

Table 3. Antithrombotic reversal strategies

Category of Antithrombotic	Name	Method/Agent of reversal				
		1 st step	2 nd step	3 rd step	4 th step	5 th step
<u>Vitamin K antagonists</u>	Warfarin	<u>Vitamin K</u> 10 mg IV, should be used with other agents as it can take up to a day to normalize INR	<u>PCC</u> 25 IU / Kg IV for INR 1.5-3.9 35 IU/Kg IV for INR 4-6 50 IU/Kg IV for INR >6 Although more expensive than FFP, it proved to be better than FFP	<u>FFP</u> 5-30 mL/Kg	<u>Recheck PT/INR</u> at 1,6 & 24 h If INR >1.5 at 1 h, 2-4 units FFP If INR >1.5 at 6 h, Vitamin K 10 mg IV	
<u>Direct factor Xa inhibitors</u>	Rivaroxaban	If ingested within 2 h, give one dose activated charcoal orally	<u>Andexanet Alfa</u> 400mg IV bolus; 480mg IV infusion if last dose >7h 800mg IV bolus; 960mg IV infusion if last dose <7h	<u>PCC</u> • If Andexanet alpha is not available • Preferably 4F-PCC (Kcentra) with a dose of 50 units/Kg • Specific anti-Xa assays are the preferred tests to evaluate the anticoagulant effects of FXa-Is Secondary end point analysis should show normalization of PT and INR	Rivaroxaban and Apixaban are not removed by dialysis	<u>Aripazine (PER977)</u> It was designed to bind to Heparin & LMWH & FXa-Is & direct thrombin inhibitors.
	Apixaban					
	Edoxaban					
<u>Direct thrombin inhibitors</u>	Dabigatran	If ingested within 2 h, give one dose activated charcoal orally	<u>Idarucizumab</u> A dose of 5 g divided into 2 doses 2.5 g given IV ≤ 15 minutes apart Approved for the reversal of dabigatran	<u>aPCC</u> (50 units/kg) or <u>4-factor PCC</u> (50 units/kg) if idarucizumab is not available	Consider emergent dialysis in patient with renal failure	

<u>Unfractionated Heparin</u>	Heparin	Discontinue heparin infusion if intracranial hemorrhage is suspected or present.	Reverse anticoagulation medications.	<u>Protamine sulfate</u> 1mg for every 100 units of heparin given in the previous 2-3 hours with a maximum single dose of 50mg If the aPTT remains elevated, repeat the protamine sulfate with a dose of 0.5mg/100 units of UFH	
<u>LMWHs and Heparinoids</u>	Enoxaparin	Discontinue LMWH infusion if intracranial hemorrhage is suspected or present.	<u>Protamine sulfate</u> If enoxaparin was given within 8 h, administer protamine sulfate at a dose of 1mg/1 mg of enoxaparin administered (up to a maximum single dose of 50 mg). If enoxaparin was given within 8–12 h, administer it at a dose of 0.5/1 mg of enoxaparin. After 3–5 half-lives have elapsed, protamine is probably not needed.		
	Dalteprain	Discontinue LMWH infusion if intracranial hemorrhage is suspected or present.	<u>Protamine sulfate</u> 1 mg/100 anti-Xa units of LMWH administered in the past 3–5 half-lives of the drug, up to a maximum single dose of 50 mg.	<u>rFVIIa</u> (90 mcg/kg IV) if protamine is contraindicated	
	Nadroparin				
Tinzaparin					
	Danaproid	Discontinue LMWH infusion if intracranial hemorrhage is suspected or present.	<u>rFVIIa</u> 90mcg/Kg IV once.		
<u>Pentasaccharides</u>	Fondaparinux	Discontinue pentasaccharide infusion if intracranial hemorrhage is suspected or present.	<u>aPCC</u> (20 IU/kg)	<u>rFVIIa</u> (90 mcg/kg), if aPCC is contraindicated or not available	
<u>Antiplatelets</u>	Aspirin	Discontinue antiplatelets if intracranial	Test platelet functions before doing unnecessary	If testing is not available, empiric platelet transfusion	A single dose of desmopressin DDAVP 0.4 mcg/kg IV in hemorrhage associated with aspirin/COX-1 inhibitors or ADP
	Ibuprofen				
	Naproxen				

	Dipyridamole	hemorrhage is suspected or present.	platelet transfusion	might be considered, if urgent neurosurgical intervention is due.	receptor inhibitors.
	Clopidogrel				
	Prasugrel				
	Ticagrelor				
	Ticlopidine				
	Cilostazol				
	Anagrelide				
	Abiciximab				
	Eptifibatide				
	Tirofiban				
	Vorpaxar				

4F PCC - 4 factor prothrombin complex concentrates, ADP - Adenosine diphosphate, aPCC - activated prothrombin complex concentrates, DDAVP - desmopressin, FFP - Fresh frozen plasma, INR - International normalized ratio, IU - International Unit, LWMH - low molecular weight heparin, PCC - prothrombin complex concentrates, rFVIIa - Recombinant factor VIIa, UFH - Unfractionated heparin