**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).

One 20 mL vial of PCC contains the following:

<table>
<thead>
<tr>
<th>Medicinal Ingredients</th>
<th>octaplex® 500</th>
<th>Beriplex® P/N 500</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human Coagulation Factor II</td>
<td>280 - 760 units</td>
<td>380 - 800 units</td>
</tr>
<tr>
<td>Human Coagulation Factor VII</td>
<td>180 - 480 units</td>
<td>200 - 500 units</td>
</tr>
<tr>
<td>Human Coagulation Factor IX</td>
<td>500 units</td>
<td>400-620 units</td>
</tr>
<tr>
<td>Human Coagulation Factor X</td>
<td>360 - 600 units</td>
<td>500 - 1020 units</td>
</tr>
<tr>
<td>Protein C</td>
<td>140 - 620 units</td>
<td>420 - 820 units</td>
</tr>
<tr>
<td>Protein S</td>
<td>140 - 640 units</td>
<td>240 - 680 units</td>
</tr>
<tr>
<td>Relevant Non-Medicinal Ingredients</td>
<td>Heparin</td>
<td>Heparin Human Antithrombin III</td>
</tr>
<tr>
<td></td>
<td>Sodium citrate</td>
<td>Human albumin</td>
</tr>
<tr>
<td></td>
<td>Solvent (water for injection)</td>
<td>Sodium chloride</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sodium citrate</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 or vitamin K deficiency in patients exhibiting major and life threatening bleeding (Intracranial hemorrhage, GI bleeding and etc.).

B. Reversal of warfarin therapy or vitamin K deficiency in patients requiring urgent (<6 hour) surgical procedures.

**Contraindicated in:**

A. Patients with a history of Heparin Induced Thrombocytopenia

**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. Coagulopathy associated with Liver dysfunction
E. Patients with recent history of thrombosis, myocardial infarction, recent ischemic stroke or Disseminated Intravascular Coagulation (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 AT 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, Apixaban) and other warfarin alternatives – See AHS Policy on Direct Oral Anticoagulants (DOAC).

ORDERING:

Each rural hospital site will have one dose consisting of 4 vials (2000 units). 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 containing human source proteins and informed consent must 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)** will require a consultation with a Transfusion Medicine Physician.

**For adult patients:**

A single reversal dose includes 80 mL of Prothrombin Complex Concentrates (X4 vials – 2000 units) and 10 mg of Vitamin K(IV).
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</td>
</tr>
</tbody>
</table>

*Reconstituted solution contains approximately 25 Units 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 100 mL** (empty of normal saline). Mixing or dilution with normal saline may decrease the potency and stability of the product. The use of an empty plastic bag for 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.

References:

1. National advisory committee on blood and blood products, Recommendation for use of Octaplex. September 16\textsuperscript{th}, 2008 and June 13\textsuperscript{th}, 2011.
5. Product Monograph, Beriplex® P/N, CSL Behring Canada Inc, November 5\textsuperscript{th} 2010.