# Urgent Anticoagulant Reversal

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Classification</th>
<th>Half-life/Duration of Anticoagulant*</th>
<th>Recommendations**</th>
</tr>
</thead>
</table>
| Alteplase (tPA) | Activase® | Thrombolytics | Half-life: ~72 minutes Duration: >50% present in plasma cleared ~5 minutes after infusion terminated, ~80% cleared within 10 minutes | - Antidote: Amicaproic acid (Amicar®) may be considered as an antidote; however, efficacy has not been established. Recommended dose is 5 gm IV over 1 hr, then 1 gm/hr infusion.  
- Other: Plasma volume expanders other than dextran may be used to replace blood volume deficits; if blood loss has been extensive, administration of packed red blood cells is preferred to whole blood. Alternatives include fresh frozen plasma or cryoprecipitate.  
- Laboratory Monitoring: plasma fibrinogen may be useful. |
| Apixaban | Eliquis® | Factor Xa Inhibitor | Half-life: 12 hours | See apixaban guidelines for use for further information.  
- Antidote: Prothrombin complex concentrate (Kcentra®) is considered an antidote (see guidelines for use).  
- Other: Consider activated charcoal if acute (<2 hours) overdose. Apixaban is not dialyzable. Fresh frozen plasma or packed red blood cells may be considered when supportive measures and control of site bleeding have failed. Prothrombin complex concentrate (PCC) has been shown in limited settings to immediately and completely reverse the anticoagulant effect of oral anti-Xa inhibitors  
- Laboratory Monitoring: no specific monitoring parameters have been established. |
| Argatroban | Argatroban | Direct Thrombin Inhibitor | Half-life: 39-51 minutes; hepatic impairment: ≤181 minutes Duration: 1-2 hours with continuous infusions | Antidote: No specific antidote is available for argatroban.  
- Other: Reversal of anticoagulant effects may be longer than 4 hours in patients with hepatic impairment. Hemodialysis may remove up to 20% of the drug; however, this is not considered clinically significant. Fresh frozen plasma or packed red blood cells may be considered when supportive measures and control of site of bleeding have failed.  
- Laboratory Monitoring: aPTT, INR (if co-administered with warfarin) |
| Bivalirudin | Angiomax® | Direct Thrombin Inhibitor | Half-life: 25-57 minutes Duration: 4-6 hours with continuous infusions | Antidote: No specific antidote is available for bivalirudin.  
- Other: Bivalirudin is hemodialyzable (~25% removed). Fresh frozen plasma or packed red blood cells may be considered when supportive measures and control of site of bleeding have failed.  
- Laboratory Monitoring: aPTT, INR (if co-administered with warfarin) |
| Dabigatran | Pradaxa® | Direct Thrombin Inhibitor | Half-life: 12-17 hours; severe renal impairment (Clcr <30 mL/min): 27.5 hours | See dabigatran guidelines for use for further information.  
- Antidote: Idarucizumab (Praxabind)  
- Other: Consider activated charcoal if acute (<2 hours) overdose. Maintain adequate diuresis as dabigatran is primarily renally eliminated. Dialysis removes 60% of drug over 2-3 hours. Fresh frozen plasma or packed red blood cells may be considered when supportive measures and control of site of bleeding have failed.  
- Laboratory Monitoring: aPTT or TT may be used; however, these are relatively insensitive tests to the effects of dabigatran. |
| Enoxaparin | Lovenox® | Low Molecular Weight Heparin | Half-life: 7-12 hours Duration: 12-24 hours | See enoxaparin guidelines for use for further information.  
- Antidote: Protamine sulfate is an antidote (neutralizes ~60% of the anti-Xa activity of enoxaparin). If enoxaparin was given within 8 hours, protamine sulfate should be administered in a dose of 1 mg per 1 mg enoxaparin. If bleeding continues a dose of protamine 0.5 mg per 1 mg of enoxaparin may be administered. Protamine should be administered by slow intravenous push at a rate of 5 mg per minute to prevent hypotension. Smaller doses of protamine should be given (no specific dosing guidelines available) if the time since enoxaparin administration was longer than 8 hours.  
- Other: Packed red blood cells may be considered useful.  
- Laboratory Monitoring: anti-Xa is considered useful. |
### UP Health System - Marquette
**Pharmacy and Therapeutics Committee**
**Medication Guideline**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Type</th>
<th>Half-life</th>
<th>Monitoring</th>
<th>Antidote:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eptifibatide</td>
<td>Integril®</td>
<td>20-60 hours</td>
<td></td>
<td>Non-specific</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Arixtra®</td>
<td>17-21 hours</td>
<td></td>
<td>Non-specific</td>
</tr>
<tr>
<td>Unfractionated Heparin</td>
<td>Panheparin®</td>
<td>1.5 hours</td>
<td></td>
<td>Protamine sulfate</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Xareito®</td>
<td>5-9 hours; elderly: 11-13 hours</td>
<td></td>
<td>Non-specific</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Coumadin®</td>
<td>20-60 hours</td>
<td></td>
<td>Vitamin K (phytonadione) and prothrombin complex concentrate (Kcentra®)</td>
</tr>
</tbody>
</table>

