THAMES VALLEY & WESSEX NEONATAL OPERATIONAL DELIVERY NETWORK

PROSTAGLANDIN INFUSIONS: NEONATAL NURSING GUIDELINE

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Related documents	**References** Akkinally.S et al (2018) Prostaglandin E1 for maintaining ductal patency in neonates with duct dependant cardiac lesions. Cochrane database of systematic reviews, Feb 2018. Cucerea.M et al (2016) Congenital heart disease requiring maintenance of ductus arteriosus in critically ill newborns admitted at a tertiary neonatal Intensive care unit. The journal of Critical care medicine, 2016, Vol 2, No 4, pp185-191. Hillig.K (2016) prostaglandin E1: Administration implications for the care provider in the treatment of neonatal duct dependant congenital heart disease, Journal of Neonatal Nursing, Feb 2016, Vol 22, No 1, pp12-15. Linney.M et al (2010) Resuscitation of the blue baby and the use of prostaglandins 2010. SRH Paediatric Guidelines group. Western Sussex Hospitals, NHS Trust. Roy.R and Park.A (2016) Trust guideline for the management of neonates requiring a prostaglandin (dinoprostone, alprostadil or epoprostenol) infusion. Norfolk and Norwich University Hospitals NHS Trust. Segar.J (2019) Protocol for use of prostaglandin E, University of Iowa, Stead Family Children's Hospital. Singh.Y and Parasekevi.M (2018) Use of prostaglandins in duct-dependent congenital heart conditions. BMJ, Vol 103, pp137-140.

	Wallis.S (2018) Alprostadil in suspected duct dependant heart conditions, Yorkshire and Humber neonatal ODN and Yorkshire and Humber Paediatric CHD network. Found at: https://www.google.co.uk/search?source=hp&ei=rDC-XvSqGoy-aYvfhPgJ&q=alpoprostadil+in+suspected+duct&oq=alpoprostadil+in+suspected+duct&gs_lcp=CgZwc3ktYWIQAzIHCCEQChCgAToFCAAQgwE6AggAOgQIABAKOgQIABANOggIABANEAoQHjoGCAAQDRAeOggIABAIEA0QHlDyBViOggFgsIwBaARwAHgAgAFciAHMEZIBAjM1mAEAoAEBqgEHZ3dzLXdpeg&sclient=psy-ab&ved=0ahUKEwj0psyRmbXpAhUMXxoKHYsvAZ8Q4dUDCAw&uact=5#spf=1589522623174 Windscheif.P (2010) Diniprostone (prostin E2) –by Continuous Intravenous Administration, Oxford University Hospitals- John Radcliffe. YHNODN (2018) Alprostadil in suspected duct dependent congenital heart conditions, Yorkshire and Humber Neonatal ODH and Yorkshire and Humber Paediatric CHD Network. **Images.** Fig 1 Showing the Foetal and Newborn heart, Found at: https://www.bing.com/images/search?view=detailV2&id=97A0F3FEEBABAA24406CB958DBE4B155237BAB57&thid=OIP.3W8FEceMOcZuiiDJHqMN6gHaFj&mediaurl=https%3A%2F%2Fi.pinimg.com%2F736x%2F3d%2F99%2Fd7%2F3d99d7381f8c9b9c1c6ac3a6694bae50--newborn-babies-newborns.jpg%3Fb%3Dt&exph=546&expw=728&q=foetal+circulation+vs+neonatal+circulation&selectedindex=22&ajaxhist=0&vt=0
Implications of race, equality & other diversity duties for this document	**This guideline must be implemented fairly and without prejudice whether on the grounds of race, gender, sexual orientation or religion.**

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1.0 Aim of Guideline Framework

To provide a framework to ensure that all infants requiring prostaglandin infusions are optimally cared for.

2.0 Scope of Guideline Framework

The guideline applies to all infants requiring within Thames Valley and Wessex Neonatal Network Operational Delivery Network.

