UAB MEDICINE

Antithrombotic/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	▪ Prothrombin Complex Concentrates (PCCs) ○ See order set titled "Oral Anticoagulant Reversal (PCC, Kcentra) coagulation factor Xa (Andexxa), idaruCIZumab (Praxbind)" ○ Guideline-directed, one time, fixed-dose PCC (Kcentra) reduces door to treatment time while maintaining hemostatic effectiveness • If fixed dosing considered, PCC 2000 units for one dose; an additional, one-time dosage of PCC 500 units allowed within 24 hours of first dosage if hemostatic control not achieved, as defined by the treating clinician • See Prothrombin Complex Concentrate (PCC) Guidelines for Use on online UAB Formulary ➢ If weight-based dosing requested by provider, administer PCC 50 units/kg (maximum dose of 5000 units) ▪ 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	Unlikely to be of value	▪ For uncontrollable bleeding: ○ Consider rFVIIa (NovoSeven RT) 90 mcg/kg ▪ Anti-Xa lab assay (specific to fondaparinux) ○ Consideration: this is a send out lab and results will be delayed
Direct Thrombin Inhibitors, Oral			
Dabigatran (Pradaxa)	— Adults: 12-17 h — Pediatrics: 12-14 h (capsules), 9-11 h (oral pellets) — Elderly: 14-17 h — Significantly prolonged in renal impairment	Yes: ~60% Likely rebound upon cessation	▪ Specific reversal agent: ○ Idarucizumab (Praxbind) 5 grams IV for one dose (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 fixed-dose PCC (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)	— Adults: 25 min — Pediatrics: 15-18 min — Significantly prolonged in renal impairment (34-57 min)	Yes: 25%; HD generally not practical	▪ Turn off the infusion ▪ If concern for clearance of bivalirudin, may consider fixed-dose PCC (Kcentra) ▪ aPTT lab assay is used to assess the degree of anticoagulation
Argatroban	— 39-51 min — Prolonged in hepatic impairment	Yes: 20%; HD	

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<table>
<tr><th>Drug</th><th>Elimination Half-life (T ½)</th><th>Removal by Hemodialysis (HD)</th><th>Reversal Strategies</th></tr>
<tr><td></td><td></td><td>generally not practical</td><td></td></tr>
<tr><td colspan="4">Heparins/Low Molecular Weight Heparins (LMWH)</td></tr>
<tr><td>Enoxaparin (Lovenox)</td><td>— 4.5-7 h
— Prolonged in renal impairment</td><td rowspan="2">Unlikely to be of value</td><td>▪ Protamine partially neutralizes anti-Xa activity (~60% to 75%)
Reversal guidance for protamine with LWMH agents (for treatment-dosed LMWH in the presence of clinically significant bleeding)
<table>
<tr><th>Time since last dose</th><th colspan="2">Dose of protamine for each 1 mg of enoxaparin or 100 units of dalteparin</th></tr>
<tr><td>≤ 8 h</td><td>1 mg</td><td rowspan="3">Maximum of 50 mg in 10 min period</td></tr>
<tr><td>8-12 h</td><td>0.5 mg</td></tr>
<tr><td>> 12 h</td><td>Not likely to be useful</td></tr>
</table></td></tr>
<tr><td>Dalteparin (Fragmin)</td><td>— 3-5 h
— Prolonged in renal impairment</td></tr>
<tr><td>Unfractionated Heparin, IV</td><td>— ~ 1.5 h
(T ½ of the anticoagulant effect)</td><td>No</td><td>▪ 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 2-3 h if given as continuous infusion)
• If required, 1 mg of protamine will neutralize ~100 units of heparin – maximum dose of 50 mg
• If aPTT remains elevated, consider repeating 0.5 mg per 100 units of heparin – maximum dose 25 mg
○ Additional protamine administration may be necessary following cardiac surgery due to heparin rebound following initial protamine reversal in the OR. Usual dose range is 25-50 mg
Reversal guidance for protamine with IV heparin boluses, if indicated:
<table>
<tr><th>Time since last dose</th><th colspan="2">Dose of protamine for each 100 units of heparin</th></tr>
<tr><td>Immediate</td><td>1 mg</td><td rowspan="3">Maximum of 50 mg in a 10 min period</td></tr>
<tr><td>30 minutes to ≤ 2 hours</td><td>0.5 mg</td></tr>
<tr><td>> 2 hours up to 3 hours</td><td>0.25 mg</td></tr>
</table></td></tr>
<tr><td>Unfractionated Heparin, subcutaneous</td><td>— ~ 1.5 h
(T ½ of the anticoagulant effect)</td><td>No</td><td>▪ Reversal of prophylactic subcutaneous heparin is generally not recommended; however, may consider if aPTT significantly prolonged and patient has clinically significant bleeding
○ If required, 1 mg of protamine will neutralize ~100 units of heparin – maximum dose of 50 mg</td></tr>
<tr><td colspan="4">Vitamin K Antagonists</td></tr>
</table>

