Calgary Zone Guidelines for Use of Prothrombin Complex Concentrates

Prothrombin Complex Concentrate (PCC) - Octaplex®/Beriplex® P/N

PRODUCT DESCRIPTION:

A lyophilized plasma concentrate that is a mixture of the vitamin K dependant coagulation factors II, VII, IX, X, Protein C and Protein S. **NOTE:** The term “units” is used in place of International Units (IU).

<table>
<thead>
<tr>
<th>Medicinal Ingredients</th>
<th>octaplex® 500 in 20 mL</th>
<th>octaplex® 1000 in 40 mL</th>
<th>Beriplex® P/N 500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Coagulation Factor II</td>
<td>280 - 760 units</td>
<td>560 – 1520 units</td>
<td>380 - 800 units</td>
</tr>
<tr>
<td>Human Coagulation Factor VII</td>
<td>180 - 480 units</td>
<td>360 – 960 units</td>
<td>200 - 500 units</td>
</tr>
<tr>
<td>Human Coagulation Factor IX</td>
<td>500 units</td>
<td>1000 units</td>
<td>500 units</td>
</tr>
<tr>
<td>Human Coagulation Factor X</td>
<td>360 - 600 units</td>
<td>720 – 1200 units</td>
<td>500 - 1020 units</td>
</tr>
<tr>
<td>Protein C</td>
<td>260 - 620 units</td>
<td>520 – 1240 units</td>
<td>420 - 820 units</td>
</tr>
<tr>
<td>Protein S</td>
<td>240 - 640 units</td>
<td>480 – 1280 units</td>
<td>240 - 680 units</td>
</tr>
<tr>
<td>Relevant Non-Medicinal Ingredients</td>
<td>Heparin Sodium citrate Solvent (Water for Injection)</td>
<td>Heparin Sodium citrate Solvent (Water for Injection)</td>
<td>Heparin Human Anti-Thrombin III Human albumin Sodium chloride Sodium citrate Solvent (Water for Injection)</td>
</tr>
</tbody>
</table>

Reconstituted solution contains approximately 25 units of prothrombin complex per mL. Standard dosing is based on Factor IX units – for simplicity, each vial of PCC’s will be assumed to contain 500 units Factor IX activity.

INDICATIONS FOR USE:

**Recommended in:**

A. Reversal of warfarin therapy in patients exhibiting major and life threatening bleeding (Intracranial hemorrhage, GI bleeding and etc.).

B. Reversal of warfarin therapy in patients requiring **urgent (less than 6 hour) surgical procedures**.

**Contraindicated in:**

A. Patients with a history of Heparin Induced Thrombocytopenia.
B. Known hypersensitivity to any of the components of the product.

**Off label use (i.e. no history of warfarin)** will require a consultation with a Transfusion Medicine Physician

**Not recommended** for:

A. Elective reversal of oral anticoagulant therapy pre – invasive procedure.
B. Treatment of elevated INRs without bleeding or need for surgical intervention.
C. Massive transfusion.
D. Disseminated Intravascular Coagulation (DIC) associated with liver dysfunction.
E. Patients with recent history of thrombosis, myocardial infarction, recent ischemic stroke or DIC.

- There may be extenuating clinical circumstances necessitating use of Prothrombin Complex Concentrates in these clinical situations. They should be evaluated on a case-by-case basis with the clinical hematologist/transfusion medicine physician on call.

*Note: If the decision is to use product in liver dysfunction and DIC patients, the assessment of Anti-Thrombin levels is recommended. This will ensure that Anti Thrombin III and/or heparin is not required prior to PCC administration.

**Special patient populations:**

A. Pregnant and lactating women – there is insufficient evidence available to allow a recommendation for use of this product in this patient population. Caution should be exercised if used in pregnancy, particularly in the peripartum/early postpartum period because of heightened tendency to thrombosis.
B. Congenital factor II or X deficient patients – use of the product should be at the discretion of the local Hemophilia clinic.
C. Reversal of Direct Xa Inhibitors (e.g. Rivaroxaban or Apixaban) and other warfarin alternatives – See AHS Policy on Direct Oral Anticoagulants (DOAC).

**ORDERING:**

This product is stocked at the Foothills Medical Center, Peter Lougheed Centre, Rockyview General Hospital, South Health Campus and Alberta Children’s Hospital. Prothrombin Complex Concentrates can be ordered through SCM. Order will be filled with either Octaplex® or Beriplex® P/N. Qualifying patients will receive only one of the above brands for each course of treatment.

**NOTE:** Prothrombin Complex Concentrates are blood products that contain human source proteins and require informed consent to be obtained by the Most Responsible Health Practitioner.

**DOsing:**

The following guidelines are based on regional recommendations approved by the Regional Transfusion Committee. The final dosing recommendation was based on review of literature and the desire to prevent thrombotic complications and it may be less than the manufacturer’s recommended dose in many individuals.
Off label use (i.e. no history of warfarin): consultation with Transfusion Medicine Physician is required.

For Adult patients:

This PCC dosing protocol has been developed in collaboration with clinical departments and is based on pre-INR results, clinical categories and variable targets for different clinical categories. Application of this dosing protocol will achieve a reversal INR of less than 1.5 in approximately 90% of the cases.

- The general recommended reversal INR for most patients is a result of less than 1.5 (excluding CNS bleeding, complex surgeries and invasive cardiac procedures).
- For patients with CNS bleeding and complex surgeries an INR result of less than 1.4 is recommended.
- Based on recommendations by the Clinical Cardiovascular group, patients undergoing invasive cardiac procedures might require partial INR reversal (1.7 – 1.9).
- For invasive procedures (ERCP etc.), PCC’s should be given less than 2 hours prior to the procedure.
- Patients requiring temporary warfarin reversal (less than 24 hours) and patients on Direct Oral Anticoagulant Factor Xa inhibitors (e.g. Rivaroxaban or Apixaban) may not need Vitamin K administration with the first dose of PCC.

