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GUIDELINES FOR REVERSAL OF ANTICOAGULANTS

NAMES	ELIMINATION HALF-LIFE	REMOVED BY HD	STRATEGIES TO REVERSE OR MINIMIZE DRUG EFFECT
apixaban *(Eliquis)*	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) 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 PTT 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)* enoxaparin *(Lovenox)*	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]) **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)* > 12hrs — Not likely to be useful *(or 25mg fixed dose)*
edoxaban *(Savaysa)*	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:** rVIIa will not effect anti-factor Xa activity and will not increase drug clearance

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UW Medicine

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<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>
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<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
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<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, may give an additional dose of 500 units if repeat INR after 15 minutes remains > 1.5
(preferred for life-threatening bleeding)</td></tr>
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