

ANTICOAGULANT AND ANTIPLATELET REFERENCE: Focus on Periprocedural Management & Reversal Strategies

GENERIC NAME (BRAND NAME) & MEDICATION CLASS	USUAL DOSE AND ROUTE OF ADMINISTRATION	RENAL AND HEPATIC DOSE ADJUSTMENTS	ELIMINATION HALF-LIFE	RECOMMENDATIONS FOR HOLDING PRIOR TO MAJOR PROCEDURES OR SURGERY	RECOMMENDATIONS FOR HOLDING FOR SPINAL ANESTHESIA/EPIDURALS	REVERSAL
<p>apixaban (Eliquis)</p> <p>anticoagulant; oral factor-Xa inhibitor</p>	<p>Atrial fibrillation: 5 mg BID; PO</p> <p>DVT/PE: 10 mg BID for 7 days, then 5 mg BID; PO</p> <p>Recurrent DVT/PE prophylaxis: 2.5 or 5 mg BID; PO</p> <p>Post-op prophylaxis: 2.5 mg twice daily; PO (starting 12 to 24 hours postop)</p>	<p>Atrial fibrillation: 2.5 mg twice daily in patients who have ≥ 2 of the following: ≥ 80 years, $TBW \leq 60$ kg, $SCr \geq 1.5$ mg/dL or on hemodialysis</p> <p>DVT/PE treatment and prophylaxis: No dose adjustment but patients with $SCr > 2.5$ mg/dL or $CrCl < 25$ mL/min excluded from trials</p> <p>Post-op prophylaxis: $CrCl < 30$ ml/min: Avoid use (excluded from trials)</p> <p>Use not recommended in severe hepatic impairment (Child-Pugh Class C)</p> <p>See DOAC Drug Interaction Document for guidance on specific drug-drug interactions</p>	<p>12 hours (reports up to 26 hours)</p>	<ul style="list-style-type: none"> • Procedure has unknown, moderate, or high risk of bleeding; patient has moderate-high bleed risk, $CrCl < 30$ mL/min (not on HD or reduced dose): discontinue at least 48 hours prior to surgery • Procedure has low risk of bleeding, bleeding can be easily controlled, patient has low bleed risk: discontinue at least 24 hours prior to surgery <p>May restart once adequate hemostasis established (onset of action 3-4 hours)</p>	<p>Hold 72 hours prior to neuraxial block; if prophylaxis dosing or unanticipated administration with indwelling catheter, hold 26-30 hours prior to catheter manipulation or withdrawal. Indwelling spinal or intrathecal catheters must be removed at least 6 hours prior to the first dose of apixaban. If traumatic puncture occurs, delay apixaban administration for 48 hours.</p>	<p>4-factor PCC (PCC>rFVIIa), charcoal if dose given within previous 2 hours; supportive care</p> <p>**Use "Anticoagulation Reversal Orders" in Epic**</p>

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bivalirudin (Angiomax) anticoagulant; parenteral direct thrombin inhibitor	Percutaneous intervention (PCI): 0.75 mg/kg IV bolus followed by 1.75 mg/kg/hour (may continue up to 4 hours post-procedure) Heparin-induced thrombocytopenia: 0.15 mg/kg/hour (adjusted based on aPTT); intravenous	CrCl <30 mL/min or on dialysis: PCI: 1 mg/kg/hour HIT: 0.06 mg/kg/hour No dose adjustment needed for hepatic impairment	25 minutes (up to 1 hour in renal impairment not on dialysis; 3.5 hours in dialysis)	Hold for at least 1 hour prior to procedure; may restart 2 hours after surgery if hemostasis achieved	Hold at least 1 hour prior to procedure (can consider checking aPTT) or prior to catheter removal; may restart 2 hours after catheter removal	No specific reversal agent; supportive care; maybe rFVIIa (use generally not recommended)
clopidogrel (Plavix) antiplatelet; oral P2Y12 inhibitor	75 mg daily; PO	No adjustment necessary	~6 hours; platelet function restored in ~5 days	Hold 5-10 days prior to procedure; may restart 24 hours after surgery if hemostasis achieved	Hold 5-7 days prior to procedure; may restart 6 hours after catheter removal (may restart immediately if no loading dose given)	no specific reversal agent; supportive infusions, case reports of using DDAVP, maybe rFVIIa (may have limited/no benefit, use generally not recommended)

