Yale New Haven Health
Department of Pharmacy
Direct Oral Anticoagulants (DOAC)– Bleeding Reversal Guidelines
YNHHS Guidelines

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Approved by: Anticoagulation & Cardiology Subcommittee, Formulary Integration Committee

STAT Labs: PT/INR, PTT, CBC, Fibrinogen, Ionized Calcium & Type & Screen

For Acute DOAC Overdose (< 2 hours) after ingestion:
Activated Charcoal 50 g PO x 1

Definitions of Reversal Situations

- Non-Urgent: Reversal is elective (> 7 days away)
- Urgent (without bleeding): Reversal needed within hours
- Urgent (with bleeding): Emergency reversal

Moderate to Severe/Life Threatening Bleeding (WHO grade 3-4)
Urgent / Emergent Procedures

- Fall with Altered Mental Status
- Spontaneous change in Mental Status (r/o Intracranial Hemorrhage)
- Gastrointestinal or Retroperitoneal Bleed

Mild Bleeding (WHO Grade 1-2) or Elective Procedure

- Fall with Normal Mental Status and hemodynamic stability
- Minor External Bleeding

Treatment

- Delay next dose of DOAC or Discontinue
- IV Hydration (if not contraindicated)
- Supportive Care
- Clinical Observation
- Bleeding source control, as appropriate
- Manage effects of other antithrombotic drugs

DOAC: Direct Thrombin Inhibitor
(*i.e. Dabigatran*)
Reversal Treatment

Step I (Initial therapy):

- Discontinue DOAC: Dabigatran (Pradaxa)
- Consider Supportive Care = **HASHTI**
- *Consider Idarucizumab (Praxbind), 5 g x 1 (2.5 g IV infusion x 2 doses)
- Consider ddAVP 0.3 mcg/kg x 1 dose (if patient uremic)
- Consider Consults (GI, Surgery, or Hematology)

Step II (Salvage Therapy):

If following treatment there is ongoing or life-threatening bleeding, consider the following:

- Consider Consults: Hematology, Surgery, etc.
- Activate "Massive Transfusion Protocol"
- Consider rFactor VIIa (Novoseven), 90 mcg/kg, Q2H, x 3 doses

"HASHTI" Acronym

- **H**old further doses of anticoagulant
- Consider **A**ntidote
- **S**upportive Treatment: Volume resuscitation, Inotropes as needed
- Local or surgical **H**emostatic measures: Topical agents (Aminocaproic acid, Tranexamic Acid)
- **T**ransfusion (red cells, platelets, fresh frozen plasma, as indicated)
- **I**nvestigate for bleeding source

DOAC: Factor Xa Inhibitor
(i.e Rivaroxaban, Apixaban)
Reversal Treatment

Step I (Initial therapy):

- Discontinue DOAC
- Consider Andexanet alpha (Andexxa) for life threatening intracranial hemorrhage (low dose or high dose). See below for dosing/restriction criteria.
- Consider Prothrombin Complex Concentartes (Kcentra) for other life threatening bleeding or if Andexanet alpha is not available. See below for dosing)
- Consider desmopressin 0.3 mcg/kg x 1 dose (if patient is uremic)
- Consider Consults (GI, Surgery, or Hematology)
- Consider Supportive Care = HASHTI

Step II (Salvage Therapy):

If following treatment there is ongoing or life-threatening bleeding, consider the following:

- Consider Consults: Hematology, Surgery, etc
- Activate "Massive Transfusion Protocol
- Consider rFactor VIIa (Novoseven), 90 mcg/kg, Q2H, x 3 doses

Prothrombin Complex Concentrates (Kcentra)		
Recommended Dosage	**Cautions**	**Recommended Follow Up Monitoring**
25 IU/kg x 1 dose (administer as a IV infusion at a rate 210 units/min Maximum dose of 2,500 units).	• Do not use in DIC, HIT, or prior hypersensitivity to any components including factors II, VII, IX, X, Proetin C, Heparin, Protein S, Antithrombin, and human Albumin • Kcentra increases thrombotic risk. Caution if history of thromboembolic event in the past 6 weeks (e.g. AMI/unstable Angina, Stroke/TIA, severe peripheral arterial disease, intravascular stent, DVT/PE) • Consider only when other measures fail. There is NO evidence that PCCs improve outcomes of reversal of DOAC anticoagulation. Potential benefits need to be weighed against increased thrombosis risk. Consider alternative measures to control bleeding first • Consider Hematology consult as need for guidance	
Andexanet alpha (Andexxa)		
Recommended Dosage	**Cautions and Criteria for Use/Restrictions**	**Recommended Follow Up Monitoring**
<u>Low Dose Strategy</u> • Bolus: 400mg IVPB over over 15 minutes • Infusion: 480mg IVPB over 2 hours (4mg/min) <u>High Dose Strategy</u> • Bolus: 800mg IVPB over over 30 minutes • Infusion: 960mg IVPB over 2 hours (8mg/min) <u>Rivaroxaban Induced bleeding</u> **Low dose strategy** • ≤ 10 mg (< 8 hrs/unknown or ≥ 8 hrs from last dose ingestion) • >10 mg (≥ 8 hrs from last dose ingestion) **High dose strategy** • >10mg or unknown dose <u>Apixaban Induced Bleeding</u> **Low Dose Strategy** • ≤ 5mg (< 8 hrs/unknown or ≥ 8 hrs from last dose ingestion) • >5 mg (≥ 8 hrs from last dose ingestion) **High dose strategy** • >5 mg or unknown dose	*Patients presenting with a life threatening traumatic or spontaneous intracerebral hemorrhage in the setting of anti-Xa inhibitor (apixaban or rivaroxaban) use.* For patients presenting to with apixaban or rivaroxaban associated coagulopathy requiring reversal in the setting of extracranial hemorrhage, please consider 4-factor prothrombin complex concentrate (KCentra). Contraindication: Patients who have received prothrombin complex-concentrate (KCentra) at any point during the current, acute presentation. All cases must be discussed with and approved by the Neurosurgery, Neurology or Critical Care attending.	Lab Monitoring: Anti Xa levels should be drawn upon presentation; a follow-up lab is not necessary. However, if there is a high clinical suspicion that apixaban or rivaroxaban was recently administered to the patient, awaiting this lab result to initiate treatment is not necessary.
Idarucizumab (Praxbind)		
Recommended Dosage	**Cautions**	**Recommended Follow Up Monitoring**
5 g x 1 dose . Administer as a 2.5g IV bolus over 5 minutes x 2 doses, no more than 15 minutes apart Idarucizumab may <u>not</u> be appropriate after the below time frames based on renal function" Do Not administer Praxbind from last dose of Dabigatran • CrCl > 50: after 48 hours • CrCl 30-50: after 72 hours • CrCl < 30: after 120 hours	• Do not use Idarucizumab if hereditary fructose intolerance (contains 4g sorbitol per dose, may cause serious adverse reactions with parenteral administration) • Consider only when other measures fail Limited clinical outcomes data available on efficacy and safety	Check aPTT for normalization 2 hours after administration and every 12 hours until normal