UAB MEDICINE

Anticoagulant/Thrombolytic Reversal Guidelines

Bold=Formulary Agent

Drug	Elimination Half-life (T ½)	Removal by Hemodialysis (HD)	Reversal Strategies
Direct Factor Xa Inhibitors, Oral			
Apixaban (Eliquis®)	– 12 h (range 7-15) – Prolonged in renal impairment	No	– Activated charcoal: ▪ Apixaban – In healthy subjects administered 2 to 6 h after ingestion of a 20 mg dose reduced AUC by 50% and 27%, respectively ▪ Edoxaban – no information available; could likely be considered if within a few hours of dose ▪ Rivaroxaban –may be considered – Prothrombin Complex Concentrates (PCCs): ▪ If considered, Kcentra® 50 units/kg (maximum dose of 5,000 units) ▪ See PowerPlan titled "Oral Anticoagulant Reversal (Kcentra®, PCC, idarucizumab [Praxbind®]) – Coagulation Factor Xa, recombinant, inactivated-zhzo (Andexanet alfa; Andexxa®) ▪ Available for reversal of apixaban and rivaroxaban ○ For patients with intracranial hemorrhage (ICH), meeting criteria for use, and approval by stroke or neurosurgery attending ○ For patients with catastrophic bleeding complications (e.g., cardiac tamponade), meeting criteria for use, and approval by interventional cardiology or electrophysiology attending physicians ▪ For patients with poor survivability, consider PCC ▪ See Andexanet alfa Guidelines for Use on online UAB Formulary – Anti-Xa lab assay only useful for detecting presence of drug and cannot be used to accurately quantitate the level of drug
Edoxaban (Savaysa®)	– 10-14 h – Prolonged in renal impairment		
Rivaroxaban (Xarelto®)	– Infants <6 months: 1.6 h – Infants ≥6 months and Children <2 years: 1.9 h – Children ≥2 years: 3 h – Adolescents: 4.2 h – Healthy adults: 5-9 h – Elderly: 11-13 h – Prolonged in renal impairment		
Factor Xa Inhibitors, Parenteral			
Fondaparinux (Arixtra®)	– 17-21 h – Prolonged in renal impairment and in the elderly	Unlikely to be of value	– For uncontrollable bleeding: ▪ Consider rFVIIa (Novoseven®RT) 90 mcg/kg – Anti-Xa lab assay (specific to fondaparinux)
Direct Thrombin Inhibitors, Oral			
Dabigatran (Pradaxa®)	– 12-17 h – Significantly prolonged in renal impairment	Yes: ~60% Likely rebound upon cessation	– Activated charcoal: ▪ May be considered if 1-2 h after ingestion – Specific reversal agent: ▪ Idarucizumab (Praxbind®) 5 grams IV x 1 (supplied as two separate 2.5 gram vials from pharmacy) ○ Although data is limited, can consider re-dosing at 5 grams for refractory bleeding ○ May consider Kcentra® in place of or with idarucizumab – Consider HD for patients with refractory bleeding or especially in those with impaired renal function – Thrombin time can be used to assess presence of drug in circulation
Direct Thrombin Inhibitors, Parenteral			
Bivalirudin (Angiomax®)	– 25 min – Significantly prolonged in renal impairment	Yes: 25%; HD generally not practical	– Turn off the infusion – If concern for clearance of bivalirudin, may consider Kcentra® – aPTT lab assay is used to assess the degree of anticoagulation
Argatroban	– 30-51 min	Yes: 20%; HD	

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	– Prolonged in hepatic impairment	generally not practical	

Drug	Elimination Half-life (T ½)	Removal by Hemodialysis (HD)	Reversal Strategies
Heparins/Low Molecular Weight Heparins (LMWH)			
Enoxaparin (Lovenox®)	– 4.5-7 h – Prolonged in renal impairment	Unlikely to be of value	– Protamine partially neutralizes anti-Xa activity (~60% to 75%) Time since last dose: ≤ 8 h → 1 mg; 8-12 h → 0.5 mg; > 12 h → Not likely to be useful Maximum of 50 mg in 10 min period
Dalteparin (Fragmin®)	– 3-5 h – Prolonged in renal impairment		
Unfractionated Heparin	– ~ 1.5 h (T ½ of the anticoagulant effect)	No	– Protamine provides rapid reversal of anticoagulant effects (measured by anti-Xa activity) ▪ Only heparin given in preceding several hours needs to be considered when calculating dose of protamine (e.g. the previous 2-2.5 h if given as continuous infusion) ▪ Additional protamine administration may be necessary following cardiac surgery due to heparin rebound following initial protamine reversal in the OR. Usual dose range is 30-50 mg. Time since last dose: Immediate → 1 mg; 30 minutes – 2 hours → 0.5 mg; > 2 hours → 0.25 mg Maximum of 50 mg in a 10 min period
Vitamin K Antagonists			
Warfarin (Coumadin®)	– Single dose terminal: ~1 week – Effective T ½ = 20-60 h	No	Based on 2012 Chest Guidelines: – Any major/life-threatening bleeding ▪ 4-factor PCC (Kcentra®) AND Vitamin K 10 mg by slow IV injection (mixed in minimum 50 mL and given over at a rate not exceeding 1 mg/min [i.e. 10 mg over 10 min]) Pre-treatment INR → Kcentra® Dose: 2 to < 4 → 25 units/kg (Maximum 2,500 units); 4 – 6 → 35 units/kg (Maximum 3,500 units); >6 → 50 units/kg (Maximum 5,000 units) – INR between 4.5 and 10 and no evidence of bleeding – suggest against the routine use of vitamin K – INR > 10 and no evidence of bleeding – suggest oral vitamin K be administered Alternative recommendations: – INR > 4.5 and no evidence of bleeding: Vitamin K PO 1 – 2.5 mg – Minor bleeding: Vitamin K PO 2.5 – 5 mg (with possible repeat dose at 24h)
Thrombolytics			
Alteplase	– Initial: ~5 min – Following 90 min infusion: 27-46 min	No	– Discontinue thrombolytic agent – Thrombolytic-associated symptomatic intracranial hemorrhage

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Tenecteplase	– Initial: 20-24 min – Terminal: 90-130 min		▪ Consider cryoprecipitate (10 units initial dose; 1 bag = 5 units) to a goal fibrinogen >150 mg/dL in patients who have received thrombolytic agent in the previous 24 hours ▪ If cryoprecipitate is contraindicated, consider aminocaproic acid 4-5 g IV over 1 hour, then a continuous infusion at a rate of 1 g/h for ~8 hours or until the bleeding is controlled, or tranexamic acid 10-15 mg/kg IV over 20 mins ▪ Consider platelet transfusion for platelet counts < 100k

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