Peripheral Administration of Noradrenaline (pNA) Clinical Guideline

V1.0

December 2023

Summary

This outlines a safe approach to administration of peripheral noradrenaline (pNA).

Key points:

- It can be used in the perioperative period with predictable post-operative weaning.
- It can be used in hypotension with shock, related predominantly to vasoplegia where central venous catheter (CVC) access is unavailable or where risks of CVC insertion outweigh benefits.
- It can only be instigated by anaesthetists around the perioperative period in patients with hypotension due to anaesthesia or their surgical condition in theatre or recovery.
- It can be instigated by critical care consultants or senior trainees for patients suitable for critical care admission with acute shock pathologies.
- It is not suitable for use in the emergency department or outside of critical care or theatre environment.
- The concentration of peripherally administered noradrenaline is different to that of centrally administered noradrenaline. **The only permitted concentration for peripheral administration is 4mg/250mL (16mcg/ml)**. Care with infusion preparation is needed.
- Its use has been demonstrated to be safe in the context of extravasation concerns and has been condoned by the Intensive Care Society (1).
- Extravasation must be monitored for and managed appropriately.

1. Aim/Purpose of this Guideline

1.1. This guideline outlines the use of peripheral noradrenaline perioperatively and applies to:

Setting: Operating Theatres, Recovery and EPOC.

Staff: all medical, nursing, and auxiliary staff utilising vasopressor infusions in the care of patients directly supervised by Anaesthetic / Critical Care staff.

Patients: adult patients with, or at risk of, vasoplegic shock and organ dysfunction.

1.2. This version supersedes any previous versions of this document.

Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation

The Trust has a duty under the Data Protection Act 2018 and General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

Data Protection Act 2018 and General Data Protection Regulations 2016/679 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the Data Protection Act 2018 and General Data Protection Regulations 2016/679 please see the Information Use Framework Policy or contact the Information Governance Team

Royal Cornwall Hospital Trust rch-tr.infogov@nhs.net

2. The Guidance

2.1. Background

2.1.1. Vasopressor therapy is required to increase systemic arterial vascular tone (or systemic vascular resistance – SVR) in conditions where this tone is reduced. Blood pressure is a useful surrogate for the diagnosis of low SVR in a euvolaemic patient. In this context a reduced SVR can lead onto inadequate organ perfusion, resulting in organ dysfunction

2.1.2. Causes of reduced SVR reversible with vasopressor therapy are:

1. Anaesthesia related
2. Central neuraxial analgesia / anaesthesia e.g. spinal / epidural techniques.
3. Septic shock.
4. Neurogenic shock.

2.1.3. Increasing the SVR back towards a normal range with concomitant and appropriate fluid administration can prevent and potentially reverse further organ dysfunction. Therefore monitoring of blood pressure and appropriate administration of both fluid and vasopressor therapy is key.

2.1.4. Noradrenaline is a mixed alpha and beta adrenoreceptor agonist, predominantly with action on the former. Its effects include direct receptor mediated action; rapid onset, titratability and offset; as well as a balanced increase in SVR with comparable additional inotropy.

2.1.5. Traditionally noradrenaline was only administered via central venous access in a more concentrated form than the peripheral version considered in the guideline. This has its own risks and has limited noradrenaline's ability to be instigated rapidly. Recent evidence has suggested that peripherally administered, more dilute, noradrenaline has a similar safety profile, in terms of extravasation and effective therapeutic benefits, to those agents which have long been considered "safe" to be delivered via peripheral venous access.

2.1.6. All vasopressor and inotropic infusions are potentially hazardous. As detailed above they should only be commenced by medical staff trained in anaesthesia or critical care. They should only be physically delivered by nursing and medical staff who have competence in intravenous drug administration, experience with vasopressor / inotrope infusions and who have read this protocol.

2.2. Starting peripheral Noradrenaline (pNA)

2.2.1. Scope of pNA administration

The use of pNA is intended in the following clinical scenarios:

a.) For short term use in the perioperative period with predictable post-operative weaning.
b.) As a short-term measure whilst central venous access is established.
c.) Where central venous access is challenging, or the risks outweigh the benefits.

It is not intended to replace the utilisation of central lines for major surgical cases, which may be needed for multiple centrally delivered drugs, electrolytes, fluid, and nutrition.

It is intended that it will be started in theatre and supported post-operatively in recovery and EPOC.

