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Title: **Alprostadil (Prostaglandin E1) for NICU**			Effective date: **01 September 2018**	
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BRIEF ADMINISTRATION GUIDE

(For more detailed guideline information please see the following pages)

Indications: To promote dilation of ductus arteriosus in infants with ductal dependant congenital heart disease[1-4]

Route: Intravenous: continuous intravenous infusion via a large vein[1,2,5]

Umbilical Artery Catheter (UAC): positioned near the ductus arteriosis[1,2]

Dose:

- Initially 5 nanogram/kg/minute (= 0.005 microg/kg/minute)
- Adjust by 5 nanogram/kg/minute increments until therapeutic response
- Maximum rate 100 nanogram/kg/minute (= 0.1 microg/kg/minute)
- After a therapeutic response has been obtained, reduce infusion rate to lowest possible dosage that maintains the desired response (weigh oxygenation versus adverse effects)
- In general, higher infusion rates do not produce greater therapeutic effects but increase the incidence of adverse effects[1-3,6]

Supplied as: Alprostadil 0.5 mg/ml ampoule[1]

Preparation and administration:

- Dilute alprostadil 150 microgram/kg to a final volume of 50 ml with compatible fluid[1,5-7]
- The final concentration of the infusion will vary depending on the weight of the neonate but will usually be 3 – 6 microgram/ml. In rare situations where fluid restriction is necessary, the maximum concentration is 20 microgram/ml[1,5-7]
- Administer by continuous infusion at the prescribed rate; 0.1 ml/hour provides a dose of 5 nanogram/kg/minute[1,5-7]
- Discard any unused portion of the ampoule remaining
- Change the solution and tubing every 24 hours

Monitoring:

- Observe respiratory effort closely. Be prepared to intubate/resuscitate[2,3,6,8]
- Monitor arterial pressure closely. If this falls, a bolus of fluid (10 - 20 ml/kg) is required. It may be necessary to decrease the rate of infusion[1,3,6]
- Pulse oximetry is mandatory due to risk of apnoea and to monitor therapeutic effect in cyanotic heart disease[1-3]
- Monitor heart rate continuously[3,6,8]
- Closely monitor infant temperature[3,6,8]
- Monitor renal function, full blood count and platelets frequently[3]

1. Purpose and scope

To facilitate the safe and effective use of alprostadil in the Neonatal Intensive Care Unit (NICU).

2. Drug

Drug	**Alprostadil, prostaglandin E1**
Drug action	Alprostadil is one of a family of naturally occurring acidic lipids. It causes vasodilation by means of a direct effect on vascular and ductus arteriosus smooth muscle. Alprostadil must be infused continuously because it is very rapidly metabolised by oxidation in the lungs with a half-life of 30 seconds to 10 minutes. 81% of alprostadil is bound to plasma proteins and its metabolites are excreted primarily by the kidney[1,8].
Indications	To promote dilation of ductus arteriosus in infants with ductal dependant congenital heart disease, including[2-4,6]: • Transposition of the great arteries • All right sided congenital heart defects associated with reduced pulmonary perfusion • Left sided congenital heart defects including hypoplastic left heart syndrome, coarctation of aorta and interrupted aortic arch
Presentation	Alprostadil 0.5 mg/ml ampoule[1] Clear solution. Contains dehydrated alcohol[1]
Route	Intravenous: continuous intravenous infusion via a large vein[1,2,5] Umbilical Artery Catheter (UAC): positioned near the ductus arteriosis[1.2]
Dose	• Initially 5 nanogram/kg/minute (= 0.005 microg/kg/minute) • Adjust by 5 nanogram/kg/minute increments until therapeutic response • Maximum rate 100 nanogram/kg/minute (= 0.1 microg/kg/minute) • After a therapeutic response has been obtained, reduce infusion rate to lowest possible dosage that maintains the desired response (weigh oxygenation versus adverse effects) • In general, higher infusion rates do not produce greater therapeutic effects but increase the incidence of adverse effects[1-3,6]
Contraindications	• Hypersensitivity to alprostadil or any component of the preparation
Precautions	• Neonates with respiratory distress syndrome (hyaline membrane disease). Full diagnostic workup should be done to differentiate between respiratory distress syndrome and cyanotic heart disease[1-3,8] • Caution in neonates with bleeding tendencies as alprostadil inhibits platelet aggregation[1-3,8] • Total anomalous venous return with obstruction[3,4] • Seizure disorders[1,3]
Incompatibilities	Compatible with glucose 5% and sodium chloride 0.9%[2,5]
Adverse effects	• Apnoea – 10-12% of neonates with congenital heart defects. Most often in babies weighing less than 2 kg and usually during first hour of infusion[2,7,8] • Transient pyrexia[1,2] • Bradycardia, hypotension, tachycardia[1,2] • Seizures[1] • Diarrhoea[1]

