<table>
<thead>
<tr>
<th>Office of Administrative Responsibility</th>
<th>Issuing Authority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Advisor to the Provincial Blood Coordinating Program</td>
<td>Dr. Lucinda Whitman</td>
</tr>
<tr>
<td>Manager, Provincial Blood Coordinating Program</td>
<td>Daphne Osborne</td>
</tr>
<tr>
<td><strong>Author</strong></td>
<td><strong>2019-12-25</strong></td>
</tr>
<tr>
<td><strong>Effective Date</strong></td>
<td><strong>6.0</strong></td>
</tr>
<tr>
<td><strong>Version</strong></td>
<td><strong>2021-12-25</strong></td>
</tr>
</tbody>
</table>
Overview

Prothrombin complex concentrates (PCC) are human plasma-derived blood clotting factors II, VII, IX and X, as well as protein C and S. PCC products are used in the treatment of active bleeding and prophylaxis of bleeding prior to invasive procedure in order to reverse the effects of vitamin K antagonists.

Another potential use for PCCs has been in the reversal of severe/life-threatening bleeding for those on Direct Oral Anticoagulants (DOACs). If there is an antidote for the DOAC then that would be the recommended first course of treatment. Thrombosis Canada has guidelines available for management of bleeding in patients on DOACs https://thrombosiscanada.ca/clinicalguides/#.

PCCs are not indicated in situations in which there is ample time to allow the prothrombin time to return to normal by discontinuing the anticoagulant or through administration of vitamin K. PCCs are not without risk so prior to use a risk versus benefit evaluation shall be completed in each individual case.

Policy

1. Regional Health Authorities (RHAs) shall implement policies, processes and procedures for ordering, receipt, handling, storage, distribution, preparation (for administration), and administration of prothrombin complex concentrates (PCC) that comply with the Newfoundland and Labrador Blood Coordinating Program (NLBCP) policies and guidelines.

2. PCCs are indicated for:
   2.1. Rapid reversal of warfarin therapy or vitamin K deficiency in patients exhibiting major bleeding manifestations.
   2.2. Rapid reversal of warfarin therapy or vitamin K deficiency in patients requiring urgent (within less than six hours) surgical procedures.

*Note: Management of vitamin K antagonist treatment with elevated INR depends on both the presence of bleeding and the severity of bleeding, Please refer to American College of Chest Physicians 2018 Antithrombotic Therapy for Atrial Fibrillation recommendations.

3. There is some published evidence to support PCC use in the reversal of severe life-threatening bleeding for those on DOACs. However, if a reversal agent/antidote is available that is the recommended first course of treatment (e.g. Praxbind® or idarucizumab for dabigatran). Each case should be looked at individually for risk versus benefit evaluation due to the prothrombotic effect of PCCs. Each facility should have a protocol for bleeding management of patients on DOACs.

4. RHAs shall adopt a process to facilitate the rapid availability and delivery of PCC for patients with major bleeding manifestations, such as expedited approval processes for
subgroups of patients, expedited delivery of product to end user, or supply availability 
(limited) in emergency departments.

5. PCCs shall be stored, transported, prepared and administered according to 
manufacturer instructions (consult product monographs).

6. PCCs shall be administered under the supervision of physicians who have access to 
aequate diagnostic and treatment facilities to ensure appropriateness of dosing, 
evaluation of treatment effect, and management of potential complications.
   6.1. PCCs shall be administered intravenously by direct IV push, syringe pump or mini-

6.2. Distribution and use of PCCs shall be limited to only facilities capable of performing 
the necessary diagnostic evaluations (i.e. PT/INR tests).

6.3. The completed blood product administration card shall be returned to the transfusion 
medicine laboratory following administration of PCCs as per facility policy.

6.4. Clinical outcome, including evaluation of mortality and thrombotic events, shall be 
completed at 24 hours post-administration of PCC.

Guidelines

1. Vitamin K (10 mg IV) co-administration is strongly recommended if reversal is required 
for longer than 6 hours (the half-life of prothrombin complex concentrates). The onset of 
action of Vitamin K is 4-6 hours when administered intravenously.

2. PCCs are not indicated for:
   2.1. Elective reversal of oral anticoagulant therapy prior to invasive procedure.
   2.2. Treatment of elevated INR **without** bleeding or need for surgical intervention.
   2.3. Massive transfusion.
   2.4. Coagulopathy associated with liver dysfunction.
   2.5. Patients with recent history of thrombosis, myocardial infarction, or disseminated 
intravascular coagulation (DIC).

3. Contraindications:
   3.1. Patients with a history of heparin induced thrombocytopenia.
   3.2. Patients who are hypersensitive to any of the components in the formulation, or 
components of the packaging.
   3.3. Patients with immunoglobulin A deficiency with known antibodies against IgA.

4. Special patient populations:
   4.1. Pregnant and lactating women: There is insufficient evidence available to allow a 
recommendation for use of PCC 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.
Prothrombin Complex Concentrates

4.2. Pediatric patients: There is insufficient evidence available to allow a recommendation for use of PCC in this patient population.

4.3. Congenital factor II or X deficient patients: Use of PCC should be at the discretion of the local Hemophilia clinic.

4.4. Reversal of direct thrombin inhibitors (DTI) – there is insufficient published evidence to allow a recommendation for this use. Idarucizumab (Praxbind®) is the antidote for dabigatran.

4.5. Reversal of direct anti-Xa inhibitors – there is some published evidence to suggest that PCCs may be effective in the reversal of direct anti-Xa therapy but no consensus has been reached on it’s efficacy for this purpose.

*Note: There may be extenuating clinical circumstances necessitating use of PCCs in these clinical situations. Use should be evaluated on a case-by-case basis by a physician experienced in the use of the product. If the decision is to use the product off-label in liver dysfunction or DIC, please consult the product monograph for further recommendations (e.g. the need for antithrombin levels or replacement).

Procedure

1. Pre-printed order forms for PCC shall be available in acute care areas where PCC may be ordered and/or administered.

2. All requests for PCCs shall be made through the transfusion medicine laboratory.

3. A PT/INR test shall be performed prior to administration of PCCs.

4. Follow (adult) PCC dosing guidelines (see attached).

5. Administer as per manufacturer instructions.

   5.1. PCCs shall be administered intravenously by direct IV push, syringe pump or mini-bag.

   5.2. The manufacturer’s recommended maximal rates of infusion are:

   • octaplex® = 3mL/min
   • Beriplex® P/N = 8 mL/min.

6. Repeat PT/INR test 15 minutes post administration (every dose).

   *Note: Do not mix two different PCC products within the same infusion.

Key Words

INR, PCC, prothrombin complex concentrate
Supplemental Materials

Appendix A: Dosing Guidelines
Appendix B: Order Form
References


Appendix A

Dosing Guidelines - Adult

<table>
<thead>
<tr>
<th>Dose of Prothrombin Complex Concentrate</th>
<th>INR &gt; 1.7 ≤ 3.0</th>
<th>INR &gt; 3.0 ≤ 5.0</th>
<th>INR &gt; 5.0 or Intracranial Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000 IU (40 mL)</td>
<td>Up to 2000 IU (80 mL)</td>
<td>Up to 3000 IU (120 mL)</td>
<td></td>
</tr>
</tbody>
</table>

*Maximum dose is 3000 IU in 24 hours

**See NAC (2014) recommendations for full dosing guidelines.
Appendix B

Pre-Printed Order (Adult)
Prothrombin Complex Concentrates

Weight: ____________ kg

<table>
<thead>
<tr>
<th>Allergies</th>
<th>□ Nil known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is informed consent confirmed?</td>
<td>□ Yes □ No</td>
</tr>
</tbody>
</table>

**Indication:**
- □ Warfarin therapy or vitamin K deficiency with active bleed.
- □ Warfarin therapy or vitamin K deficiency with **imminent emergency** operative or invasive procedure within six (6) hours.
- □ Reversal for **severe/life threatening bleeding** for those on Direct Oral Anticoagulants (DOACs). If there is an antidote for the DOAC that is the recommended treatment. DOAC presently on: ____________

**Contraindications:**
- □ Yes □ No Recent thromboembolic event (within 30 days), e.g. AMI, thrombotic stroke, PE, DVT.
- □ Yes □ No History of heparin-induced thrombocytopenia (HIT) or allergy to heparin.

**Physician Orders:**
- □ Vitamin K 10 mg IV.
- □ PCC ________ International Units (IU). (Administer as per product monograph/ facility policy.) RHA may specify PCC/dose/ infusion rate here.

REPEAT INR **15 minutes post every dose.**

<table>
<thead>
<tr>
<th>Dose of Prothrombin Complex Concentrate</th>
<th>INR &gt; 1.7 ≤ 3.0</th>
<th>INR &gt; 3.0 ≤ 5.0</th>
<th>INR &gt; 5.0 or Intracranial Hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1000 IU (40 mL)</td>
<td><strong>Up to 2000 IU</strong> (up to 80 mL)</td>
<td><strong>Up to 3000 IU</strong> (up to 120 mL)</td>
</tr>
</tbody>
</table>

*Maximum dose is 3000 IU in 24 hours*

**Physician Signature:** ___________________________  **Print Name:** ___________________________  **Date:** DD/MONTH/YYYY

**Incomplete order forms may result in delays in treatment and may require consult with Laboratory Hematologist/Hematopathologist**

**Monitoring:**
Vital signs every 5 min during infusion; 15 min post infusion (**every** dose).
**Prothrombin Complex Concentrates**

**LAB USE ONLY**

Indications Confirmed □ Yes □ No

1. Initial Dose: ______________
2. Additional Dose: ______________ INR: _______
3. Additional Dose: ______________ INR: _______

<table>
<thead>
<tr>
<th>Human Coagulation Factor (per vial)</th>
<th>octaplex® 500 Dose</th>
<th>octaplex® 1000 Dose</th>
<th>Beriplex® P/N 500 Dose</th>
<th>Beriplex® P/N 1000 Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor II</td>
<td>280-760 IU</td>
<td>560-1520 IU</td>
<td>380-800 IU</td>
<td>760-1600 IU</td>
</tr>
<tr>
<td>Factor VII</td>
<td>180-480 IU</td>
<td>360-960 IU</td>
<td>200-500 IU</td>
<td>400-1000 IU</td>
</tr>
<tr>
<td>Factor IX</td>
<td>500 IU</td>
<td>1000 IU</td>
<td>500 IU</td>
<td>1000 IU</td>
</tr>
<tr>
<td>Factor X</td>
<td>360-600 IU</td>
<td>720-1200 IU</td>
<td>500-1020 IU</td>
<td>1000-2040 IU</td>
</tr>
<tr>
<td>Protein C</td>
<td>260-620 IU</td>
<td>520-1240 IU</td>
<td>420-820 IU</td>
<td>840-1640 IU</td>
</tr>
<tr>
<td>Protein S</td>
<td>240-640 IU</td>
<td>480-1280 IU</td>
<td>240-680 IU</td>
<td>480-1360 IU</td>
</tr>
<tr>
<td>Heparin</td>
<td>80-310 IU</td>
<td>160-620 IU</td>
<td>8-40 IU</td>
<td>16-80 IU</td>
</tr>
<tr>
<td>Antithrombin</td>
<td>none</td>
<td>none</td>
<td>4.3-30 IU</td>
<td>8.6-80 IU</td>
</tr>
</tbody>
</table>

*Note: Beriplex P/N contains 343 Mg of Sodium per 100mL. Consider effect on renal impaired or sodium restricted patients.*