Hypovolaemic states should be corrected prior to, or concurrent with administration of pNA.

2.2.2. Practitioners initiating pNA

Initiation of pNA can be done by an anaesthetic / critical care consultant or senior anaesthetic trainee. This can only happen in theatres/recovery/ EPOC.

pNA must not be commenced in the Emergency Department or any ward.

Delivery of the therapy can be performed by any medical or nursing staff, with competence in intravenous drug administration, experience with vasopressor infusions and who have read this protocol. Prolonged or increasing use should prompt senior medical review and escalation to critical care if required.

2.2.3. Intended patient population

1) Adult patients with peri-operative hypotension, where vasodilation is secondary to ongoing or residual effects of anaesthesia/surgery.

2) Adult patients suitable for critical care admission with a clinical picture consistent with a shock state (predominantly due to low SVR) who are at risk of, or with established end organ dysfunction. This will usually manifest as hypotension unresponsive to first line therapy of fluid administration, where a primary cause of hypovolemia/cardiogenic shock is not suspected. pNA can be used prior to initiation of noradrenaline via central access which should be done prior to critical care.

2.2.4. Making up pNA

pNA must be made as a concentration of 16 micrograms/ml solution. Please note this is **different** to the centrally administered noradrenaline concentration. Centrally administered noradrenaline concentrations should **NEVER** be given peripherally.

1) Remove 4ml of fluid from a 250mL bag of 0.9% sodium chloride or 5% glucose.

2) Add 4mg (4mls of 1mg/ml) of noradrenaline to the 246mL bag of 5% glucose/0.9% sodium chloride. This gives a total volume of 250mls.

3) Best practice is to use a single syringe drawing of 50mls from the 250mls solution and discard the remains.

However this may not be practicable, if so, draw off 2 x 50ml syringes of the solution from this bag, to be run through a syringe driver. These syringes are only for use in the same patient and must be clearly labelled in accordance with trust policy – a fully completed white drug additive label.

It is anticipated the second syringe will be used within 24hours. If not, it must be discarded, and a fresh infusion made.

2.2.5. Administering pNA

2.2.5.1. Venous access:

A 20G (pink) peripheral venous cannula or larger, in a large vein with good flow, blood returns on insertion and the cannula flushes easily with 0.9% sodium chloride. The cannula should be located in the forearm, at or proximal to the wrist. Avoid sites where multiple venepunctures have occurred (increased risk of extravasation).

A 2nd cannula must be available, with the same requirements as the first, as a contingency in case of primary cannula failure. This may be a cannula used for other drug/fluid administration in whom a break is not detrimental to enable a new cannula to be inserted. Prior to use this **must** be flushed with 0.9% sodium chloride.

In theatre the cannula should be visible, ideally the arm into which the pNA is being administered should be out on a board to prevent any kinking of veins. This will allow early visualisation of any extravasation.

2.2.6. Prescribing pNA

2.2.6.1. Prescribing:

Within theatres this should be prescribed on the anaesthetic chart.

Outside of theatres the infusion should be prescribed ideally on EPMA, or in an emergency on the RCHT fluid infusion prescription, as: either ‘Noradrenaline 0.8mg made up to 50ml with 5% glucose / 0.9% sodium chloride’ or “Noradrenaline 4mg made up to 250mls with 5% glucose / 0.9% sodium chloride” to run intravenously.

The rate should be charted as: ‘0.05- 0.1micrograms/kg/minute to achieve a desired MAP, or systolic BP range.

2.2.6.2. Rate of administration:

At all times, follow table 1 (below) and titrate by flowchart 1. A specified blood pressure (BP) target end point should be documented before commencing the infusion.

