

Optimizing Outcomes for Patients With DOAC-Related Bleeding:

A Multidisciplinary Appraisal of Data-Driven Management Strategies Using Specific Reversal Agents

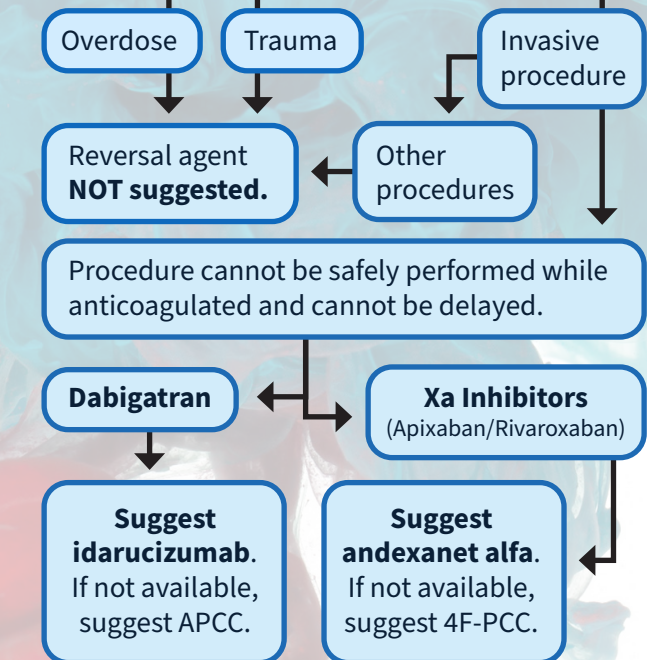
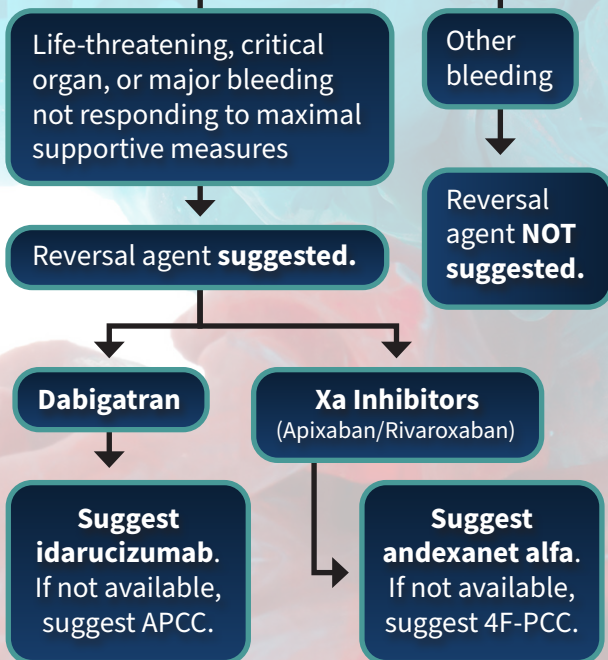
 CORNERSTONE CLINICAL TOOL

Anticoagulation Forum Pathway

Adapted from: Cuker A, et al.
Am J Hematol. 2019.

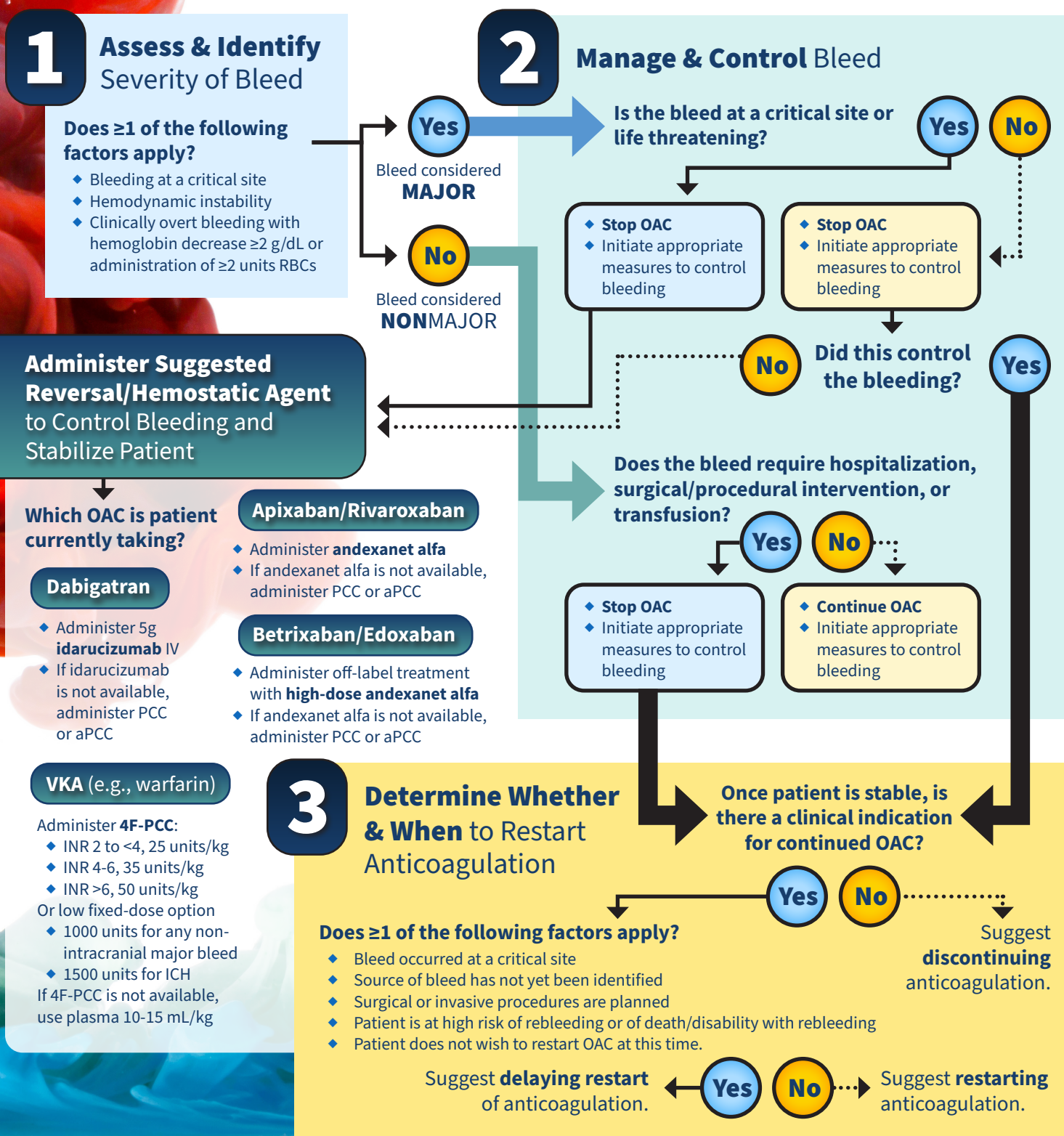
Patient on **Direct Oral Anticoagulant (DOAC)**

