## GUIDELINES FOR REVERSAL OF ANTICOAGULANTS

<table>
<thead>
<tr>
<th>NAMES</th>
<th>ELIMINATION HALF-LIFE</th>
<th>REMOVED BY HD</th>
<th>STRATEGIES TO REVERSE OR MINIMIZE DRUG EFFECT</th>
</tr>
</thead>
</table>
| apixaban     | 8-15 hours (longer in renal impairment) | NO            | • Drug activity can be assessed with anti-factor Xa activity assay (UWMedicine: apixaban assay [APIXN1])  
• If ingested within 2 hours, administer activated charcoal  
• Consider 4-factor PCC (KCentra) 50 units/kg (maximum 5000 units) (25 unit/kg, maximum 2500 units for intraparenchymal hemorrhage)  
NOTE: PCC may partially correct PT/aPTT but will not affect anti-factor Xa activity and will not increase drug clearance; correlation of shortening PT/aPTT with reduction in bleeding risk is unknown |
| argatroban   | 40 – 50 minutes       | ~ 20%         | • Turn off infusion  
• Degree of reversal can be assessed with PTT and/or plasma-diluted thrombin time (UWMedicine: DTI assay [DTPAT]) |
| bivalirudin  | 25 minutes (up to 1 hr in severe renal impairment) | ~ 25%         | • Turn off infusion  
• Degree of reversal can be assessed with plasma-diluted thrombin time (UWMedicine: DTI assay [DTPAT]) |
| dabigatran   | 14-17 hours (up to 34 hrs in severe renal impairment) | ~ 65%         | • Drug activity can be assessed with aPTT and/or plasma-diluted thrombin time (UWMedicine: dabigatran assay [DABIG])  
• If ingested within 2 hours, administer activated charcoal  
• For life-threatening bleeding or emergency surgery, consider idarucizumab (Praxbind) 5gm IV  
NOTE: idarucizumab will likely correct aPTT and plasma-diluted thrombin time but the correlation of lab results with improved outcomes is not established  
NOTE: Plasma dabigatran concentrations can increase more than 12-24 hours after idarucizumab, likely due to re-distribution from the extravascular compartment.  
NOTE: The risks and benefits of repeat idarucizumab administration are not known |
| dalteparin   | 3-5 hours (longer in renal impairment) | ~ 20%         | • Use protamine for partial neutralization (~ 60%)  
• Degree of reversal can be assessed with anti factor Xa activity (UWMedicine: anti-Xa for LMWH [LMWXA]) |
| enoxaparin   | 10-14 hours (longer in renal impairment) | ~ 25%         | • There is no assay for edoxaban at this time.  
• If ingested within 2 hours, administer activated charcoal  
• Consider 4-factor PCC (KCentra) 50 units/kg (maximum 5000 units) (25 unit/kg, maximum 2500 units for intraparenchymal hemorrhage)  
NOTE: PCC may partially correct PT/aPTT but will not affect anti-factor Xa activity and will not increase drug clearance; correlation of shortening PT/aPTT with reduction in bleeding risk is unknown |
| fondaparinux | 17 – 21 hours (significantly longer in renal impairment) | NO            | • Fondaparinux levels can be assessed by anti-factor Xa activity (UWMedicine: fondaparinux assay [FNDXT])  
• Consider rFVIIa (Novoseven) 90 mcg/kg  
NOTE: rVIIa will not effect anti-factor Xa activity and will not increase drug clearance |

### Protamine Dosing Table

<table>
<thead>
<tr>
<th>Time since last dose of LMWH</th>
<th>Dose of protamine for each 100 units of dalteparin or 1mg of enoxaparin administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 8 hrs</td>
<td>1mg (or 50mg fixed dose)</td>
</tr>
<tr>
<td>8-12 hrs</td>
<td>0.5mg (or 25mg fixed dose)</td>
</tr>
<tr>
<td>&gt; 12hrs</td>
<td>Not likely to be useful (or 25mg fixed dose)</td>
</tr>
</tbody>
</table>

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Heparin

30 – 90 minutes (dose dependent)

Partial

- Use protamine for heparin neutralization (100%)
- Degree of reversal can be assessed with PTT and/or anti factor Xa activity (UWMedicine: Heparin Activity for Heparin [HIXA])

<table>
<thead>
<tr>
<th>Time since last dose of heparin</th>
<th>Dose of protamine for each 100 units of heparin administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate</td>
<td>1mg (or 25mg fixed dose)</td>
</tr>
<tr>
<td>30 minutes – 2 hrs</td>
<td>0.5mg (or 10mg fixed dose)</td>
</tr>
<tr>
<td>&gt;2 hrs</td>
<td>0.25mg (or 10mg fixed dose)</td>
</tr>
</tbody>
</table>

Rivaroxaban (Xarelto)

Healthy: 5-9 hrs
Elderly: 11-13 hrs
(longer in renal impairment)

NO

- Drug activity can be assessed with anti-factor Xa activity (UWMedicine: rivaroxaban assay [RIVAR1])
- If ingested within 2 hours, administer activated charcoal
- Consider 4-factor PCC (KCentra) 50 units/kg (maximum 5000 units) (25 unit/kg, maximum 2500 units for intraparenchymal hemorrhage)

**NOTE:** PCC may partially correct PT/aPTT but will not affect anti-factor Xa activity and will not increase drug clearance; correlation of shortening PT/aPTT with reduction in bleeding risk is unknown

Warfarin (Coumadin)

<table>
<thead>
<tr>
<th>INR</th>
<th>CLINICAL SCENARIO</th>
<th>MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4.5</td>
<td>No bleeding</td>
<td>• Hold warfarin until INR in therapeutic range</td>
</tr>
</tbody>
</table>
|          | Rapid reversal required | • Hold warfarin
|          |                    | • Consider vitamin K 2.5mg oral                                           |
| 4.5-10   | No bleeding       | • Hold warfarin until INR in therapeutic range                              |
|          | Rapid reversal required | • Hold warfarin
|          |                    | • Consider vitamin K 2.5mg oral                                           |
| >10      | No bleeding       | • Hold warfarin until INR in therapeutic range                              |
|          | Rapid reversal required | • Give vitamin K 2.5mg oral or 1mg IV infusion
|          |                    | (IV administration of vitamin K has faster onset of action)               |
| Any INR  | Serious or life-threatening bleeding | • Hold warfarin
|          |                    | • Give vitamin K 10mg IV infusion over 30 minutes
|          |                    | • Give 4 units FFP/plasma
|          |                    | • OR consider 4-factor PCC (Kcentra) (preferred for life-threatening bleeding)
|          |                    | (INR 1.5 – 3.9: 25 units/kg (maximum 2500 units)
|          |                    | INR 4.0 – 6.0: 35 units/kg (maximum 3500 units)
|          |                    | INR > 6.0: 50 units/kg (maximum 5000 units))                             |