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<p>dabigatran (Pradaxa)</p> <p>anticoagulant; oral direct thrombin inhibitor</p>	<p>Atrial fibrillation: 150 mg twice daily; PO</p> <p>DVT/PE: 150 mg twice daily (after 5-10 days parenteral anticoagulation)</p> <p>Post-op prophylaxis: 110 mg 1-4 hours after surgery or 220 mg >24 hours after surgery when hemostasis achieved</p>	<p>Atrial fibrillation: CrCl 15-30 ml/min or when used with certain P- gp inhibitors: 75 mg PO BID CrCl < 15 ml/min or HD, or CrCl 15-30 mL/min with concomitant P-gp inhibitors: Use not recommended</p> <p>DVT/PE: CrCl ≤ 30 mL/min or HD excluded from trials CrCl ≤50 mL/min with P-gp inhibitors: Avoid use</p> <p>See DOAC Drug Interaction Document for guidance on specific drug-drug interactions</p>	<p>12-17 hours (up to 34 hours in renally impaired)</p>	<ul style="list-style-type: none"> • CrCl ≥50 mL/min: Hold 1-2 days prior to procedure • CrCl <50 mL/min: Hold 3-5 days prior to procedure <p>*May consider longer times for major surgery or spinal surgery/puncture</p> <p>May restart when full anticoagulation deemed safe (therapeutic anticoagulation will occur 0-2 hours after administration)</p>	<ul style="list-style-type: none"> • Hold a minimum of 120 hours (~5 days) prior to catheter manipulation or withdrawal if renal function not reliably determined <p>If renal function known:</p> <ul style="list-style-type: none"> • CrCl 30-40 mL/min: hold at least 120 hours • CrCl 50-70 mL/min: hold at least 96 hours • CrCl ≥80 mL/min: hold at least 72 hours <p>Neuraxial block not recommended if CrCl <30 mL/min on dabigatran pre-procedure; ; if unanticipated administration with indwelling catheter, hold for 34-36 hours prior to catheter removal; avoid use while catheter in place; may restart when full anticoagulation deemed safe, usually 6-8 hours after atraumatic puncture/ removal or 24 hours after traumatic procedures (therapeutic anticoagulation will occur 0- 2 hours after administration)</p>	<p>Praxbind® (idarucizumab)-specific reversal agent; charcoal if dose given within previous 2 hours; hemodialysis if major hemorrhage or overdose (limited evidence); limited literature with PCC (may use if Praxbind not available) maybe rFVIIa (may have limited/no benefit, use generally not recommended)</p> <p>**Use "Anticoagulation Reversal Orders" in Epic**</p>

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<p>edoxaban (Savaysa)</p> <p>anticoagulant; oral factor-Xa inhibitor</p>	<p>Atrial fibrillation: 60 mg daily; PO</p> <p>DVT/PE: 60 mg daily; PO (after 5-10 days parenteral anticoagulation)</p>	<p>Atrial fibrillation CrCl 15-50 ml/min: 30 mg daily CrCl > 95 ml/min: Avoid use</p> <p>DVT/PE: 30 mg daily if the patient has any of the following: CrCl 15-50 mL/min, TBW ≤60 kg, certain P-gp inhibitors</p> <p>Use not recommended if moderate or severe hepatic impairment (Child-Pugh Class B or C)</p> <p>See DOAC Drug Interaction Document for guidance on specific drug-drug interactions</p>	10-14 hours	<ul style="list-style-type: none"> Discontinue edoxaban at least 24 hours prior to procedures May hold at least 48 hours if unknown or high bleeding risk <p>Restart when adequate hemostasis established (onset 1-2 hours)</p>	<p>Hold at least 72 hours prior to neuraxial block; if unanticipated administration with indwelling catheter, hold for 20-28 hours prior to catheter removal Hold the next dose of edoxaban at least 6 hours after removal of the catheter.</p>	<p>4-factor PCC (PCC>rFVIIa),; charcoal if dose given within previous 2 hours; supportive care</p> <p>**Use "Anticoagulation Reversal Orders" in Epic**</p>
<p>enoxaparin (Lovenox)</p> <p>anticoagulant; low-molecular weight heparin</p>	<p>Therapeutic dose: 1 mg/kg twice daily or 1.5 mg/kg once daily; SUBQ</p> <p>DVT prophylaxis: 40 mg daily (or 30 mg twice daily for hip fracture or TKA)</p>	<p>Therapeutic dose: CrCl<30 ml/min: 1 mg/kg once daily</p> <p>DVT prophylaxis: CrCl <30 mL/min: 30 mg daily</p>	4.5 to 7 hours (longer if renally impaired)	<p>Hold 24 hours prior to procedure</p> <p>May restart 24-72 hours after surgery if hemostasis achieved (peak effect 3-5 hours after dose)</p>	<p>Prophylaxis: hold at least 12 hours before needle placement</p> <p>Therapeutic: hold at least 24 hours before needle placement (may consider anti-Xa level)</p> <p>Avoid use while catheter in place; may restart 4 hours after removal of the catheter or at least 24 hours after catheter placement (whichever is greater)</p> <p>If CrCl <30 mL/min, remove catheter at least 24 hours after last prophylactic doses & at least 48 hours after treatment doses</p>	<p>Protamine neutralizes ~60% of the drug; consider hemodialysis if major hemorrhage or overdose; supportive care, rFVIIa if contraindication to protamine or refractory bleeding (limited evidence)</p> <p>**Use "Anticoagulation Reversal Orders" in Epic**</p>

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<p>fondaparinux (Arixtra)</p> <p>anticoagulant; parenteral factor Xa inhibitor</p>	<p>DVT prophylaxis: 2.5 mg daily; SUBQ (contraindicated in patients <50 kg)</p> <p>DVT/PE treatment: <50 kg: 5 mg daily 50-100 kg: 7.5 mg daily >100 kg: 10 mg daily</p>	CrCl < 30 ml/min: Contraindicated	17-21 hours (longer if renally impaired and in elderly)	hold 24 hours prior to procedure although effects may persist for 2-4 days after discontinuation (longer in renal impairment); may restart 6-8 hours after surgery if hemostasis achieved	hold a minimum of 36-42 hours prior to procedure; avoid use while catheter in place; may restart 6 hours after catheter removal (if placement was atraumatic and single-pass) or 12 hours after catheter removal that does not meet these criteria	no specific reversal agent; supportive care; PCC or maybe rFVIIa (if PCC contraindicated or unavailable)
<p>Heparin</p> <p>anticoagulant</p>	Variable based on indication (see ACS and Afib/VTE/Other panels in Epic for specific dosing), weight; IV or SUBQ	May adjust according to anti-Xa	1.5 hours (IV)	Hold 4-6 hours prior to procedure; may restart when hemostasis achieved	<p>Intravenous heparin:</p> <ul style="list-style-type: none"> Discontinue 4-6 hours (consider sending anti-Xa) prior to neuraxial blockade Remove indwelling catheters 4-6 hours after last heparin dose (consider anti-Xa level) May resume heparin 1 hour after catheter removal <p>Subcutaneous heparin:</p> <p><i>Prophylaxis:</i></p> <ul style="list-style-type: none"> 5000 units BID-TID (low-dose): neuraxial block 4-6 hours after heparin; remove catheter 4-6 hours after heparin; may be continued while catheter is in place; resume heparin 1 hour after catheter removal 7500-10000 units BID: neuraxial block 12 hours after heparin <p><i>Treatment (>20,000 units total daily dose):</i> Neuraxial block 24 hours after heparin</p>	<p>protamine; supportive care; maybe rFVIIa (use generally not recommended)</p> <p>**Use "Anticoagulation Reversal Orders" in Epic**</p>

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<p>prasugrel (Effient)</p> <p>antiplatelet; oral P2Y12 inhibitor</p>	<p>10 mg daily; PO</p> <p>May consider 5 mg daily in patients <60 kg and/or ≥ 75 years</p>	<p>No adjustment necessary</p>	<p>~7 hours; platelet function restored in ~7 days</p>	<p>hold 7-10 days prior to procedure; may restart 24 hours after surgery if hemostasis achieved</p>	<p>hold 7-10 days prior to procedure may restart 6 hours after catheter removal (may restart immediately if no loading dose given)</p>	<p>no specific reversal agent; supportive care (platelet infusions, case reports of using DDAVP, maybe rFVIIa (may have limited/no benefit, generally not recommended)</p>
<p>rivaroxaban (Xarelto)</p> <p>anticoagulant; oral factor-Xa inhibitor</p>	<p>Atrial fibrillation: 20 mg PO daily</p> <p>DVT/PE: 15 mg PO BID for 3 weeks, then 20 mg PO once daily</p> <p>Chronic CAD/PAD: 2.5 mg PO twice daily</p> <p>Post-op prophylaxis: 10 mg daily; PO</p>	<p>Atrial fibrillation: CrCl 15-50 ml/min: 15 mg PO daily CrCl < 15 ml/min: Avoid use</p> <p>DVT/PE: Avoid if CrCl<30 ml/min</p> <p>Post-op Prophylaxis: CrCl < 30 ml/min: Avoid use</p> <p>Use not recommended in moderate or severe hepatic impairment (Child-Pugh Class B or C)</p> <p>See DOAC Drug Interaction Document for guidance on specific drug-drug interactions</p>	<p>5-9 hours; 11-13 hours in elderly</p>	<p>hold at least 24 hours prior to procedure; consider holding at least 48 hours if unknown or high bleeding risk; may restart 6-10 hours after surgery if hemostasis achieved</p>	<p>hold at least 72 hours prior to procedure; if prophylaxis dosing or unanticipated administration with indwelling catheter, hold for 22-26 hours prior to catheter manipulation or removal; may restart 6 hours after removal of the catheter if placement was atraumatic or 24 hours after traumatic punctures</p>	<p>4-factor PCC (PCC>rFVIIa), charcoal if dose given within previous 2 hours; supportive care</p> <p>**Use "Anticoagulation Reversal Orders" in Epic**</p>

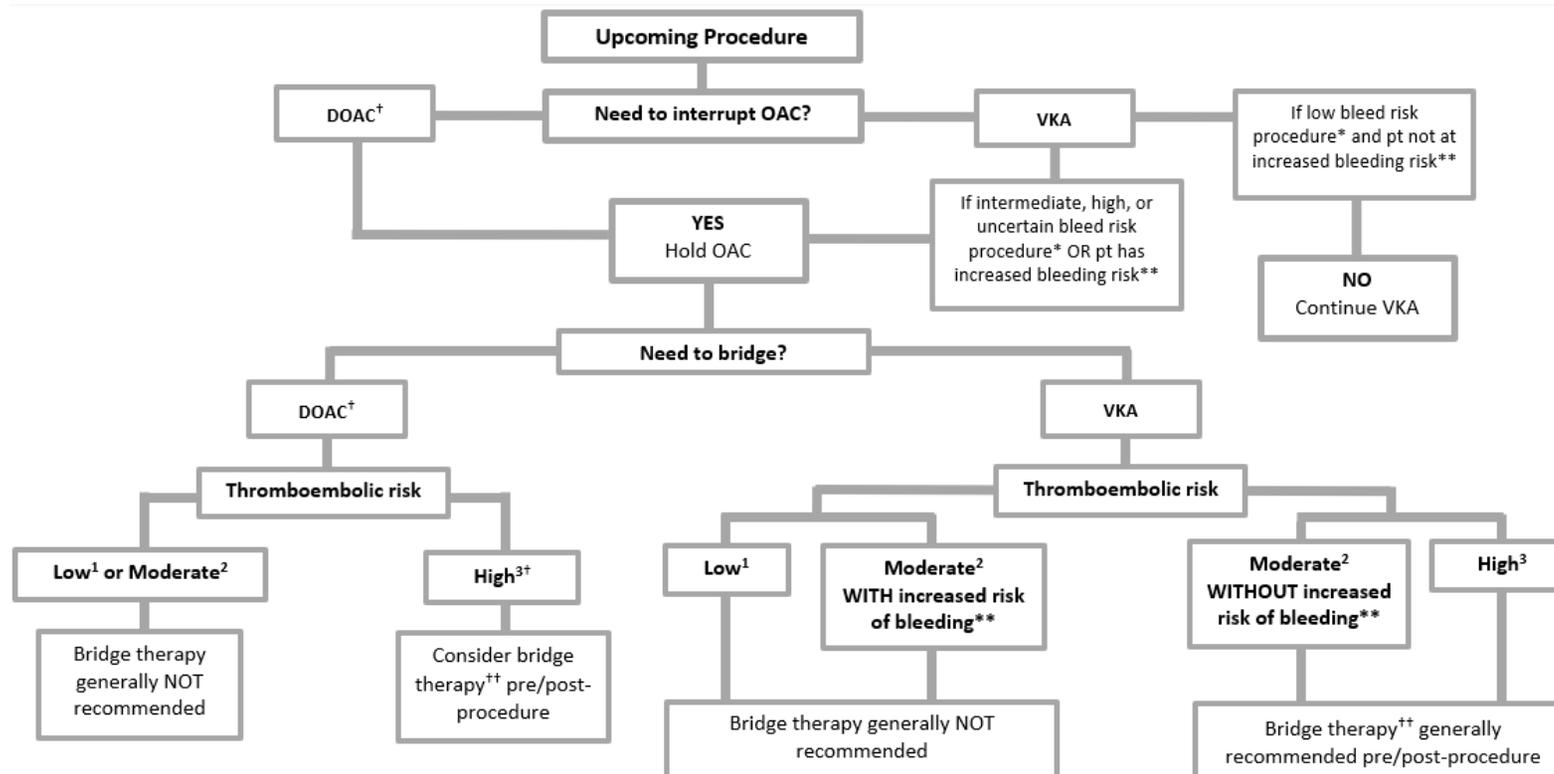
ANTICOAGULANT AND ANTIPLATELET REFERENCE: Focus on Perioperative Management & Reversal Strategies

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ticagrelor (Brilinta) antiplatelet; oral P2Y12 inhibitor	90 mg twice daily; PO Continued therapy after initial 12 months for patients with high ischemic risk: 60 mg twice daily; PO	No adjustment necessary Use not recommended in severe hepatic impairment (Child-Pugh Class C)	7-9 hours; platelet function restored in ~5 days	hold a minimum of 5 days prior to procedure; may restart 24 hours after surgery if hemostasis achieved	no official recommendations from manufacturer; consider holding 5-7 days prior to procedure; avoid use while neuraxial catheter is in place; may restart 6 hours after catheter removal (may restart immediately if no loading dose given)	no specific reversal agent; supportive care (platelet infusions, case reports of using DDAVP, maybe rFVIIa (may have limited/no benefit, use generally not recommended)
Tirofiban (Aggrastat) antiplatelet; parenteral GP IIb/IIIa inhibitor	25 mcg/kg loading dose followed by 0.15 mcg/kg/minute infusion for 18-48 hours; IV	Reduce infusion dose to 0.075 mcg/kg/minute if CrCl <60 mL/min No dose adjustment necessary for hepatic impairment	2 hours (prolonged in renal impairment)	Hold 4 hours prior to surgery (8 hours if CrCl <60 mL/min); may restart 24 hours after surgery if hemostasis achieved	Hold at least 8 hours prior to procedure; may restart 24 hours after	no specific reversal agent; supportive care (platelet infusions, case reports of using DDAVP, maybe rFVIIa (may have limited/no benefit, use generally not recommended)
warfarin (Coumadin) anticoagulant; vitamin K antagonist	Variable based on patient-specific factors and goal INR; PO	Adjust based on INR (may be affected by renal or hepatic function or drug interactions)	7 days	Hold 5 days prior to procedure; monitor INR and utilize short-acting bridging agents (e.g. IV heparin) when appropriate; may restart 12-24 hours after surgery	hold 4-5 days prior to procedure or until INR ≤1.4 prior to needle insertion; may restart after catheter removal; remove catheter while INR < 1.5	vitamin K; PCC > FFP; cryoprecipitate; supportive care; rFVIIa if other treatments failed

PCC: prothrombin complex concentrate: Four Factor PCC (Kcentra) is on formulary with the below restrictions: one-time dose only, prescribing provider (ED physicians, intensivists, surgeons, anesthesiologists, hematologists, hospitalists with verbal/telephone consultation with one of the approved specialties), indication (reversal of warfarin and DOACs in the setting of severe, life-threatening bleeding; reversal of warfarin and DOACs prior to emergent invasive procedures where potential bleeding may be life-threatening, not on anticoagulants: life-threatening bleeding refractory to massive transfusions). See "Restricted Medications" policy for more information. 3 factor complex (Profilnine) is also available on formulary.
 FFP: Fresh frozen plasma; DDAVP: Desmopressin; rFVIIa: recombinant Factor VIIa

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General Perioperative & Bridging Considerations for Anticoagulants



*Procedural bleeding risk: see 2017 ACC Consensus Online Appendix (http://jaccjacc.acc.org/Clinical_Document/PMAC_Online_Appendix.pdf)

**Patient factors for increased bleeding risk: Assess HAS-BLED (hypertension, renal or liver dysfunction, history of stroke, anemia or major bleeding history, labile INR, elderly (age >65), concomitant antiplatelets, NSAIDs, alcohol (≥8 drinks/week) or drug usage); other factors may include intracranial hemorrhage within 3 months, platelet abnormality, or bleeding during bridging or prior procedure

† Interrupting DOAC therapy: Recommended for any procedural bleeding risk or uncertain risk. Not enough evidence to routinely support uninterrupted DOAC therapy periprocedurally. Package insert recommendations recommend holding for at least 24 hours. Longer duration may be indicated based on CrCl, estimated DOAC half-life, & procedural risk (see 2017 ACC Expert Consensus for Periprocedural Anticoagulation in Non-Valvular Atrial Fibrillation [J Am Coll Cardiol. 2017;1-28]). Bridging generally not recommended with DOACs unless high thrombotic risk unable to tolerate resumption of oral medications post-procedure or additional procedures planned.

Thromboembolic risk considerations:

1. **Low**: VTE, stroke, or TIA >12 months prior with no other risk factors, mechanical aortic valve replacement without any additional risk factors for stroke, CHA2DS2VASc score 0-4
2. **Moderate**: VTE, stroke, or TIA 3-12 months prior or >12 months prior with additional risk factors, mechanical aortic valve replacement AND at least one additional risk factor for stroke (eg. AF, prior stroke/TIA, HTN, DM, CHF, age >75), history of recurrent VTE, active cancer, CHA2DS2VASc score 5-6
3. **High**: VTE, stroke, or TIA <3 months prior, mechanical mitral valve or caged-ball or tilting disc mechanical aortic valve replacement, hypercoagulable condition, CHA2DS2VASc score ≥7 (Exception: no bridge therapy recommended if major bleed or ICH <3 months)

When to restart OAC post-procedure: If hemodynamically stable, may resume within 24 hours post-procedure if low bleed risk; may resume within 48-72 hours if high bleed risk.

††Weight-based dosing of enoxaparin should be preferred bridge therapy if CrCl >30 mL/min. If CrCl <30 mL/min may need to consider inpatient admission for IV unfractionated heparin

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Package inserts.