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# Antithrombotic Management in Regional Anesthesia

This table provides information on management of antithrombotics in **surgical** patients before, during, and after **epidural or spinal anesthesia**. *The information in the table is from the 2018 guidelines from the American Society of Regional Anesthesia and Pain Medicine (**reference 1**) unless otherwise noted*. Most of the recommendations are based on Level C evidence and the drugs' pharmacokinetics due to a paucity of higher-level evidence. The suggested timing for stopping/restarting anticoagulants does not take into account surgical bleeding risks that might require a more conservative approach. Fortunately, spinal hematomas appear to be rare, but they are likely underreported. Consider reporting spinal hematomas to FDA's MedWatch at https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home. Note that there are **separate guidelines and recommendations**[3] for patients undergoing interventional pain procedures (e.g., spinal cord stimulator implant, celiac plexus block, etc) which are beyond the scope of this document.

**—Information in table may differ from FDA-approved labeling—**

**Abbreviations**: CrCl = creatinine clearance; INR = international normalized ratio

| Drug | Suggested Approach |
|---|---|
| **Anticoagulants, Oral** | |
| Apixaban (*Eliquis*) | • Stop apixaban 72 hours before neuraxial block.<br>• Wait at least 6 hours after neuraxial catheter removal to start/restart apixaban.<br>• If apixaban is given to a patient with an indwelling epidural catheter (e.g., emergently or by accident), hold apixaban 26 to 30 hours before catheter removal. |
| Betrixaban (*Bevyxxa*) | • Stop betrixaban at least three days before neuraxial block. In patients taking a P-glycoprotein inhibitor, or taking a dose >80 mg/day, allow a washout of 76 to 135 hours. If CrCl is <30 mL/min., guidelines suggest against neuraxial block in betrixaban patients. However, if used in patients with CrCl 15 to 29 mL/min., allow a washout of 76 to 135 hours.<br>• Wait at least 5 hours after neuraxial catheter removal to start/restart betrixaban.<br>• If betrixaban is given to a patient with an indwelling epidural catheter (e.g., emergently or by accident), hold betrixaban for at least 72 hours before catheter removal. |
| Dabigatran (*Pradaxa*)<br><br>*Continued…* | • Stop dabigatran 120 hours before neuraxial puncture. However, if CrCl is <30 mL/min., guidelines suggest against neuraxial block in dabigatran patients. For patients with good renal function (see below), without additional bleeding risk factors such as age >65 years, hypertension, or antiplatelet use, earlier institution could be considered as follows: |

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| **Drug** | **Suggested Approach** |
|---|---|
| Dabigatran, continued | • If CrCl is ≥80 mL/min., allow 72 hours between the last dabigatran dose and neuraxial puncture.<br>• If CrCl is 50 to 79 mL/min., allow 96 hours between the last dabigatran dose and neuraxial puncture.<br>• Wait at least 6 hours after catheter removal to start/restart dabigatran.<br>• If dabigatran is given to a patient with an indwelling epidural catheter (e.g., emergently or by accident), hold dabigatran for 34 to 36 hours before catheter removal. |
| Edoxaban (*Savaysa*) | • Stop edoxaban 72 hours before neuraxial block.<br>• Wait at least 6 hours after catheter removal to restart edoxaban.<br>• If edoxaban is given to a patient with an indwelling epidural catheter (e.g., emergently or by accident), hold edoxaban for 20 to 28 hours before catheter removal. |
| Rivaroxaban (*Xarelto*) | • Stop rivaroxaban 72 hours prior to neuraxial block.<br>• Wait at least 6 hours after catheter removal to start/restart rivaroxaban.<br>• If rivaroxaban is given to a patient with an indwelling epidural catheter (e.g., emergently or by accident), hold rivaroxaban for 22 to 26 hours before catheter removal. |
| Warfarin | • Ideally, stop warfarin five days before neuraxial block, and confirm normalization of INR.<br>• In patients beginning warfarin pre-operatively (e.g., low-dose for thromboprophylaxis), check INR before neuraxial block if the first dose was given >24 hours earlier or if a second dose of warfarin has been given.<br>• Postoperatively, for patients on low-dose warfarin (for thromboprophylaxis) receiving epidural anesthesia, monitor for neurodeficits. Use drugs that minimize sensory and motor block to facilitate monitoring.<br>  • Remove catheter when INR is <1.5 (e.g., within 12 to 24 hours after the first perioperative warfarin dose).<br>  • Maintain catheter with caution if INR is 1.5 to 3.<br>  • Check INR daily. If INR is >3, hold or reduce the warfarin dose.<br>  • Concomitant use of other anticoagulants or antiplatelets is not recommended.<br>  • Monitor for neurodeficits for 24 hours after catheter removal. |
| **Antiplatelets, Oral** | |
| Aspirin | • Aspirin can be continued, but consider risk/benefit in the event that another antithrombotic is needed. |
| Cilostazol | • Stop cilostazol two days before neuraxial block.<br>• Wait 6 hours after catheter removal to restart cilostazol. |
| Clopidogrel (*Plavix*, generics) | • Stop clopidogrel five to seven days before neuraxial block.<br>• Clopidogrel can be restarted immediately after catheter removal provided that a loading dose is not given. If a loading dose is given, wait 6 hours after catheter removal before administration. |

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| **Drug** | **Suggested Approach** |
|---|---|
| Dipyridamole | • Stop dipyridamole 24 hours before neuraxial block.<br>• Wait 6 hours after catheter removal to restart dipyridamole. |
| Prasugrel (*Effient*, generics) | • Stop prasugrel seven to ten days before neuraxial block.<br>• Prasugrel can be restarted immediately after catheter removal provided that a loading dose is not given. If a loading dose is given, wait 6 hours after catheter removal before administration. |
| Ticagrelor (*Brilinta*) | • Stop ticagrelor five to seven days before neuraxial block.<br>• Ticagrelor can be restarted immediately after catheter removal provided that a loading dose is not given. If a loading dose is given, wait 6 hours after catheter removal before administration. |
| Ticlopidine | • Stop ticlopidine ten days before neuraxial block.<br>• Ticlopidine can be restarted immediately after catheter removal provided that a loading dose is not given. If a loading dose is given, wait 6 hours after catheter removal before administration. |
| **Injectable Antithrombotics** | |
| Cangrelor (*Kengreal*) | • Stop cangrelor 3 hours before neuraxial block.<br>• Wait 8 hours after catheter removal to restart cangrelor. |
| Fondaparinux (*Arixtra*, generics), **prophylaxis** dose | • Not recommended unless neuraxial techniques are identical to those used in clinical trials (e.g., single needle pass, atraumatic placement, no indwelling catheter). May not be feasible in practice.<br>• Allow 36 to 42 hours after administration before neuraxial puncture.<br>• Wait at least 6 hours after catheter removal to start/restart fondaparinux. |
| LMWH, **prophylaxis** dose | • Allow 12 hours after administration before neuraxial puncture. Consider a longer washout if CrCl <50 mL/min.[2]<br>• Post-op, **twice-daily prophylactic** dosing: give the first dose the next day (assuming surgical hemostasis has been achieved) AND no sooner than 12 hours after needle/catheter placement AND at least 4 hours after catheter removal.<br>• Post-op, **once-daily (q 24 h) prophylactic** dosing: the first dose should be given at least 12 hours after needle/catheter placement. Catheter may be maintained, but do not use any additional drugs with antihemostatic effects. Wait 12 hours after the last dose of LMWH to remove catheter. Wait at least 4 hours after catheter removal to resume LMWH.<br>• Check platelets if used for more than five days. |

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| **Drug** | **Suggested Approach** |
|---|---|
| LMWH, **treatment** dose | • Allow 24 hours after administration before neuraxial puncture. Consider a longer washout if CrCl <50 mL/min.[2]<br>• Wait at least 4 hours after catheter removal to start/restart LMWH.<br>• It is recommended that at least 24 hours elapse between needle/catheter placement and removal.<br>• Check platelets if used for more than five days. |
| Heparin infusion | • Stop heparin drip 4 to 6 hours prior to neuraxial puncture AND check coagulation labs to ensure they are normal.<br>• Check platelet count prior to catheter insertion/removal for patients receiving heparin for more than four days (due to possibility of heparin-induced thrombocytopenia).<br>• Avoid use of other antithrombotics. Review med list daily.<br>• May start/restart heparin 1 hour after catheter removal. |
| Heparin, low-dose subcutaneous (5,000 units two or three times daily) | • Wait 4 to 6 hours (or check coagulation labs) after heparin administration to perform neuraxial block,<br>• Check platelet count prior to catheter insertion/removal for patients receiving heparin for more than four days (due to possibility of heparin-induced thrombocytopenia).<br>• Postoperatively, a neuraxial catheter may be maintained despite low-dose subcutaneous heparin. Wait 4 to 6 hours after heparin administration to remove/manipulate catheter. May restart low-dose subcutaneous heparin 1 hour later. |
| Heparin, higher-dose subcutaneous (7,500 to 10,000 units twice daily, or a daily dose ≤20,000 units) | • Wait 12 hours after heparin administration to perform neuraxial block, AND check coagulation labs.<br>• Check platelet count prior to catheter insertion/removal for patients receiving heparin for more than four days (due to possibility of heparin-induced thrombocytopenia).<br>• Postoperatively, the safety of maintaining a neuraxial catheter at these doses is unclear. Consider risk/benefit, and use drugs that minimize sensory and motor block to facilitate monitoring for neurodeficits. Monitor closely.<br>• May start/restart subcutaneous heparin 1 hour after catheter removal. |
| Heparin, therapeutic subcutaneous dose (>10,000 units per dose or >20,000 units total daily dose) | • Wait 24 hours after heparin administration to perform neuraxial block, AND check coagulation labs.<br>• Check platelet count prior to catheter insertion/removal for patients receiving heparin for more than four days (due to possibility of heparin-induced thrombocytopenia).<br>• May start/restart subcutaneous heparin 1 hour after catheter removal. |

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| **Drug** | **Suggested Approach** |
|---|---|
| Platelet GP IIb/IIIa inhibitors (abciximab, eptifibatide, tirofiban) | • Avoid neuraxial anesthesia until platelet function has recovered. Platelet aggregation usually recovers within 8 hours (48 hours for abciximab). Also check for thrombocytopenia.<br>• If a patient who has undergone neuraxial anesthesia emergently requires a GP IIb/IIIa inhibitor post-op, use drugs that minimize sensory and motor block to facilitate monitoring for neurodeficits. Monitor closely. No specific recommendations are given for timing of catheter removal in this situation. Balance need for continued antiplatelet therapy vs potential for spinal bleeding during catheter maintenance or removal. |
| Thrombolytics (e.g., alteplase) | • Avoid neuraxial anesthesia.<br>• If neuraxial anesthesia is performed, it is suggested that at least 48 hours elapse after thrombolytic dose, AND clotting studies, including fibrinogen, be checked to ensure they have normalized. Use drugs that minimize sensory and motor block to facilitate monitoring. Neurological checks at least every 2 hours are suggested. |
| Direct thrombin inhibitors (argatroban, bivalirudin, desirudin) | • Neuraxial anesthesia is not recommended in these patients. |

*Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication*

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## *Levels of Evidence*

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

| Level | Definition | Study Quality |
|---|---|---|
| **A** | Good-quality patient-oriented evidence.* | 1. High-quality RCT<br>2. SR/Meta-analysis of RCTs with consistent findings<br>3. All-or-none study |
| **B** | Inconsistent or limited-quality patient-oriented evidence.* | 1. Lower-quality RCT<br>2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings<br>3. Cohort study<br>4. Case control study |
| **C** | Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening. | |

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).
**RCT** = randomized controlled trial; **SR** = systematic review
[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. http://www.aafp.org/afp/2004/0201/p548.pdf.]

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## *References*


1. Horlocker TT, Vandermeuelen E, Koop SL, et al. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine evidence-based guidelines (fourth edition). *Reg Anesth Pain Med* 2018;43:263-309.
2. DeCarolis DD, Thorson JG, Clairmont MA, et al. Enoxaparin outcomes in patients with moderate renal impairment. *Arch Intern Med* 2012;172:1713-8.
3. Narouze S, Benzon HT, Provenzano D, et al Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications (second edition): guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society and the World Institute of Pain. *Reg Anesth Pain Med* 2018;43:225-62.


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