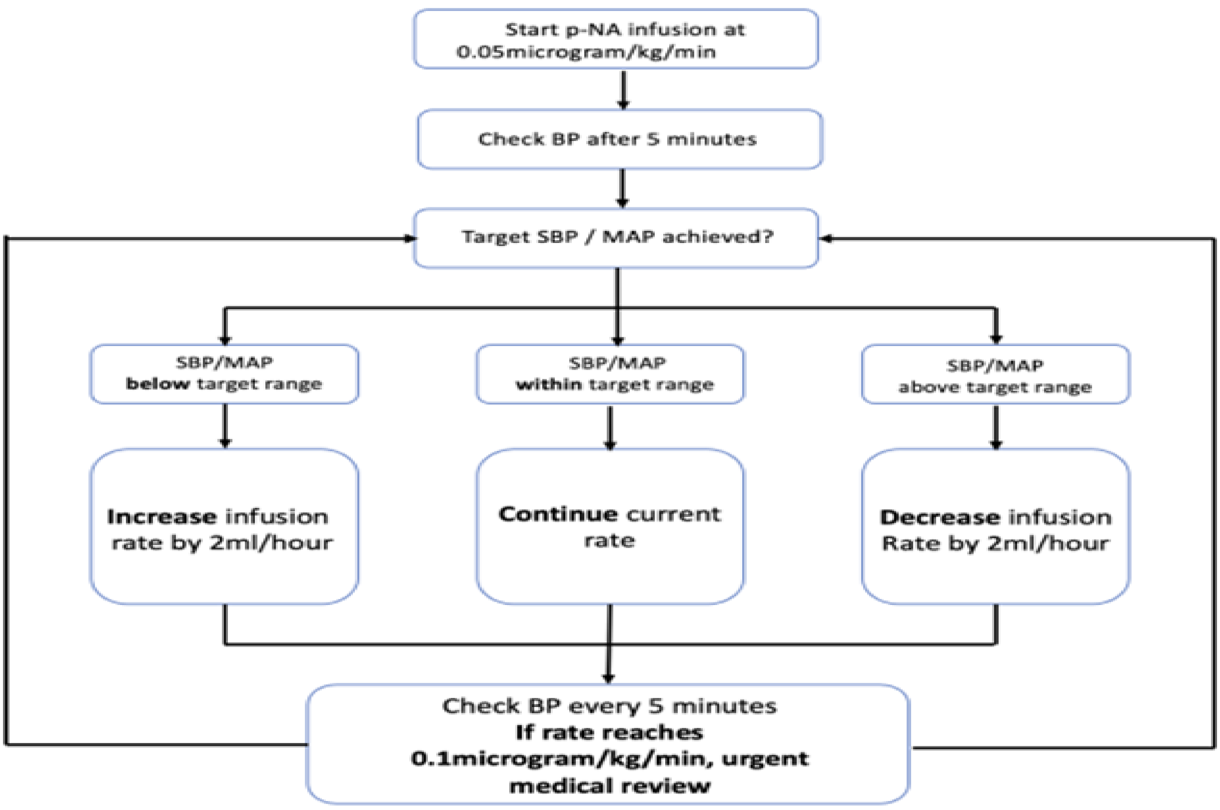
Start at 0.05 micrograms/kg/min dosing. This has been dose banded for ease. An estimated body weight is acceptable. If continuous invasive arterial blood pressure monitoring is in place, the infusion rate may be titrated more frequently than the 5 minute intervals, as clinically indicated.

2.2.6.3. Noradrenaline rate (mls/hr) – using a 16microgram/ml solution

Weight (kg)	Starting Rate (0.05 micrograms / Kg / min)	Maximum Rate (0.1 micrograms / Kg / min)	Maximum enhanced rate after clinician review (0.15 micrograms / Kg / min)
< 50Kg	8.5	18	26.5
50 – 59 Kg	10	20	30
60 – 69 Kg	12	24	36
70 – 79 Kg	14	28	42
80 – 89 Kg	16	32	48
90 – 99 Kg	18	36	54
100 – 109 Kg	20	40	60
110 – 119 Kg	22	44	66
At or over 120 Kg	22.5	45	67.5

2.2.6.4. Increasing infusion rate of pNA

The infusion rate should be titrated to target BP. Dose changes have been adjusted to mls/hr for ease. **The chart below relates to a 70-79kg patient** where 2mls/hr relates to 0.005-0.01mcg/kg/min increase. Where invasive arterial pressure monitoring is present this increase can occur more rapidly to achieve target BP



Flowchart 1 – Titration of p-NA infusion rate based on BP targets.

2.2.6.5. Urgent clinician review if BP not at target and the infusion reaches 0.1 micrograms/kg/min:

- Ensure delivery of the p-NA is effective (pump, line, cannula, and soft tissue)
- Ensure other causes of hypotension are investigated and treated (hypovolemia/ sepsis / cardiac causes).
- If there is still a requirement for higher doses of noradrenaline following senior review a central venous catheter (CVC) should be inserted and centrally delivered noradrenaline concentrations should be used.
- Whilst the CVC is being placed, doses up to 0.15mcg/kg/min of pNA maybe delivered for a short period under specialist anaesthetic or critical care supervision.

2.2.6.6. Syringe changes

Due to the low concentration of the infusion and low dosages used with pNA, double pumping is not required for syringe changes. Instead, a rapid change over of infusion syringe/bag should occur. Bolusing of pNA is not sanctioned.

In the context of pump failure change to an alternative pump.

Should this not be achieved quick enough a supply of pre-filled metaraminol syringes (0.5 mg/ml – total of 5 mls) should be kept within EPOC drug cupboard.

2.2.6.7. Co-administration:

pNA should be administered via a dedicated cannula. The concomitant administration of noradrenaline and other medicines via a Y-site should be avoided where possible (to prevent the inadvertent bolus of noradrenaline). If this is unavoidable, pNA is Y-site compatible with Hartmann's solution, 0.9% saline, propofol, and remifentanil.

It is anticipated that during surgery it will be co-administered with a dedicated infusion line and the chosen isotonic fluids. However it can be administered as the vasopressor component of total intravenous anaesthesia (TIVA) using a dedicated TIVA giving set.

2.2.6.8. Recording of administration

Within theatres administration will be recorded on the anaesthetic chart.

Within recovery and EPOC administration of pNA should be recorded on Nerve Centre in the fluid balance chart. A separate column should be dedicated to this and be titled 'pNA.' This will then be included in the fluid balance calculations.

Where there is significant change hourly readings should be recorded, however commentary should be clearly documented.

2.3. Monitoring of vital signs

2.3.1. All patients must have their cardiovascular state monitored continuously during pNA therapy. This includes continuous 3 lead ECG, continuous SpO2 and blood pressure monitoring. As BP is the target to which pNA will be titrated, an arterial line (IABP) is preferrable, although not mandatory at low infusion rates.

2.3.2. There may be occasions where insertion of an IABP is either not possible, or not practical. In these situations, utilising frequent NIBP measurements is acceptable. The maximum interval between NIBP measurements should be 5 minutes.

2.4. Duration of therapy

Active review of pNA should occur after 24 hours infusion and should not routinely be utilised for > 48 hours. If there is an ongoing requirement for vasopressor therapy at 48hrs of infusion, a Consultant review should be undertaken to assess why. At this point a CVC should be considered an infusion of central concentration noradrenaline started. If not undertaken already the patient should be referred for Critical Care.

2.5. Monitoring for adverse events

2.5.1. The peripheral venous cannula (PVC) should be assessed for infection and extravasation as per the Trust’s Use of Intravascular Catheters in Adults Clinical Guideline.

2.5.2. Extravasation is the inadvertent leakage of any drug or fluid into the surrounding tissues. Regular monitoring of the infusion site is essential to enable early recognition and management of extravasation events. Extravasation is uncommon, with a recent study suggesting it occurs in 3.4% of peripherally administered vasopressor situations(5). Of these incidents, none led onto serious side effects such as tissue necrosis or limb ischaemia. See below for the suggested immediate management of extravasation and see the trust Use of Intravascular Catheters in Adults Clinical Guideline for further details.

2.5.3. Suggested management of pNA extravasation

1. Stop the infusion and disconnect the line from the extravasated peripheral cannula.

2. Run pNA infusion through the spare cannula.

3. Attempt to aspirate 3-5mL from the extravasated peripheral cannula.

4. Remove the extravasated cannula and apply a dressing to the removal site.

5. Mark the extravasation area, if possible, in order to allow monitoring of any developing injury.

6. Elevate the affected limb if able to do so to reduce swelling.

7. Consider application of a warm compress and/or topical vasoactive agent such as GTN cream to encourage local blood flow.

8. Administer analgesia if required.

9. Consider need for phentolamine.

   Make up 10mg phentolamine into 10mls 0.9% saline. Inject 0.5 – 1ml aliquots in 5 separate places subcutaneously around the leading edge of the extravasation using a 25g (orange) needle.

