

NETWORK MONOGRAPH

Guideline:	DINOPROSTONE (Prostaglandin E2): Produced for Routine Intravenous Administration to Neonates for Maintenance of the Patent Ductus Arteriosus
Version:	01
Date:	January 2024
Review Date:	January 2027
Approval:	EMNODN Clinical Governance Group
Authors:	EMNODN Pharmacy Group
Consultation:	EMNODN Pharmacy Group & EMNODN Clinical Governance Group
Distribution:	Neonatal Units within EMNODN
Risk Managed:	

This document is a guideline. Its interpretation and application remains the responsibility of the individual clinician, particularly in view of its applicability across the different Trusts in the East Midlands Neonatal Operational Delivery Network. Please also consult any local policy/guideline document where appropriate and if in doubt contact a senior colleague.

Caution is advised when using guidelines after a review date.

REVIEW AND AMENDMENT LOG

Version	Type of Change	Date	Description of Change
01	New	January 2024	-

1. Product Description

Name	Dinoprostone (Prostaglandin E ₂ , Prostin E ₂)
Classification	Prostaglandin
Product Presentation	Clear, colourless, particle-free solution for injection

2. Dosage

To maintain patency of ductus arteriosus	<p>Dose range</p> <ul style="list-style-type: none"> • 5-20 nanograms / kg / minute • Usual initial dose of 5 nanogram/kg/min increased in increments of 5 nanogram/kg/min • Doses up to 100 nanograms / kg / minute have been used but are associated with increased side effects <p>Frequency & infusion rate</p> <ul style="list-style-type: none"> • Continuous IV infusion
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3. Preparation

The information included in this section is not comprehensive
For diluents and drugs not listed contact Pharmacy or Medicines Information

Reconstitution	No required
<p>Dilution</p> <p>Be careful. Dinoprostone injection is very concentrated and has to be diluted twice to get the small doses required.</p> <p>(Remember 1mg = 1000micrograms 1 microgram = 1000nanograms)</p>	<p>Brand: Dinoprostone 1mg/ml (Pfizer)</p> <p>Single strength Step 1: Dilute 0.5mg (=0.5ml) to 5ml with sodium chloride 0.9% or glucose 5% to give a 100 microgram/ml solution</p> <p>Step 2: Draw up 15 micrograms/kg (=0.15ml/kg) of the above 100 microgram/ml solution and further dilute to 50ml with sodium chloride 0.9% or glucose 5%</p> <p>Double strength (only suitable for doses of 10 nanogram/kg/min or greater).</p> <p>Step 1: as for single strength Step 2: Draw up 30 micrograms/kg (=0.3ml/kg) of the above 100 microgram/ml solution and further dilute to 50ml with sodium chloride 0.9% or glucose 5%</p> <p>Quadruple strength (only suitable for doses of 20 nanogram/kg/min or greater) Step 1: as for single strength</p>

	Step 2: Draw up 60 micrograms/kg (=0.6ml/kg) of the above 100 microgram/ml solution and further dilute to 50ml with sodium chloride 0.9% or glucose 5%
Resultant strength per ml (after step 2)	<p>Single strength: 300 nanograms/kg/ml (=0.3 micrograms/kg/ml)</p> <p>Double strength: 600 nanograms/kg/ml (=0.6 micrograms/kg/ml)</p> <p>Quadruple strength: 1200 nanograms/kg/ml (=1.2 micrograms/kg/ml)</p> <p>Double or quadruple strength may be preferred where doses exceed 10 and 20 nanogram/kg/minute respectively, and the baby is fluid restricted or has multiple co-infusions running.</p>
Compatible drugs	Sodium chloride 0.9%, glucose 5%, glucose 10%
Incompatible drugs and diluents	Do not mix with any other drugs, infuse via a separate line.
Compatible flush	Sodium chloride 0.9% infused at the same rate as the dinoprostone infusion – do not bolus the flush!

4. Method of Administration

Central or peripheral line	Can be administered via central or peripheral lines
Rate of infusion	<p>Continuous infusion via an infusion pump (or smart pump with drug library where available)</p> <p>When diluted as above to:</p> <p>Single strength 300 nanograms/kg/ml 1-4ml/hour = 5-20 nanogram/kg/min</p> <p>Double strength 600nanogram/kg/ml 1-2ml/hour = 10-20 nanogram/kg/minute</p> <p>Quadruple strength 1200nanogram/kg/ml 1ml/hr = 20 nanogram/kg/min</p> <p>DO NOT USE AN IN-LINE FILTER</p> <p>Infusion rates should not fall below 1ml/hour to ensure rapid and effective doses are reaching the patient</p>

5. Precautions

Adverse effects due to IV administration	Local reactions and erythema
Side effects	<p>Apnoea, bronchospasm, tachycardia, bradycardia, vasodilatation, hypotension, hypertension, metabolic acidosis, hypoglycaemia, seizures, pyrexia, shivering, raised white cell count, and see BNF for Children. Use >5 days may cause gastric-outlet obstruction.</p> <p>Respiratory side effects more common with high doses and in low birth-weight neonates.</p> <p>If apnoea occurs intubate and ventilate the patient. Consider reducing dose if possible. If hypotension occurs, consider reducing dose and commencing inotropic support.</p>
Essential monitoring required	Saturations, arterial oxygenation where facilities available, respiratory rate & apnoeas, heart rate, blood pressure (arm & leg), core temperature, urine output, blood glucose. Injection site
Notes	<p>Facilities for intubation and ventilation must be available</p> <p>Use lowest effective dose</p> <p>Use caution in handling this product to prevent contact with skin. Wash hands thoroughly with soap and water after administration</p>

6. Example calculations

<p>a) 1.4kg baby. Starting dose of 5nanogram/kg/minute with range of 5-20 nanogram/kg/minute infusion – single strength</p> <p>Dilute 0.5mg (=0.5ml) to 5ml with sodium chloride 0.9% or glucose 5% to give a 100 microgram/ml solution</p> <p>Draw up 15 micrograms/kg (=0.15ml/kg) of the above 100 microgram/ml solution</p> <p>$=0.15\text{ml/kg} \times 1.4\text{kg} = 0.21\text{ml}$</p> <p>and further dilute to 50ml with sodium chloride 0.9% or glucose 5%</p> <p>1-4ml/hour = 5-20 nanogram/kg/min – start at 1ml/hr and increase in steps of 1ml/hour= 5nanogram/kg/minute to a maximum rate of 4ml/hr</p>
<p>b) 1.6kg baby needing 20-30nanogram/kg/minute – double strength</p> <p>Dilute 0.5mg (=0.5ml) to 5ml with sodium chloride 0.9% or glucose 5% to give a 100 microgram/ml solution</p>

Draw up 30 micrograms/kg (=0.3ml/kg) of the above 100 microgram/ml solution

$$=0.3\text{ml/kg} \times 1.6\text{kg} = 0.48\text{ml}$$

and further dilute to 50ml with sodium chloride 0.9% or glucose 5%

1-2ml/hour = 10-20 nanogram/kg/minute, therefore 20nanogram/kg/minute = 2ml/hour so 30nanogram/kg/ minute must =3ml/hr $((30 \div 20) \times 2 = 3)$

2-3ml/hour gives 20-30 nanogram/kg/minute

c)0.9kg baby stable on 20 nanogram/kg/minute. Fluid overloaded - plan to change to quadruple strength dinoprostone

Dilute 0.5mg (=0.5ml) to 5ml with sodium chloride 0.9% or glucose 5% to give a 100 microgram/ml solution

Draw up 60 micrograms/kg (=0.6ml/kg) of the above 100 microgram/ml solution

$$=0.6\text{ml/kg} \times 0.9\text{kg} = 0.54\text{ml}$$

and further dilute to 50ml with sodium chloride 0.9% or glucose 5%

1ml/hr = 20 nanogram/kg/min

7. References

1. BNF for Children, BMJ Publishing group Ltd London. Accessed online 14/12/2023.
2. SmPC Prostin E2 Sterile Solution 1mg/ml Intravenous Prostin E2. Pfizer. Last revision 05/2022. Accessed online 14/12/2023.
3. University Hospitals of Leicester Children's Hospital. Procedure for intravenous administration of dinoprostone, April 2023.
4. Guy's and St Thomas' paediatric formulary. Accessed 14/12/2023 via app available from www.ubqo.com/paediatricformulary
5. Personal communication, Aleksandra Stach, Pfizer November 2018 (filtration).
6. Ainsworth S. Neonatal Formulary. 8th Edition, 2020. Oxford University Press.
7. Neonatal and Paediatric Pharmacist Group (2019). Glucose 5% vs glucose 10% as an infusion diluent
8. Medusa, NHS Injectable Medicines Guide, Dinoprostone Neonate and Child IV monograph, version 7-T1, published 11/11/2023