### DOAC Bleeding Management (v1 1/2/2019)

#### Assess for Clinically Relevant Drug Levels

<table>
<thead>
<tr>
<th>Drug</th>
<th>Specialized Test</th>
<th>Drug Level Interpretation</th>
<th>General Test</th>
<th>Drug Level Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>dTT, ECT, ECA</td>
<td>Normal: not clinically relevant</td>
<td>TT</td>
<td>Normal: not clinically relevant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Results correlate with drug level</td>
<td></td>
<td>Prolonged: may/may not be clinically relevant</td>
</tr>
<tr>
<td></td>
<td>aPTT</td>
<td>Normal: likely indicates lower drug level but can’t exclude drug presence</td>
<td></td>
<td>Prolonged: clinically relevant</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Anti-Xa</td>
<td>Absent activity: not clinically relevant</td>
<td>PT</td>
<td>Normal: does not exclude clinically relevant levels</td>
</tr>
<tr>
<td>Betrixaban</td>
<td></td>
<td>Results correlate with drug level (if calibrated for specific DOAC)</td>
<td></td>
<td>Prolonged: clinically relevant levels</td>
</tr>
<tr>
<td>Edoxaban</td>
<td></td>
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<tr>
<td>Rivaroxaban</td>
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</tbody>
</table>

- Apixaban: anti-factor Xa. aPTT = activated partial thromboplastin time; dTT = dilute thrombin time; ECA = ecarin chromogenic assay; ECT = ecarin clotting time; PT = prothrombin time; TT = thrombin time.

#### Determine Bleed Severity

- Bleeding in critical site (examples below):
  - Central nervous system bleeds (intracranial, spinal, intracerebral)
  - Pericardial tamponade
  - Airway, including posterior epistaxis
  - Hemothorax
- Intra-abdominal
- Retroperitoneal
- Intra-articular
- Intra-muscular

- Hemodynamic instability (examples below):
  - Elevated heart rate
  - Decrease in SBP >40 mm Hg
  - Mean arterial pressure (intra-artificial) <65 mm Hg
  - SBP <90 mm Hg
  - Orthostatic blood pressure changes
  - Urine output <0.5 mL/kg/hr

- Overt bleeding with either:
  - Hemoglobin drop of ≥2 g/dL
  - Administration of ≥2 U of packed RBCs

#### Manage Bleeding

- If last dose taken at least 24 hr ago in patients with normal renal function, drug levels probably not clinically relevant.†
- If patient taking dabigatran, a TT can be used to rule out clinically relevant drug levels. Specialized tests can quantify drug levels.
- If apixaban, edoxaban, rivaroxaban, or betrixaban, anti-Xa is the preferred test and can be used to rule out relevant drug levels or quantify levels.
- Don’t wait for results before administering reversal agents in life-threatening bleeds†

#### DOAC Reversal

- **Dabigatran**
  - Admin. ANDEXXA per package insert (Apix/Riva only)
  - If ANDEXXA not avail. Admin 4F-PCC 50 units/kg IV
  - If 4F-PCC not available, consider aPCC 50 units/kg IV (refer to prescribing information for max units)
  - Activated charcoal (50 g) can be considered if ingested within 2-4 hours
  - Fresh-frozen plasma is not recommended for DOAC reversal

- **Apixaban, Betrixaban, Edoxaban, Rivaroxaban**
  - Most patients benefit from restarting anticoagulation after bleeds, but make sure there is still a valid indication.
  - eg. CHA₂DS₂-VASc is ≥ 1 (in AF), length of treatment hasn’t reached (for VTE treatment or post-op prophylaxis).
  - Base plan on the balance between bleeding and thromboembolic risks and discussions with other appropriate practitioners (eg. surgeons), the patient, and caregivers.
  - Stop DOAC
  - Provide supportive care
  - Secure airway and large-bore IV access
  - Aggressive volume resuscitation (NS or LR)
  - Correct hypothermia and acidosis
  - Early involvement of other services (eg. surgery)
  - RBC transfusions to achieve Hgb ≥7 g/dL (28 g/dL if pt has CAD)
  - Platelet transfusion to achieve counts >50 x 10⁹/L
  - Cryoprecipitate transfusion to maintain fibrinogen >100 mg/dL
  - Stop any antplatelets
  - Consider surgical/procedural management
  - *Administer reversal agent if above not effective*

#### Continue Antiplatelet Therapy

- If patients with GI bleed should typically wait at least 7-14 days. Patients with intracranial hemorrhage (and no mechanical valve) should wait at least 4 weeks.² In patients with moderate to high risk of recurrent VTE without high risk of recurrent bleeding, ASH suggests resuming anticoagulation within 90 days rather than discontinuation.³

- Make sure dose is correct based on age, renal function, weight, and indication and address any reversible risk factors such as interacting medications or unnecessary antiplatelet therapy.
References


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