Thames Valley	
Buckinghamshire Healthcare NHS Trust	- Stoke Mandeville Hospital, Aylesbury
Frimley Health NHS Foundation Trust	- Wexham Park Hospital, Slough
Milton Keynes University Hospital NHS Foundation Trust	- Milton Keynes General Hospital
Oxford University Hospitals NHS Foundation Trust	- John Radcliffe Hospital, Oxford
Royal Berkshire NHS Foundation Trust	- Reading
Wessex	
Dorset County Hospital NHS Foundation Trust	- Dorset
Hampshire Hospitals NHS Foundation Trust	- Basingstoke
Hampshire Hospitals NHS Foundation Trust	- Winchester
Isle of Wight NHS Trust	- St Mary's Hospital
Poole Hospital NHS Foundation Trust	- Poole Hospital
Portsmouth Hospitals NHS Trust	- Queen Alexandra Hospital
Salisbury NHS Foundation Trust	- Salisbury
University Hospital Southampton NHS Foundation Trust	- Princess Anne Hospital
Western Sussex Hospitals NHS Foundation Trust	- St Richard's Hospital, Chichester

3.0 Guideline Summary

- The baby should be nursed in a bed space with immediate access to resuscitation equipment, and facilities for intubation and ventilation should also be available.
- There is a risk of apnoea when a baby receives a prostaglandin infusion - so all babies should be continuously monitored with ECG leads and pulse oximetry.
- There is a risk of hypotension, so blood pressure should be measured every 30 minutes initially, then reduced to hourly.
- Hourly observations and recording should occur of;
    - Heart rate.
    - Respiratory rate.
    - Blood pressure.
    - Oxygen saturation levels, both pre and post ductal.
    - Temperature on initiation of prostaglandin infusion, and then 2-4 hourly during ongoing administration.

- The drug takes effect very rapidly, but also has a rapid short life so requires continuous intravenous infusion for effective treatment.

- Both the prostaglandins alprostadil and dinoprostone are unstable drugs, so should be run in a separate intravenous line, not used for other medication.

- The baby should have spare IV access at all times when receiving a prostaglandin infusion.

- The intravenous line with a prostaglandin infusion running should never be flushed.

- Observe for side effects from the medication. The most commonly occurring are hyperthermia, respiratory depression/ apnoea, flushing and hypotension.

- The infusion will be prescribed in nanograms per kilo per minute (ng/kg/min).

- It is usual practice to start the infusion at 5nanograms/kg/min.

- The infusion rate can be calculated using the following formula;

$$\text{Infusion rate (ml/hr)} = \frac{\text{Dosage (nanograms/kg/min)} \times \text{weight in kg} \times \text{60 min/1 hour}}{\text{Concentration of infusion (nanograms/ml)}}$$

- A prostaglandin infusion should only be stopped under the guidance of the cardiologist.

4.0 Background information

Ductus Arteriosus.

The ductus arteriosus is a blood vessel connection found in the foetus that lies between the pulmonary artery (supplying blood to the lungs) and the aorta (supplying blood to the body). It allows most of the blood from the right ventricle to bypass the foetus's fluid-filled non-functioning lungs. Normally the ductus is open before birth (foetal circulation) and closes naturally within the first day after birth as the baby transitions to a 'neonatal circulation' See Fig1 on page 6.

However, in certain heart conditions, where there is a block to the blood flow either to the lungs or the body, the baby will deteriorate if the ductus closes because the newly evolving neonatal circulation is not compatible with life. These heart conditions are classified as 'duct dependent' and include transposition of the great arteries, hypoplastic left heart, critical co-arctation of the aorta, pulmonary atresia and interrupted aortic arch. Many of these conditions can be corrected or managed using a surgical procedure, however, time is required to confirm a formal diagnosis, plan for surgery, and in some situations give the baby time to grow larger so the surgery has more chance of success.

In order to enable time for this planning and growing to occur, an intravenous infusion of prostaglandin can be administered to a neonate. It maintains the patency of the ductus, and therefore allows blood to mix between the two distinct circulatory pathways that can exist with certain heart conditions.

Prostaglandins.

The prostaglandins are a group of naturally occurring, physiologically active compounds. They have diverse hormone-like effects and are found in almost every tissue in the human body. Prostaglandins differ in structure, and it is these differences that account for their varied biological activities. The name of each specific prostaglandin is derived from its chemical structure, being named with a letter first, followed by a number. For example, prostaglandin E1 is abbreviated PGE1 or PGE_1, and prostaglandin I2 is abbreviated PGI2 or PGI_2.

Two different prostaglandins medications can be used in neonatal medicine to maintain the patency of the ductus arteriosus; Prostaglandin E1 (PGE1) also known as alprostadil and prostaglandin E2 (PGI2), also known as dinoprostone. Both are potent vasodilators that are effective for maintaining the patency, and both need to be administered with great care as they have a number of potential side effects for the neonate. In current neonatal practice prostaglandin E2 (dinoprostone) is used as a first line treatment, with prostaglandin E1 (alprostadil) only being used if E1 is not available.

