Management of Warfarin-related elevated INR and/or bleeding

Severe bleeding or urgent surgical intervention?

- YES
  - Severe bleeding or bleeding at critical site*
    - Hold warfarin
    - 4F-PCC (Kcentra) IV x 1 dose AND Phytodione (Vit K) 10mg IV over 30 mins
    - Recheck INR in 1 hour after infusion & at 12 hours

- NO
  - Elevated INR with need for surgical intervention
    - Urgent intervention
      - Hold warfarin
      - 4F-PCC (Kcentra) IV x 1 dose AND Phytodione (Vit K) 10mg IV over 30 mins
      - Recheck INR in 30 minutes after transfusion and at 12 hours
    - Semi-urgent intervention
      - Hold warfarin
      - Phytodione (Vit K) 2.5mg po
      - recheck INR within 24h

INR > 10?

- YES
  - INR >4.5: hold warfarin. Consider phytonadione (Vit K) 2.5mg po x 1 based on clinical situation and risk for bleeding

- NO
  - INR<4.5: reduce or hold dose

INR < 4.5:

- NO
  - Reduce or hold dose

- YES
  - Recheck INR within 24h
    - Consider FFP 10-20 ml/kg if INR not within target range prior to procedure

*Critical sites:
Intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome

4F-PCC (Kcentra) dosing based on INR

<table>
<thead>
<tr>
<th>INR</th>
<th>Dose of 4F-PCC (Kcentra)</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to &lt;4</td>
<td>25 units/kg</td>
<td>2500 units</td>
</tr>
<tr>
<td>4 to 6</td>
<td>35 units/kg</td>
<td>3500 units</td>
</tr>
<tr>
<td>&gt;6</td>
<td>50 units/kg</td>
<td>5000 units</td>
</tr>
<tr>
<td>unknown</td>
<td>35 units/kg</td>
<td>3500 units</td>
</tr>
</tbody>
</table>
**Direct Oral Anticoagulant (DOAC) Reversal Guidelines for Life-threatening Bleeding**

**Life-threatening hemorrhage or bleeding at critical site?**

- **NO**  
  - Supportive care with fluids and transfusion as needed

- **YES**
  - **Direct thrombin inhibitor:** Dabigatran (Pradaxa)
    - Administer **idarucizumab (Praxbind)** 5g IV x 1 dose over 5-10 minutes through dedicated line. Flush with 0.9% saline before & after. Provide supportive care as needed
  - **Factor Xa inhibitors:** Apixaban (Eliquis) or Rivaroxaban (Xarelto)
    - Known use of apixaban or rivaroxaban in the last 18 hours **AND** an emergent procedure is indicated?
      - Administer andexanet alfa (AndexXa)  
        - Low dose = 400 mg IV bolus 30 mg/min, then infusion of 4 mg/min up to 120 min.  
        - High dose = 800 mg IV bolus 30 mg/min, then infusion of 8 mg/min up to 120 min.  
        - Apixaban ≤ 5mg or ≥ 8 hours since dose: low dose  
        - Apixaban > 5mg AND < 8 hours since last dose: high dose  
        - Rivaroxaban ≤ 10mg or ≥ 8 hours since last dose: low dose  
        - Rivaroxaban > 10mg AND <8 hours since last dose: high dose

**Other Factor Xa inhibitors:** Edoxaban (Savaysa)

**Reversal Guidelines for Antiplatelet Agents: Aspirin, Clopidogrel (Plavix), Prasugrel (Effient), Dipyridamole, Ticagrelor (Brilenta), Cilostazol**

**Life-threatening hemorrhage or bleeding at critical site?**

- **NO**  
  - Supportive care with fluids and transfusion as needed

- **YES**
  - Administer platelets x1 unit if an emergent procedure is indicated or platelets <100

**Critical sites:** Intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome

References: