1. **Indications:** Urgent and rapid reversal of warfarin related life-threatening bleed
   
   **Criteria:** Patient is taking warfarin with an INR > 2.0 with life threatening bleed (traumatic bleeding, bleeding into a critical organ, hemoglobin drop > 5 g/dL, requiring reversal in 2 hours)

2. **Relative Contraindications**
   - Hemorrhage thought not survivable
   - Disseminated intravascular coagulation (DIC), fibrinolysis or sepsis
   - Known thrombotic tendency or recent (6 weeks) thrombotic event (PE, DVT, MI, stroke)
   - History of heparin-induced thrombocytopenia
   - Fibrinogen < 100 mg/dL or thrombocytopenia (platelets < 70,000)

3. **Diagnostics/Labs:**
   - Baseline PT / INR, aPTT, CBC, and fibrinogen before administration
   - PT / INR 30 minutes after dose
   - PT / INR at 2 hours after infusion then every 4 hours

4. **Dosing and Administration Guidelines for Warfarin Reversal:**
   (See backer for guidelines regarding reversal of other anticoagulants)
   - If INR less than 2, consider the use of 2 units FFP rather than PCC
   - Vitamin K (phytonadione) 10 mg IV in 50 mL 0.9% NaCl infused over 15 min X 1 dose

<table>
<thead>
<tr>
<th>Baseline INR</th>
<th>2 – 3.99</th>
<th>4 – 5.99</th>
<th>≥ 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose of Kcentra® (units of factor IX)/ kg total body weight</td>
<td>25 units/kg Max of 2,500 units</td>
<td>35 units/kg Max of 3,500 units</td>
<td>50 units/kg Max of 5,000 units</td>
</tr>
</tbody>
</table>

- Prothrombin Complex concentrate (Kcentra®) (available in approximately 500 unit vials, dosage units based on factor IX content)
  - 25 units/kg IV x 1 dose (Max dose of 2,500 units)
  - 35 units/kg IV x 1 dose (Max dose of 3,500 units)
  - 50 units/kg IV x 1 dose (Max dose of 5,000 units)

Dose Ordered: ______________ units IV once (will be rounded to the nearest available vial size)

*Repeat dosing was not studied and is not recommended*

- Infuse at a rate of 0.12 mL/kg/min (~3 units/kg/min) up to a maximum rate of 8.4 mL/min (~210 units/min)

- Diphenhydramine (Benadryl®) 25 – 50 mg IV x 1 dose PRN hypersensitivity

5. **Monitoring and Follow-Up**
   Monitor patient should be monitored post-dose for signs and symptoms of arterial and venous thrombosis such as:
   - DVT and PE
   - Stroke
   - Ischemia
   In the case of allergic reaction, administer diphenhydramine (Benadryl®) as ordered above STAT and notify Physician.

Date __________ Time _______ Physician/Provider Signature ____________________________
PHSW Pharmacy Guidelines: Critical Reversal of Anticoagulants
(Reversal of life or brain/spinal cord threatening bleeding)

*Approved by PHSW Pharmacy and Therapeutics committee 1/16/2014

*These are off-label uses. Recommendations are based on anecdotal reports and theory in the absence of randomized or even cohort trials and case reports. See contraindication and relative contraindications‡

Balance the use of a procoagulant against the risk for serious thrombotic events.

**Direct Xa Inhibitors:**

Rivaroxaban (Xarelto®) or Apixaban (Eliquis®)
Reverse if patient shows signs of bleeding and has an INR > 1.5

1. Withhold drug, give activated charcoal if last dose taken within 2 hours (charcoal contraindicated in GI bleed)
2. Recommend 4-factor PCC* (Kcentra®) 50 units/kg [total body weight] pharmacy will round to the nearest whole vial

**Direct Thrombin Inhibitor:**

Dabigatran (Pradaxa®)
Reverse if patient shows signs of bleeding and had an elevated aPTT > 45 seconds

1. Withhold drug, give activated charcoal if last dose taken within 2 hours (charcoal contraindicated in GI bleed) if greater than 2 hours, consult nephrology for dialysis to remove dabigatran
2. Consider 4-factor PCC* (Kcentra®) 50 units/kg [total body weight] pharmacy will round to the nearest whole vial

Note: The aPTT may be a qualitative indicator of anticoagulation status. If the aPTT is less than 45 seconds, then minimal drug may be present.

**Pentasaccharide:**

Fondaparinux (Arixtra®)
Major Bleeding Reversal - Protamine ineffective

1. Consider 4-factor PCC* (Kcentra®) 50 units/kg [total body weight] pharmacy will round to the nearest whole vial

‡ Contraindications to PCC use: known anaphylactic or severe systemic reactions to Kcentra®, disseminated intravascular coagulation, patients with known heparin-induced thrombocytopenia (Kcentra® contains heparin). Relative contraindications to PCC use: venous or arterial thrombotic events in the past 3 months, underlying conditions that increase the risk of thrombosis (crush injury, sepsis, recent major surgery), liver disease (except in certain limited circumstances such as ICH), intracranial hemorrhage not felt to be survivable.

References: