1. Introduction and Who Guideline applies to

Prothrombin complex concentrate (PCC) is the treatment of choice when rapid reversal of anticoagulation with Warfarin, other Vitamin K antagonists or a direct inhibitor of activated factor X (factor Xa – e.g. rivaroxaban, apixaban or edoxaban) is required.

At any given time, one or the other of the two products licensed in the UK - Octaplex or Beriplex P/N - is available within UHL. The product is stored in the transfusion laboratories at each of the three hospitals as well as the ER drug cupboard in the LRI Emergency Department.

Its use requires verbal authorization from a haematology registrar or consultant via telephone.

Please note that PCC contains clotting factors II, VII, IX and X, derived from multi-pooled donor plasma. It is pasteurised and nanofiltered to remove viruses, but certain viruses such as Hepatitis A virus (HAV) and parvovirus may resist the inactivation process. The risk of transmission for prion diseases including variant Creutzfeldt-Jakob disease (vCJD) is as yet unknown.

This guideline applies to all UHL staff who request, prescribe or administer PCC as well as haematology and pharmacy staff involved in the logistics of dispensing and replenishing PCC stocks. It has been created to ensure that PCC is used as effectively as possible.

2. Guideline Standards and Procedures

2.1 Administration of PCC carries a risk of thrombosis and it should generally be avoided in patients with disseminated intravascular coagulation (DIC) or decompensated liver disease

2.2 Detach the request form shown in Appendix E and gather all necessary information (patient’s weight, indication for anticoagulation, latest INR and PCC indication) before contacting the haematology duty doctor

2.3 ED staff should follow the algorithm shown in Appendix A as well as the Beriplex P/N and Octaplex administration aid shown in Appendix C

2.4 Staff in all other clinical areas should follow the algorithm shown in Appendix B as well as the Beriplex P/N and Octaplex administration aid shown in Appendix C

2.5 Give the patient information leaflet (PIL) shown in Appendix D to all patients deemed to have capacity before obtaining and documenting their verbal consent

3. Education and Training

No additional skills are required to follow this guideline.

4. Monitoring Compliance

<table>
<thead>
<tr>
<th>What will be measured to monitor compliance</th>
<th>How will compliance be monitored</th>
<th>Monitoring Lead</th>
<th>Frequency</th>
<th>Reporting arrangements</th>
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<tbody>
<tr>
<td>Appropriate PCC use</td>
<td>• ED audit • Trust audit</td>
<td>Medication safety team</td>
<td>annually</td>
<td>Anticoagulation Committee</td>
</tr>
<tr>
<td>Timely PCC use</td>
<td>• ED audit • Trust audit</td>
<td>Medication safety team</td>
<td>annually</td>
<td>Anticoagulation Committee</td>
</tr>
</tbody>
</table>
5. Supporting References and Related Policies
1. Oral anticoagulation with warfarin and coumarins UHL guideline (Trust Ref: B44/2016)
2. DOAC (Direct Oral Anticoagulants) reversal in bleeding patients UHL Emergency Department guideline (Trust Ref: C13/2017)
3. Injectable Medicines Guide (‘Medusa’) – Dried prothrombin concentrate (Beriplex P/N)
4. Injectable Medicines Guide (‘Medusa’) – Dried prothrombin concentrate (Octaplex)

6. Key Words
Bleed, haemorrhage, coagulation, warfarin, DOAC, octaplex, beriplex, prothrombin, PCC, reversal, clotting, haematology, blood product

<table>
<thead>
<tr>
<th>CONTACT AND REVIEW DETAILS</th>
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<td>Guideline Lead (Name and Title)</td>
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<td>Hafiz Qureshi, Consultant Haematologist</td>
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Details of Changes made during review:

PCC stock replenishment request process for ED changed only; ED algorithm and PCC request form amended accordingly
Appendix A. **PCC algorithm for clinical users – ED only.**

ED clinician considers urgent anticoagulation reversal for life, limb or sight threatening bleeding using PCC

- Print off this guideline from INsite or ED on-demand print screen ‘ER – Other’
- Gather all necessary information to complete PCC request form (last sheet of this guideline)
- Contact haematology duty doctor **NOW**

Does the haematology duty doctor confirm need for PCC?

- Record final details, including PCC dose recommended, on PCC request form during phone call to haematology duty doctor. **(NB: haematology doctor to round dose to nearest 500 units)**
- Ensure patient receives Vitamin K 5mg IV STAT **UNLESS**
  - already given
  - advised differently by haematology
  - patient is taking rivaroxaban, apixaban or edoxaban

- Give patient the information leaflet (PIL; see page 7)
- Obtain verbal informed consent if patient has capacity OR document absence of capacity in patient’s ED record using the ED capacity assessment form (available from the ED on-demand print screen ‘ER – Other’)
- On the prescribing page of the patient’s ED notes, prescribe each 500- or 1000-unit vial of PCC separately; each 500-unit vial to be given over 2min, 1000-unit vials over 4min