	• Cutaneous vasodilation (flushing)[2,7] • Uncommon: Cardiac arrest, oedema, sepsis, disseminated intravascular coagulation (DIC)[1,2] • Extravasation may cause tissue sloughing and necrosis[2,5,7]

3. Administration

Competency for administration	This procedure is carried out by, or under, the direct supervision of a registered nurse/registered midwife who holds current Waikato DHB Generic Medicine Management and IV certification as well as Neonatal specific competency NCV/NAC.
Preparation & Administration	• Dilute alprostadil 150 microgram/kg to a final volume of 50 ml with compatible fluid[1,5-7] • When diluting alprostadil, draw up diluent first as undiluted alprostadil may turn hazy when in contact with plastic. If haziness occurs, discard solution[1,6] • The final concentration of the infusion will vary depending on the weight of the neonate but will usually be 3 – 6 microgram/ml. In rare situations where fluid restriction is necessary, the maximum concentration is 20 microgram/ml[1,5-7] • Administer by continuous infusion at the prescribed rate; 0.1 ml/hour provides a dose of 5 nanogram/kg/minute[1,5-7] • Discard any unused portion of the ampoule remaining • Change the solution and tubing every 24 hours
Observations and management	• Observe respiratory effort closely. Be prepared to intubate/resuscitate[2,3,6,8] • Monitor arterial pressure closely. If this falls, a bolus of fluid (10 - 20 ml/kg) is required. It may be necessary to decrease the rate of infusion[1,3,6] • Pulse oximetry is mandatory due to risk of apnoea and to monitor therapeutic effect in cyanotic heart disease[1-3] • Monitor heart rate continuously[3,6,8] • Closely monitor infant temperature[3,6,8] • Monitor renal function, full blood count and platelets frequently[3] • Monitor for side effects associated with prolonged therapy[8]
Special considerations (storage)	• Store ampoules in the fridge (2-8°C), do not freeze[1] • Prepare fresh infusion solutions every 24 hours[1,2]
Rescue medication	• Apnoea, bradycardia, pyrexia, hypotension and flushing may be signs of drug overdosage[1] • If apnoea or bradycardia occurs, discontinue the infusion and provide appropriate medical treatment. Caution should be used in restarting the infusion[1] • If pyrexia or hypotension occurs, reduce the infusion rate until these symptoms subside[1] • Flushing is usually the result of incorrect intra-arterial catheter placement and the catheter should be repositioned[1]

4. Guardrails Information

Alprostadil is Guardrail profiled on the CC pump for NICU. Following are the guardrail limits[9]:

Guardrails Drug Name	**Alprostadil**			
Pump	**CC**			
	0.4 – 1 kg	**1 – 2 kg**	**2 – 3 kg**	**3 – 5 kg**
Concentration (microgram/ml)				
Minimum	1.2	3	3	3
Maximum	10	20	20	20
Dose rate (nanogram/kg/min)				
Default	5	5	5	5
Soft minimum	5	5	5	5
Soft maximum	20	20	20	20
Hard max	100	100	100	100

5. References

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