Reversal of Anticoagulants and Management of Bleeding Guideline
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
- May consider an additional 5 gram dose if:
  - Re-bleeding and TT is elevated
  - 2nd emergent surgery is needed and TT is elevated
- Dabigatran taken 24 - 48 hrs ago
  - AND TT is elevated:
    - Praxbind® 5 grams IV x 1

**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.

 Origination date: 5/2014
 Revisions: 5/2015, 1/2016, 2/2019
 Approved by Anticoagulation Safety Committee: 3/2019
 Approved by P&T: 5/2019
Unfractionated Heparin (UFH)

Time since UFH last given

Time elapsed: Immediate
Protamine 1–1.5 mg slow IV for every 100 units of UFH the patient has received*
Max dose: 50 mg in a 10 minute period

Time elapsed: 30 - 60 minutes
Protamine 0.5–0.75 mg slow IV for every 100 units of UFH the patient has received *
Max dose: 50 mg in a 10 minute period

Time elapsed: >2 hours
Protamine 0.25–0.375 mg slow IV for every 100 units of UFH the patient has received *
Max dose: 50 mg in a 10 minute period

* 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 (≤ 0.5 mg of protamine for every 100 units of heparin) if bleeding continues and if the heparin assay (AntiXa level) remains elevated
Repeat dosing of protamine can elevate the aPTT and ACT. A normal thrombin time is useful to confirm reversal of heparin

Enoxaparin (Lovenox ®)

Time since enoxaparin last given

Time elapsed: < 8 hours
1 mg of Protamine per 1 mg of enoxaparin the patient has received
Max dose: 50 mg in a 10 minute period

Time elapsed: 8 -12 hours
0.5 mg Protamine per 1 mg of enoxaparin the patient has received
Max dose: 50 mg in a 10 minute period

Time elapsed: >12 hours
Protamine likely not needed if 3 – 5 half-lives have elapsed

* Additional protamine dose should be guided by clinical bleeding. May repeat dose x 1 if bleeding continues and if the LMW heparin assay (AntiXa level) remains elevated.
Protamine neutralizes 60% - 75% of anti-Xa activity of enoxaparin

Fondaparinux (Arixtra®)

- 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.

Argatroban and Bivalirudin (Angiomax®)

- 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

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