### PCC Dosing Protocols with Target INR Result

<table>
<thead>
<tr>
<th>Clinical Groups</th>
<th>Target INR</th>
<th>Pre INR &lt; 2.0</th>
<th>Pre INR 2.0 – 2.4</th>
<th>Pre INR 2.5 – 3.4</th>
<th>Pre INR 3.5 – 6.9</th>
<th>Pre INR ≥ 7.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS Bleeding</td>
<td>&lt;1.4</td>
<td>1500 Units</td>
<td>1500 Units</td>
<td>2000 Units</td>
<td>2000 Units</td>
<td>2500 Units</td>
</tr>
<tr>
<td>Active Bleeding</td>
<td>&lt;1.5</td>
<td>1000 Units</td>
<td>1500 Units</td>
<td>1500 Units</td>
<td>2000 Units</td>
<td>2500 Units</td>
</tr>
<tr>
<td>Urgent/EM Surgery</td>
<td>&lt;1.5</td>
<td>1500 Units</td>
<td>1500 Units</td>
<td>1500 Units</td>
<td>2000 Units</td>
<td>2500 Units</td>
</tr>
<tr>
<td>Complex Surgeries*</td>
<td>&lt;1.4</td>
<td>1500 Units</td>
<td>1500 Units</td>
<td>2000 Units</td>
<td>2000 Units</td>
<td>2500 Units</td>
</tr>
<tr>
<td>Lumbar Puncture &amp; Tissue Biopsies</td>
<td>&lt;1.5</td>
<td>1000 Units</td>
<td>1000 Units</td>
<td>1000 Units</td>
<td>1500 Units</td>
<td>2500 Units</td>
</tr>
<tr>
<td>Thoracentesis (Plural Tap) &amp; Paracentesis (Abdominal Tap)</td>
<td>&lt;2.0</td>
<td>NA</td>
<td>500 Units</td>
<td>1000 Units</td>
<td>1000 Units</td>
<td>1000 Units</td>
</tr>
<tr>
<td>Inv. Cardiac Procedure**</td>
<td>1.7 – 1.9</td>
<td>N/A</td>
<td>500 Units</td>
<td>1000 Units</td>
<td>1000 Units</td>
<td>1500 Units</td>
</tr>
</tbody>
</table>

* Complex surgeries: Cardiac/vascular/trauma/thoracotomy and laparotomic surgeries.
** Invasive cardiac procedures: Angiography, angioplasty and stent placement.

Transfusion Medicine (TM) staff will consult a TM Physician for the following:
- PCC orders are greater than 2500 Units.
- Patients not on Warfarin.
- Patients requiring a second dose in less than 24 hours.

**Note:**
- For **Adult** patients weighing less than 60 kg weight, a maximum single dose of 2000 units is recommended.
- Patients requiring temporary warfarin reversal (less than 6 hours) may not need Vitamin K administration.

The Calgary Zone Transfusion Committee and the ACH Transfusion Committee has given approval for the use of PCCs in the pediatric population.

**For Pediatric patients:**

The pediatric dosing guidelines have been developed in collaboration with the pediatric hematology group for warfarin reversal. Pediatric dosing for PCC is a weight based protocol.

<table>
<thead>
<tr>
<th>Weight</th>
<th>PCC Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 20 kg</td>
<td>25 Units/kg*</td>
</tr>
<tr>
<td>20 – 40 kg</td>
<td>500 Units, repeat if required</td>
</tr>
<tr>
<td>40 – 60 kg</td>
<td>1000 Units</td>
</tr>
<tr>
<td>Greater than 60 kg</td>
<td>Follow the Adult PCC table or SCM for dosing</td>
</tr>
</tbody>
</table>

*Reconstituted solution contains approximately 25 IU of prothrombin complex per mL.

**RECONSTITUTION AND ADMINISTRATION:**

**Reconstitution:** *Follow the instructions included in the appropriate product monograph.*

**Note:**

1. PCC’s should be administered intravenously within 30-60 minutes after making the solution.
2. PCC’s should not be mixed with other medication/normal saline in the same infusion set.
3. For infusion rate see below.
4. Signed consent form must be on the patient’s chart before the product is reconstituted and infused.

**INFUSION RATE:**

PCC’s may be administered by minibag infusion/SIVP (slow IV push) or syringe pump.

1. Initial Rate: 1 ml/minute (to watch for allergic/anaphylactic reactions) for 5 – 10 minutes.
2. Rate: 2-3 ml/minute. (The maximum recommended rate by manufacturer is 3 mL/minute).
Notes:

1. **Reconstituted PCC’s must be transferred into the empty plastic minibag** (empty of normal saline) or use an empty sterile bag. Mixing or dilution with normal saline may decrease the potency and stability of the product. The minibag infusion for administration of PCC’s is widely used across Canada and European countries.

2. The recommendation outlined in this guideline including indications, dosage, route of administration and rate of infusion only applies to Prothrombin Complex Concentrates and not other factor concentrates.

3. In case of allergic/anaphylactic reactions the infusion must be stopped. Any reaction and complications (DIC and thromboembolic events) due to the infusion of this product are considered as transfusion associated reactions and require an official report to Transfusion Medicine.

POST-INFUSION MONITORING & REPEAT DOSES:

1. Follow-up PT/INR and PTT should be performed 10-15 minutes after completion of the PCC infusion.

2. In case of persistent bleeding 1 hour after the completion of the infusion of the recommended dose, and the target INR has not been reached, a minimum repeat dose of 1000 units may be considered. A TM physician consult is required to receive the second dose.

References: