Target-Specific Oral Anticoagulant Reversal Guideline

M·TQIP

	Drug Profile			Laboratory Assessment Options					
	Half-life (hours)	5 Half-Lives (days)	Renal Excretion (%)	PT	APTT	TT	Anti-factor Xa Activity	Clearance Capacity	Adjunct Testing
Dabigatran (Pradaxa)	12-17 14-17** 15-18† 28‡	2.5-3.5	80	↑ or ↔	↑* (qualitative)	↑* nl = no drug (qualitative)	N/A	CrCl	Hct (anemia) Plt (thrombocytopenia) Electrolytes
Apixaban (Eliquis)	12	1 – 2	27	↑ or ↔	↑ or ↔	N/A	↑* enoxaparin calibrated (quantitative)	CrCl LFT's	
Rivaroxaban (Xarelto)	5-9	1.5 – 3.5	33	↑ or ↔* (qualitative)	↑ or ↔	N/A	↑* rivaroxaban calibrated (quantitative)	CrCl LFT's	

**Elderly, †Mild to moderate renal impairment, ‡Severe renal impairment

*Preferred, ↑ Simple increase, ↔ No change

	Assessment		Interventions		
	History	Exam	General	Major Blood Loss	Critical Blood Loss (Life-threatening)
Dabigatran (Pradaxa)	• Last dose • Potential for unintentional overdose • Renal or hepatic disease • Concomitant agents associated with bleeding (e.g. clopidogrel)	• Hemodynamic assessment • Active blood loss • Blood loss severity • Blood loss location	Stop anticoagulant IV access – large bore Hemodynamic optimization	1. Antifibrinolytic 2. Oral activated charcoal (if last dose within 2 hrs) 3. Hemodialysis	1. Major blood loss interventions 2. Idarucizumab (Praxbind)
Apixaban (Eliquis)				1. Antifibrinolytic 2. Oral activated charcoal (if last dose within 6 hrs)	1. Major blood loss interventions 2. Unactivated or activated 4-factor PCC*
Rivaroxaban (Xarelto)				1. Antifibrinolytic 2. Oral activated charcoal (if last dose within 8 hrs)	

** Pro-hemostatic products (e.g. PCC) carry substantial risk of thrombosis.*

	Prothrombin Complex Concentrates					
	Factors	Parameter	Dosing	Max Dosage	Infusion Time	Duration of Effect
Unactivated 4 Factor *Kcentra*	II, VII, IX, X	Not defined	25-50 units/kg IV	5000 units	20 min	~12-24 hours
Unactivated 3 Factor *Bebulin VH*	II, IX, X	Moderate bleeding Major bleeding	50-65 units/kg IV 75-90 units/kg IV	5000 units	15 min	
Activated 4 Factor *FEIBA NF*	II, IX, X VII (activated)	Mucous membrane Soft tissue Severe hemorrhage	50-100 units/kg IV Q 6 hrs 100 units/kg IV Q 12 hrs 100 units/kg IV Q 6-12 hrs	200 units/kg	15 min	

No current approved antidote is available for TSOAC-induced anticoagulation. While reversal is felt to be prudent in the setting of critical blood loss, evidence from randomized control trials is not available to confirm the efficacy of this practice. Some experts report need to redose PCC regardless of coagulation testing results.

	Antifibrinolytics		
	Indication	IV Dosing	PO Dosing
Aminocaproic acid	Excessive bleeding	5 g followed by 1 to 1.25 g hourly. This method of treatment would ordinarily be continued for about 8 hours or until the bleeding situation has been controlled. Administration of more than 30 g per 24 hours is not recommended.	5 g administered during the first hour of treatment. A continuing rate of 1 g (tablet) or 1.25 g (syrup) per hour. This method of treatment would ordinarily be continued for about 8 hours or until the bleeding situation has been controlled.
	Subarachnoid hemorrhage *(FDA off-label)*	Initiate therapy with 4 g IV as a loading dose, followed by a 1 g/h infusion for up to 72 hours after subarachnoid hemorrhage onset. Infusion should be discontinued 4 hours prior to angiography or 2 hours prior to endovascular ablation of the aneurysm.	
	Traumatic hyphema *(FDA off-label)*		50 mg/kg/dose every 4 hours (maximum daily dose: 30 g) for 5 days.
Tranexamic acid	Massive transfusion *(FDA off-label)*	1 g IV over 10 min followed by 1 g infusion over 8 hours within 8 hours of injury.	
	Subarachnoid hemorrhage *(FDA off-label)*	1 g IV immediately upon diagnosis followed by 1 g every 6 hours, not to exceed 72 hours after the initial bleed.	
	GI hemorrhage *(FDA off-label)*	3 to 6 g/day IV in divided doses every 6 to 8 hours for 2 to 3 days, followed by 3 to 6 g/day orally for an additional 3 to 5 days.	

	Monoclonal Antibody Fragment
	Dosing
Idarucizumab (Praxbind)	5 g IV x 1 (2 vials, each contains 2.5 g)

	Activated Charcoal
	Dosing
Charcoal	Initial dose: 50-100 g followed by 25-50 g PO every 4 hours.

Abbreviations	
APTT	activated partial thromboplastin time
CrCl	creatinine clearance
FFP	fresh frozen plasma
Hct	hematocrit
hrs	hours
IV	intravenous
kg	kilogram
LFTs	liver function tests
max	maximum
mg	milligram
min	minute
N/A	not applicable
PCC	prothrombin complex concentrate
Plt	platelets
PO	oral
PT	prothrombin time
QID	four times a day
TSOAC	target-specific oral anticoagulant
TT	thrombin time