**Antidote:**
- No specific antidote is available for the glycoprotein IIb/IIIa inhibitors.
- No specific antidote is available for the factor Xa inhibitors.
- Vitamin K (phytonadione) and prothrombin complex concentrate (Kcentra®) are considered antidotes.

**Laboratory Monitoring:**
- PT or aPTT, ACT
- Anti-Xa

**Antidote:**
- Protamine sulfate is an antidote. Recommended dose is 1 mg per 100 units of heparin based on the total heparin units given within past 3 hours.
- Fondaparinux is hemodialyzable (~20% removed). Fresh frozen plasma or packed red blood cells may be considered when supportive measures and control of site of bleeding have failed. Protamin sulfate is an antidote. Recommended dose is 50 units/kg for INR > 6 (do not exceed 5000 units).

**Laboratory Monitoring:**
- Anti-Xa
- Heparin anti-Xa 30 minutes after protamine administered.

**Antidote:**
- Vitamin K (phytonadione) and prothrombin complex concentrate (Kcentra®) are considered antidotes. Recommended doses and routes below are based on INR values and bleeding.

**Laboratory Monitoring:**
- INR

<table>
<thead>
<tr>
<th>INR</th>
<th>Bleeding</th>
<th>Recommended Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.5-10</td>
<td>No</td>
<td>Continue with lower dose OR omit dose and resume therapy at lower dose when INR is in therapeutic range; if only minimally above therapeutic range, no dose reduction may be required. Routine use of vitamin K is not recommended.</td>
</tr>
<tr>
<td>&gt;10</td>
<td>No</td>
<td>Hold warfarin and administer vitamin K 2.5 – 5 mg PO; administer additional vitamin K every 24 to 48 hours as needed; resume therapy at lower dose when INR is in therapeutic range.</td>
</tr>
<tr>
<td>Any</td>
<td>Major bleeding</td>
<td>Consider prothrombin complex concentrate (Kcentra®) and vitamin K 5 to 10 mg. Kcentra® dosing:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 25 units/kg for INR 2 to &lt; 4 (do not exceed 2500 units)</td>
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<tr>
<td></td>
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<td>• 35 units/kg for INR 4 to 6 (do not exceed 3500 units)</td>
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<tr>
<td></td>
<td></td>
<td>• 50 units/kg for INR &gt; 6 (do not exceed 5000 units)</td>
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<tr>
<td></td>
<td></td>
<td>• Dose should not be repeated</td>
</tr>
</tbody>
</table>

**Notes:**
- Half-life indicated for patients with normal renal and hepatic function unless indicated otherwise.
- Recommendations universally include discontinuation of anticoagulant and providing supportive care which includes (but is not limited to) blood transfusions and control of bleeding site.

*Cross Reference: See Anticoagulant Guidelines for Use.*

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UP Health System - Marquette
A Duke LifePoint Hospital
Marquette, MI 49855
References: