

Name	Mechanism	Reversal Agent/Dose	Comments/Ref
Vitamin K Antagonist			
warfarin (Coumadin)	Blocks conversion of Vit K & activation of Vit K-dependent factors FII, FVII, FIX, FX	Kcentra (4-factor PCC: FII, FVII, FIX, FX) + Vitamin K 10 mg IV Consider Heme consult Consider FFP, platelets or cryo Consider rFVIIa	½ life = 40 hrs Hirsh J, et al. AHA/ACC Foundation guide to warfarin therapy. Circulation 2003 Hanley JP. Warfarin reversal. J Clin Pathol 2004 Lin Y, et al. Emergency reversal of warfarin anticoagulation. CMAJ 2010 Yee J, et al. Emergency reversal of anticoagulation. West J Emerg Med 2019 Peck KA, et al. Early anticoagulant reversal after trauma_ A WTA critical decisions algorithm. JTACS 2021
Unfractionated Heparin & Low-Molecular-Weight-Heparins			
unfractionated heparin	Activates ATIII, inactivates thrombin (FIIa) & factor Xa	Protamine (consult Pharmacy for dose)	½ life = 1-2 hrs Hold IV heparin 4 hrs & SQ 12 hrs before operation Resume in 12-48 hrs Yee J, et al. Emergency reversal of anticoagulation. West J Emerg Med 2019
enoxaparin (Lovenox)	Inhibit FXa > FIIa	Protamine (consult Pharmacy for dose) Consider dialysis Consider rFVIIa	½ life = 4.5 hrs Hold 12 hrs prior to MAJOR operation Iqbal Z, et al. Enoxaparin: a pharmacologic and clinical review. Expert Opin Pharmacother 2011 Gordon JL, et al. Anticoagulant & antiplatelet medications encountered in emergency surgery patients: a review of reversal strategies. J Trauma 2013 Thomas S, et al. The reversal of anticoagulation in clinical practice. Clin Med (Lond) 2018
fondaparinux (Arixtra)	Inhibits FXa	Protamine ineffective Consider Kcentra Consider rFVIIa	½ life = 17-21 hrs Ansani NT. Fondaparinux: the 1 st pentasaccharide anticoagulant. P&T 2002 Nagler M, et al. Fondaparinux – data on efficacy and safety in special situations. Thromb Res 2012 Thomas S, et al. The reversal of anticoagulation in clinical practice. Clin Med (Lond) 2018

Kcentra - contains FII, FVII, FIX, FX, protein C & S

rFVIIa = recombinant factor VII activated

Name	Mechanism	Reversal Agent/Dose	Comments/Ref
Factor Xa Inhibitors (DOACs, previously NOACs)			
apixaban (Eliquis)	Inhibits FXa	Kcentra (based on reports of similar reversal to Xarelto) Andexanet Alfa ³ (Not on WakeMed formulary – yet) Consider Heme consult Consider activated charcoal	½ life = 10-14 hrs 1. Baumann Kreuziger LM, et al. New anticoagulants: a concise review. J Trauma 2012 2. Moorman ML, et al. Emergency surgery & trauma in patients treated with the new oral anticoagulants: dabigatran, rivaroxaban, & apixaban. J Trauma 2014 3. Siegal, DM et al Andexanet Alfa for the Reversal of Factor Xa Inhibitor Activity. NEJM 2015 4. Yee J, et al. Emergency reversal of anticoagulation. West J Emerg Med 2019
rivaroxaban (Xarelto)	Inhibits FXa	Kcentra ³ Andexanet Alfa ⁴ (Not on WakeMed formulary – yet) Consider Heme consult Consider TXA Consider activated charcoal	½ life = 5-9 hrs (>13 hrs with impaired renal function) 1. Baumann Kreuziger LM, et al. New anticoagulants: a concise review. J Trauma 2012 2. Moorman ML, et al. Emergency surgery & trauma in patients treated with the new oral anticoagulants: dabigatran, rivaroxaban, & apixaban. J Trauma 2014 3. Baumann Kreuziger LM, et al. Management of the bleeding patient receiving new oral anticoagulants_ a role for prothrombin complex concentrates. Biomed Res Int 2014 4. Siegal, DM et al Andexanet Alfa for the Reversal of Factor Xa Inhibitor Activity. NEJM 2015 5. Yee J, et al. Emergency reversal of anticoagulation. West J Emerg Med 2019
edoxaban (Savaysa)	Inhibits FXa	No specific reversal agent Kcentra Consider Heme consult Consider rFVIIa Activated charcoal if dose within 2 hrs	½ life = 10-14 hrs Hold 24 hrs prior to procedure, 48 hrs for high risk, 72 hrs for neuraxial block & 20-24 hrs for catheter removal. Resume >6 hrs after catheter removal. Yee J, et al. Emergency reversal of anticoagulation. West J Emerg Med 2019

rFVIIa = recombinant factor VII activated

Kcentra - contains FII, FVII, FIX, FX, protein C&S

TXA = tranexamic acid - Adapted from controversial CRASH-2 trial (2010) - TXA affords significant reduction in all-cause mortality in trauma patients with significant hemorrhage

Name	Mechanism	Reversal Agent/Dose	Comments/Ref
Direct Thrombin Inhibitors			
hirudin (lepirudin, desirudin) - IV	Isolated from leech saliva	Remove the leech No specific reversal agent Stop infusion Consider FFP Consider dDAVP Consider Heme consult Consider Kcentra Consider dialysis	½ life = 1-2 hrs Schulman S, et al. Anticoagulants & their reversal. Transfus Med Rev 2007
argatroban - IV	Binds free & clot-bound thrombin, prevents conversion of fibrinogen to fibrin	No specific reversal agent Stop the infusion Consider FFP Consider dDAVP Consider Heme consult Consider Kcentra Consider dialysis	½ life = 45-50 min Schulman S, et al. Anticoagulants & their reversal. Transfus Med Rev 2007
bivalirudin (Angiomax) - IV	Binds free & clot-bound thrombin, prevents conversion of fibrinogen to fibrin	No specific reversal agent Stop the infusion Consider FFP Consider dDAVP Consider Heme consult Consider Kcentra Consider dialysis	½ life = 25 min Schulman S, et al. Anticoagulants & their reversal. Transfus Med Rev 2007
dabigatran (Pradaxa) - po	Binds free & clot-bound thrombin (factor IIa), prevents conversion of fibrinogen to fibrin	Idarucizuma (Praxbind) Consider charcoal Consider dialysis Consider Kcentra Consider rFVIIa Consider TXA	½ life = 14-17 hrs (>18 hrs in elderly) Moorman ML, et al. Emergency surgery & trauma in patients treated with the new oral anticoagulants: dabigatran, rivaroxaban, & apixaban. J Trauma 2014 Pollack CV, et al. Idarucizumab for Dabigatran Reversal. N Engl J Med 2015; 373:511-520

dDAVP = 1-desamino-8-dextro-arginine vasopressin

FFP = fresh frozen plasma, less favorable to Kcentra (25x less concentration of coagulation factors, requires large volume, requires thawing, etc...)

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TXA = tranexamic acid

Name	Mechanism	Reversal Agent/Dose	Comments/Ref
Antiplatelet Agents			
acetylsalicylic acid (ASA)	Inhibits platelet aggregation	No specific reversal agent (irreversible for the life of the platelet ~ 10 days) Consider platelet transfusion Consider dDAVP 0.3 mcg/kg	Hold aspirin 5-10 days before elective surgery Cahill RA, et al. Duration of increased bleeding tendency after cessation of aspirin therapy. JACS 2005 Taylor G, et al. Is platelet transfusion efficient to restore platelet reactivity in patients who are responders to aspirin and-or clopidogrel before emergency surgery. J Trauma 2013
Dipyridamole (Persantine) (Aggrenox = ASA & dipyridamole)	Reversible Phosphodiesterase inhibitor	Consider platelet transfusion Consider dDAVP 0.3 mcg/kg	
ticlopidine (Ticlid) 1 st generation thienopyridine	Inhibits platelet aggregation	No specific reversal agent (irreversible for the life of the platelet ~ 10 days) Consider platelet transfusion Consider dDAVP	Hold 5-7 (or more) days before surgery Associated with blood dyscrasias Replaced by Plavix
clopidogrel (Plavix) 2 nd generation thienopyridine	Inhibits platelet aggregation	No specific reversal agent (irreversible for the life of the platelet ~ 10 days) Consider platelet transfusion Consider rFVIIa Consider dDAVP 0.3 mcg/kg	Hold 5-7 (or more) days before surgery Grujic D, et al. Perioperative clopidogrel is 7 days enough? Am Surg 2009 Taylor G, et al. Is platelet transfusion efficient to restore platelet reactivity in patients who are responders to aspirin +/-or clopidogrel before emergency surgery? J Trauma 2013 Gleason LJ, et al. Preoperative management of anticoagulation & antiplatelet agents. Clin Geriatr Med 2014 Joseph B, et al. Clinical outcomes in traumatic brain injury patients on preinjury clopidogrel: a prospective analysis. J Trauma 2014 Patel PA, et al. Aspirin, clopidogrel, and the surgeon. Adv Surg 2014
prasugrel (Effient) 3 rd generation thienopyridine	Inhibits platelet aggregation	No specific reversal agent (irreversible for the life of the platelet ~ 10 days) Consider platelet transfusion Consider rFVIIa Consider dDAVP 0.3 mcg/kg	Hold 5-7 (or more) days before surgery Cattaneo M. Update on antithrombotic therapy; new P2Y ₁₂ inhibitors. Circulation 2010
ticagrelor (Brilinta) cyclopentyltriazolopyrimidine	Reversible platelet inhibition	No specific reversal agent Consider platelet transfusion Consider rFVIIa Consider dDAVP 0.3mcg/kg	½ life = 7 hrs Hold 5 days before surgery Wallentin L, et al. Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes. NEJM 2009 Cannon CP, et al. Comparison of ticagrelor with clopidogrel in patients with a planned invasive strategy for acute coronary syndromes (PLATO)_ a randomised double-blind study. Lancet 2010

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Name	Mechanism	Reversal Agent/Dose	Comments/Ref
Glycoprotein IIb/IIIa Inhibitors			
abciximab (ReoPro)	Inhibit GpIIb/IIIa platelet receptor	Stop the infusion Consider platelet transfusion	½ life ~ 10 min
eptifibatide (Integrillin)	Inhibit GpIIb/IIIa platelet receptor	Stop the infusion Platelet transfusion + 10 units cryo Consider dDAVP 0.3 mcg/kg Consider dialysis	½ life ~ 2.5 hrs
tirofiban (Aggrastat)	Inhibit GpIIb/IIIa platelet receptor	Stop the infusion Platelet transfusion + 10 units cryo Consider dDAVP 0.3 mcg/kg Consider dialysis	½ life ~ 2 hrs

dDAVP = 1-desamino-8-dextro-arginine vasopressin