BLEEDING | **NOT BLEEDING**



2020 American College of Cardiology Expert Consensus Decision Pathway

Adapted from:
Tomaselli G, et al.
J Am Coll Cardiol. 2020.



Administer Suggested Reversal/Hemostatic Agent to Control Bleeding and Stabilize Patient

Which OAC is patient currently taking?

Dabigatran

- Administer 5g **idarucizumab** IV
- If idarucizumab is not available, administer PCC or aPCC

Apixaban/Rivaroxaban

- Administer **andexanet alfa**
- If andexanet alfa is not available, administer PCC or aPCC

Betrixaban/Edoxaban

- Administer off-label treatment with **high-dose andexanet alfa**
- If andexanet alfa is not available, administer PCC or aPCC

VKA (e.g., warfarin)

- Administer **4F-PCC**:
- INR 2 to <4 , 25 units/kg
 - INR 4-6, 35 units/kg
 - INR >6 , 50 units/kg
- Or low fixed-dose option
- 1000 units for any non-intracranial major bleed
 - 1500 units for ICH
- If 4F-PCC is not available, use plasma 10-15 mL/kg

Reversal Agent Quick Reference

Adapted from: [ClinicalTrials.gov](https://www.clinicaltrials.gov/);
FDA Prescribing Information.

Idarucizumab

Andexanet alfa

DOAC Target	Dabigatran	Apixaban, Rivaroxaban
Mechanism of Action	Humanized monoclonal antibody fragment that binds to dabigatran and its acylglucuronide metabolites with higher affinity than the binding affinity of dabigatran to thrombin.	Engineered variant of factor Xa that binds and sequesters factor Xa inhibitors with high affinity. Can also increase thrombin generation by binding and inhibiting the activity of tissue-factor pathway inhibitor.
FDA-Approved Indication	Patients treated with dabigatran when reversal of the anticoagulant effects of dabigatran is needed, including emergent surgent/urgent procedures and life-threatening or uncontrolled bleeding	Patients treated with rivaroxaban or apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding
Admin. Route	Intravenous	Intravenous
Dose	5 g in 2 separate vials of 2.5 mg/50 mL	Dosed based on specific FXa inhibitor, dose of FXa inhibitor, and time since patient's last dose of FXa inhibitor.
Common Adverse Events	Headache, constipation, nausea	Urinary tract infection, pneumonia
Prominent Studies	RE-VERSE AD (non-RCT)	ANNEXA-A (RCT), ANNEXA-R (RCT), ANNEXA-4 (non-RCT), ANNEXA-I (RCT)

Anticoagulants Reversal Strategies in the Emergency Department

Adapted from:
Baugh CW, et al.
Ann Emerg Med. 2020.

Anticoagulated Patient enters emergency department.

Is the patient bleeding? **OR**
Non-bleeding and needs emergent surgery/urgent procedure?

Yes

Is the bleed life threatening or at a critical site? **OR** Does the non-bleeding patient need emergent surgery/urgent procedure?

Yes

Class	DTI	Direct Xa Inhibitor			AT-Mediated Inhibition of Xa	Inhibition of Thrombin; Indirectly Inactivates Xa		Vitamin K Antagonist
Agent	Dabigatran	Rivaroxaban/ Apixaban	Edoxaban	Betrixaban	Fondaparinux	Unfractionated Heparin	Enoxaparin/ Daltaparin	Warfarin
Last Dose	<8-12 hrs	<18 hrs	10-14 hrs	19-24 hrs	17-21 hrs	PTT Based 1-2 hrs	3-5 hrs	INR Based 20-60 hrs
Tier 1	Idarucizumab	Andexanet alfa			4F-PCC	Protamine		Vit K & 4F-PCC
Tier 2	PCC Dialysis	PCC			PCC			PCC FFP

Reassess: Clinical | Labs | Imaging

Consider redosing and hospital admission

No

← Patient improving? →

Yes

Consider hospital admission