Reversal Agents	Indication	Mechanism	Dosing	Monitoring	Pearls	JHHS RESTRICTIONS
KCENTRA®	First line Vitamin K antagonist (VKA) reversal in patients with acute major bleeding or need for an urgent surgery/invasive procedure	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	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. **Pretreatment INR 2 to <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 >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.*	INR (baseline and at 30 minutes post dose) Clinical response during and after treatment Signs of thromboembolism and hypersensitivity reactions	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	For patients with intracranial hemorrhage in association with an INR > 1.4 in the setting of warfarin therapy For patients with cardiac wall perforation and/or cardiac tamponade in association with an INR > 1.4 in the setting of warfarin therapy Life threatening hemorrhage in a patient on warfarin resulting in initiation of the massive transfusion protocol
FEIBA®	Second line reversal agent for several anticoagulants	4 Factor Activated PCC	50 unit/kg/dose (max dose is 100 units/kg; TDD is 200 units/kg) Maximum infusion rate is 2 units/kg/min	Signs/symptoms of disseminated intravascular coagulation (DIC), acute coronary ischemia, and thromboembolic events, especially if >100 units/kg is administered; hemoglobin and hematocrit Signs/symptoms of hypersensitivity reactions	Reconstituted preparations should be used within 3 hours **Onset of action:** ~15-30 minutes	FEIBA can only be ordered by ED, ICU for NOAC (Non-Vitamin K Oral Anticoagulant) reversal, or Hematology for hematologic indications
Idarucizumab [PRAXBIND®]	Dabigatran reversal	Humanized Monoclonal Antibody	2.5 g IV x 2 doses within 15 minutes of each other (doses should be administered within an hour of removal from vials)	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	**Onset of action:** Effects observed within minutes and hemostasis is restored at a median of 11.4 hours	Restricted to use for reversal of dabigatran for emergency surgery/procedure or in life-threatening bleeding

Andexanet Alfa [Andexxa®]	First line reversal of anticoagulation from apixaban, rivaroxaban, or edoxaban with life-threatening bleeding	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	**Low dose**: 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 ≥8 hours - use for apixaban ≤ 5mg - use for rivaroxaban ≤ 10mg - use for edoxaban ≤ 30mg **High dose:** 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 > 5mg/unknown - use for rivaroxaban > 10mg/unknown - use for edoxaban > 30mg/unknown	Signs/symptoms of arterial and venous thromboembolic events, ischemic events, or cardiac arrest, hemostasis, and hypersensitivity reactions	Reconstituted ANDEXXA in IV bags is stable at room temperature for up to 8 hours **Onset of Action:** Rapid	Restricted to approval by Intensivists/ER Physicians for use in patients with intrcranial 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
PROTAMINE	First line Heparin/LMWH reversal	Combines with heparin to form a neutralized salt	**Heparin reversal (<2.5 hrs):**1 mg of protamine to 100 units of heparin **Enoxaparin reversal (<8 hrs):** 1 mg of protamine to 1 mg of enoxaparin **Enoxaparin reversal (>8 hrs):** 0.5 mg of protamine to 1 mg of enoxaparin ***Max dose is 50 mg over 10 mins***	Signs/symptoms of hypersensitivity reactions	**Onset of action: IV:** Heparin neutralization: ~5 minutes	
Vitamin K / Phytonadione [MEPHYTON®]	Warfarin reversal	Replaces coagulation factors II, VII, IX, and X	**INR supratherapeutic but < 4.5:** Hold warfarin dose, no vitamin K **INR 4.5-10:** Hold warfarin dose; no vitamin K **INR ≥ 10:** Hold warfarin, administer vitamin K 2.5-5 mg PO **Major bleeding despite INR:** 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. Signs/symptoms of hypersensitivity reactions	Subcutaneous and IM routes are not recommended **Onset of action:** 6-10 hours (oral); 1-2 hours (IV)	

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