- Remove prescribed quantity of PCC from designated ER drug cupboard and record details in ER CD register
- Administer PCC **NOW** (i.e. within 30min of authorization)

- When administration is complete, peel off a batch number sticker from each vial and place it against the prescription on the ED notes prescribing page
- Peel off a further sticker and place it on the back of the request form to help pharmacy keep track

Ask porter to take form to Windsor pharmacy **NOW** **(NB: ask them to drop it in letter box under window marked ’Prescription Collection’ if pharmacy closed)**

Recheck INR within 1h of PCC administration **(NB: This can also be done immediately if more convenient)**

- Pharmacy to replenish used product as detailed on the returned PCC request form using CD delivery process (sealed red bag)
- ER nurse signs for delivery, discards red bag and **IMMEDIATELY** places PCC vials into designated ER drug cupboard

Pharmacy porter returns sign sheet to pharmacy

**NB:** Request forms dropped off out of hours will be processed early next day

**Ideally involves 2 people (nurses or doctors; NB:** Any IV-trained nurse may administer PCC:**
- One person reconstitutes PCC as shown on page 5
- The other gives each 20mL syringe over 2min (HINT: The 40mL content of a 1000-unit vial is best drawn up in two 20mL syringes)**
Appendix B.  PCC algorithm for clinical users – excluding ED.

Clinician considers urgent anticoagulation reversal for life, limb or sight threatening bleeding using PCC

Clinician
- Prints off this guideline from INsite (unless paper copy readily available)
- Gathers all necessary information to complete PCC request form (last sheet of this guideline)
- Contacts haematology duty doctor immediately

Does the haematology duty doctor confirm need for PCC?

Y

Clinician
- Completes PCC request form during phone call to haematology duty doctor who will round dose to nearest 500 units
- Sends form to transfusion laboratory by porter immediately
- Ensures patient receives Vitamin K 5mg IV STAT UNLESS
  - already given
  - advised differently by haematology
  - patient is taking rivaroxaban, apixaban or edoxaban

Clinician
- Gives patient the information leaflet (PIL; see page 7)
- Obtains verbal informed consent if patient has capacity OR documents ‘no capacity’ including reason in patient’s record
- Prescribe each 500- or 1000-unit vial of PCC separately; each 500-unit vial to be given over 2min, 1000-unit vials over 4min

Haematology duty doctor
- Informs transfusion laboratory staff immediately of required dose (rounded up to nearest number of full vials – maximum dose 3000 units)

Porter
- Takes PCC request form to transfusion laboratory and remains there until vials ready to be released

Transfusion laboratory staff
- Releases PCC to waiting porter within 5min of receiving the PCC request form
- Completes ‘FOR TRANSFUSION LABORATORY USE ONLY’ section of request form then files it in designated place

Porter
- Takes PCC to clinical area

Patient’s team
- Gives PCC within 30min of authorization
- Rechecks INR within 1h of administration (NB: May also be done immediately if that is more convenient)

Nursing staff
- Return orange ‘transfusion receipts’ to transfusion laboratory by usual process

How to administer PCC efficiently

- Any IV-trained nurse may give PCC
- Return any unused PCC vials to the lab within 2h of issue. Late returns cannot be reused – your CMG will be charged!
- To administer PCC efficiently, ask a nursing colleague or doctor to help:
  - Open one PCC box and reconstitute its contents as per administration aid on page 5.
  - Pass syringe to your colleague – solution to be administered over 2min
  - Complete required details on orange ‘transfusion receipt’, including time
  - Place the adhesive batch sticker from orange ‘transfusion receipt’ onto the blood component prescription chart
  - Open next box and prepare syringe while colleague is still completing administration of the previous one
  - Continue in this manner until all PCC has been given
  - Finally, sign/countersign, time & date blood component prescription chart
1. Open the Mix2Vial package by peeling off the lid. Do **not** remove the Mix2Vial from the blister package!

2. Place the solvent vial on an even, clean surface and hold the vial tight. Take the Mix2Vial together with the blister package and push the spike of the blue adapter end **straight down** through the solvent vial stopper.

3. Carefully remove the blister package from the Mix2Vial set by holding at the rim, and pulling **vertically** upwards. Make sure that you only pull away the blister package and not the Mix2Vial set.

4. Place the product vial on an even and firm surface. Invert the solvent vial with Mix2Vial set attached and push the spike of the transparent adapter end **straight down** through the product vial stopper. The solvent will automatically flow into the product vial.

5. With one hand grasp the product-side of the Mix2Vial set, and with the other hand grasp the solvent-side and unscrew the set carefully into two pieces. Discard the solvent vial with the blue Mix2Vial adapter attached.

6. Gently swirl the product vial with the transparent adapter attached until the substance is fully dissolved. Do not shake.

7. Draw air into an empty, sterile 20mL syringe. While the product vial is upright, connect the syringe to the Mix2Vial's Luer Lock fitting. Inject air into the product vial.

8. While keeping the syringe plunger pressed, invert the system upside down and draw the solution into the syringe by pulling the plunger back slowly.

9. Now that the solution has been transferred into the syringe, firmly hold on to the barrel of the syringe (keeping the syringe plunger facing down) and disconnect the transparent Mix2Vial adapter from the syringe. Without delay, **college to give syringe over 2min by IV push while you prepare the next syringe.**

**NB:** For vials containing 1000 units, repeat steps 7 and 8 using a second 20ml syringe as the total volume contained in the vial is 40mL

**Repeat process until all vials have been administered**
Prothrombin Complex Concentrate
(Octaplex or Beriplex P/N)

Patient Information Leaflet (PIL)

At present your blood is too thin (you are ‘over-anticoagulated’) because of a drug (Warfarin or a similar drug, rivaroxaban, apixaban or edoxaban) that you have been taking. When your blood is too thin it may lead to bleeding problems (as you may have already experienced). Your doctors feel that it is important to reverse the effects of the blood-thinning drug and return your blood to a state where it can clot normally.

It is felt that, in your particular situation at the moment, your blood-clotting problem is best treated using a treatment called Prothrombin Complex Concentrate, or ‘PCC’. This is a clotting factor concentrate that is given by intravenous injections. It is manufactured from plasma drawn from several blood donations that are pooled together and then specially processed. The treatment contains all the clotting factors needed to reverse the effects of the blood-thinning drug you have been taking.

As large numbers of plasma donations may have been used to produce this product, there is a theoretical risk of transmitting an infection. However, each plasma donation is carefully screened. In addition all clotting factor concentrates undergo a special procedure to eliminate certain viruses. Further, PCC is heated (pasteurised) to inactivate any potential viruses. This is a very effective additional safety measure. Virus inactivation processes such as pasteurisation might also reduce the possibility of transmitting any unknown viruses. The combination of testing, virus inactivation processes and the way PCC is manufactured all serve to make this treatment as safe as is possible.

Some concerns remain that illnesses such as new variant Creutzfeldt-Jakob disease (vCJD, or ‘mad cow disease’) could be transmitted by blood products, but the actual risk is unknown and probably very, very small. Some patients also experience a temporary rise in their body temperature (or fever). Also, as the purpose of giving you PCC is to restore the ability of your blood to clot, there is a small risk that it might cause a thrombosis (an abnormal blood clot) to occur.

All in all, PCC and other similar clotting factor concentrates have been used for many years and have helped many thousands of patients.

Very occasionally, allergic reactions occur with clotting factor concentrates but these are indeed quite rare. When you first receive the clotting factor concentrate, precautions are taken to monitor you for these reactions and to treat them should they occur.

Using the above precautions, PCC has been shown to be safe and effective and will correct your clotting problem very rapidly - within minutes of receiving the injections.

If you have any further questions about PCC that you wish to cover, please ask one of our doctors.
### Appendix E. PCC request form.

**Patient details**
- Full name
- DOB
- Unit number (use sticker if available)

**CLINICAL DETAILS**
- **PCC indication**
  - ☐ Intracranial bleed
  - ☐ Intraocular bleed
  - ☐ Life-threatening blood loss (state source)
  - ☐ Other (give details)
- **Consultant**
- **Location**
- **Extn**
- **Hospital**
  - ☐ LRI
  - ☐ GGH
  - ☐ LGH

**Indication for anticoagulation**
- **Weight** (mandatory)
- **Latest INR**
- **Vitamin K given yet?**
  - ☐ Yes, dose:
  - ☐ IV
  - ☐ PO

**AUTHORISATION**
- **Time**
  - Use 24h clock

**REQUESTED BY**
- **Print name**
- **Signature**
- **Role**
- **Contact phone or bleep number**

**TRANSFUSION LABORATORY USE ONLY (NB: IF LEFT BLANK, PHARMACY TO SUPPLY PCC TO ED)**
- **Did haematology doctor call transfusion lab staff?**
  - ☐ No had to be called
  - ☐ Yes
- **To replace stock, GGH/LGH transfusion lab staff fax this form to LRI lab on 6607, LRI lab staff fax it to LRI pharmacy on 6924.**

**PHARMACY USE ONLY**
- **Stock supplied by**
- **Product**
  - Beriplex P/N
  - Octaplex
- **Expiry date**
- **Batch number**
- **Number of vials received**
- **Stock received by (LRI)**
- **Stock received by (GGH / LGH)**
- **Print Name**
- **Initials**
- **Date**
- **Time**
- **Faxed by (GGH / LGH staff)**
- **Date**
- **Time**
- **Faxed by (LRI staff)**
- **Date**
- **Time**
- **Next Review:** Oct 2021

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**NB:** Paper copies of this document may not be most recent version. The definitive version is held on INsite Documents.
FOR ED USE ONLY

Peel off a batch number sticker from each of the used PCC vials and stick them down in the space below

Pharmacy may contact ER nurse coordinator on extns 0027, 0028, 0167 or 1168 if further information needed