Guideline for the Reversal of Anticoagulants and Management of Bleeding

Patients with trauma and/or life-threatening hemorrhage (ICH, intra-abdominal, intra-thoracic) or needs emergent operative intervention

Warfarin (Coumadin®)

Check INR

INR 1.4 - 3.9
Kcentra® 25 units/kg IV x 1
Max dose: 2500 units

INR 4 - 6
Kcentra® 35 units/kg IV x 1
Max dose: 3500 units

INR > 6
Kcentra® 50 units/kg IV x 1
Max dose: 5000 units

5-10 mg Vitamin K IV over 30 minutes x 1

Recheck INR 30 minutes after Kcentra® dose

Kcentra®=4-Factor PCC

Dose based on actual body weight up to 100 kg. Cannot re-dose Kcentra®

Direct Oral Anticoagulants (DOAC)

Rivaroxaban (Xarelto®), Apixaban (Eliquis®) or Edoxaban (Savaysa®)

Last dose taken within 3-5 half-lives of DOAC

Yes or Unknown Kcentra®
50 units/kg IV x 1
Max dose: 5000 units

No
Provide supportive care

Dabigatran (Pradaxa®)

Check Thrombin Time (TT)
(A normal thrombin time excludes clinically significant levels of dabigatran)

Dabigatran taken within 24 hrs:
Praxbind®
5 grams IV x 1

Dabigatran taken 24 - 48 hrs ago
AND TT is elevated:
Praxbind®
5 grams IV x 1

May consider an additional 5 gram dose if:
- Re-bleeding and TT is elevated
- 2nd emergent surgery is needed and TT is elevated

Kcentra®=4-Factor PCC
If signs/symptoms of allergic reaction to infusion – stop infusion.
Avoid Kcentra® in patients with history of HIT or allergy to albumin.

Praxbind®=Idarucizumab
Given as 2 consecutive 2.5 gram infusions
Praxbind contains 4 grams sorbitol. Consider this if calculating total daily amount of sorbitol/fructose in patients with hereditary fructose intolerance.
If patient was on a continuous infusion, only consider heparin given in the preceding 2 - 3 hours.

Additional protamine dose should be guided by clinical bleeding. May repeat dose x 1 \((\leq 0.5 \text{ mg of protamine for every 100 units of heparin})\) if bleeding continues and if the heparin assay (Anti\(\text{Xa}\) level) remains elevated.

Repeat dosing of protamine can elevate the aPTT and ACT. A normal thrombin time is useful to confirm reversal of heparin.

Protamine neutralizes 60% - 75% of anti-Xa activity of enoxaparin.

There is no FDA-approved reversal agent for Fondaparinux.

Reversal agent is likely not needed if 3 – 5 half-lives have elapsed (half-life 17 - 21 hours).

Recombinant factor VIIa (NovoSeven ®) 90 mcg/kg has been shown to partially normalize a prolonged aPTT, endogenous thrombin potential, and prothrombin activation in vivo.

Protamine likely not needed if 3 – 5 half-lives have elapsed.

There is no FDA-approved reversal agent for Argatroban or Bivalirudin.

Reversal agent is likely not needed if 3 – 5 half-lives have elapsed:

- Argatroban half-life 40 - 50 minutes
- Bivalirudin half-life 25 minutes, extended up to 3.5 hour in patients on dialysis
- Recombinant factor VIIa (NovoSeven ®) 90 mcg/kg has been shown to reverse the anticoagulation effect of direct thrombin inhibitors.
### Management of Bleeding

<table>
<thead>
<tr>
<th>Name of Anticoagulant</th>
<th>Dialysis</th>
<th>Management</th>
<th>Reversal Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin (Coumadin®)</td>
<td>Not dialyzable</td>
<td>Hold warfarin</td>
<td>Kcentra® and Vitamin K</td>
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<tr>
<td></td>
<td></td>
<td>Supportive measures*</td>
<td></td>
</tr>
<tr>
<td>Rivaroxaban (Xarelto®)</td>
<td>Not dialyzable</td>
<td>Discontinue anticoagulant</td>
<td>Kcentra®</td>
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<tr>
<td></td>
<td></td>
<td>Supportive measures*</td>
<td></td>
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<td></td>
<td></td>
<td>Overdose: Charcoal by mouth if ingested within 1–2 hours</td>
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<tr>
<td>Apixaban (Eliquis®)</td>
<td>Not dialyzable</td>
<td>Discontinue anticoagulant</td>
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<tr>
<td>Edoxaban (Savaysa®)</td>
<td>Not dialyzable</td>
<td>Discontinue anticoagulant</td>
<td>Protamine</td>
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<td></td>
<td></td>
<td>Supportive measures*</td>
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<tr>
<td>Dabigatran (Prada®)</td>
<td>Hemodialysis removes ~57% over 4 hours</td>
<td>Discontinue anticoagulant</td>
<td>Praxbind®</td>
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<td>Supportive measures*</td>
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<td></td>
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<td>Overdose: Charcoal by mouth if ingested within 1–2 hours</td>
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</tr>
<tr>
<td>Unfractionated Heparin (UFH)</td>
<td>Not dialyzable</td>
<td>Discontinue anticoagulant</td>
<td>Protamine</td>
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<td>Supportive measures*</td>
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<tr>
<td>Enoxaparin (Lovenox®)</td>
<td>Not dialyzable</td>
<td>Discontinue anticoagulant</td>
<td>Protamine</td>
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<td></td>
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<td>Supportive measures*</td>
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</tr>
<tr>
<td>Fondaparinux (Arixtra®)</td>
<td>Clearance increased by 20%</td>
<td>Discontinue anticoagulant</td>
<td>NovoSeven®</td>
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<td></td>
<td>Supportive measures*</td>
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</tr>
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<td>Argatroban</td>
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<tr>
<td>Bivalirudin (Angiomax®)</td>
<td>Hemodialysis removes ~25% over 4 hours</td>
<td>Discontinue anticoagulant</td>
<td>NovoSeven®</td>
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<tr>
<td></td>
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<td>Supportive measures*</td>
<td></td>
</tr>
</tbody>
</table>

* Supportive measures include management of airway, breathing, circulation, transfusions, compression, surgical hemostasis

### References:
4. Idarucizumab (PRAXABIND®) package insert, Boehringer Ingelheim, December 2015

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