This guideline is written to provide nursing staff with a clear outline of why, how and when to pharmacologically administer a prostaglandin infusion to the newborn neonate. For clarity within this guideline the term prostaglandin infusion will be used to refer to either/or prostaglandin E1 and prostaglandin E2, unless otherwise specified. In addition, prostaglandin infusion will be abbreviated to PGI for brevity.

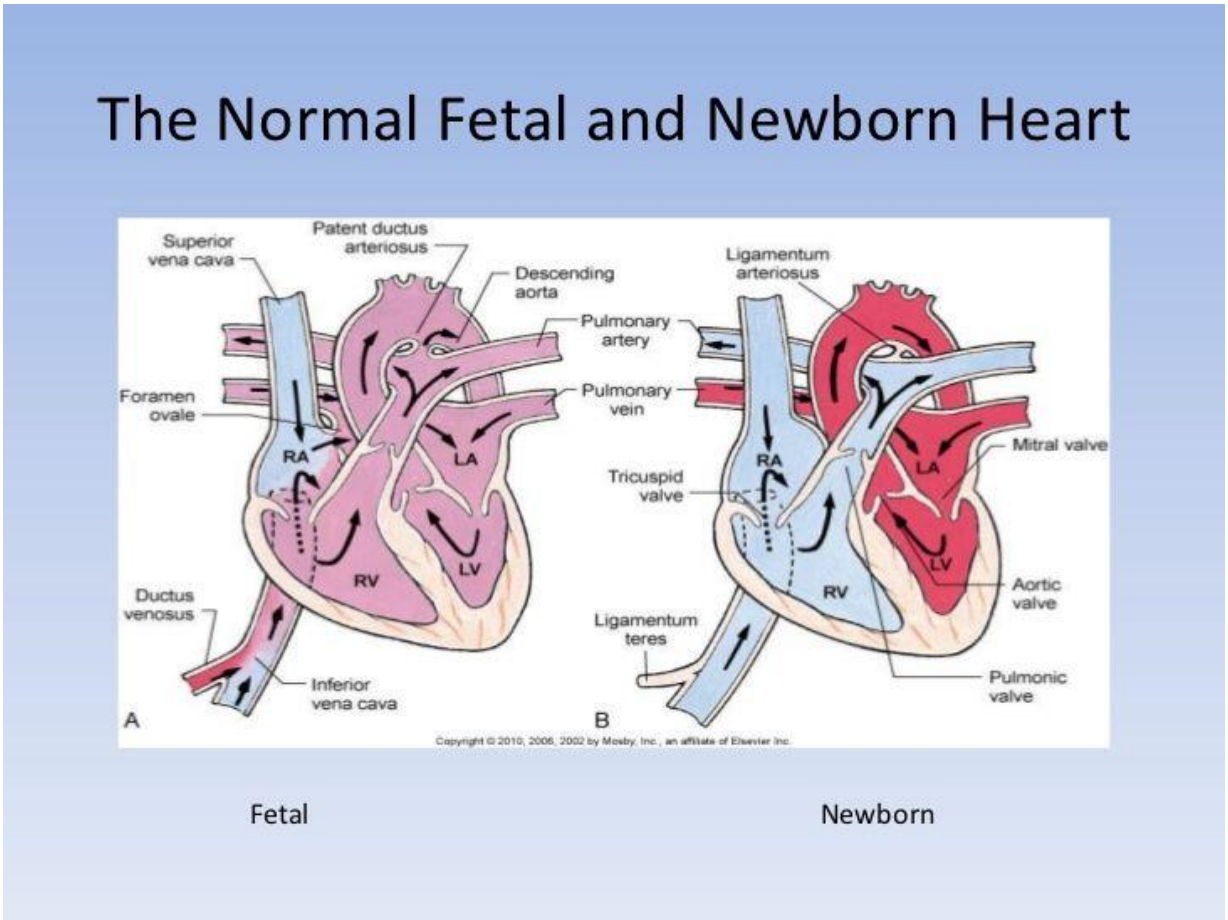

Fig 1 Showing the foetal and newborn heart.

5.0 Practice Guidelines

- PGIs are identified by many neonatal unit nursing staff as stressful and difficult aspects of their nursing practice. This is largely because a number of nursing care needs can arise at the same time, often unexpectedly with urgent action required.

- One aspects of the baby's care will relate to the need to administer the PGI safely and effectively.

- A second aspect of the baby's care is the context in which the infusion is required.

- This may be for a baby who is antenatally diagnosed with a cardiac condition- where the need for admission and a PGI has been anticipated and planned for.

- In other situations a previously well baby could be unexpectedly declining- and a cardiac condition is being considered as a potential diagnosis. This requires nursing staff to make up an unfamiliar infusion - at the same time as they may also be trying to stabilise a fragile or declining infant.

5.1 Admission of a baby requiring Prostaglandin Infusion.

- The baby should be nursed in a bed space with immediate access to resuscitation equipment- such as a Neopuff ™ or bag valve mask system. This would usually be in an intensive care environment.

- Facilities for intubation and ventilation should also be available, and intubation and ventilation should be considered for babies who will be transferred with a PGI.

- Where a baby has been antenatally diagnosed/ suspected with a duct dependant cardiac condition the PGI can be prepared in advance of the birth. Using an estimated weight (based on the baby's gestation or most recent growth scan) the prepared PGI can then be commenced in delivery suite, or immediately after admission to the neonatal unit- when a cannula is sited.

- There is a risk of apnoea when a baby receives a PGI, so all babies should be continuously monitored with ECG leads and pulse oximetry in place.

- There is a risk of hypotension, so blood pressure should be measured every 30 minutes initially, then reduced to hourly.

- The baby will require IV access. A central line is preferred, as there is more certainty that the line is patent and delivering the infusion consistently into the blood stream. If central access is unavailable, the infusion can be given via a peripheral venous line (a large vein and ideally NOT a scalp vein).

- For the newly admitted baby also consider:

    - Is a chest x ray required? - this is usually part of the diagnosis process.
    - Is a blood gas required? - the baby can be compromised, and this is part of the process of checking if this is so.
    - Do they need to be placed nil by mouth? –if the baby's circulation is compromised, it is common practice to stop milk feeds, until stabilised, as blood flow to the gut may be compromised and place the baby at risk of developing Necrotising Enterocolitis.
    - If available can the baby be reviewed urgently by cardiologist?
    - Contact the local level three unit to inform of probable cardiac diagnosis and likely need for intensive care bed and transfer.

5.2 The prostaglandin infusion.

The process for making up the infusion will vary from one hospital trust to another, so cannot be outlined within this guideline, but a range of principles will apply, however the infusion is made. These include;

- The drug takes effect very rapidly, but also has a rapid short life so requires continuous intravenous infusion for effective treatment. (80% of PGE1 is rapidly metabolised after one pass through the pulmonary bed, the remainder is excreted by the kidneys and is fully eliminated within 24 hours of stopping the medication.)

- The baby should have spare IV access at all times when receiving a PGI, so that if one IV access stops working the infusion can be transferred immediately to another cannula or central line.

- Observe for side effects from the medication. but the most commonly occurring are;

    - Hyperthermia (14%)
    - Respiratory depression/ Apnoea (12%) particularly with high doses >10ng/kg/min and in low birth weight babies.
    - Flushing (10%)
    - Hypotension (due to its properties as a vasodilator)

- However, others include;
    - nausea
    - vomiting
    - diarrhoea
    - hypoglycaemia
    - bradycardia
    - cardiac arrest
    - breathlessness
    - cyanosis
    - bronchospasm
    - raised white cell count
    - hypokalaemia
    - convulsions
    - hypothermia
    - oedema
    - degradation of central line- if infusion given through same line over many weeks

- If apnoea or hypotension occurs, DO NOT STOP THE INFUSION. Complications should be dealt with by providing Intensive Care Support. When breathing has been re-established, it is probably appropriate to lower the prostaglandin dose, in discussion with the cardiology team

- The size of the duct will be assessed initially by the medical team, who will scan the baby's heart using an echocardiogram. The duct will then be regularly rescanned to assess its size and patency.

- The infusion will be prescribed in nanograms per kilo per minute (nanograms/kg/min).

- It is usual practice to start the infusion at 5 nanograms/kg/min.

- If the duct is very large after commencing the PGI, the rate might be reduced to 3nanograms/kg/min.

- If the duct is not as open as desired, the infusion dose can be increased in 5 nanograms/kg/min increments, up to 20 nanograms/kg/min.

- Doses between 40-100 nanograms/kg/min have been given, for short durations of 30-60 mins in intensive care units when a baby is deeply desaturated or has circulatory collapse. However, doses greater than 100 nanograms/kg/min have not been found to be more effective and are more likely to cause adverse reactions.

