Management of Warfarin-related elevated INR and/or bleeding

Severe bleeding or urgent surgical intervention?

NO

INR > 10?

NO

INR < 4.5: reduce or hold dose

YES

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

Severe bleeding or bleeding at critical site*

Hold warfarin

Elevated INR with need for surgical intervention

NO

INR > 10?

YES

Hold warfarin

Urgent intervention

Hold warfarin

Semi-urgent intervention

Hold warfarin

recheck INR within 24h

Phytonadione (Vit K) 2.5mg po

Phytonadione (Vit K) 2.5mg po x 1 dose

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

4F-PCC (Kcentra) IV x 1 dose

AND Phytonadione (Vit K) 10mg IV over 30 mins

Recheck INR in 1 hour after infusion & at 12 hours

Recheck INR in 30 minutes after transfusion and at 12 hours

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

<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>
**Novel Oral Anticoagulant (NOAC) 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 x1 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?
      - **YES**
        - Administer andexanet alfa (AndexXa) (requires attending approval, may not be given after 4F-PCC)
          - 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 >10 mg AND <8 hours since last dose: high dose

    - **NO**
      - Administer 4F-PCC (Kcentra) 25 units/kg IV x 1 dose

      - Consider additional 4F-PCC (Kcentra) 25 units/kg IV x 1 dose if intracranial hemorrhage AND INR remains elevated after 1st dose

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**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**
  - Consider transfusing platelets x1 unit or 6 pack in addition to supportive care. Discuss with neurosurgery prior to administration in intracranial hemorrhage

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**References:**