Continuous Veno Venous Haemofiltration (CVVH) and Continuous Veno Venous Haemodiafiltration (CVVHDF) within the paediatric critical care unit (PCCU)

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Author (include email and role):	Nicole Justice, Paediatric Renal Critical Care Educator nicole.justice1@nhs.net Dusan Raffaj, Paediatric Intensivist d.raffaj@nhs.net Andrew Wignell, PCCU Lead Pharmacist a.wignell@nhs.net
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This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.	

Document Control

Document Amendment Record

Version	Issue Date	Lead Author	Changes from previous version
V1	Sept 22	Kate Peace	Original document
V2	Nov 24	Nicole Justice, Dusan Raffaj, Andrew Wignall	Guideline reviewed due to changes in anticoagulation choice and revised guidance for Citrate accumulation

Key words

CVVH, CVVHDF, Anticoagulation, Citrate, Flow Rates

Contents

1. Executive summary of guideline

Patient requires **CVVH/CVVHDF**

For **Peritoneal Dialysis** liaise with renal team and refer to guideline: **Peritoneal Dialysis Acute**

First line **anticoagulation** on PCCU is **Citrate**; consider using Epoprostenol if any of the following contraindications present:

- Patients with hepatic failure (as the Calcium-Citrate complex is metabolised by the liver) as in:
  - Severe Liver Disease
  - Baseline INR >3.5
  - Paracetamol hepatitis with gross elevation of AST, INR and with elevated lactate
- <1 year of age
- Clinical risk of bleeding considered too great for ANY CRRT anticoagulation
- Previous Citrate accumulation, if organ dysfunction persists
- Additional Citrate load e.g. on-going massive transfusion

(Alternatively, Epoprostenol may be used. For more information, refer to page 10 and appendix 2 on page 25)

Prior to commencing therapy:

- Obtain a full set of bloods, paying particular attention to electrolytes
- It is not necessary to have cross matched blood available before commencing therapy and should not be a reason for delay, unless there is a clinical reason for the patient to have a blood transfusion prior to starting.
- Ensure appropriate size VasCath is insitu
- Complete prescription chart
- Assemble PrisMax and all necessary equipment

The following groups of patients require extra consideration:

- Low body weight (See pg 17)
- Septic (see pg 18)
- Hyperammonaemia or other Metabolic Emergency **(Time critical)**, Hyperkalaemia, Hyperuraemia or Hypernatraemia (see clearance chart on pg 23 for information on adjusted flow rates)

Use a **CVVHDF daily prescription and observation chart**

Prescribing checklist:

- Heparin line lock
- Priming fluids – 1st prime: 0.9% Sodium Chloride with Heparin, 2nd prime: Plasmalyte 148
- Pre Blood Pump, Replacement and Dialysate fluid bags
- Flow rates
- Fluid removal rate
- Calcium Gluconate infusion / Epoprostenol infusion
- When on Citrate, please indicate Calcium compensation algorithm arm required (with consideration for liver impairment)

Considerations during therapy:

Initiating therapy:
Haemodynamic stability
Fluid balance
Electrolytes: pay close attention to Mg^{++}, PO_4^- and K^+
Drug clearance
Temperature control

Potential problems:
Fluid & electrolyte shift
Citrate accumulation
Infection
Air embolism

Monitoring during therapy:
Arterial blood gas within 1hr of commencing then every 4hrs thereafter
U&Es 6hrs after commencing then every 6hrs thereafter
FBC daily

<u>Additional monitoring: Citrate</u>
Filter Ca and Patient Ca within 1 hour of commencing then 4hourly once stable
(See algorithm on pg 19)
T:i ratio every 6hrs
Clotting every 12hrs
More frequent bloods may be required in those at risk of Citrate accumulation

<u>Additional monitoring: Epoprostenol</u>
Clotting every 6 hours

2. Introduction and description of therapies

Continuous renal replacement therapy (CRRT) is a supportive therapy used for the management of fluid balance and metabolic derangement, with or without evidence of acute injury kidney injury (AKI), in critically ill patients.

Aims of the therapy include:

- Relieving hypervolaemia and maintaining fluid balance
- Removing excess urea & creatinine
- Correcting and maintaining metabolic and electrolyte balance
- Removing toxins

Indications for commencing treatment:

- Fluid overload
- Electrolyte imbalance
- Acute Kidney Injury (AKI)
- Inborn errors of metabolism
- Sepsis*
- Rhabdomyolysis
- Tumour lysis*
- Drug intoxications
- Optimising nutrition*

  (* other indication(s) needed to support decision, not enough on its own)

In the East England, East Midlands and South Yorkshire (EMEESY) Children's Kidney Network, CRRT is utilised in the following forms; Peritoneal Dialysis (PD), Continuous Veno Venous Haemofiltration (CVVH) and Continuous Veno Venous Haemodiafiltration (CVVHDF). This guideline focuses on the use of CVVH and CVVHDF; these are both delivered using the PrisMax (Baxter) machine.

As Citrate is the first line anticoagulant for CVVH/CVVHDF, this will be the main focus of this guideline. There may be times when Citrate cannot be used, in which case the second line anticoagulant is Epoprostenol. Information for this can be found in Appendix 2 (see page 25).

Using a dedicated double lumen vascath and an extracorporeal circuit, blood is continuously removed and returned to the patient. This continuous technique allows fluid and waste

products to be removed gradually over a 24hr period. This provides more haemodynamic stability for critically ill children than other intermittent therapies.

The extracorporeal circuit incorporates a blood pump and a filter containing a semi-permeable membrane. A pressure gradient within the circuit forces fluid and solutes across the membrane to form effluent fluid. Dialysis fluid can also be added to the other side of the filter, this causes molecules to move across with a concentration gradient. The processes utilised are ultrafiltration, convection and diffusion.

2.1. Ultrafiltration

This is the movement of fluid through a semi-permeable membrane driven by a hydrostatic pressure gradient. On the PrisMax a positive pressure is generated by the blood pump on the blood side of the semi-permeable membrane and a negative pressure by the effluent pump on the other side. This results in the movement of fluid from the positive pressure side (blood side) to the negative pressure side (effluent side).

2.2. Convection

This occurs when large volumes of fluid crossing the semi-permeable membrane down the hydrostatic pressure gradient results in solvent drag across the membrane. Large molecules can be moved efficiently if the flow is fast enough. Pre blood pump and replacement fluid is added to the circuit to increase the flow across the semi-permeable membrane.

2.3. Diffusion

This is the movement of solutes across a semi-permeable membrane caused by a concentration gradient. Solutes move from an area of higher concentration to an area of lower concentration. On the PrisMax this is achieved by the addition of dialysate fluid which is run counter-currently to the blood flow on the other side of the semi-permeable membrane, to ensure the concentration gradient is maintained the whole length of the filter.

The movement of molecules in CRRT are driven by the above processes but are limited by the size of the solute particles. The PrisMax filters have pores that allow passage of molecules up to 35,000 Daltons. This allows for free movement of small ions and molecules (e.g. urea, creatinine, ammonia) across the membrane as well as some larger molecules such as myoglobin (17,200 Daltons), insulin (active) and interleukins (varies). Small molecules are more efficiently removed by diffusion and larger molecules by convection.

Please note that diffusion is a two way process, so particles will move into the blood from the dialysate fluid if the concentration in the blood is lower than the fluid. After some time, the concentration within the blood should match that within the fluid.

2.4. Adsorption

Some molecules are removed in CRRT by adherence to the artificial semi-permeable membrane; this is the process by which inflammatory markers are thought to be removed. High levels of these molecules can cause the filter to clog and become less effective.

On PCCU the Baxter PrisMax machine is used and has several different modes. The two main modes are Continuous Veno Venous Haemofiltration (CVVH) and Continuous Veno Venous Haemodiafiltration (CVVHDF). Slow Continuous Ultrafiltration (SCUF) is used on some units as a rest mode to assess if a patient is ready to stop treatment however this is currently not used on PCCU.

2.5. CVVH

This mode of CRRT utilises the principles of ultrafiltration and convection and is ideal for removing medium sized and large molecules.

- Biochemistry is controlled by removing large volumes of filtrate and replacing it with electrolyte containing fluid (replacement fluid). The more filtrate removed and replaced the more efficient haemofiltration is in controlling biochemical disturbance.

- As most solutes are distributed within the extracellular and intracellular fluid compartments (total body water), the volume of filtration (replacement) necessary to control biochemistry relates to total body water. Clinical experience has shown that a replacement of approximately 50% of bodyweight (1kg = 1litre) is usually adequate for solute and electrolyte removal.

- Low blood flow rate, high haematocrit and high plasma protein concentration will limit the rate at which filtration can occur and solutes (particularly of higher molecular weight) can be removed.

2.6. CVVHDF

This mode of CRRT utilises the principles of ultrafiltration, convection and diffusion. Using both convective and diffusive transport systems will optimise the clearance of molecules of varying sizes.

- The addition of dialysate flow with CVVHDF will improve the efficiency of acid base, waste removal and control of electrolyte balance. Waste and electrolytes diffuse from the patient's blood into the dialysate fluid surrounding the fibres. The "saturated" dialysate fluid (effluent) is removed from the filter and discarded.

- Diffusion is a two way process, molecules that are at a low concentration in the blood and high in the dialysate fluid will diffuse into the blood and vice versa (e.g. bicarbonate).

- Convective transport systems utilised in CVVH are limited by the blood flow achieved. If higher replacement rates are indicated, but not achievable, adding in dialysate flow will optimise clearance. Reasons for not achieving desired replacement rates could be due to patient stability or issues with access limiting the blood flow rates.
- This is practically important when treating children with inborn errors of metabolism, for overdose of drug or therapeutic agents and for patients with a high lactate.

- Increasing dialysate flow will at least theoretically improve clearance; however this is limited by the relatively low dialysate flow rates generated by CRRT equipment.

2.7. Which therapy?

***CVVHDF** should always be selected when setting up the PrisMax.*

When performing filtration with Epoprostenol anticoagulation it is possible to switch between CVVH and CVVHDF whilst treatment is running depending on the patient's clinical condition.

*However, when using Citrate anticoagulation **CVVHDF** will always be the therapy of choice.*
This is due to the additional benefits of running dialysate with Citrate, such as off-loading Citrate into the effluent bag which can help prevent Citrate accumulation and reducing high bicarbonate levels in the patient's blood. If therapy is proving to be too efficient, move the patient down a weight bracket (see clearance table on page 23).

3. Coagulation

As with any extracorporeal circuit, the circuits used for CRRT require the administration of anticoagulation to prevent the development of clots and keep the blood flowing in the circuit. Historically, the most common anticoagulant used for CRRT within PCCU was heparin, which is run as an infusion into the circuit. In recent years there has been a shift to use regional Citrate anticoagulation. This is more beneficial than heparin as it can be used in patients that are at an increased risk of bleeding and have contraindications to heparin. It has also been shown to increase the life of the circuit, resulting in fewer interruptions to treatment and ensuring a more efficient treatment for the patient. Regional Citrate will be the anticoagulation of choice on PCCU and therefore the focus of this guideline, however there may be times when Citrate cannot be used and Epoprostenol should be used instead as an anticoagulant.

For information on Epoprostenol anticoagulation please see Appendix Two.

3.1. What is Citrate?

Citrates are a family of compounds, but in relation to anticoagulation for CRRT, Trisodium Citrate and Citric Acid are the two relevant compounds.

The Citrate solution used on PCCU is PrismoCitrate 18/0; this contains Trisodium Citrate 18mmol/L and 0mmol/L of Citric Acid.

Trisodium Citrate is a salt of Citric Acid sometimes referred to as Sodium Citrate. It is metabolised in the liver to bicarbonate. Trisodium Citrate binds with ionised calcium and magnesium.

Sodium Citrate is widely used in blood collection tubes and for the preservation of donated blood products. It is now becoming an increasingly popular alternative to heparin for the anticoagulation of the extracorporeal circuits used in CRRT.

3.2. How it works

In the blood, calcium circulates primarily either in a free form or bound to plasma protein. The free portion, termed ionized calcium (iCa), is the form of calcium which is key to the activation of the coagulation cascade. Through binding and forming a complex with iCa, Citrate prevents coagulation in the extracorporeal circuit. Citrate anticoagulation is referred to as regional anticoagulation as it is delivered to the circuit and filter without anticoagulating the patient, offering a significantly reduced risk of bleeding. However, it is still vital that iCa

levels in both the circuit and the patient are closely monitored to ensure adequate anticoagulation of the circuit and minimise risk to the patient.

Citrate solution is delivered to the patient's blood pre-filter, on the pre-blood pump (PBP) scale; this ensures that both the filter and circuit are anti-coagulated. The concentration of Citrate added to the patient's blood before entering the filter depends on the blood flow rate and Citrate infusion (PBP) flow rate. The amount of Citrate is expressed, as Citrate dose, in mmol/L blood. On PCCU the starting Citrate dose will be 4mmol/L for most patients, aim for a filter iCa concentration of 0.25-0.35mmol/L for optimum anticoagulation of the circuit. For patients with liver impairment/failure, please use a lower Citrate dose of 3mmol/L and aim for a filter iCa concentration of 0.4-0.45mmol/L.

Blood flow rates and Citrate infusion rates determine the ionised calcium level in the circuit; if the blood flow rate is adjusted the Citrate infusion rate will automatically be altered by the PrisMax. This synchronization of the blood flow rate and PBP Citrate flow rate is necessary to maintain the Citrate dose at the desired level.

Citrate also non-specifically binds to positively charged ions such as magnesium and phosphate, so a reduction in serum magnesium and phosphate levels is to be expected. Urea and Electrolyte blood testing should be checked at least 6 hourly whilst patient is on the filter to monitor electrolytes closely and correct as needed.

Most of the Citrate infused into the circuit is cleared by the filter and lost in the effluent. Consequently, only a portion of the infused Citrate is delivered to the patient. Based on the Citrate infusion rate and the rate of Citrate loss in the effluent, the amount of Citrate delivered to the patient can be calculated. This is called the 'Patient Citrate Load'. Citrate will be rapidly metabolised by the patient so will not have any anticoagulation effect, however if this Citrate is not metabolised it can lead to Citrate accumulation. Please refer to the 'Citrate Accumulation' section for more details on how to recognise and manage this.

3.3. Contraindications (please discuss with consultant)

- Patients with severe hepatic failure (as the calcium-Citrate complex is metabolised by the liver), as in:
- Liver disease or INR >3.5
- Paracetamol hepatitis with gross elevation of AST, INR and elevated lactate
- Patient is aged <1yr as they will have an immature liver
- Clinical risk of bleeding considered too great for ANY CRRT anticoagulation

- Previous Citrate accumulation, if organ dysfunction persists
- Additional Citrate load e.g. on-going massive transfusion

If any of these contraindications are present, Citrate anticoagulation can still be used but start at a lower dose (3.0mmol/L blood) and monitor iCa and filter calcium closely. In this case, a higher filter calcium can be accepted, please see the algorithm for liver impairment/failure on page 19 for more information. Alternatively, use Epoprostenol anticoagulation (See appendix 2).

4. Calcium Gluconate infusion

A certain percentage of Citrate in the blood in the circuit is cleared by the filter and lost in the effluent. This Citrate is bound to some of the patient's ionised calcium so in order to avoid systemic ionised hypocalcaemia a separate infusion of calcium is required. The rate of this is adjusted to maintain patient ionized calcium levels between 1.0-1.2mmol/L. This infusion is delivered via the PrisMax syringe pump directly to the patient via a **central line**, not into the circuit. If central access is problematic then this infusion can be delivered via the return lumen, however this may increase the risk of clots forming within the central line so this must be discussed with the PCCU consultant or paediatric renal critical care nurse beforehand.

Based on the estimated calcium loss in the effluent, the PrisMax calculates the amount of compensatory calcium to be delivered by the machine syringe pump. This calculation takes into account the concentration of the calcium solution in the syringe.

Calcium compensation is expressed in % and can be modified during treatment. Complete replacement of the calcium lost in the effluent corresponds to a calcium compensation of 100%. The range of calcium compensation % is variable and is dependent on the set used, weight of the child and flow rates.

The PrisMax software calculates the syringe flow rate based on the calcium compensation selected, CRRT dose, patient body weight and calcium concentration in the syringe. The syringe flow rate cannot be set directly. The same applies for the calculation of the calcium rate i.e. the amount of calcium administered per hour.

4.1. Calcium gluconate concentration

For all patients
40ml of Calcium Gluconate 10% with 10ml Sodium Chloride 0.9% (Total of 9mmol/50ml or **0.18mmol/ml**)

Calcium syringe needs to be changed every 24 hours and calcium syringe lines every 72 hours.

Calcium gluconate must be administered centrally, if separate central access is not available then it can be run on return line using a 3-way tap. Monitor VasCath closely for signs of clotting and keep filter iCa in lower end of range, discuss with paediatric renal critical care nurse if any issues.

5. Citrate, Dialysate and replacement solutions

The fluid bag required for each scale (Pre blood pump, Dialysate and Replacement) will depend on the type of anticoagulation used. **For Citrate** the following fluid bags will be used:

The Citrate solution used on PCCU will be *PrismoCitrate 18/0* and will be used on the *Pre Blood Pump* scale:

PrismoCitrate 18/0 (all values in mmol/L)									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	0	0	0	86	0	0	0	0	18

The Dialysate solution will be *Prism0cal B22*; calcium-free solutions should be used on the *dialysate* scale to prevent restoration of ionized calcium levels and coagulation in the filter.

Prism0cal B22									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	4	0	0.75	120.5	0	3	22	6.1	0

Phoxilium will be the first line fluid for the *replacement* scale. The use of Phoxilium will aid in the restoration of phosphate lost during filtration, however it contains no glucose so close monitoring of the patient's glucose level is essential. Phoxilium contains calcium so the return line should be closely observed for signs of clotting.

Phoxilium									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	4	1.25	0.6	115.9	1.2	0	30	0	0

Please discuss any patients with high potassium levels with consultant before commencing treatment.

Fluid bags need to be mixed prior to use and must be changed every 24 hours.

5.1. Adding electrolytes to fluid bags

With the exception of sodium, no additives should be added to any of the fluid bags.

If the patient requires additional phosphate then please discuss this with the consultant and pharmacist. This should then be given as a direct correction to the patient.

In cases of hypernatraemia in patients requiring CRRT it may be necessary to add sodium to replacement/dialysis fluids to ensure sodium correction does not occur too rapidly. The sodium content of Prism0cal B22 and Phoxilium is 140mmol/L, so without the addition there is a significant risk the patient's serum sodium could drop too quickly.

If an addition is required this must be clearly documented on the patients CVVH/CVVHDF Daily Prescription and Record Chart and the patient's serum sodium must be closely monitored. If the patient's plasma sodium is greater than 150mmol/L follow the guidance below for adding sodium (sodium should **NOT** be added to the Citrate 18/0 fluid bag):

Target Na^+ (mmol/L)	**Addition to 5 litre bag (Prism0cal B22/Phoxilium)**	
150	10mls of sodium chloride 30%	Remove same volume from replacement/dialysate bag before addition (e.g. for target 150mmol/L remove 10mls from Prism0cal B22/Phoxilium, then add 10mls sodium chloride 30%)
155	15mls of sodium chloride 30%	
160	20mls of sodium chloride 30%	
165	25mls of sodium chloride 30%	
170	30mls of sodium chloride 30%	
175	35mls of sodium chloride 30%	
180	40mls of sodium chloride 30%	
185	45mls of sodium chloride 30%	
190	50mls of sodium chloride 30%	

For patients on Epoprostenol please see **Appendix Two** for more information on adding electrolytes.

6. Prior to commencing therapy

6.1. Access

Temporary central venous lines (CVL) are used for CRRT within PCCU. Follow the guideline for insertion of CVL in PCCU. The use of ultrasound guidance should strictly be adhered to during insertion.

Tego connectors need to be used on temporary CVL when they are being used for CRRT. Usually on PCCU, needle free connectors are used on all temporary venous lines, however these do not accommodate the high flow rates required for CRRT. Tego connectors allow flow rates of up to 600ml/minute and provide a reduced risk of catheter related blood stream infections. These must be changed every 7 days whilst the CVL is in situ.

Weight	Type	Size	Line lock	
<10kg	**Braun or similar**	2 x 18G (green) peripheral cannula	0.2ml or 1.3ml with connection **Heparin 100units/ml**	Prescribe on front of CVVHDF chart
	Gam Cath	6.5Fr x 7.5cm	Lock using volume of line plus 0.2ml (Add 0.3ml total if a Tego connector is used) **Heparin 100units/ml**	
		6.5Fr x12.5cm		
10-20kg	**Gam Cath**	8Fr x 10cm		
		8Fr x12.5cm		
>20kg	**Gam Cath**	11Fr x15cm		
		11Fr x 20cm		

Heparin line lock MUST be aspirated and discarded before connection to patient.

6.2. Prior to connecting

Obtain baseline bloods: to include ABG, FBC, U+E, LFT, magnesium, phosphate, total calcium and clotting.

Check the patient's iCa and magnesium levels are within normal limits. When commencing therapy the calcium compensation is usually started at 100%, but if the calcium is out of range:

- If iCa >1.2 start calcium compensation at 90%
- If iCa <1.0 start calcium compensation at 110%

If patients iCa level is very low consider giving a correction prior to commencing treatment. If the patient already has a calcium infusion running then keep this going whilst filtration is established. Once patient's iCa levels are at desired level the calcium infusion **not** being delivered by the PrisMax can be weaned and stopped.

Magnesium levels <0.7mmol/L should be corrected (if arrhythmias present then correct if <1mmol/L). This should be done according to unit policy. Discuss with consultant and pharmacist before replacing.

With Citrate, effectiveness of anticoagulation is monitored by taking iCa levels from the filter so Activated Clotting Times (ACTs) are not required prior to or during treatment.

6.3. Equipment required

- PrisMax circuit - HF20/ST60/ST100/Oxiris (see prescription for size guide)
- If patient requires less efficient treatment then a smaller circuit can be used, for more efficient treatment next size up filter can be used. Discuss with Paediatric Renal Critical Care Nurse prior to commencing treatment using a different filter to the one which is recommended.
- TherMax disposable if using ST circuits
- 50mL luer lock syringe and dedicated calcium infusion line (CA250)
- Calcium Gluconate 10% and 0.9% Sodium Chloride for Calcium infusion
- 5 litre bag PrismoCitrate 18/0 to be used on the pre blood pump scale
- 5 litre bag Prism0cal B22 to be used on the dialysate scale
- 5 litre bag Phoxilium to be used on replacement scale
- 1 litre bag 0.9% Sodium Chloride with 2000 units of Heparin for 1st prime
- 1 litre bag Plasmalyte 148 for 2nd prime

Aseptic non-touch technique should be utilised when setting up and connecting PrisMax.

6.4. Priming

Plasmalyte 148 is now the priming fluid of choice; this will be suitable for the majority of patients. If the patient has a high potassium level, 0.9% sodium chloride can be used instead. Circuits will initially be primed with 0.9% Sodium Chloride and Heparin (2000 units of Heparin added to a 1 litre bag of 0.9% Sodium Chloride), then primed with a plain bag of Plasmalyte 148.

A 4.5% Human Albumin Solution (HAS) prime can be used if required, please discuss with consultant.

Blood priming should **not** be routinely practiced; however there might be an occasion when this is necessary such as in very low weight babies. Please discuss with PCCU consultant and paediatric renal critical care nurse if this is indicated. If a patient requires blood please run a **transfusion** prior to or during commencement of therapy.

6.5. Starting parameters

- Always set up in CVVHDF
- Initial starting Citrate dose 4mmol/L unless liver impairment is present, in which a starting dose of 3mmol/L is used. Only change after discussion with consultant or paediatric renal critical care nurse.
- If patient's iCa within normal range start calcium compensation at 100%
- Due to the blood pump speed being considerably slower than previously used, there is no need to commence treatment at half the blood pump speed for patients <50kg.
- For patients >50kg, start at a lower blood pump speed and build up when the patient is haemodynamically stable.

6.6. Flow rates

Initial Treatment Settings						
	<5kg	5-11kg	11-18kg	18-30kg	30-50kg	>50kg
Blood flow rate	20ml/min	30ml/min	55ml/min	3ml/kg/min		
PBP Citrate	Starting dose: 4mmol/L. Adjust during treatment according to algorithm. (in liver impairment or <1yr, start at 3mmol/L and monitor systemic iCa closely)					
Dialysate	Commence at 20ml/kg/hr (can increase up to 50ml/kg/hr)					
Replacement	20ml/hr	30ml/hr	50ml/hr	100ml/hr	150ml/hr	200ml/hr
Calcium syringe	Initially start at 100% if patient calcium normal. Adjust during treatment according to algorithm.					
Set patient gain/loss limit	This is set at 10ml/kg over 3 hours, once set this limit cannot be changed during treatment.					

These are initial flows for commencing treatment and can be altered depending on patient's condition. For example: if patient has hyperammonaemia then start dialysis rate at 50ml/kg/hr and titrate rate according to ammonia level. If patient has high sodium or high urea then the flow rates should be slowed down. Please see **Appendix One** for clearance

table, to increase efficiency go up the weight brackets and to decrease efficiency then go down the weight brackets.

6.7. Unintended patient fluid loss or gain limit

This is the difference between the fluid removal measured on the machine and the set fluid removal rate over the last 3 hours. Once this limit has been reached the PrisMax will stop and will not allow treatment to continue. The default limit is 60-400mls over 3 hours, but should be set based on patient's weight, clinical condition and haemodynamic stability.

6.8. Patient fluid removal rate

This is calculated on an hourly basis depending on actual patient fluid balance, desired fluid balance and condition and stability of the patient. Individual prescription depends on input (i.e. nutrition, IV fluids, drugs) and output (i.e. urine, gastric, drain losses). The PrisMax will continue to run at the set hourly rate until changed by staff. The rate **must** be reviewed every hour. Beware of removing fluid too quickly.

If a negative balance is required this needs to be prescribed in ml/hr. Net fluid removal rate refers to desired net removal (e.g. 0ml/hr would mean a neutral balance to the patient, 10ml/hr would mean -10ml/hr to the patient). Net fluid removal rate and hourly actual fluid balance both need to be added together to work out patient fluid removal rate to be programmed (e.g. if total hourly input amount of IV fluids and infusions is 45ml/hr and 10ml/hr net removal is prescribed = 55mls/hr needs to be programmed into the machine). Do not remove fluid bolus given to support blood pressure or intravascular loss. Blood products which have **not** been administered for volume should be added to the programed fluid removal rate and removed over the duration of the transfusion.

If the machine shows a minus number that means that it has gained that amount of fluid. This may occur when treatment is first commenced, but should readjust itself after a few minutes.

Deciding exactly how much fluid to remove from the patient is complex as it depends on many clinical factors including urine output, insensible loss, hypervolaemia/hypovolaemia and clinical observations.

EXTREME CAUTION should be used when setting the patient fluid loss rate, as the PrisMax will try to remove that fluid; it has no way of assessing the effect on the patient. It will continue to remove fluid even when the patient is **HYPOVOLAEMIC.** In low body weight children extra caution is advised in assessing and programming fluid removal rates. No Paediatric CRRT equipment is accurate ml for ml and there may be some discrepancies in what the machine actually achieves.

Always treat the patient NOT the machine.

7. During therapy

7.1. Care and clinical monitoring of patient

- Continuous monitoring of cardiovascular and respiratory parameters should be undertaken.
- Ensure cardiovascular observations are recorded hourly on PCCU chart or half hourly depending on stability of patient.
- All patients who are receiving CVVH/CVVHDF should have central/peripheral temperature*, heart rate and arterial blood pressure (*****central temperature does not have to be a rectal temperature).
- Fluid balance needs careful monitoring because of the large volumes of fluid being removed/infused. Weigh patient on daily basis if possible.
- There are inherent errors in all the measures of fluid balance therefore it is wise to assess the following factors before deciding upon the hydration status of the patient in relation to CRRT:
    - Fluid balance
    - Clinical examination (Heart Rate, Arterial Blood Pressure, Central Venous Pressure, Capillary Refill Time etc.)
    - Biochemistry
    - Haematocrit
    - Weight (preferably use a bed with weighing scales inbuilt)

Always treat the patient NOT the machine.

7.2. Pharmacological considerations

Drug removal by haemofiltration/haemodiafiltration depends on molecular weight, albumin binding, water solubility and volume of distribution, therefore some drugs' handling properties are changed by the therapy. Filtration will remove non-protein bound, water soluble drugs, which are available in the circulation. Adding dialysate flow will cause more efficient drug removal by diffusion. Drug dose changes should be checked with a pharmacist.

