific action on the tissues of the ductus arteriosus Inhibitor of platelet aggregation</p>
<b>Dose</b>	<p>5-100 nanograms/kg/minute <b>Dependent upon presentation, follow flow chart</b> See regional guideline for full guidance</p>
<b>Route of administration</b>	<p>Intravenous infusion (central or peripheral)</p>
<b>To prepare an infusion</b>	<p>1ml ampules of 500microgram/mL</p> <p><b>Preferred diluent:</b> glucose 5% Other diluents: sodium chloride 0.9%</p> <p><b>300 micrograms in 50mL:</b> Draw up 0.6mL of the 500 micrograms/mL Alprostadil (300 micrograms) and add to 49.4mL of diluent</p> <p>Note: 50 nanograms/kg/minute = 0.5mL/kg/hour</p>
<b>Compatibilities</b>	<p>Caffeine citrate, cefotaxime, dobutamine, dopamine, fentanyl, furosemide, gentamicin, vancomycin, parenteral nutrition – vamin only. Can add terminally, when necessary, to a line containing adrenaline, glyceryl trinitrate, heparin, lidocaine, midazolam, morphine, sodium nitroprusside, pancuronium, phenobarbital. <b>Incompatible</b> with lipid part of parenteral nutrition.</p>
<b>Notes</b>	<p>Always prescribe as ALPROSTADIL. Never prescribe as Prostaglandin E1 or Prostin. The continuous infusion should NOT be stopped. An infant on Alprostadil should have 2 routes of intravenous access (one for the Alprostadil and the other as a spare for other IV infusions). <b>Remember to prime the giving set to minimise delay in Alprostadil reaching the patient.</b> <b>Running alongside a continuous dextrose infusion allows quicker delivery of alprostadil and may allow quicker recognition if the line tissues or is clamped</b></p> <p>At low infusion rates it may take time for Alprostadil to reach the patient. For example - priming volume for 4Fr UVC = 0.26mL for each lumen.</p> <p>Do not store undiluted solution in plastic syringes. Dilute immediately after drawing up the solution as Alprostadil can react with the plastic causing formation of a haze. If this occurs the solution and syringes should be discarded immediately and replaced with fresh solution. Syringes should be stable for 24 hours. Alprostadil use can potentially cause line degradation over time. Line failure / breakage has occasionally been reported where infusions have run through the same line for long periods (weeks).</p> <p>If there is no compatibility information for specific drugs, do not assume compatibility. For incompatible drugs or those with no compatibility information use a separate line.</p>
<b>References</b>	<p>Regional guideline on the use of alprostadil in duct dependent congenital heart conditions in neonates. July 2015. Yorkshire and Humber Neonatal Network and Yorkshire Paediatric Congenital Cardiac Network. Neonatal Formulary 7<sup>th</sup> edition. Medusa. Handbook of Injectable Drugs. BNFc.</p>

## Aims

To improve the management of duct dependent congenital heart conditions.

## Objectives

1. To provide evidence-based recommendations for starting the appropriate dose of Alprostadil depending upon the clinical presentation of duct dependent or suspected duct dependent congenital heart conditions.
2. To provide guidance on management of duct dependent or suspected duct dependent congenital heart conditions.
3. To enhance the uniformity of practice in management of duct dependent congenital heart conditions across the Yorkshire and Humber Neonatal ODN and Yorkshire Paediatric Congenital Cardiac Network.

## Background:

Infants with suspected duct dependent congenital heart disease (CHD) require Alprostadil infusion to promote patency of the ductus arteriosus.

Alprostadil is a Prostaglandin E1 and paediatric preparation is marketed as: *Prostin VR*.

Duct dependent conditions include:

1. Left ventricular outflow obstruction: Coarctation of aorta, critical aortic stenosis, severe hypoplastic / interrupted arch of aorta
2. Right ventricular outflow tract obstruction: Pulmonary atresia, critical pulmonary stenosis, tricuspid atresia
3. Transposition of great arteries (TGA). May require urgent transfer for atrial septostomy

**Sepsis, respiratory or metabolic conditions are far more common than duct dependent CHD in neonatal period and these can mimic similar clinical presentation or can be associated with duct dependent CHD - Treat these conditions if any clinical suspicion!**

## Indications of Alprostadil:

Alprostadil is a potent vasodilator which is effective in maintaining the patency of the ductus arteriosus in duct dependent congenital heart conditions. The common indications for starting Alprostadil are:

1. Antenatally diagnosed left ventricular (LV) or right ventricular (RV) outflow tract obstruction or TGA
2. High suspicion of CHD with poor pulses or significant cyanosis
3. Confirmed or suspected duct dependent congenital heart condition on echocardiogram

## Dosing regimen:

The dose of Alprostadil ranges from 5 to 100 nanograms/Kg/min.

