MHealth/UMMC Summary of Anticoagulation Reversal

<table>
<tr><th>Drug</th><th>Drug class</th><th>Elimination half-life</th><th>Summary of emergent reversal for life threatening bleeding or need for emergent surgery</th></tr>
<tr><td>Apixaban (Eliquis)</td><td>Direct FXa inhibitor</td><td>12h (longer with renal impairment)</td><td>-If ingested within 2 hours, consider giving activated charcoal 1g/kg (max 50g)
-Administer Kcentra (4-factor PCC) 50units/kg x1 (max 5000units)
-If Kcentra ineffective, consult hematology and consider recombinant activated factor VII (Novoseven) 90 mcg/kg IV once, max 10 mg
-Drug activity can be assessed with anti-factor Xa assay. However, this may not accurately reflect the degree of anticoagulation
-If anti-factor Xa level is <0.1 IU/mL, consider other causes for bleeding
-Reversal agent adexanet alpha not yet available</td></tr>
<tr><td>Argatroban</td><td>Direct thrombin inhibitor</td><td>40-50 min (longer in pts with hepatic dysfunction)</td><td>-Turn off infusion
-Degree of reversal can be assessed with PTT
-Consider KCentra (4-factor PCC) 50units/kg x 1 (max 5000units)for life threatening bleeding</td></tr>
<tr><td>Betrixaban (Bevyssa)</td><td>Direct FXa inhibitor</td><td>20-27h</td><td>-Administer 4-factor PCC(Kcentra) 50u/kg x 1 (max 5000u)
-If Kcentra ineffective, consult hematology and consider recombinant Novoseven (activated factor VII) 90 mcg/kg IV once, max 10 mg
-If anti-factor Xa level is <0.1 IU/mL, consider other causes for bleeding</td></tr>
<tr><td>Bivalrudin</td><td>Direct thrombin inhibitor</td><td>25 min (longer in pts with renal impairment)</td><td>-Turn off infusion
-Degree of reversal can be assessed with PTT
-Consider Kcentra (4 factor PCC) 50units/kg x 1 (max 5000units) for life threatening bleeding</td></tr>
<tr><td>Dabigitran (Pradaxa)</td><td>Direct thrombin inhibitor</td><td>14h (up to 34h in severe renal impairment)</td><td>-If ingested within 2 hours, consider giving activated charcoal 1g/kg (max 50g)
-Administer idarucizumab (Praxbind)5 mg IV once (given as 2 consecutive IV infusions of 2.5 g vials over 5 min each. The 2nd vial must be given within 15 min of the first).
-If Praxbind ineffective, consider recombinant activated factor VII (Novoseven) 90 mcg/kg IV once, max 10 mg
-Plasma transfusion not expected to reverse effects</td></tr>
<tr><td>Dalteparin (Fragmin)
Enoxaparin (Lovenox)</td><td>LMWH</td><td>3-5h (longer with renal impairment)</td><td>-Use protamine for partial neutralization (~60%)
<table>
<tr><th>Time since last dose of LMWH</th><th>Dose of protamine for each 100u of dalteparin or 1 mg of enoxaparin given</th></tr>
<tr><td><8 hours</td><td>1mg (or 50 mg fixed dose)</td></tr>
<tr><td>8-12 hours</td><td>0.5mg (or 25 mg fixed dose)</td></tr>
<tr><td>>12 hours</td><td>Not likely to be useful (or 25mg fixed dose)</td></tr>
</table>
-Monitor anti-factor Xa activity level to confirm reversal
-For refractory or life threatening bleeding, administer Kcentra (4 factor PCC) 50u/kg x 1 (max dose 5000u)</td></tr>
<tr><td>Edoxaban (Savaysa)</td><td>Direct FXa inhibitor</td><td>10-14h (longer with renal impairment)</td><td>-If ingested within 2 hours, consider giving activated charcoal 1g/kg (max 50g)
-Administer 4 factor PCC (Kcentra) 50units/kg x1 (max 5000units)
-If Kcentra ineffective, consult hematology and consider recombinant activated factor VII (Novoseven) 90 mcg/kg IV once, max 10 mg
-Drug activity can be assessed with anti-factor Xa assay. However, this may not accurately reflect the degree of anticoagulation
-If anti-factor Xa level is <0.1 IU/mL, consider other causes for bleeding</td></tr>
<tr><td>Fondaparinux (Arixtra)</td><td>Antithrombin mediated inhibition of FXa</td><td>17-21h (++ longer with renal impairment)</td><td>-Administer Kcentra (4 factor PCC) 50u/kg x 1 (max 5000u)
-Monitor aPTT/ anti factor Xa levels</td></tr>
<tr><td>Heparin</td><td>AT III enhancer</td><td>30-90 min</td><td>-Administer protamine:
For each 1000 units of heparin, administer 1mg of protamine
-Do not exceed rate of 5 mg/min, max dose is 50 mg</td></tr>
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<table>
<tr><td>Rivaroxaban (Xarelto)</td><td>Direct FXa inhibitor</td><td>5-9h
Elderly: 11-13h (longer with renal impairment)</td><td>-If ingested within 2 hours, consider giving activated charcoal 1g/kg (max 50g)
-Administer Kcentra (4-factor PCC) 50units/kg x1 (max 5000units)
-If Kcentra ineffective, consult hematology and consider recombinant activated factor VII (Novoseven) 90 mcg/kg IV once, max 10 mg
-Drug activity can be assessed with anti-factor Xa assay. However, this may not accurately reflect the degree of anticoagulation
-If anti-factor Xa level is <0.1 IU/mL, consider other causes for bleeding
-Reversal agent adexanet alpha not yet available</td></tr>
<tr><td>Warfarin (Coumadin)</td><td>Vit K antagonist</td><td colspan="2">
<table>
<tr><td>Clinical Scenario</td><td>INR</td><td>Management</td></tr>
<tr><td>No bleeding</td><td colspan="2"><4.5 Hold Warfarin or lower dose and check daily INR

4.5 – 9.9 Preferred treatment
• Omit next 1-2 doses. Resume at adjusted dose once INR therapeutic
• If INR remains the same or increases despite holding ≥3 doses, consider giving vit K
o High risk thrombosis patients- avoid vit K if possible; If needed give 1-2 mg PO x 1
o All other patients- 2.5 – 5 mg PO x 1
• INR daily

>10 Hold Warfarin AND give vit K at the following doses
o High risk thrombosis patients- avoid vit K if possible; If needed give 1-2 mg PO x 1
o All other patients- 2.5 – 5 mg PO x 1
• INR daily
• For patients at very high risk for bleeding consider FFP/ Kcentra</td></tr>
<tr><td>Mild to moderate bleeding OR surgical procedure <24h</td><td colspan="2">1.8 – 4.5 Hold Warfarin, daily INR, 2 mg IV vit K once

4.5 – 9.9 Hold Warfarin, daily INR, 5 mg IV vit K once

>10 Hold Warfarin, daily INR, 10 mg IV vit K once

If patient continues to bleed despite Vit K or INR remains elevated above acceptable level, consider
• FFP transfusion
• Kcentra 25U/kg IV once max 2500 units. Recheck INR 30 min after Kcentra</td></tr>
<tr><td>Major life threatening bleed OR requiring emergent procedure</td><td colspan="2">Any > 1.4
• Hold warfarin AND
• Vitamin K 10 mg IV once (over 30 minutes) AND
• Kcentra (4 factor PCC)
o INR <2: 25 units/kg IV once (max 2500 units)
o INR 2- 3.9: 25 units/kg IV once (max 2500 units)
o INR 4-6: 35 units/kg IV once (max 3500 units)
o INR >6: 50 units/kg IV once (max 5000 units)

Recheck INR 30 minutes after Kcentra, then q6h x 24h

• If INR > 2.0 and/or bleeding heavily AFTER Kcentra, consider
o TEG
o Hematology consult
o 4-6 units FFP
o Pro-hemostatic agents
o If all above not effective, consider recombinant factor VII (Novoseven) 20 mcg/kg once</td></tr>
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