Andexanet alfa (Andexxa)

****Andexanet alfa (Andexxa) was NOT ADDED to the UW Medicine formulary at this time due to unclear risk vs benefit and high cost. Providers should continue to order 4F-PCC (Kcentra) for urgent reversal of anti-Xa inhibitors per UW Medicine guidelines.****

****Portola pharmaceuticals, maker of andexanet alfa (Andexxa), received approval for their Generation 2 manufacturing process on Dec 31st, 2018. UW hospitals DO NOT have access to andexanet alfa at this time.****

A recombinant modified human coagulation factor Xa that binds to and sequesters factor Xa inhibitors (such as rivaroxaban and apixaban) to neutralize their anticoagulant effects as measured by anti-Xa activity. Andexanet alpha may have “off-target” prothrombotic effects, possibly resulting from its effects on Tissue Factor Pathway Inhibitor (TFPI).

**Approved for reversal of the anticoagulant effect rivaroxaban and apixaban in the setting of:**

- Life-threatening bleeding

**Relevant Clinical Trials**


**Therapeutic Monitoring**

- Prior to use, assess the patient for recent administration of rivaroxaban or apixaban.
- Monitor for signs/symptoms of clinically relevant bleeding and thromboembolic events.
- Andexanet alfa will likely correct anti-Xa values, but the correlation of lab results with improved clinical outcomes has not been established.
- Anti-Xa activity can rebound after completing the infusion of andexanet. Clinical trials suggest peak anti-Xa activity at 4 hours after infusion, then decrease at a rate similar to clearance of the factor Xa inhibitor.
- The safety and efficacy of repeated doses of andexanet alfa have not been established.

**Dosing and Administration**

- There are two dosing regimens (Low or High dose) of andexanet alfa based on the last dose and timing of rivaroxaban or apixaban.

**Table 1: ANDEXXA Dosing Regimes**

<table>
<thead>
<tr>
<th>Dose*</th>
<th>Initial IV Bolus</th>
<th>Follow-On IV Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low dose</td>
<td>400 mg at target rate of 30 mg/min</td>
<td>4 mg/min for up to 120 minutes</td>
</tr>
<tr>
<td>High dose</td>
<td>800 mg at a target rate of 30 mg/min</td>
<td>8 mg/min for up to 120 minutes</td>
</tr>
</tbody>
</table>

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The safety and efficacy of more than one dose have not been evaluated.

Table 2: ANEXXA Dose Based on Rivaroxaban or Apixaban Dose (Timing of FXa Inhibitor Last Dose Before ANDEXXA Initiation)

<table>
<thead>
<tr>
<th>FXa Inhibitor</th>
<th>FXa Inhibitor Last Dose</th>
<th>&lt; 8 Hours or Unknown</th>
<th>≥ 8 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban</td>
<td>≤ 10 mg</td>
<td>Low Dose</td>
<td>Low Dose</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>&gt; 10 mg / Unknown</td>
<td>High Dose</td>
<td>Low Dose</td>
</tr>
<tr>
<td>Apixaban</td>
<td>≤ 5 mg</td>
<td>Low Dose</td>
<td>Low Dose</td>
</tr>
<tr>
<td>Apixaban</td>
<td>&gt; 5 mg / Unknown</td>
<td>High Dose</td>
<td>Low Dose</td>
</tr>
</tbody>
</table>

- After reconstitution, andexanet must be used within 8 hours at room temperature.
- Administer through a 0.2-0.22 micron in-line polyethersulfone or equivalent low protein-binding filter.
- Administer the IV bolus dose at approximately 30 mg/min.
- Within 2 minutes following the IV bolus, administer the continuous IV infusion for up to 120 minutes.

**Drug Interactions**

- There are no known drug interactions

**Other Considerations**

- The safety and efficacy of repeat treatment with andexanet has not been established.
- There are no recommendations for dose adjustments due to renal or hepatic dysfunction.
- Andexanet may have off-target prothrombotic effects; therefore, therapeutic anticoagulation should be restarted as soon as clinically appropriate after treatment with andexanet.

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