Atlantic Collaborative Recommendations for Managing the Bleeding Patient on Apixaban, Dabigatran or Rivaroxaban

Pharmacologic Properties of Apixaban, Dabigatran & Rivaroxaban

<table>
<thead>
<tr>
<th>Pharmacologic Properties</th>
<th>Apixaban&lt;sup&gt;7&lt;/sup&gt;</th>
<th>Dabigatran&lt;sup&gt;8&lt;/sup&gt;</th>
<th>Rivaroxaban&lt;sup&gt;5&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak level</td>
<td>3 – 4 hours</td>
<td>2 hours</td>
<td>1.5 - 4 hours</td>
</tr>
<tr>
<td>Renal clearance</td>
<td>27%</td>
<td>80%</td>
<td>66 %</td>
</tr>
<tr>
<td>Half-life</td>
<td>12 hours</td>
<td>11-17 hours</td>
<td>5 - 9 hours</td>
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Assessment of Bleeding Patient Receiving Apixaban, Dabigatran or Rivaroxaban

There is limited clinical data related to reversal of apixaban, dabigatran and rivaroxaban. With no proven antidote available at the current time, the recommendations below may change as new evidence becomes available.

Patient on apixaban/dabigatran/rivaroxaban presents with bleeding

- Initiate appropriate resuscitation measures if required
- Blood work: CBC, creatinine, INR, aPTT.
- Hold or discontinue apixaban/dabigatran/rivaroxaban (Document time of the last dose)
- Consider holding or reducing other medications known to increase a patient’s bleeding risk (NSAIDs, ASA, Clopidogrel (Plavix®), Prasugrel (Effient®), Ticagrelor (Brilinta®), Ginkgo Biloba, Ginseng, Omega-3 Fatty Acids) or known to interact by increasing the dabigatran plasma levels (Amiodarone, Verapamil, Ketoconazole, Rifampin).

MILD BLEEDING

- Local hemostatic measures
- Keep hydrated

MILD BLEEDING directive AND:

- Manage bleeding (compression, surgery)
- Fluid replacement → Maintain good urine output
- Transfuse RBCs, FFP and platelets as needed

MODERATE - SEVERE BLEEDING<sup>1</sup>

MODERATE - SEVERE BLEEDING directive AND:

- Activate the Massive Transfusion Protocol
- Consider tranexamic acid (1g IV followed by 1g infusion over 8 hours)
- Consult with Transfusion Medicine Specialist

LIFE - THREATENING BLEEDING<sup>1</sup>

- Local hemostatic measures
- Keep hydrated
- Initiate appropriate resuscitation measures if required
- Blood work: CBC, creatinine, INR, aPTT.
- Hold or discontinue apixaban/dabigatran/rivaroxaban (Document time of the last dose)
- Consider holding or reducing other medications known to increase a patient’s bleeding risk (NSAIDs, ASA, Clopidogrel (Plavix®), Prasugrel (Effient®), Ticagrelor (Brilinta®), Ginkgo Biloba, Ginseng, Omega-3 Fatty Acids) or known to interact by increasing the dabigatran plasma levels (Amiodarone, Verapamil, Ketoconazole, Rifampin).

There is limited clinical data related to reversal of apixaban, dabigatran and rivaroxaban. With no proven antidote available at the current time, the recommendations below may change as new evidence becomes available.

The anticoagulant effect of apixaban, dabigatran or rivaroxaban will not be reversed by the administration of vitamin K or plasma infusion. DO NOT TRANSFUSE PLASMA to reverse an elevated aPTT or INR.

There is insufficient evidence to recommend the use of Prothrombin Complex Concentrates (octaplex® or Beriplex® P/N), FEIBA or rFVIIa (NiaStase®) for the reversal of these medications.

In overdose situations without bleeding, activated charcoal may be considered for apixaban, dabigatran and rivaroxaban. Hemodialysis may be considered for patients with renal failure while taking dabigatran however apixaban and rivaroxaban are not expected to be dialyzable.

**Moderate to severe bleeding** – a reduction in Hgb ≥ 20g/L, symptomatic bleeding in an organ or critical area, e.g. intraocular, intracranial, intramuscular, retroperitoneal, intra-articular or pericardial bleeding.

**Life-threatening bleeding** – a reduction in Hgb ≥ 50g/L, symptomatic intracranial bleed, hypotension requiring inotropic agents, e.g. dopamine, bleeding requiring surgery.

References:
5. Bayer Inc., 2013 Xarelto® Product Monograph

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