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<th>Reversal Agents</th>
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<td><strong>KCENTRA®</strong></td>
<td>First line Vitamin K antagonist (VKA) reversal in patients with acute major bleeding or need for an urgent surgery/invasive procedure</td>
<td>4 Factor unactivated PCC Prothrombin complex concentrate provides an increase in the levels of the vitamin K-dependent coagulation factors (II, VII, IX, and X) with the addition of protein C and protein S</td>
<td>Individualize dosing based on current pre-dose INR. Dosage is expressed in units of factor IX activity. Administer with vitamin K concurrently. Repeat dosing is not recommended.</td>
<td>Pretreatment INR 2 to &lt;4: Administer 25 units/kg; maximum dose: 2,500 units Pretreatment INR 4 to 6: Administer 35 units/kg; maximum dose: 3,500 units Pretreatment INR &gt;6: Administer 50 units/kg; maximum dose: 5,000 units **Patients can be given a conservative dose of 1500 units x 1 dose with a repeat INR taken 30-60 minutes post dose administration. It is recommended to give KCentra® 1500 units x 1 dose, wait 30-60 minutes post dose and then recheck the INR. If the INR ≥ 2, a supplemental dose based upon the INR reading should be given.</td>
<td>INR (baseline and at 30 minutes post dose) Clinical response during and after treatment Signs of thromboembolism and hypersensitivity reactions</td>
<td>For ICH, 10 mg IV phytonadione (vitamin K) must be ordered and administered to ALL PATIENTS receiving the Kcentra®. This can also be considered for patients with cardiac wall perforation, but is not required. The administration of phytonadione must not delay the administration of Kcentra®.*** Reconstituted preparations should be used within 4 hours Onset of action: Rapid; significant INR decline within 10 minutes Life threatening hemorrhage in a patient on warfarin resulting in initiation of the massive transfusion protocol</td>
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<td><strong>FEIBA®</strong></td>
<td>Second line reversal agent for several anticoagulants</td>
<td>4 Factor Activated PCC</td>
<td>50 unit/kg/dose (max dose is 100 units/kg; TDD is 200 units/kg) Maximum infusion rate is 2 units/kg/min</td>
<td>Signs/symptoms of disseminated intravascular coagulation (DIC), acute coronary ischemia, and thromboembolic events, especially if &gt;100 units/kg is administered; hemoglobin and hematocrit Signs/symptoms of hypersensitivity reactions</td>
<td>Reconstituted preparations should be used within 3 hours Onset of action: ~15-30 minutes</td>
<td>FEIBA can only be ordered by ED, ICU for NOAC (Non-Vitamin K Oral Anticoagulant) reversal, or Hematology for hematologic indications</td>
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<td><strong>Idarucizumab [PRAXBIND®]</strong></td>
<td>Dabigatran reversal</td>
<td>Humanized Monoclonal Antibody</td>
<td>2.5 g IV x 2 doses within 15 minutes of each other (doses should be administered within an hour of removal from vials)</td>
<td>Monitor for re-elevation of coagulation parameters (i.e. aPTT) In patients overdosed with dabigatran, consider: Baseline aPTT, repeat at 2 hours postexposure (if known) or post-presentation (if exposure time is unknown) and every 12 hours thereafter until aPTT returns to normal Signs/symptoms of clinically relevant bleeding, thromboembolic events, and hypersensitivity</td>
<td>Onset of action: Effects observed within minutes and hemostasis is restored at a median of 11.4 hours</td>
<td>Restricted to use for reversal of dabigatran for emergency surgery/procedure or in life-threatening bleeding</td>
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<td>Andexanet Alfa [Andexxa®]</td>
<td>First line reversal of anticoagulation from apixaban, rivaroxaban, or edoxaban with life-threatening bleeding</td>
<td>Andexanet alfa binds and sequesters the FXa inhibitors rivaroxaban and apixaban. In addition, andexanet alfa inhibits the activity of Tissue Factor Pathway Inhibitor (TFPI), increasing tissue factor-initiated thrombin generation. <strong>Low dose:</strong> 400 mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 4 mg/minute IV infusion for up to 120 minutes - use for any ingestion ≥ 24 hours - use for apixaban ≤ 5 mg - use for rivaroxaban ≤ 10 mg - use for edoxaban ≤ 30 mg <strong>High dose:</strong> 800 mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 8 mg/minute IV infusion for up to 120 minutes - use for apixaban &gt; 5 mg/unknown - use for rivaroxaban &gt; 10 mg/unknown - use for edoxaban &gt; 30 mg/unknown</td>
<td>Signs/symptoms of arterial and venous thromboembolic events, ischemic events, or cardiac arrest, hemostasis, and hypersensitivity reactions</td>
<td>Reconstituted ANDEXXA in IV bags is stable at room temperature for up to 8 hours <strong>Onset of Action:</strong> Rapid</td>
<td>Restricted to approval by Intensivists/ER Physicians for use in patients with intracranial hemorrhage meeting all of the following criteria: - last dose of apixaban, rivaroxaban, or edoxaban within 18 hours - Glasgow Coma Scale Score ≥ 5 - No administration of Kcentra, FEIBA or NovoSeven within 48 hours</td>
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<td>PROTAMINE</td>
<td>First line Heparin/LMWH reversal</td>
<td>Combines with heparin to form a neutralized salt <strong>Heparin reversal (&lt;2.5 hrs):</strong> 1 mg of protamine to 100 units of heparin <strong>Enoxaparin reversal (&lt;8 hrs):</strong> 1 mg of protamine to 1 mg of enoxaparin <strong>Enoxaparin reversal (&gt;8 hrs):</strong> 0.5 mg of protamine to 1 mg of enoxaparin <strong>Max dose is 50 mg over 10 mins</strong></td>
<td>Signs/symptoms of hypersensitivity reactions</td>
<td><strong>Onset of action:</strong> IV: Heparin neutralization: ~5 minutes</td>
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<td>Vitamin K / Phytonadione [MEPHYTON®]</td>
<td>Warfarin reversal</td>
<td>Replaces coagulation factors II, VII, IX, and X <strong>INR supratherapeutic but &lt; 4.5:</strong> Hold warfarin dose, no vitamin K <strong>INR 4.5-10:</strong> Hold warfarin dose; no vitamin K <strong>INR ≥ 10:</strong> Hold warfarin, administer vitamin K 2.5-5 mg PO <strong>Major bleeding despite INR:</strong> Administer vitamin K 5-10 mg IV with Kcentra INR will decrease over ~24-48 hours (oral) and ~12-14 hours (IV); more frequent INR monitoring and additional vitamin K doses may be necessary.</td>
<td>Signs/symptoms of hypersensitivity reactions</td>
<td>Subcutaneous and IM routes are not recommended <strong>Onset of action:</strong> 6-10 hours (oral); 1-2 hours (IV)</td>
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**APIXABAN:**
*Conversion from warfarin to apixaban:* Discontinue warfarin and initiate apixaban when INR is <2

*Conversion from apixaban to warfarin: Note:* Apixaban affects the INR; measuring the INR during warfarin therapy may not be useful for determining an appropriate dose of warfarin. If continuous anticoagulation is necessary, discontinue apixaban and begin both a parenteral anticoagulant with warfarin when the next dose of apixaban is due; discontinue parenteral anticoagulant when INR reaches an acceptable range

*Conversion between apixaban and other non-warfarin anticoagulants:* Discontinue anticoagulant being taken and begin the other at the next scheduled dose

**DABIGATRAN:**
*Conversion from a parenteral anticoagulant:* Initiate dabigatran ≤2 hours prior to the time of the next scheduled dose of the parenteral anticoagulant (eg, enoxaparin) or at the time of discontinuation for a continuously administered parenteral drug (eg, IV heparin); discontinue parenteral anticoagulant at the time of dabigatran initiation.

*Conversion to a parenteral anticoagulant:* Wait 12 hours (CrCl ≥30 mL/minute) or 24 hours (CrCl <30 mL/minute) after the last dose of dabigatran before initiating a parenteral anticoagulant.

*Conversion from warfarin:* Discontinue warfarin and initiate dabigatran when INR <2.0

*Conversion to warfarin:* Since dabigatran contributes to INR elevation, warfarin’s effect on the INR will be better reflected only after dabigatran has been stopped for ≥2 days. Start time must be adjusted based on CrCl:
- CrCl >50 mL/minute: Initiate warfarin 3 days before discontinuation of dabigatran
- CrCl 31 to 50 mL/minute: Initiate warfarin 2 days before discontinuation of dabigatran
- CrCl 15 to 30 mL/minute: Initiate warfarin 1 day before discontinuation of dabigatran (dabigatran use is contraindicated in Canadian labeling when CrCl <30 mL/minute).
- CrCl <15 mL/minute: There are no recommendations provided in the U.S. manufacturer’s labeling.

**RIVAROXABAN:**
*Conversion from warfarin:* Discontinue warfarin and initiate rivaroxaban as soon as INR falls to <3.0 (U.S. labeling) or ≤2.5 (Canadian labeling)

*Conversion to warfarin: Note:* Rivaroxaban affects INR; therefore, initial INR measurements after initiating warfarin may be unreliable.

- Discontinue rivaroxaban and initiate both warfarin and a parenteral anticoagulant at the time the next dose of rivaroxaban would have been taken

*Conversion from continuous infusion unfractionated heparin:* Initiate rivaroxaban at the time of heparin discontinuation

*Conversion to continuous infusion unfractionated heparin:* Discontinue rivaroxaban and initiate continuous infusion heparin at the time the next dose of rivaroxaban would have been taken.

*Conversion from anticoagulants (other than warfarin and continuous infusion unfractionated heparin):*
- Discontinue current anticoagulant and initiate rivaroxaban ≤2 hours prior to the next regularly scheduled evening dose of the discontinued anticoagulant.

*Conversion to other anticoagulants (other than warfarin):* Discontinue rivaroxaban and initiate the anticoagulant at the time the next dose of rivaroxaban would have been taken