EVIS: Clinical information Sheet for Participant Medical Records

Study: **EVIS:** Early Vasopressors in Sepsis

EudraCT No: 2021-006886-39

EVIS Participant No.:		Insert Patient ID/Addressograph label
Randomisation: This patient has been randomised to the **EARLY PERIPHERAL VASOPRESSOR / INTERVENTION arm** of the EVIS study.		

Study treatment duration: 48 hours (from time of randomisation)

Participant randomised on:
_____ *(insert date)* **at** _____ *(insert time hh:mm)*

IMPORTANT:
Contact the Research Team if you have any questions or need advice.
Further information can be found on the study website XXXXXXXXX

Key information for EARLY PERIPHERAL VASOPRESSOR / INTERVENTION arm

Intervention arm – study treatment period 48 hours post-randomisation

- Starting dose of norepinephrine is 0.05 micrograms/kg/minute. Dose can be increased to 0.10 micrograms/kg/min and subsequently to 0.15 micrograms/kg/min (maximum protocol permitted norepinephrine dose).
- Titrate the dose of norepinephrine to target MAP of 65 mm Hg.
- *Rescue IV fluids:* If target MAP not reached at maximum norepinephrine dose of 0.15 micrograms/kg/min or clinician concerns of organ hypoperfusion, administer 250-1000ml balanced crystalloid via peripheral IV route.
- *Maintenance IV fluids:* At clinician discretion, maintenance rather than resuscitation IV fluid can be administered but only after resuscitation is complete and at a rate of no more than 125 ml/hour. The reason for fluid administration must be clear ie. maintenance versus resuscitation
- *Rescue vasopressors:* If target MAP not reached using maximum permitted dose and use of rescue IV fluids/concerns of organ hypoperfusion then rescue vasopressor can be administered via a CENTRAL route. Discontinue peripheral infusion.
- All other care should be as per UK/local treatment guidelines.

Suspected extravasation:
Extravasation is a rare complication of norepinephrine peripheral infusion. Monitor the infusion site regularly. If the patient reports sustained pain or itching at infusion site or there is pallor, oedema or erythema at the peripheral cannula site then

- **IMMEDIATELY STOP THE INFUSION**. Disconnect the infusion line from the cannula.
- Attempt to aspirate 3-5ml from the peripheral venous cannula
- Remove the cannula and apply a dressing
- Mark the extravasation area and elevate the limb if able to reduce swelling
- Contact the research team for further advice.

Other information:

- Any brand of norepinephrine (noradrenaline) 1 mg/ml Concentrate for solution for infusion stocked by hospital can be used. .

Research Team Contact Details

Research Nurse:	**Name:** **Telephone:** **E-mail:**
Principal Investigator:	**Name:** **Telephone:** **E-mail:**
Location of local study information:	
Completed and inserted into medical notes by:	*(insert name & designation)* **on** *(insert date)*

Intervention Arm: Norepinephrine dosing and administration guidance

Guidance on peripheral IV catheter use for norepinephrine administration

- Chose at least a 20G (pink) or larger peripheral venous catheter (PVC)
- Locate in a site according to standard practice. Peripheral long lines can be used if this is normal practice at site
- If possible, avoid sites of flexion in awake patients due to the risk of occlusion
- Avoid sites requiring more than 1 venepuncture
- Ensure there is a return of blood following insertion of the PVC and that the PVC flushes easily with 5-10mL of 0.9% sodium chloride
- Site a second PVC in case of failure of the primary site (if possible)

Infusion preparation

Norepinephrine must be prepared by dilution in either 0.9% sodium chloride injection or 5% glucose to provide **a final concentration of 16 micrograms/ml**.

Norepinephrine dosing guidance for peripheral infusion

(based on a solution containing norepinephrine 16 micrograms/ml)

Patient weight*	Starting dose of 0.05 micrograms / kg / min		Dose of 0.10 micrograms / kg / min		Maximum dose of 0.15 micrograms / kg / min	
	Total drug dose per hour (micrograms / hour)	Flow rate per hour ** (ml / hr)	Total drug dose per hour (micrograms / hour)	Flow rate per hour ** (ml / hr)	Total drug dose per hour (micrograms / hour)	Flow rate per hour ** (ml / hr)
40kg	120	7.5	240	15.0	360	22.5
50kg	150	9.4	300	18.8	450	28.1
60kg	180	11.3	360	22.5	540	33.8
70kg	210	13.1	420	26.3	630	39.4
80kg	240	15.0	480	30	720	45.0
90kg	270	16.9	540	33.8	810	50.6
100kg	300	18.8	600	37.5	900	56.3
110kg	330	20.6	660	41.3	990	61.9
120kg***	360	22.5	720	45.0	1080	67.5

* Round to nearest 10 kg for dosing purposes
**Round to nearest whole ml if pumps cannot accommodate 1 decimal place
*** Calculate to exact kg for weights above 120kg as per the worked example below

Calculation for participants over 120kg

Step 1: Dose (micrograms/minute) = Starting dose (microgram/kg/min) x Patient Weight (kg)

Step 2: Convert dose (microgram/minute) to *micrograms/hour* = Dose (micrograms/minute) x 60

Step 3: $\text{Infusion rate (millilitres/hour)} = \frac{\text{Dose (micrograms/hour)}}{\text{Concentration of norephinepherine solution (16 micrograms/ml)}}$

Worked example for 123kg patient with norepinephrine starting dose of 0.05 micrograms/kg/min

1. Dose (micrograms/minute)
   = 0.05 micrograms/kg/min x 123 kg = 6.15 micrograms/minute
2. Convert Dose to *micrograms/hour*
   = 6.15 micrograms/minute x 60 = 369 micrograms/hour
3. Infusion rate (millilitres per hour) = $\frac{\mathbf{=369\ micrograms/hour}}{\mathbf{16\ micrograms/ml}}$ = 23.1 ml/hour