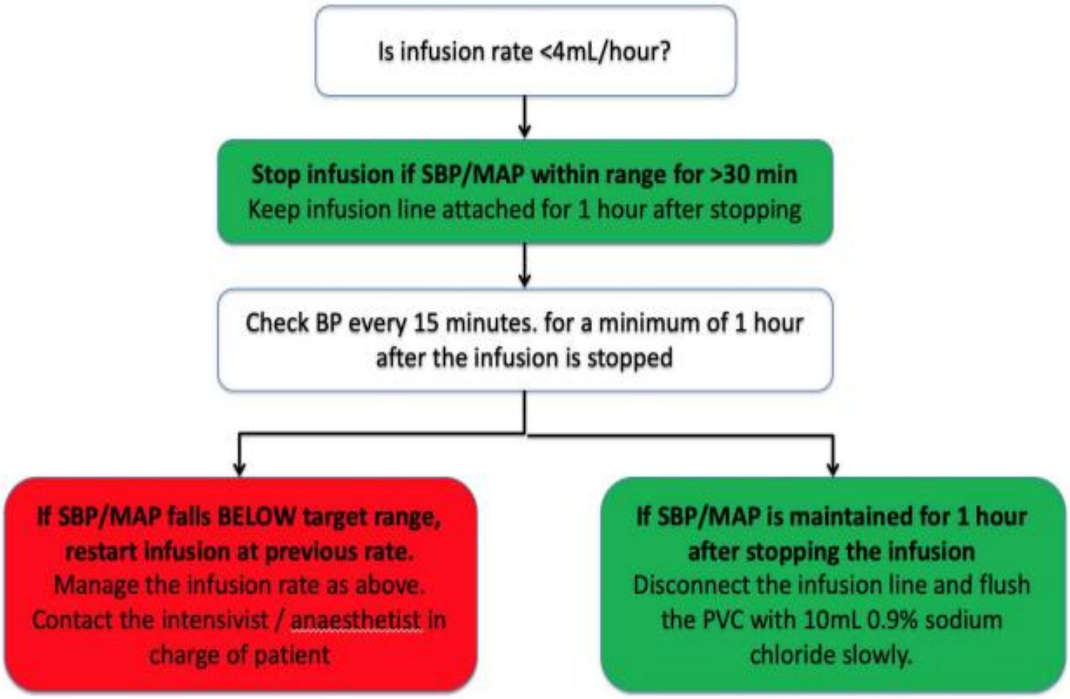
10. Seek advice from a surgeon or local tissue viability service if concerned.

11. Document the incident and report via datix.

2.6. Cessation of therapy

When the infusion weans to less than 4ml/hr (0.01mcg/kg/hr – 0.02mcg/kg/hr), follow flowchart 2 below to safely stop the p-NA infusion.

On ceasing p-NA administration, the PVC should be infused with 10mls of 0.9% sodium chloride, delivered at the same rate as the prior p-NA infusion was running. This will prevent sudden increases in blood pressure related to bolus noradrenaline administration.



Flowchart 2 – Safe cessation of p-NA infusion.

3. Monitoring compliance and effectiveness

Information Category	Detail of process and methodology for monitoring compliance
Element to be monitored	Audit compliance with guideline and rate of extravasation.
Lead	Dr Robert Hartley.
Tool	Datix of events plus audit of pNA use.
Frequency	Yearly.
Reporting arrangements	Report to local governance structures.
Acting on recommendations and Lead(s)	Guideline author in collaboration with governance structure.
Change in practice and lessons to be shared	Guideline changes via MPC and local governance structures. Extravasation reported via medication safety pharmacist.

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the Equality Diversity And Inclusion Policy or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Information Category	Detailed Information
Document Title:	Peripheral Administration of Noradrenaline (PNA) Clinical Guideline V1.0
This document replaces (exact title of previous version):	New Document
Date Issued/Approved:	8 December 2023
Date Valid From:	December 2023
Date Valid To:	December 2026
Directorate / Department responsible (author/owner):	Dr Robert Hartley, Consultant Anaesthetist. Department of Anaesthesia and Perioperative Medicine.
Contact details:	01872 25 8195
Brief summary of contents:	Guideline for use of peripheral noradrenaline for hypotension due to anaesthesia / surgery / shock.
Suggested Keywords:	Noradrenaline, hypotension.
Target Audience:	**RCHT:** Yes **CFT:** No **CIOS ICB:** No
Executive Director responsible for Policy:	Chief Medical Officer
Approval route for consultation and ratification:	Medicines Practice Committee (MPC) approved on 08.12.2023.
Manager confirming approval processes:	Doug Riley
Name of Governance Lead confirming consultation and ratification:	James Masters.
Links to key external standards:	None
Related Documents:	References: (1) Guidance For: The use of Vasopressor Agents by Peripheral Intravenous Infusion in Adult Critical Care Patients. The Intensive Care Society. Nov 2020.

