Anticoagulant & Antiplatelet Medication Reversal

1: Identify the medication 2: Stop the medication 3: Confirm time of last dose

Emergent- Life threatening bleeding- Immediate action needed:
Hold anticoagulants and consider giving a specific antidote and/or a pro-coagulant agent (see table below) Consider laboratory analysis for baseline values and if necessary to modify the therapy. Therapy may be initiated prior to lab results being posted

Urgent-non-life-threatening bleeding- potential intervention within 6-12 hours:
hold anticoagulants and consider giving a specific antidote and/or a pro-coagulant agent (see table below) Consider laboratory analysis for baseline values and if necessary to modify the therapy.

Non-urgent- non-bleeding patient- 12-24 hours or greater**:**
Hold the anticoagulant. Consider additional laboratory analysis and reassess bleeding risks.

Drug: Agent Type	Monitor	Half-life (t1/2)	Reversal Recommendation	Administration /Miscellaneous
Vitamin K antagonist: Coagulation factors II, VII, IX, X; anticoagulant proteins C, S	Monitor PT/INR	20-60 hrs	Determine risk (emergent, urgent, non-urgent for appropriate intervention) • **Non-urgent:** Hold the anticoagulant. Consider additional laboratory analysis and reassess bleeding risks. Consider Vitamin K 10 mg PO x 1 based on INR. • **Urgent:** Phytonadione (Vitamin K) 10 mg IV over 30 minutes ○ *Vit K ALONE can significantly reverse the INR within change to 6-8 hours) so should be considered as sole agent if no intervention is needed until that time.* • **Emergent:** PCC 4 factor (Kcentra) 1500 units IV **PLUS** vitamin K 10 mg IV over 30 minutes ○ Dose may be repeated (max 5000 units)	• FFP: *plasma can be used if 4FPCC is unavailable.* ○ FFP may require 2 or more adult doses for total reversal and may exceed 6 hours ▪ *single adult plasma dose = 10-15ml/kg* • If INR remains elevated post single dose and/or the patient is still experiencing uncontrolled bleeding, redosing of PCC can be considered. Max dose is 5000 units. Redosing of Vitamin K is rarely indicated, but may be given after 12 hours of original dose.
Anticoagulant: Heparin (UFH); binds to antithrombin; inactivates Xa; inactivates IIa; indirect thrombin inhibitor	aPTT Platelets	90 minutes	• 1mg protamine/100 units of IV heparin infused over 10 mins; max dose = 50mg protamine repeating to calculated amount	• IV slowly ~over 10 mins • Beware anaphylactoid reaction; >50mg/dose
Anticoagulant: enoxaparin (Lovenox; LMWH); binds to antithrombin; inactivates Xa	aPTT Monitor anti-Xa; platelets	7-12 hrs ~ upon renal function	• Activity 60% neutralized by protamine; ≤ 8hrs; give 1mg protamine/mg enoxaparin. Last dose > 8hrs - give 0.5mg protamine/1mg enoxaparin • Second dose needed: 0.5mg protamine/1mg of enoxaparin 2-4 hrs after the first.	• See UFH
Anticoagulant: fondaparinux (Arixtra); binds to antithrombin; inactivates Xa; a heparinoid.	Monitor platelets anti-Xa; thrombocytopenia is rare.	17-21 hours	• None • *(None of the following products has been shown to reduce bleeding in these pts; however, there is no direct antidote for fondaparinux)*	• Supportive care; blood components, • PCC 4 factor (Kcentra contains heparin) 25units/kg with repeat dose of 25 units/kg(max 5000 units)
Thrombolytic: recombinant tissue plasminogen activator	Monitor neurologic exam; PT and aPTT, fibrinogen, platelets.	~5min	• TXA 1gm IV bolus over 10 mins followed by 1gm gtt over 8 hours • 1 Cryoprecipitate dose *(1 adult dose = 5 pooled units)* • Platelets *(single adult dose= 1 unit)*	If TXA contraindicated- use Amicar (contact pharmacy for dosing) Keep fibrinogen ≥150 mg/dl
Factor Xa inhibitor: oral 1. Rivaroxaban (Xarelto) 2. Apixaban (Eliquis) 3. Edoxaban (Savaysa) 4. Betrixaban (Bevyxxa)	**PT**/INR (if normal, less likely that drug is contributing to ongoing bleeding)	1) 5-9 hrs & elderly 11-13 hrs 2) 8-15 hrs 3) 9-11 hrs 4) 19-25 hrs	• **Vitamin K is NOT effective** • Supportive care • PCC 4 factor (Kcentra contains heparin) 25 units/kg with repeat dose of 25 units/kg if needed(max 5000 units; *off label-but is an option in life threatening situation.*)	• If initial interventions do not control bleeding, consider: ○ Consider Plasma *(adult dose =15ml/kg)*
Oral platelet inhibitors: 1. Clopidogrel (Plavix- $P2Y_{12}$) 2. Prasugrel (Effient -$P2Y_{12}$) 3. Ticagrelor (Brilinta-$P2Y_{12}$) 4. Vorapaxar (Zontivity -Par1)	Monitor bleeding, Hct, platelet function testing.	1) ~ 6 hrs 2) ~ 7 hrs 3) ~ 7 hrs 4) ~ 8 **days**	• Platelets • *Start with single unit (single unit= 1 adult dose)* • *Utility of platelet transfusion in critical bleeding patients remains under investigation.* • DDAVP (caution: fluid overload) 0.3 mcg/kg IV x 1	• Platelet count > 50 for major surgery/100k for neurosurgical/ophthalmic. • DDAVP 0.3 mcg/kg in 50ml NS over 15-30 mins • Platelet transfusions have not been shown to improve clinical outcomes; however, the recommendations provided are based on the most recent neuro/critical care guidelines.
Direct thrombin inhibitor: (oral) dabigatran (Pradaxa)	APTT: (if normal, less likely that drug is contributing to ongoing bleeding)	(t1/2=12-17 hours but much longer with renal impairment)	• Idarucizumab 5g, provided as two separate vials each containing 2.5g/50ml; give one after the other. Limited data supports administration of an additional 5g of idarucizumab (Praxbind)	

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