Higher doses, up to 200 nanograms/kg/min, can be used on advice of the paediatric cardiologist, neonatologist or intensivist.

## Dosing regimen:

An open duct (e.g. shortly after birth in antenatally diagnosed duct dependent cases) requires a small dose to keep it patent. A closing or closed duct requires higher dose to open and maintain it. However, echocardiogram facilities may not be available in emergency situations or out of hours.

### Clinical presentation and dose regimen

- **Antenatally diagnosed TGA or duct dependent circulation (LV or RV obstruction):** Start on 10 nanograms/Kg/min and monitor for the response.
- **Cyanotic infant who is non-acidotic and well with suspected duct dependent CHD:** Start on 10 nanograms/Kg/min. If there is poor response (no improvement in oxygen saturation), increase the dose stepwise (double the dose up to a maximum of 100 nanograms/Kg/min) every 20 minutes aiming to achieve a clinical improvement of oxygen saturation levels (to between 75-85% providing infant remains well). Remember to consider alternative non-cardiac diagnoses.
- **Infant with poorly palpable femoral pulses who is non-acidotic and otherwise well:** Start on 25 nanograms/Kg/min. These infants may take longer to respond. Increase dose every 20 minutes (double the dose up to a maximum of 100 nanograms/Kg/min) to achieve a clinical improvement of palpable pulses with lactate maintained below 2 mmol/L.
- **Acidotic / unwell infants and suspected duct dependent CHD:** Start on 100 nanograms/Kg/min and consider mechanical ventilation. These infants usually need mechanical ventilation for severe hypoxaemia, acidosis or cardio-respiratory failure.

If not ventilated there is clearly a higher risk of apnoea in non-ventilated infants on high doses of Alprostadil (>25nanogram/Kg/min).

Rarely some of these infants may need a much higher dose (upto 200 nanograms/kg/min) which should be used after urgent discussion with the paediatric cardiologist or intensivist. The infusion rate can be reduced to 50 nanograms/Kg/min if there is rapid improvement but this is usually done after cardiology assessment.

### General management of acidotic / unwell infants with suspected duct dependent CHD:

- **DO NOT FORGET common differential diagnosis like Sepsis, Respiratory / PPHN and Metabolic conditions. These conditions are far more common than duct dependent CHD and can mimic similar clinical presentation.**
- Manage as per newborn life support (NLS) or advanced paediatric life support (APLS) guideline for sick infant
- Correcting severe acidosis may help in improving cardiac function.
- Discuss with neonatologist or PICU intensivist via Embrace for further support.

### Important notes on starting Alprostadil:

1. **DO NOT DELAY IN STARTING Alprostadil if there is clinical suspicion of duct dependent CHD** while waiting for paediatric cardiology opinion or echocardiogram, even when in-house echo facilities are present.
2. **Alprostadil infusion can be given via peripheral or central line.**
3. Infusion rates, particularly for small babies can be low. This may cause a delay between starting Alprostadil and it reaching the patient. In these instances, giving Alprostadil alongside a continuous maintenance dextrose infusion can improve flow rate and allow quicker recognition if the line tissues. Other drugs such as antibiotics or fluid boluses need to be given through a separate line and a second line should be available so that Prostin can be quickly switched if the first line fails
4. Remember to **prime the giving set** to minimise delay in Alprostadil reaching the patient. Ideally the infusion should be connected via a Y connector close to the cannula with an anti-syphon valve to prevent backtracking up the line.
5. All cases suspected to have duct dependent congenital heart condition should be discussed with the on-call paediatric cardiologist at the first opportunity but collapsed or sick infants will need immediate stabilisation, including starting Alprostadil.
6. If likely transfer to Leeds, use of the Embrace (0845 147 2472) number when calling the Paediatric Cardiologist will allow discussion of transport options at an early stage.

### Desired response to Alprostadil:

In absence of echocardiographic diagnosis aim for palpable pulses, resolving acidosis and improving oxygen saturation.

If PPHN remains a differential diagnosis then appropriate respiratory support should be provided with an aim to maximise oxygenation.

