**Reversal and Treatment Strategies for DOAC-Related Bleeding**

**BOTTOM LINE**

<table>
<thead>
<tr>
<th>DO</th>
<th>DON’T</th>
<th>CONSIDER</th>
<th>CAUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Do determine the time of last dose of anticoagulant administration 1,2</td>
<td>• Do not give FFP for DOAC reversal 1,2</td>
<td>• Consider reversing life-threatening or uncontrolled bleeding with specific reversal agent unavailable 1,2</td>
<td>• Be cautious as there are no comparison trials for reversal strategies</td>
</tr>
<tr>
<td>• Do reverse life-threatening or uncontrolled bleeding with andexanet alfa in patients taking dabigatran, rivaroxaban, or edoxaban, if available 1</td>
<td></td>
<td>• Consider activated charcoal for known recent ingestion (within 2-4 hours) 1</td>
<td></td>
</tr>
<tr>
<td>• Do reverse life-threatening or uncontrolled bleeding with idarucizumab in patients taking dabigatran, if available 1,2</td>
<td>• Do formulate an anticoagulation restart plan 1</td>
<td>• Consider hemodilisation for dabigatran removal if drug administered recently and idarucizumab not available 1</td>
<td>• Be cautious about reversal agent re-dosing due to limited safety and efficacy data</td>
</tr>
</tbody>
</table>

**Assumption:** In the setting of bleeding with hemodynamic compromise, standard supportive care and resuscitative measures should always be applied.

**Laboratory Assessment for “Clinically Significant” DOAC Levels**

“Clinically significant” refers to DOAC levels that may contribute to bleeding. The minimum DOAC level that may contribute to bleeding is unknown. The International Society on Thrombosis and Haemostasis suggests consideration of DOAC reversal in patients with serious bleeding and a plasma DOAC concentration > 50 ng/mL.10

<table>
<thead>
<tr>
<th>Drug</th>
<th>Assays suitable for quantitation of DOAC levels</th>
<th>Screening assays Not suitable for quantification, may be useful for screening “clinically significant” DOAC levels</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>dTT, ECA, LC-MS/MS</td>
<td>TT, Urine DOASENSE®</td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td>Apixaban anti-Xa, LC-MS/MS</td>
<td>Heparin or LMWH anti-Xa</td>
<td></td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Edoxaban anti-Xa, LC-MS/MS</td>
<td>Urine DOASENSE®</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Rivaroxaban anti-Xa, LC-MS/MS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Example: A normal thrombin time or negative Urine DOASENSE® indicates the absence of “clinically significant” dabigatran levels. A heparin or LMWH anti-Xa assay below the lower limit of quantitation or negative Urine DOASENSE® indicates the absence of “clinically significant” apixaban, edoxaban, or rivaroxaban levels. Note: DOASENSE® is currently not available in the United States.

**Definitions and Abbreviations:**
- Critical Organ Sites: central nervous system (intracranial, intracocular, or spinal), airway (including posterior epistaxis), hematoma, intra-abdominal (non-gastrointestinal), retroperitoneal, intramuscular, intra-articular
- aPCC: activated prothrombin complex concentrate
- dTT: dilute thrombin time
- ECA: etamin chromogenic assay
- FFP: fresh frozen plasma
- LC-MS/MS: liquid chromatography tandem mass spectrometry
- LMWH: low molecular weight heparin
- PCC: prothrombin complex concentrate
- TT: thrombin time

**Background and Scope**

Despite improved safety with direct oral anticoagulants (DOACs) compared to vitamin K antagonists, 2.1% to 3.6% of patients taking DOAC therapy in Phase III clinical trials had major bleeding.1,2 Guidance has been offered by the Anticoagulation Forum2,7, American College of Cardiology4, American College of Chest Physicians1, American Society of Hematology3, and the American College of Emergency Physicians1 for management of patients with major hemorrhages while on anticoagulant therapy. This Rapid Resource provides summarized evidence-based guidance for DOAC reversal and bleeding management.

**Reversal Strategy by DOAC Agent**

**Dabigatran**

- Idarucizumab
  - 5 grams IV x 1
- Consider activated charcoal for known recent ingestions within 2-4 hours

  - If idarucizumab not available:
    - aPCC or PCC 50 units/kg IV x 1 (max 4,000 units)
    - Hemodialysis
      - (if hemodynamically stable and idarucizumab not available)

**Factor Xa Inhibitor**

**Andexanet alfa**

- aPCC or PCC 50 units/kg IV x 1 (max 4,000 units)
- Hemodialysis
  - (if hemodynamically stable and idarucizumab not available)

**Considerations**

- Andexanet alfa: Clinical judgement advised when selecting dose regimen based on time cut-offs in patients presenting with acute or chronic renal dysfunction and life-threatening bleeding, receiving non-renally dose adjusted baseline DOAC regimens

**References**


**Rapid Resources**

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