*Contrast is efficiently removed by filtration

*IVIG does not pass through the haemofilter most commonly used on PCCU

7.3. Temperature control

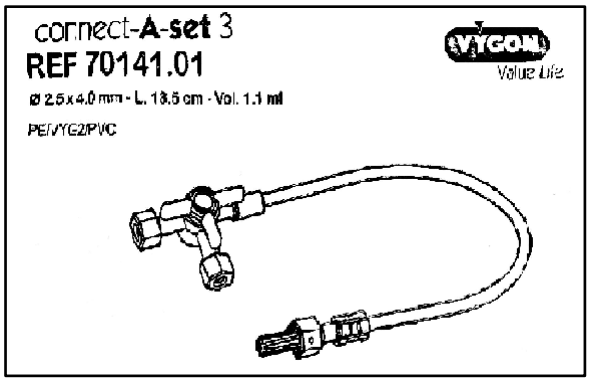
As the patient's blood is removed from their body and pumped through the circuit it significantly cools down so it is essential that a blood warming device is used during treatment. There are two options to heat the patient's blood: the TherMax for ST circuits and the Prismacomfort (Barkey) for HF20 circuits. Please see **Appendix Three** for instructions of how to swap the heaters on the PrisMax. There will also be on screen instructions when setting up PrisMax which will guide through the set up of both devices

- The Prismacomfort should be set 1-2ºC above the desired patient temperature and attached to the Return line.
- As the heater sleeve covers the Return line it is essential that a portion of the line is left exposed next to the patient's catheter so any air will be visible.
- The TherMax should be set at 37°C.
- Additional warming devices may be required (e.g. overhead heater, Bair hugger).
- Beware of both blood warming devices masking pyrexia.

8. Low body weight patients (<4kg)

8.1. Access

If siting a 6.5fg or 8fg double lumen central venous catheter is not possible in very small patients, siting two 18G cannulas in separate sites is advised. A short connection line with a 3-way tap (see right) will need to be attached to these cannulas prior to connecting the CRRT circuit. If the cannula needs to be used as a point of access in an emergency then the blood pump must be stopped.



8.2. Temperature Control

As hypothermia is a serious complication of CRRT, particularly within this group of patients, additional warming devices will be required. Both Access and Return limbs of the circuit should be actively heated with original heating sleeves provided by manufacturer. Close monitoring of the patient's temperature is paramount.

9. Septic patients

9.1. Calcium infusion

Many of the septic patients on PCCU will already be on a calcium infusion due to their inotropic requirements. If this is the case, still continue to run this infusion whilst treatment via the PrisMax is commenced. Once the patient's iCa is within normal range then the calcium infusion being delivered via the external syringe pump can be turned off. The calcium infusion being delivered via the PrisMax can be used to maintain optimum patient iCa levels.

Please be aware that if the PrisMax is discontinued for any reason then the patient won't be receiving any calcium. If treatment is going to be stopped for a while then please recommence a calcium infusion on an external syringe pump as soon as possible to prevent a decrease in the patient's iCa.

This is only applicable if patient was on a calcium infusion for inotropic support pre CVVHDF.

9.2. Transmembrane pressure (TMP)

TMP is the hydrostatic pressure gradient across the filter membrane i.e. the difference in pressure between the blood compartment and the dialysate compartment. This is the driving force that causes ultrafiltration. A rise in TMP suggests that there is clogging occurring in the filter. This is a natural occurrence during treatment and can occur more frequently in septic patients, thought to be due to the adsorption of inflammatory markers to the filter membrane. Unfortunately once the TMP starts to rise there isn't much that can be done to resolve the issue. Making the PrisMax work less by reducing the patient fluid removal or replacement rate may stop TMP rising too quickly but this will mean treatment is less effective. So ultimately the only solution is to electively stop treatment and set up a new circuit.

9.3. High flow replacement

When using heparin for anticoagulation it was possible to increase the flow rates to achieve a more efficient treatment. However this is more complicated with Citrate anticoagulation, mainly due to not being able to manually change the pre blood pump flow rate. If a more efficient treatment is required then this can be achieved by moving the patient up the weight brackets until desired treatment is achieved (see **Appendix One**). When doing this change blood pump, dialysate and replacements flow rates simultaneously.

9.4. Oxiris Circuit

In septic patients who require fluid and uremic toxin removal, an Oxiris set should be used. This set is intended for patients with excessive endotoxin, cytokine and inflammatory mediators. Due to the adsorption properties of the set, the first set should be electively changed after approximately 12 hours. Following this, each set should only be in use for 24-48 hours, at which point it should be changed electively. This can either be for another Oxiris set, or for a standard ST set if inflammatory mediators have been reduced but further uremic toxin removal or fluid/electrolyte management is required.

10. Monitoring

10.1. iCa – Post filter and Patient systemic

Within the first hour after treatment has been commenced, the iCa level of the filter and the patient need to be checked. Take a post filter blood sample from the blue port on the circuit (filter sample) and another blood sample from the patient's arterial line (systemic sample). Compare the results to the table below and alter the Citrate dose and/or calcium compensation accordingly. After initial blood samples repeat both again 1 hour later even if first results in the normal range. If the second set of levels remain in the normal range then these can monitored 4 hourly.

Patients > 1yr and normal liver function:

	Filter Ca^{2+} >0.35	Filter Ca^{2+} 0.25-0.35	Filter Ca^{2+} <0.25
Patient Ca^{2+} <1.0	Increase Citrate dose by 0.5mmol/L blood Increase calcium compensation by 10%	Increase calcium compensation by 10%	Decrease Citrate dose by 0.5mmol/L blood
Patient Ca^{2+} 1.0-1.2	Increase Citrate dose by 0.5mmol/L blood	**Normal Ideal Values - No change needed.**	Decrease Citrate dose by 0.5mmol/L blood
Patient Ca^{2+} >1.2	Decrease calcium compensation by 10%	Decrease calcium compensation by 10%	Decrease calcium compensation by 10% Decrease Citrate dose by 0.5mmol/L blood

Patients with liver impairment/failure, <1yr or mitochondrial disorders:

Aim for a higher filter calcium as below:

	Filter Ca^{2+} >0.45	Filter Ca^{2+} 0.4-0.45	Filter Ca^{2+} <0.4
Patient Ca^{2+} <1.0	Increase Citrate dose by 0.5mmol/L blood Increase calcium compensation by 10%	Increase calcium compensation by 10%	Decrease Citrate dose by 0.5mmol/L blood
Patient Ca^{2+} 1.0-1.2	Increase Citrate dose by 0.5mmol/L blood	**Normal Ideal Values - No change needed.**	Decrease Citrate dose by 0.5mmol/L blood
Patient Ca^{2+} >1.2	Decrease calcium compensation by 10%	Decrease calcium compensation by 10%	Decrease calcium compensation by 10% Decrease Citrate dose by 0.5mmol/L blood

- Changes must be documented and checked by two nurses and signed for on prescription chart.
- After any adjustments to Citrate dose and calcium compensation are made, iCa must be checked in both the patient and the filter after 1 hour.
- Check post filter and patient iCa hourly until ideal values have been established and are stable for two consecutive hours, then 4 hourly.
- Frequent increased requirements for calcium compensation could indicate Citrate accumulation, so check *Total Calcium/iCa patient ratio (see below).*
- If the Citrate dose is reduced, pre blood pump and total effluent will reduce. If total effluent falls below 30mL/kg/hr, gradually increase replacement flow rate until a dose of 30mL/kg/hr is achieved.

10.2. Total Calcium/iCa patient ratio (calcium T:i ratio)

Perform blood total calcium 6 hours after treatment has been commenced, and take a blood gas at the same time. Divide patient's total calcium (from lab sample) by the patient's iCa (from blood gas) and then action as below. If stable repeat every 6 hours, or more frequently if clinically indicated. Inform paediatric renal critical care nurse if ratio >2.5 and follow actions on pages 8-9 in prescription (Also see Page 22 of this guideline).

Calcium T:i ratio	Action
<2.5	No change needed. Check 6 hourly.
>2.5	Aim for post filter iCa 0.35-0.4mmol/L (or 0.45-0.5 if using liver impairment/failure arm of algorithm) by decreasing Citrate dose in 0.5mmol/L increments every 30 minutes or until range achieved, check calcium T:i ratio after one hour See *Citrate Accumulation* section (Page 22) if calcium T:i ratio still >2.5 after one hour

10.3. What bloods to take and when

Calcium monitoring – timing summary	**Initially**	**And then**
Post filter ionised Ca (blood gas from ***blue*** port in circuit) Target 0.25-0.35mmol/L	Within the first hour after commencing then 1 hour after initial test	4 hourly once stable (for two consecutive hours)
Patient systemic iCa (blood gas from patient) Target 1.0-1.2mmol/L		
Post filter gas and patient gas must be taken at the same time		
Patient total calcium (not corrected calcium) Target 2.2-2.5mmol/L	6 hours after commencing	6 hourly once stable (more frequently if concerned about Citrate accumulation)
Calcium ratio (total Ca/patient systemic iCa) Target ratio <2.5	***If the calcium compensation is being increased frequently and patient systemic iCa is not improving, send a total calcium urgently and calculate a T:i ratio to check for Citrate Accumulation. Discuss with paediatric renal critical care nurse and consultant.***	
Blood sampling and frequency		
Arterial blood gas Pay particular attention to pH, lactate, bicarbonate, sodium, potassium, glucose, iCa	Within the first hour after commencing then 1 hour after initial test	4 hourly once stable
U's & E's, plus magnesium and phosphate	6 hours after commencing	6 hourly once stable
Clotting	Every 12 hours	
FBC	Daily	

10.4. pH acid/base balance

Aim for pH 7.35-7.45

Metabolic acidosis (pH <7.35, BE <4mmol/L, HCO_3 <22mmol/L)

Most patients with AKI have some degree of metabolic acidosis on commencement of treatment. This should improve over the first few hours of treatment. If there is a failure to improve BE/HCO_3 towards normal, consider:

- Decreasing dialysate rate by up to 50% from baseline, therefore more Citrate will reach the patient
- Increasing blood flow rate which will increase Citrate delivery
- Giving systemic sodium bicarbonate to the patient (consider respiratory acidosis contribution in first instance, so ventilation is optimised)

These will have different effects on clearance, potential for Citrate toxicity and cardiovascular status and should be discussed with consultant and paediatric renal critical care nurse prior to making any changes.

If the patient has developed Metabolic Acidosis and high lactate alongside a persistently low iCa which is not improving despite increasing calcium concentration then Citrate Toxicity should be suspected. Send a T:i ratio urgently and follow actions on pages 8-9 in prescription (Also see Page 22 of this guideline).

Metabolic alkalosis (pH >7.45, BE >+4mmol/L, HCO3 >25mmol/L)

Please ensure other causes for Metabolic Alkalosis have been considered and optimised these (i.e. ventilation). This can occur due to the metabolism of Citrate into bicarbonate (1mmol Citrate converts to 3mmol bicarbonate), plus the addition of bicarbonate via the dialysate fluid. This may also indicate Citrate Accumulation/Net overload so check calcium T:i ratio. Consider:

- Doubling baseline dialysate flow, this will increase Citrate clearance
- Decreasing blood flow (min 20mL/min) which will reduce Citrate intake
- Be aware of other reasons for the alkalosis and ensure ventilation is optimised

These options will have differing effects on clearance, potential for Citrate toxicity and cardiovascular status and should be discussed with consultant and paediatric renal critical care nurse.

11. Potential problems whilst undergoing treatment

11.1. Emergency Disconnection

In some circumstances emergency disconnection is required such as when lines have clotted, technical failure or evacuation of the unit. In these circumstances wash back of the patient's blood should be considered if possible. CVVH/CVVHDF catheter should then be flushed with sodium chloride 0.9% and locked with heparin.

11.2. Cardiac Arrest

In the event of cardiac arrest while the patient is undergoing CVVH/CVVHDF, treatment should be stopped and the line aspirated, flushed and locked as time allows. It may be an option to wash back the blood in the circuit to the patient, if deemed necessary. In some circumstances continuing filtration may be appropriate (e.g. if being used for life threatening electrolyte disturbance such as **Hyperkalaemia**). Haemofiltration catheters are central venous access and can be used instead of standard central lines in an emergency.

11.3. Air Embolism

In the event of the patient having an air embolism, attempt to aspirate air using the central line. To do so, put the patient on their left side with their head down. Summon emergency assistance.

11.4. Citrate Accumulation

When more Citrate is being infused than can be cleared by either metabolic or dialysis pathways, the calcium-Citrate complex remains in the patient's circulation. As most of this complex is metabolised by the liver, Citrate accumulation is more likely to occur in patients with liver impairment/failure. The Citrate molecule itself is not toxic however the aim is to avoid the secondary effects which are hypocalcaemia and metabolic acidosis.

The main indicator for Citrate accumulation is an increasing total calcium with decreasing patient iCa and a calcium T:i ratio of >2.5. If the calcium compensation is being increased each hour because of low patient iCa THINK: <u>Could this be Citrate Accumulation?</u>

As per section 9.2 calculate Total Calcium/iCa patient ratio (calcium T:i ratio):

- If the ratio is high, aim for post filter iCa 0.35-0.4mmol/L (or 0.45-0.5mmol/L if using liver impairment/failure arm of algorithm) by decreasing Citrate dose in 0.5mmol/L increments every 30 minutes or until range achieved, check calcium T:i ratio after one hour.
- Also consider decreasing blood pump speed (min 20mls/min), this will also decrease the total administered Citrate.
- Discuss with paediatric renal critical care nurse and PCCU consultant.

If the T:i ratio calculated after one hour still remains high, take the following actions to resolve the problem:

- Stop Citrate dose by reducing rate to 0mmol/L and quadruple the baseline dialysate flow (or increase to maximum dialysate flow rate possible for set), this will increase the Citrate clearance
- Increase blood flow rate, this will prevent clotting in the circuit whilst there is no anticoagulant running
- Send a total calcium urgently after one hour and repeat ratio (if result does not come back within an hour contact the laboratory on 84932 and chase result)

If improvement seen:

- Restart Citrate at 50% of previous Citrate dose and half dialysate rate, monitor patient calcium and T:i ratio closely
- Monitor the iCa of the circuit hourly to ensure adequate anticoagulation of the circuit, aim for a new target of 0.4-0.45mmol/L (see 'Liver impairment' section of *iCa Filter and Patient Algorithm* on Pg 19 for suggested ranges). This will mean less Citrate is needed to maintain within target range.

If despite these actions the calcium T:i ratio remains high do not restart Citrate and discuss converting to alternative anticoagulation with consultant.

12. Appendix One - Clearance table (Citrate)

If there is either not enough clearance or too efficient clearance, then use the following table to alter the flow rates on the PrisMax. This will either increase or decrease the overall effluent dose making the treatment more or less efficient depending on what is to be achieved. When going up or down a weight bracket, change all of the flow rates shown in the table. Movement up or down several weight brackets may be required, depending on the clinical picture. The patient must then be closely monitored, including regular blood gas and bloods, to ensure changes in flow rates are effective.

Decrease Clearance ↓

Weight	BFR	Dialysate	Replacement	Estimated Effluent dose
80	200	1600	200	54
70	200	1400	200	59
60	180	1200	200	61
50	150	1000	150	61
45	135	900	150	61
40	120	800	150	62
35	105	700	150	62
30	90	600	100	61
25	75	500	100	62
20	60	400	100	63
18	55	360	50	61
16	55	320	50	67
14	55	280	50	73
12	55	240	50	82
11	55	220	50	88
10	30	200	30	61
9	30	180	30	66
8	30	160	30	71
7	30	140	30	79
6	30	120	30	88
5	30	100	30	102
4	20	80	20	88
3	20	60	20	111
2	20	40	20	157

↑ Increase Clearance

Special Considerations

Hyperkalaemia – High potassium levels can cause arrhythmias and lead to cardiac arrest if not treated. Do not delay commencing therapy in these patients and consider moving the patient up a weight band if clearance is needed quickly.

Hyperammonaemia (Time Critical) – The higher the ammonia level and the longer it stays at that level, the higher the risk of brain damage to the patient. It is essential that ammonia is cleared as quickly as possible to reduce this risk. When starting CVVHDF on a patient with hyperammonaemia move them up one or two weight bands, depending on ammonia level. The dialysate flow can also be increased to rates up to 50ml/kg/hr to improve clearance. **(Also applies to Metabolic emergencies)**

Hypernatraemia and Hyperuraemia – If sodium and urea are cleared too quickly, disequilibrium syndrome can occur and the osmotic gradient in the brain will change causing cerebral oedema. When starting CVVHDF in these patients, start slowly by moving the patient down one or two weight bands, depending on sodium and urea levels. A smaller filter size can also be used to decrease clearance.

For all patients, it is essential that a full set of bloods (including U&Es) are taken and reviewed before commencing treatment and at regular intervals throughout. This allows treatment to be adjusted and tailored to the patient's clinical condition.

13. Appendix Two - CVVH/CVVHDF with Epoprostenol Anticoagulation

In the event that Citrate is contraindicated for a patient e.g. in Citrate accumulation or hepatic impairment/failure, then Epoprostenol can be used as an anticoagulant. Epoprostenol is used to anticoagulate the patient and therefore the blood that is traveling through the circuit.

13.1. Properties

Epoprostenol is a member of the prostaglandin family and is a powerful platelet aggregation inhibitor, which means it stops platelets being able to adhere to one another and create a clot. It also has vasodilating properties and can be used in patients with pulmonary hypertension.

13.2. Administration and dosage

Epoprostenol has a short half-life, so must be administered continuously directly to the patient using an external syringe driver, not through the PrisMax machine. Use a dedicated central line for administration. If access is a problem, a 3-way tap may be added onto return line of circuit. Prepare infusion using the following table:

Patient weight	Amount of drug to be added to 50ml syringe	Dilute to 50ml with	Syringe concentration	1ml/hr =	Dose range
Under 10kg	10ml of 10 microgram/ ml solution	40ml 0.9% sodium chloride	100 microgram in 50ml	Equivalent to x nanogram/kg/minute where x = 33.3 / patient weight in kg	**Starting dose = 4 nanogram/kg/minute.** If filter life is under 48hours, increase by 2 nanogram/kg/minute incrementally to the usual maximum rate of 8 nanograms/kg/minute Rates up to 10 nanogram/ kg/minute have been used.
10-30kg	25ml of 10 microgram/ ml solution	25ml 0.9% sodium chloride	250 microgram in 50ml	Equivalent to x nanogram/kg/minute where x = 83.3 / patient weight in kg	
30kg and over	Use reconstituted solution without further dilution		500 microgram in 50ml	Equivalent to x nanogram/kg/minute where x = 167 / patient weight in kg	

Due to its vasodilating effects, Epoprostenol should not be stopped suddenly to avoid rebound pulmonary hypertension. If planning to discontinue CVVH, wean Epoprostenol gradually by reducing by 2 nanograms/kg/minute every 15 minutes prior to stopping therapy. If CVVH stops unexpectedly (i.e if it clots or the patient's access stops working), continue Epoprostenol and wean by 2 nanogram/kg/minute every 15 minutes until off. Observe for signs of rebound pulmonary hypertension.

13.3. Flow rates for Epoprostenol

When using Epoprostenol for anticoagulation, the flow rates used are quicker than when using Citrate to prevent the circuit from clotting.

Initial Treatment Settings	
Blood flow rate Affected by vascular access and patient's condition	6-9ml/kg/min (30-240ml/min) *Can increase to 12-15ml/kg/min in low weight babies* Blood flow rates will not affect clearances There is no such thing as too much blood flow (other than max limit set by filter size). In patients >30kg aim for a blood pump speed of 180-240mL/min, rates above this are not always achievable or necessary. Blood flows should be adjusted in high flow CRRT to compensate for excessive haemoconcentration of the filter.
Replacement rate Ultrafiltration and Convection *Medium and large molecule clearance (e.g. products of inflammation/cytokines)*	Standard replacement rate = 30ml/kg/hr On PrisMax this is programmed as: - 10ml/kg/hr for Pre Blood Pump - 20ml/kg/hr for Replacement *Higher rates up to 100ml/kg/hr may be used in sepsis and hyperammonaemia (Increase incrementally and monitor patient response closely in higher rates)* Increasing % pre-dilution may be required when having problems with the filter pressures increasing. Majority pre-dilution may be needed in certain patients (**Max 90% pre, 10% post.**)
Dialysate rate Diffusion *Small molecule clearance (e.g. urea/ammonia)*	Usually 20ml/kg/hr *Higher rates up to 50ml/kg/hr may be used in order to increase clearance (ie in Hyperammonia, Hyperkalaemia etc)* *(Increase incrementally and monitor patient response closely in higher rates)*
Set patient gain/loss limit	This is set at 10ml/kg over 3 hours (60-400ml/hr) *Once set this limit cannot be changed during treatment*

In AKI no evidence exists to support one mode over another. A combination of convection and diffusion to optimise the removal of small and medium sized molecules may be preferred.

Typical starting prescription for fluid overload and/or oliguria would be: 30ml/kg/hr total convection (replacement), with the addition in SIRS/Sepsis of 20ml/kg/hr diffusion (dialysate).

13.4. Monitoring

There is no bed side monitoring required when administering Epoprostenol, but close monitoring of the patient's coagulation status should be carried out by sending regular laboratory bloods. Clotting should be sent every 6 hours alongside routine bloods and if abnormal, Epoprostenol rate should be reduced.

When titrating Epoprostenol, the speed of increase is limited by the occurrence of side effects. Consider the patient's blood pressure in conjunction with the filter pressures and evidence of clots in the circuit:

- If filter pressures are rising then the Epoprostenol rate can be increased, but monitor the patient closely for signs of hypotension.
- If the patient becomes hypotensive, the rate will need to be decreased to reduce vasodilator effects. This will increase the risk of the filter clotting so observe for rising filter pressures.

13.5. Side Effects

- Hypotension due to vasodilation
- Patients can develop raised intracranial pressure
- Inhibition of platelet aggregation can cause unwanted bleeding, therefore monitor coagulation status carefully, particularly if on other anticoagulants
- Nausea, vomiting, headache, hypotension, flushing, chest pain, anxiety, dizziness, bradycardia, dyspnoea, abdominal pain and tachycardia - although these are mainly described in adults who are not on CRRT.

13.6. Contraindications

- Treat any hypovolaemia before commencing infusion
- Avoid sudden withdrawal due to the potential for rebound pulmonary hypertension
- Contraindicated in severe left ventricular dysfunction and pulmonary veno-occlusive disease
- Contraindicated in patients with oesophageal varices due to the inhibition of platelets and increased blood flow in the portal venous system
- Vasodilator effect may augment or be augmented by other vasodilators
- Caution if patient has abnormal coagulation prior to heamofiltration

13.7. Pre-Blood Pump, Dialysate and Replacement Solutions

Phoxilium is the first line fluid on all three scales if Phosphate is <3mmol/L or glucose >5mmol/L. The use of Phoxilium will aid in the restoration of phosphate lost during filtration, although it contains no glucose so close monitoring of the patient's glucose level is essential.

Phoxilium									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	4	1.25	0.6	115.9	1.2	0	30	0	0

Prismasol 4 is used as a second line option on all three scales.

Prismasol 4 (all values in mmol/L)									
Sodium	Potassium	Calcium	Magnesium	Chloride	Phosphate	Lactate	Bicarbonate	Glucose	Citrate
140	4	1.75	0.5	113.5	0	3	32	6.1	0

13.8. Adding electrolytes to fluid bags

Currently, additives can only be added to Prismasol 4 due to the unknown stability of additives in Phoxilium fluid. Additives are always prescribed to be added per litre of fluid and as a total dose. Care needs to be taken when making up the fluid as a result. When additives are required, more frequent blood sampling will be required.

Electrolyte	Indication	Additive
Phosphate	Serum Phosphate <2mmol/L	Sodium glycerophosphate 1mmol/L (5mmols added to 5 litre bag)
Glucose	Serum glucose <6mmol/L	Glucose 1.1 grams/L (6mmol/L) (5.5 grams glucose to 5 litre bag of Hemosol BO,11mls of 50% glucose).

13.9. Management of hypernatraemia

This is the same as with Citrate anticoagulation, the only difference being sodium chloride can be added to all three fluid bags.

Please see pharmacopeia for more information:

http://nuhnet/nuh_documents/Guidelines/Family%20Health/Children%27s%20Hospital%20-%20PICU/2560.pdf

14. Appendix Three - Swapping Blood Warmers

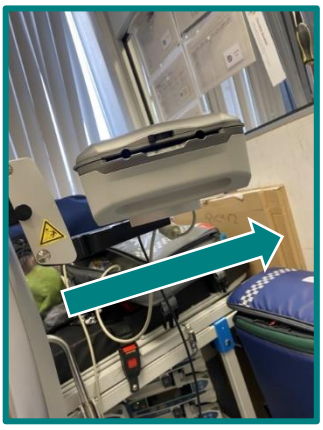
The TherMax can only be used on the ST circuits as the HF20 circuit does not have a break in the circuit to attach the TherMax disposable warming pouch. Therefore for the HF20 circuit the Prismacomfort (Barkey) heating device is used.

TherMax **Prismacomfort**

In order to swap between the devices, please use the following instructions:

- Disconnect the Thermax cable from the back of the PrisMax (when reconnecting, cable needs to go in the middle socket)
- Use an allen key to remove the long screws from the base plate
- Carefully slide the TherMax off the base plate to the right
- Secure the Prismacomfort to the base plate using the allen key and the short screws

Ensure the heater is held at all times whilst removing from or securing it to the base plate to avoid it falling on the floor.



Follow the procedure in reverse to swap back to the TherMax

15. References

Aldairi N, Al Ali A S, Alabdulqader M, et al. (2023). Efficacy of Prostacyclin Anticoagulation in Critically Ill Patients Requiring Extracorporeal Support: A Systematic Review and Meta-Analysis. *Cureus.* **15** (6)

Brophy P, Somers M, Baum M et al. (2005). Multi-centre evaluation of anticoagulation in patients receiving continuous renal replacement therapy (CRRT). *Nephrology Dialysis Transplant.* **20** (7), 1416-21

Brophy P, Mottes T, Kudelka T et al. (2001). AN-69 membrane reactions are pH-dependent and preventable. *American Journal of Kidney Disease.* **38** (1), 173-8

Brunet S, Leblanc M, Geadah. D et al. (1999). Diffusive and convective solute clearances during continuous renal replacement therapy at various dialysate and ultrafiltration flow rates. *American Journal of Kidney Disease.* **34**, 486-92.

Buccine E (2022). Regional Citrate anticoagulation and systemic anticoagulation during pediatric continuous renal replacement therapy: A systemic literature review. *Journal of Clinical Medicine.* **11**, 3121

Bunchman T, Maxvold N, Kershaw D et al. (1994). Continuous venovenous hemodiafiltration in infants and children. *Pediatric Nephrology.* **8**, 96-9

Davenport A and Tolwani A (2009). Citrate anticoagulation for continuous renal replacement therapy (CRRT) in patients with acute kidney injury admitted to intensive care. *NDT Plus.* **2**, 439-447

Deep A, Mohammad Z and Dutta Kukreja P (2017). Prostacyclin as an anticoagulant for continuous renal replacement therapy in children. *Blood purification.* **43**, 279-289

Deep, A (2022). Anticoagulation strategies in continuous kidney replacement therapy – does one size fit all? *Paediatric Nephrology*. **37** (11), 2525-2529

Deep, A et al. (2024). Epoprostenol (Prostacyclin Analog) as a Sole Anticoagulant in Continuous Renal Replacement Therapy for Critically Ill Children With Liver Disease: Single-Center Retrospective Study, 2010–2019*. *Paediatric critical care medicine.* **25** (1), 15-23

Fernandez S et al. (2014). Citrate anticoagulation for CRRT in children: Comparison with heparin. *Biomed Research International.* Article ID 786301

Goldstein SL et al. (2004). The Prospective Pediatric Continuous Renal Replacement Therapy (ppCRRT) Registry: design, development and data assessed. *Int J Artif Organs.* **27**, 9-14

Goldstein S. (2003). Overview of pediatric renal replacement therapy in acute renal failure. *Artifical Organs.* **27** (9), 781-5

Goldstein S, Somers M, Baum M et al. (2005) Pediatric patients with multi-organ system failure receiving continuous renal replacement therapy. *Kidney Int.* **67** (2), 653-8

John JC, Taha S, Bunchman TE. (2019). Basics of continuous renal replacement therapy in pediatrics. *Kidney Res Clin Pract.* **38** (4), 455-461

Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney inter., Suppl. 2012; 2: 1–138.

National institute for health and care excellence (2019). Acute kidney injury: prevention, detection and management (online). NICE Guidance NG148

Rupesh R et al. (2020). Consensus guidelines for management of hyperammonaemia in paediatric patients receiving continuous kidney replacement therapy. *Nephrology Nature Reviews.* **16**

Ronco C et al. (2000). Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial. *The Lancet.* **356**, 26-30

Shaheen I, Harvey B, Watson A (2009). Haemofiltration Therapy *Paediatrics and Child Health.* **19** (3), 121-126

Steves-Harris I, Raffaj D, Davies P (2017). Pressure-related flow rates for continuous renal replacement therapy in very small children: an invitro study. *BMJ Paediatrics Open*

Strazdins V, Watson A, Harvey B (2004). European Pediatric Peritoneal Dialysis Working Group: Renal replacement therapy for acute renal failure in children: European guidelines. *Pediatric Nephrology.* **19** (2), 199-207

Szamosfalvi B et al. (2021). Regional Citrate anticoagulation protocol for patients with presumed absent Citrate metabolism. *Kidney 360.* **2**

15.1. Other useful resources:

www.baxterhealthcare.co.uk

www.pcrrt.com