**After** confirming diagnosis monitor for response as:

1. Suspected LV obstruction with acidosis: aim for palpable pulses and resolving acidosis.
2. Cyanotic heart disease with restricted pulmonary blood flow (PBF): aim for saturations 75-85%. Accept saturations down to 70% if lactate is maintained below 2mmol/L.

### Time critical emergency:

Some infants with TGA will have restrictive mixing despite opening of the duct. These infants constitute a time critical emergency and are at significant risk of death without a balloon septostomy. Arrange for urgent transfer (Embrace) and discuss with the paediatric cardiologist.

Consider this diagnosis in any infant whose saturations do not increase above 70% or do not show improvement in their acidosis or lactate levels despite 100 nanograms/Kg/min of Alprostadil for at least 20 minutes duration.

### Antenatally diagnosed or suspected TGA:

Infants known to have a TGA antenatally should be delivered wherever possible in a centre able to carry out a septostomy (Leeds General Infirmary for Yorkshire). **Acute in-utero transfers can be organised by calling Embrace (0845 147 2472).**

## Side effects:

The common side effects are apnoea, hypotension, fever, tachycardia and looking flushed. Other known side effects include hypothermia, cardiac arrest; bradycardia, convulsions, diarrhoea and disseminated intravascular coagulation.

Side effects after prolonged Alprostadil infusion therapy include gastric outlet obstruction secondary to antral hyperplasia and hypertrophic osteoarthropathy

**In practice the major complication on starting therapy is apnoea requiring ventilator support. Apnoea after starting Alprostadil:**

- Apnoea after starting Alprostadil is the most common side effect.
- Apnoea is a less likely a complication on a dose of <15 nanograms/kg/min of Alprostadil<sup>1-2</sup>.
- Apnoea as a side effect normally occurs within 1 hour after starting Alprostadil unless dose is being increased.

In acidotic or collapsed infants the recommended dose of Alprostadil is much higher and likely to cause apnoea needing mechanical ventilation.

## Monitoring while on Alprostadil

During the infusion the newborn requires the normal close physiological monitoring of heart rate, oxygen saturation, blood pressure, respiratory rate, and core body temperature.

a) Stable infants on Alprostadil: Side effects like apnoea, profound bradycardia, or severe hypotension may warrant more intensive care support. Recurrent or prolonged apnoea may require ventilatory support in order for the infusion to be continued.

b) Critically sick infants: Alprostadil infusion MUST NOT be stopped and complications should be dealt with by providing intensive care support.

## Transfer of infants on Alprostadil

- Infants with severe hypoxaemia, acidosis and cardiorespiratory failure will need mechanical ventilation.
- Alprostadil is the drug of choice for transfer of duct dependant infants because of the lower incidence of apnoeas (compared to Dinoprostone) and is used by the Embrace transport service.
- Collapsed babies / those on higher doses of Alprostadil (e.g. 100nanograms/kg/min) will need intubation and ventilation. However at lower doses, if the infant is not suffering apnoeas after 1 hour of fixed dose infusion then ventilation is not necessary. However, it is recommended that these infants are transferred by a person who is competent to manage the airway if it becomes necessary.
- Elective intubation and ventilation may be required if the infant is to be transferred immediately after starting Alprostadil infusion. This will be agreed with the Embrace team.
- An infant on Alprostadil should have 2 routes of intravenous access.

## Indications for mechanical ventilation

1. Severe hypoxemia, acidosis or cardio respiratory failure
2. Apnoea following the introduction of Alprostadil
3. Elective ventilation may be required for transfer, especially if dose > 25 nanograms/Kg/min or has recently been increased.

## Audit and monitoring compliance

Guideline will be audited yearly. Audit criteria will include dosing of Alprostadil in different conditions, time taken to start the infusion and apnoeas following starting infusion. Dr Fatemah Rajah will be responsible for auditing the guideline.

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Clinical condition: **Duct dependent congenital heart conditions**

Target patient group: **Neonates across the Yorkshire and Humber Neonatal Operational Delivery Network and Yorkshire Paediatric Congenital Cardiac Network**

Target group: **Doctors, nurses and pharmacists involved in the care of neonates across Yorkshire and Humber Neonatal Operational Delivery Network and Yorkshire Paediatric Cardiology Network**



## Evidence Base

Evidence: B (Robust experimental and observational studies)

References and evidence levels:

- A. Meta-analyses, randomised controlled trials/systematic reviews of RCTs
- B. Robust experimental or observational studies
- C. Expert consensus.
- D. Leeds consensus. (where no national guidance exists or there is wide disagreement with a level C recommendation or where national guidance documents contradict each other)

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