- PGIs are unstable drugs, so should be run in a separate line, not used for other medication or parenteral nutrition.

- If at all possible, do not flush a line with a PGI running. This will cause an overdose, due to the small volume of medication.

- PGIs need to be replaced every 24 hours.
- If running the PGI through a central line it is best practice to have the infusion running at a minimum of 1ml/hr to ensure the line remains patent.
- PGIs can be made up in higher concentrations for the fluid restricted baby. The standard concentration is often referred to as 'single strength'- meaning the standard concentration used on that neonatal unit. However, they can also be made up 'double' or 'quadruple strength'. This option is usually selected when a large amount of the baby's fluid allowance is being taken up by the PGI. By concentrating the infusion, there is more fluid allowance remaining for other critical care infusions, or nutrition such as TPN.
- Prostaglandins come in more than one preparation depending on the manufacturer, so take care to check the strength/ formulation of the product you are about to use.
- PGIs can be made up using 5% Glucose- first preference, Sodium Chloride 0.9% or Glucose 10%
- Do not store undiluted drug solution in plastic syringes. Dilute immediately after drawing up, as the prostaglandin solution can react with the plastic causing formation of a haze. If this occurs, the solution and the syringes should be discarded immediately, and replaced with fresh solution.
- The PGI needs to run continuously without interruption. Always prepare the replacement new syringe before the old syringe runs out.
- If a baby is noted to be very sensitive to the PGI, -noted by oxygen saturation dropping when the syringe is changed - consider double pumping during the change of syringes.
- The infusion rate can be calculated using the following formula;

$$\text{Infusion rate (ml/hr)} = \frac{\text{Dosage (nanograms/kg/min)} \times \text{weight in kg} \times \text{60 min/1 hour}}{\text{Concentration of infusion (nanograms/ml)}}$$

Question for drug checkers	Yes/ No
Is the patient's current weight correctly recorded on the drug chart?	
Is the prescription signed	
Is the prescription in nanograms/kilo/minute?	
Has the correct dose been prescribed based on the weight? *Each checker to check dose separately.*	
Is the medication thoroughly mixed and all lines purged	
Is the infusion pump set to the correct rate/dose?	
Are baby and drug details programmed correctly into the pump- where this is possible.	

- Refer to local policy for how to make up the PGI.
- Only appropriately trained staff should be preparing the prostaglandin solution for administration.
- Whenever possible- one of the staff preparing the prostaglandin solution will be an experienced neonatal nurse and will have prepared the PGI before.

5.3 Ongoing care of the patient.

- Check blood gases regularly, especially after initiation of PGI.

- Watch for signs of deterioration/ reaction to medication (see list page 7)

- Hourly observations and recording of;
    - Heart rate.
    - Respiratory Rate.
    - Blood Pressure.
    - Oxygen Saturation, both pre and post ductal.
    - Temperature on initiation of the PGI and then 2-4 hourly during its administration.

- Take care to maintain the baby's saturations within the target level identified by the medical team. Different cardiac conditions will enable different safe levels of oxygen saturation to be maintained and giving excess oxygen to attain higher oxygen saturations can be harmful to the baby- by encouraging their PDA to close when it needs to remain open.

- Be aware that if the baby's condition declines it may not be due to the cardiac condition. Either because the possible cardiac diagnosis is incorrect, or because the baby has multiple health problems. These other conditions could be causing the problems and will need to be managed separately. For example, respiratory distress, PPHN, Meconium aspiration, Congenital abnormality/ condition or infection.

- A PGI should only be stopped under the guidance of the cardiologist. This would usually be following surgery to correct the cardiac condition, or if the medical diagnosis shows that the condition is not duct dependant.

5.4 Parents

- Keep parents informed about their baby's condition, and the most current finding/ concerns/ plans for care.

- Encourage and support parents to be involved with their baby and its care as much as possible. For example, facilitating cuddles, taking photographs, enrolling in electronic video sharing sites such as Vcreate™.

- If the baby needs to be transferred to a level three unit inform the mothers midwife, so that transfer of the mother/ parents can be arranged.

Version Control:

Version	Date	Details	Author(s)	Comments
Draft 1	Jan 2021	New Guideline circulated to TV&W Lead Nurses for comments/feedback.	KR (Chair)	
Final Draft	Feb 2021	Amendments made to guideline following feedback. Sent for ratification.		
Final Draft v1	Oct 2021	Added Monograph to appendix	MM	Ratified Dec 2021
Review Date:	**Dec 2024**			

Appendix 1
Drug**: Dinoprostone – Prostin E2** – Monograph Neonatal

Dose & Frequency	Formulation/ Presentation	Preparation / Administration	Compatibilities	Notes
Critical Care Area/Unit only with ECG, heart rate and blood-pressure (BP) monitoring: CONTINUOUS INFUSION Titrate slowly to desired response: **Starting at 5nanograms/kg/min** increased by 5nanograms/kg/min up to 20nanograms/kg/min If there is a good response to the initial dose, consider reduction to 3nanograms/kg/minute. Note: doses up to 100nanograms/kg/minute have been used but are associated with increased side effects.	0.75mg in 0.75ml ampoule (750micrograms in 0.75ml= 1mg in 1ml* MUST BE DILUTED BEFORE USE *if unavailable, 10mg/ml can be used (with appropriate dilution)	*CONTINUOUS INFUSION*: **Standard concentration-single strength** Dilute to a concentration of 1microgram in 1mL = **1000nanograms/ml** Withdraw 0.5mL (500micrograms) from the ampoule and add to 500ml bag of compatible diluent. Infusion rate of 0.3ml/kg/hour will provide 5nanograms/kg/minute. **Double strength** Dilute to a concentration of 2microgram in 1mL = **2000nanograms/ml** Withdraw 1mL (1000micrograms) from the ampoule and add to 500ml bag of compatible diluent. Infusion rate of 0.15ml/kg/hour will provide 5nanograms/kg/minute. Withdraw the required strength from the ampoule of dinoprostone using a filter needle. Change the needle and add dinoprostone to a 500mL bag of diluent and mix well. Withdraw 50mL from the bag into a syringe and attach a label. Discard the bag immediately. [1] Do not flush dinoprostone infusions.	**Diluents: -** Glucose 5%, sodium Chloride 0.9%, Glucose 10% [2] **Y-site compatibility:** No compatibility information is known. Do not infuse with any other medicines.	Monitoring: heart rate, blood pressure (arm and leg), respiratory status – breathing rate, apnoea, arterial oxygenation and core body temperature, urine output. ALL BABIES ON DINOPROSTONE MUST BE ON AN APNOEA ALARM Dinoprostone may be associated with NEC. [2] Side effects: nausea, vomiting, diarrhoea, flushing, bradycardia, hypotension, cardiac arrest, respiratory depression and apnoea (particularly with high doses >10nanograms and in LBW infants), bronchospasm, pyrexia and raised WBC. Half life: 95% inactivated within 90 seconds of administration. Use caution in handling this product to prevent contact with skin. Wash hands thoroughly with soap and water after administration.

Indications	*Calculation example: for a 2.3kg neonate*	References:
Unlicensed – to maintain the patenty of the ductus arteriosus in babies with congenital heart defects dependent on the duct for survival, prior to corrective surgery	*To prepare the standard continuous infusion: withdraw 0.5ml (=0.5mg=500micrograms) and add to 500ml of compatible diluent to get a 1microgram in 1ml solution. Rate of 0.69ml/h will provide 5nanograms/kg/min [5nanograms x 2.3(kg) x 60(min)/1000(nanograms/ml)]* *To prepare double strength: withdraw 1ml (=1mg=1000micrograms) and add to 500ml of compatible diluent to get a 2micrograms in 1ml solution. Rate of 0.34ml/h will provide 5nanograms/kg/min [5nanograms x 2.3 (kg) x60 (min) /2000(nanograms/ml)]*	1. Medusa National Injectable monographs accessed 12/07/21 2. Evelina London Paediatric formulary accessed 12/07/21 3.Ainsworth, S., (2020) Neonatal formulary 8th Ed. (suggested concentration 600nanograms/kg/ml) 4.Akkinally, S. et al (2018) Prostaglandin E1 for maintaining ductal patency in neonates with duct dependant cardiac lesions. Cochrane database of systematic reviews, Feb 2018. 4.Cucerea, M. et al (2016) Congenital heart disease requiring maintenance of ductus arteriosus in critically ill newborns admitted at a tertiary neonatal Intensive care unit. The journal of Critical care medicine, 2016, Vol 2, No 4, pp185-191. 5.Hillig,K. (2016) prostaglandin E1: Administration implications for the care provider in the treatment of neonatal duct dependant congenital heart disease, Journal of Neonatal Nursing, feb 2016, Vol 22, No 1, pp12-15.