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 (Eliquis) | 8-15 hours (longer in renal impairment) | NO            | • Drug activity can be assessed with anti-factor Xa activity assay (UWMedicine: apixaban assay [APIXNI])  
• If ingested within 2 hours, administer activated charcoal  
• Consider 4-factor PCC (KCentra) 2000 units  
**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 PT and/or plasma-diluted thrombin time (UWMedicine: DTI assay [DTIPAT]) |
| betrixaban (Bevyxxa) | 19-27 hours (longer in renal impairment) | Unknown | • There is no assay for betrixaban at this time.  
• If ingested within 2 hours, administer activated charcoal  
• Consider 4-factor PCC (KCentra) 2000 units  
**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 |
| bivalirudin (Angiomax) | 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 [DTIPAT]) |
| dabigatran (Pradaxa) | 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*  
• If idarucizumab is not available, consider 4-factor PCC (KCentra) 2000 units  
**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 (Fragmin) | 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 (Lovenox) | 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) 2000 units  
**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 (Arixtra) | 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:** rFVIIa will not effect anti-factor Xa activity and will not increase drug clearance |

**Time since last dose of LMWH** | **Dose of protamine for each 100 units of dalteparin or 1mg of enoxaparin administered**
--- | ---
< 8 hrs | 1mg (or 50mg fixed dose)
8-12 hrs | 0.5mg (or 25mg fixed dose)
> 12 hrs | Not likely to be useful (or 25mg fixed dose)

*October 2019*
### Heparin

- **30 – 90 minutes** (dose dependent)
- Partial

<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>

**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])

**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])

**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])

### 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 [RIVA])

- **If ingested within 2 hours, administer activated charcoal**

- **Consider 4-factor PCC (KCentra) 2000 units**

**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>
<tr>
<td></td>
<td>Rapid reversal required</td>
<td>• Hold warfarin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Consider vitamin K 2.5mg oral</td>
</tr>
<tr>
<td>4.5-10</td>
<td>No bleeding</td>
<td>• Hold warfarin until INR in therapeutic range</td>
</tr>
<tr>
<td></td>
<td>Rapid reversal required</td>
<td>• Hold warfarin</td>
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<tr>
<td></td>
<td>Rapid reversal required</td>
<td>• Hold warfarin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Give vitamin K 2.5mgoral or 1mg IV infusion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(IV administration of vitamin K has faster onset of action)</td>
</tr>
<tr>
<td></td>
<td>Any INR</td>
<td>• Hold warfarin</td>
</tr>
<tr>
<td></td>
<td>Serious or life-threatening bleeding</td>
<td>• Give vitamin K 1-2mg IV infusion over 30 minutes, and repeat q24h as needed</td>
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<td>(IV administration of vitamin K has faster onset of action)</td>
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<tr>
<td></td>
<td></td>
<td>• Give vitamin K 10mg IV infusion over 30 minutes</td>
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<td></td>
<td>• Give 4 units FFP/plasma</td>
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<td></td>
<td>• OR consider 4-factor PCC (Kcentra) 2000 units if INR &gt; 1.5</td>
</tr>
</tbody>
</table>

**Rapid reversal required**

- Hold warfarin
- Give vitamin K 1-2mg IV infusion over 30 minutes, and repeat q6-24h as needed

**Rapid reversal required**

- Hold warfarin
- Give vitamin K 10mg IV infusion over 30 minutes
- Give 4 units FFP/plasma
- OR consider 4-factor PCC (Kcentra) 2000 units if INR > 1.5
  
(preferred for life-threatening bleeding)