UW Medicine

GUIDELINES FOR REVERSAL OF ANTICOAGULANTS

<table>
<tr><th>NAMES</th><th>ELIMINATION HALF-LIFE</th><th>REMOVED BY HD</th><th>STRATEGIES TO REVERSE OR MINIMIZE DRUG EFFECT</th></tr>
<tr><td>apixaban

(Eliquis)</td><td>8-15 hours

(longer in renal impairment)</td><td>NO</td><td>• 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) 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</td></tr>
<tr><td>argatroban</td><td>40 – 50 minutes</td><td>~ 20%</td><td>• Turn off infusion
• Degree of reversal can be assessed with PTT and/or plasma-diluted thrombin time (UWMedicine: DTI assay [DTIPAT])</td></tr>
<tr><td>bivalirudin

(Angiomax)</td><td>25 minutes

(up to 1 hr in severe renal impairment)</td><td>~ 25%</td><td>• Turn off infusion
• Degree of reversal can be assessed with plasma-diluted thrombin time (UWMedicine: DTI assay [DTIPAT])</td></tr>
<tr><td>dabigatran

(Pradaxa)</td><td>14-17 hours

(up to 34 hrs in severe renal impairment)</td><td>~ 65%</td><td>• 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.</td></tr>
<tr><td>dalteparin

(Fragmin)
enoxaparin

(Lovenox)</td><td>3-5 hours

(longer in renal impairment)</td><td>~ 20%</td><td>• Use protamine for partial neutralization (~ 60%)
• Degree of reversal can be assessed with anti factor Xa activity (UWMedicine: anti-Xa for LMWH [LMWXA])
<table>
<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>
<tr><td>< 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>> 12hrs</td><td>Not likely to be useful (or 25mg fixed dose)</td></tr>
</table></td></tr>
<tr><td>Edoxaban

(Savaysa)</td><td>10-14 hours

(longer in renal impairment)</td><td>~ 25%</td><td>• 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</td></tr>
<tr><td>fondaparinux

(Arixtra)</td><td>17 – 21 hours

(significantly longer in renal impairment)</td><td>NO</td><td>• 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</td></tr>
</table>

December 2018

UW Medicine

<table>
<tr>
<td>Heparin</td>
<td>30 – 90 minutes

(dose dependent)</td>
<td>Partial</td>
<td>

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>
<tr><th>Time since last dose of heparin</th><th>Dose of protamine for each 100 units of heparin administered</th></tr>
<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>>2 hrs</td><td>0.25mg (or 10mg fixed dose)</td></tr>
</table>
</td>
</tr>
<tr>
<td>Rivaroxaban

(Xarelto)</td>
<td>Healthy: 5-9 hrs
Elderly: 11-13 hrs

(longer in renal impairment)</td>
<td>NO</td>
<td>

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) 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
</td>
</tr>
<tr>
<td>Warfarin
(Coumadin)</td>
<td colspan="3">
<table>
<tr><th>INR</th><th>CLINICAL SCENARIO</th><th>MANAGEMENT</th></tr>
<tr><td rowspan="2">< 4.5</td><td>No bleeding</td><td>• Hold warfarin until INR in therapeutic range</td></tr>
<tr><td>Rapid reversal required</td><td>• Hold warfarin
• Consider vitamin K 2.5mg oral</td></tr>
<tr><td rowspan="2">4.5-10</td><td>No bleeding</td><td>• Hold warfarin until INR in therapeutic range
• Consider vitamin K 2.5mg oral</td></tr>
<tr><td>Rapid reversal required</td><td>• Hold warfarin
• Give vitamin K 2.5mg oral or 1mg IV infusion
(IV administration of vitamin K has faster onset of action)</td></tr>
<tr><td rowspan="2">>10</td><td>No bleeding</td><td>• Hold warfarin until INR in therapeutic range
• Give vitamin K 2.5mg oral or 1-2mg IV infusion over 30 minutes, and repeat q24h as needed
(IV administration of vitamin K has faster onset of action)</td></tr>
<tr><td>Rapid reversal required</td><td>• Hold warfarin
• Give vitamin K 1-2mg IV infusion over 30 minutes, and repeat q6-24h as needed</td></tr>
<tr><td>Any INR</td><td>Serious or life-threatening bleeding</td><td>• 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)</td></tr>
</table>
</td>
</tr>
</table>