Information Category	Detailed Information
	(2) Rhodes A, Evans L, Alhazzani W et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016, Critical Care Medicine: March 2017 - Volume 45 - Issue 3 - p 486-552. (3) Avni T, Lador A, Lev S et al. Vasopressors for the Treatment of Septic Shock: Systematic Review and Meta-Analysis. PLoS One. 2015 Aug 3;10(8):e0129305. (4) Levy, B, Klein, T, Kimmoun, A. Vasopressor use in cardiogenic shock. Current Opinion in Critical Care: August 2020 - Volume 26 - Issue 4 - p 411-416. (5) D. H. Tian, C. Smyth, G. Keijzers et al. Safety of peripheral administration of vasopressor medications: A systematic review. Emergency Medicine Australasia, vol. 32, no. 2, pp. 220-227, 2020. (6) C. Pancaro, N. Shah, W. Pasma, L et al. Risk of Major Complications After Perioperative Norepinephrine Infusion Through Peripheral Intravenous Lines in a Multicenter Study. Anesthesia and Analgesia, vol. 131, no. 4, pp. 1060-1065, 2020.
Training Need Identified?	No – standard training for staff in ACCT care group.
Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet and Intranet
Document Library Folder/Sub Folder:	Clinical / Anaesthetics

Version Control Table

Date	Version Number	Summary of Changes	Changes Made by
October 2023	V1.0	Initial issue	Dr Robert Hartley, Consultant Anaesthetist

All or part of this document can be released under the Freedom of Information Act 2000

All Policies, Strategies and Operating Procedures, including Business Plans, are to be kept for the lifetime of the organisation plus 6 years.

This document is only valid on the day of printing.

Controlled Document

This document has been created following the Royal Cornwall Hospitals NHS Trust The Policy on Policies (Development and Management of Knowledge Procedural and Web Documents Policy). It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Equality Impact Assessment

Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity, and Inclusion Team rcht.inclusion@nhs.net

Information Category	Detailed Information
Name of the strategy / policy / proposal / service function to be assessed:	Peripheral Administration of Noradrenaline (PNA) Clinical Guideline V1.0
Directorate and service area:	Department of Anaesthesia and Perioperative Medicine.
Is this a new or existing Policy?	New
Name of individual completing EIA (Should be completed by an individual with a good understanding of the Service/Policy):	Dr Robert Hartley, Consultant Anaesthetist.
Contact details:	01872 25 8195

Information Category	Detailed Information
1. Policy Aim - Who is the Policy aimed at? (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed)	Provides guidance and clarification of the Peripheral Administration of Noradrenaline (PNA).
2. Policy Objectives	To provide guidelines on the use of peripheral noradrenaline perioperatively and applies to: **Setting**: Operating Theatres, Recovery and EPOC. **Staff:** all medical, nursing, and auxiliary staff utilising vasopressor infusions in the care of patients directly supervised by Anaesthetic / Critical Care staff. **Patients**: adult patients with, or at risk of, vasoplegic shock and organ dysfunction.
3. Policy Intended Outcomes	As above.

Information Category	Detailed Information
4. How will you measure each outcome?	Datix of events plus audit of pNA use.
5. Who is intended to benefit from the policy?	Patients and RCHT
6a. Who did you consult with? (Please select Yes or No for each category)	• Workforce: Yes • Patients/ visitors: No • Local groups/ system partners: No • External organisations: No • Other: No
6b. Please list the individuals/groups who have been consulted about this policy.	**Please record specific names of individuals/ groups:** Medicines Practice Committee.
6c. What was the outcome of the consultation?	Approved.
6d. Have you used any of the following to assist your assessment?	**National or local statistics, audits, activity reports, process maps, complaints, staff, or patient surveys:** No.

7. The Impact

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

Protected Characteristic	(Yes or No)	Rationale
Age	No	
Sex (male or female)	No	
Gender reassignment (Transgender, non-binary, gender fluid etc.)	No	
Race	No	
Disability (e.g. physical or cognitive impairment, mental health, long term conditions etc.)	No	

Protected Characteristic	(Yes or No)	Rationale
Religion or belief	No	
Marriage and civil partnership	No	
Pregnancy and maternity	No	
Sexual orientation (e.g. gay, straight, bisexual, lesbian etc.)	No	

A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment: Dr Robert Hartley, Consultant Anaesthetist.

If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:
Section 2. Full Equality Analysis