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Warfarin (Coumadin)	— Single dose terminal: ~1 week — Effective T ½ = 20-60 h	No	Based on 2022 Chest Guidelines: ▪ Any major/life-threatening bleeding ○ Fixed-dose PCC (Kcentra) 2000 units AND Vitamin K 10 mg by slow IV injection (mixed in minimum 50 mL and given over a rate not exceeding 1 mg/min [i.e., 10 mg over 10 min]) • An additional, one-time dosage of PCC 500 units allowed within 24 hours of first dosage if hemostatic control not achieved, as defined by the treating clinician Guidance for utilization of vitamin K in the presence of elevated INR and non-life-threatening bleeding: ▪ INR above therapeutic range but < 4.5 and no evidence of bleeding: routine administration of vitamin K is not recommended ▪ INR between 4.5 and 10 and no evidence of bleeding: suggest against the routine use of vitamin K, but if administered, one dose of vitamin K PO 1 – 2.5 mg is recommended ▪ INR > 10 and no evidence of bleeding: suggest oral vitamin K be administered; one dose PO 2 – 5 mg is recommended (may administer a second dose if INR recheck remains elevated) ▪ 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 ○ 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 – usual dose is 1000 mg IV once over 20 mins ○ Consider platelet transfusion for platelet counts < 100k
Tenecteplase	— Initial: 20-24 min — Terminal: 90-130 min		
Antiplatelets, Oral and Parenteral			
Aspirin	— 3.5-4.5 h	Yes; unlikely to be of value if not for salicylate toxicity	▪ Desmopressin IV 0.4 mg/kg IV once may be beneficial in reversal of aspirin, clopidogrel, prasugrel, ticagrelor, naproxen, or ibuprofen ▪ Platelet transfusion is recommended ONLY if sending for a neurosurgical procedure for ICH related to aspirin or an ADP inhibitor (clopidogrel, prasugrel, or ticagrelor) – not NSAIDs ○ Platelet pheresis 1 Unit STAT
ADP Inhibitors (e.g., clopidogrel, prasugrel, ticagrelor)	— 6 h (clopidogrel) — ~7 h; range 2-15 h (prasugrel) — 7 h (ticagrelor)	No	

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NSAIDs (e.g., ibuprofen, naproxen)	— ~2 h (ibuprofen) — 2-4 h (naproxen)	No	• When possible, test platelet function prior to platelet transfusion – not recommended for normal platelet function or documented antiplatelet resistance ▪ Platelet transfusion NOT recommended for GP 2b/3a inhibitors (eptifibatide, tirofiban) or non-ADP inhibitors (anagrelide, cilostazol, dipyridamole, and vorapaxar)
GP 2b/3a inhibitors (**eptifibatide,** tirofiban)	— 2.5 h (eptifibatide)	Yes; ~73-83% removed after 1 h	
Non-ADP inhibitors (e.g., anagrelide, cilostazol, dipyridamole, vorapaxar**)**	— 1.3 h (anagrelide) — 11-13 h (cilostazol) — 10 h (dipyridamole)	No	
Cangrelor (Kengreal)	— 3-6 min	No	▪ Turn off the infusion ○ Upon discontinuation of cangrelor, platelet function rapidly returns to baseline (within 1 hour); however, residual activity from other concurrently administered antiplatelet agents (e.g., aspirin, clopidogrel, ticagrelor) may persist ▪ Clinicians should assess the overall antiplatelet burden and evaluate the need for additional reversal strategies

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