CONSIDERATIONS FOR ANTICOAGULATION REVERSAL/HEMOSTASIS*

This fact sheet provides clinician guidance for administering anticoagulant reversal/hemostatic agents. Reversal/hemostatic agents may be required for a life-threatening or critical site bleed, or in situations in which bleeding cannot be controlled with other measures. Please consult with other specialists involved in the patient's care as appropriate. When possible, therapeutic options should be determined after discussion between the patient and their care provider.

Vitamin K Antagonists (warfarin)		
Reversal Strategy	**Dosage**	
4F-PCC†		**Note regarding vitamin K:** When PCCs are used to reverse VKAs, vitamin K should also always be given. If bleed is considered **major**: Administer 5-10 mg IV vitamin K If bleed is considered **nonmajor**: Administer 2-5 mg PO/IV vitamin K
• INR 2 to <4	25 units/kg	
• INR 4-6	35 units/kg	
• INR >6	50 units/kg	
4F-PCC low fixed-dose option	1000 units for any non-intracranial major bleed	
	1500 units for intracranial hemorrhage	
If 4F-PCC not available, administer plasma	10-15 mL/kg (1)	

Direct Thrombin Inhibitor (dabigatran)	
Reversal Strategy	**Dosage**
Idarucizumab	5g idarucizumab IV‡
If idarucizumab is not available, administer either PCC or aPCC	50 units/kg IV §
Consider activated charcoal for known recent ingestion (within 2-4 h)	(n/a)

Factor Xa Inhibitor (edoxaban and betrixaban)	
Reversal Strategy	**Dosage**
Off-label treatment with andexanet alfa ‖ ¶	Initial IV Bolus 800 mg at a target rate of 30 mg/min, follow-up IV infusion 8 mg/min for up to 120 minutes
If andexanet alfa is not available, administer PCC or aPCC	50 units/kg IV§
Consider activated charcoal for known recent ingestion (within 2-4 h)	(n/a)

4F-PCC = four-factor prothrombin complex concentrate; aPCC = activated prothrombin complex concentrate; h = hours; IV = intravenous; PCC = prothrombin complex concentrate; INR = international normalized ratio

*Reversal/hemostatic agents include repletion strategies such as PCCs, plasma, vitamin K, and specific reversal agents for DOACs (e.g., idarucizumab for dabigatran; andexanet alfa for apixaban or rivaroxaban)

† When PCCs are used to reverse vitamin K antagonists, vitamin K should also always be given

‡ If bleeding persists after reversal and there is laboratory evidence of a persistent dabigatran effect, or if there is concern for a persistent anticoagulant effect before a second invasive procedure, a second dose of idarucizumab may be reasonable

§ Refer to prescribing information for max units. To control bleeding in hemophilia patients with inhibitors, aPCC is typically administered intravenously in doses ranging from 50 U/kg to 100 U/kg, with a daily maximum of 200 U/kg. There are no randomized data regarding dosing in patients with factor Xa inhibitor–related major bleeding. Based on preclinical evidence, case reports, and case series data, an initial intravenous dose of 50 U/kg is suggested for patients with FXa inhibitor major bleeding and who are known or likely to have clinically significant anticoagulant levels.

‖ ANNEXA-4 full report excluded patients with DOAC levels <75 ng/ml because those patients were considered to have clinically insufficient levels for reversal agent. If drug effect/level can be assessed without compromising urgent clinical care decisions, then assessment should be performed before andexanet alfa is administered

¶ Andexanet alfa is not currently available at every institution; please refer to product locator on manufacturer's website.

(1) Sarode R, Milling TJ, Jr., Refaai MA, et al. Efficacy and safety of a 4-factor prothrombin complex concentrate in patients on vitamin K antagonists presenting with major bleeding: a randomized, plasma controlled, phase IIIb study. Circulation. 2013; 128:1234-43.

Reference:

Tomaselli GF, Mahaffey KW, Cuker A, Dobesh PP, Doherty JU, Eikelboom JW, Florido R, Gluckman TJ, Hucker W, Mehran R, Messé SR, Perino AC, Rodriguez F, Sarode R, Siegal D, Wiggins BS. 2020 ACC expert consensus decision pathway on management of bleeding in patients on oral anticoagulants: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2020 Aug, 76(5) 594-622. doi:10.1016/j.jacc.2020.04.053

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Factor Xa Inhibitor (apixaban)					
Reversal Strategy			**Dosage**		
	Last dose of apixaban	**Timing of last dose**	**Low/High**	**Initial IV Bolus**	**Follow-On IV Infusion**
Andexanet alfa ‖ ¶	≤ 5 mg	< 8 hours or unknown	Low dose	400 mg at a target rate of 30 mg/min	4 mg/min for up to 120 minutes
		≥ 8 hours	Low dose	400 mg at a target rate of 30 mg/min	4 mg/min for up to 120 minutes
	> 5 mg or unknown	< 8 hours or unknown	High dose	800 mg at a target rate of 30 mg/min	8 mg/min for up to 120 minutes
		≥ 8 hours	Low dose	400 mg at a target rate of 30 mg/min	4 mg/min for up to 120 minutes
If andexanet alfa is not available, administer PCC or aPCC			50 units/kg IV§		
Consider activated charcoal for known recent ingestion (within 2-4 h)			(n/a)		

Factor Xa Inhibitor (rivaroxaban)					
Reversal Strategy			**Dosage**		
	Last dose of rivaroxaban	**Timing of last dose**	**Low/High**	**Initial IV Bolus**	**Follow-On IV Infusion**
Andexanet alfa ‖ ¶	≤ 10 mg	< 8 hours or unknown	Low dose	400 mg at a target rate of 30 mg/min	4 mg/min for up to 120 minutes
		≥ 8 hours	Low dose	400 mg at a target rate of 30 mg/min	4 mg/min for up to 120 minutes
	> 10 mg or unknown	< 8 hours or unknown	High dose	800 mg at a target rate of 30 mg/min	8 mg/min for up to 120 minutes
		≥ 8 hours	Low dose	400 mg at a target rate of 30 mg/min	4 mg/min for up to 120 minutes
If andexanet alfa is not available, administer PCC or aPCC			50 units/kg IV§		
Consider activated charcoal for known recent ingestion (within 2-4 h)			(n/a)		

4F-PCC = 4-factor prothrombin complex concentrate; aPCC = activated prothrombin complex concentrate h=hours

*Reversal agents include repletion strategies such as PCCs, plasma, Vitamin K, and specific reversal agents for DOACs (e.g., idarucizumab for dabigatran; andexanet alfa for apixaban or rivaroxaban).

§ Refer to prescribing information for max units. To control bleeding in hemophilia patients with inhibitors, aPCC is typically administered intravenously in doses ranging from 50 U/kg to 100 U/kg, with a daily maximum of 200 U/kg. There are no randomized data regarding dosing in patients with factor Xa inhibitor–related major bleeding. Based on preclinical evidence, case reports, and case series data, an initial intravenous dose of 50 U/kg is suggested for patients with FXa inhibitor major bleeding and who are known or likely to have clinically significant anticoagulant levels.

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This tool represents content found in the above referenced ACC Expert Consensus Decision Pathway. Any drugs or advice not mentioned in that document are not currently covered by this tool.

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