

<b>Guideline/Protocol Title:</b>	GUIDELINES FOR THE USE OF ANTITHROMBOTIC AGENTS IN THE SETTING OF NEURAXIAL PROCEDURES
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<b>Last revision Date:</b>	Version 3.0, May 2015

<b>PURPOSE/SCOPE:</b>	To allow the safe performance of neuraxial procedures in patients on antithrombotic medication.
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<b>EXECUTIVE SUMMARY</b>
The intention of this guideline is to allow the safe performance of neuraxial procedures in patients on antithrombotic medication. Such neuraxial procedures include lumbar punctures, subarachnoid block (spinal), and the placement of intrathecal (e.g. lumbar drains) and epidural catheters. For high-risk neuraxial and other chronic pain procedures such as spinal cord stimulator or intrathecal delivery system implants, we advise providers to follow the guidelines of their specialty societies (Narouze et al, RAPM 2018).

<b>BACKGROUND / INTRODUCTION</b>
The primary concern for neuraxial procedures and anthithrombotics is the risk for epidural hematoma. The consequences of this complication include paralysis and permanent bowel/bladder dysfunction. The historic approximate risk of this complication is estimated to be 1 in 150,000 for epidurals and 1 in 220,000 for subarachnoid blocks (Bonica’s Management of Pain, 4th ed.) although evidence supports that the incidence may be as high as 1/9,000 for perioperative epidurals (MPOG- 2013). Thus, we have a very rare, high consequence complication associated with an elective procedure. The risks vs benefit ratio must be assessed in each situation.
The table presented in the appendix is a collection of expert recommendations from UCSF, American Society of Regional Anesthesia (ASRA), European Society of Regional Anaesthesia (ESRA), and the Scandinavian Society of Anaesthesiology using retrospective data on several agents. For the newer agents lacking substantial data, such as betrixaban, anagrelide and vorapaxar, times have been calculated taking their plasma half-life and stating arbitrarily that reduction by 96.9% (5 maximum half-lives) is acceptable. These numbers may be considered conservative. The purpose of the table presented in the appendix is to provide recommendations-- they do not replace an individual’s judgment in specific situations.

### **Risks of Ceasing Antithrombotic Therapy & the Role of Bridging**

In patients at very high risk for thromboembolism during anticoagulation interruption (see UCSF SFVA periop anticoagulation guidance) bridge therapy with short acting agent may be recommended, however this intervention is associated with increased bleeding risk and therefore assessment of net clinical benefit should be assessed.

As a general rule, the discontinuation or holding of anticoagulants for VTE prophylaxis to facilitate the removal of indwelling catheters is discouraged and hardly ever necessary.

### **Peripheral Regional Anesthesia & Antithrombotics**

Depending on the type of peripheral nerve block, the risks and potential consequences of hematoma formation are less severe than for neuraxial anesthesia. However, there are no guidelines or studies to base recommendations for specific peripheral regional techniques. We recommend that for patients undergoing perineuraxial, deep plexus, or deep peripheral blocks, the guidelines regarding neuraxial techniques be applied, whereas for patients undergoing other plexus or peripheral techniques, we suggest management based on site compressibility, vascularity, and consequences of bleeding, should it occur.

### **Hepatic & Renal Impairment**

These values are valid for patients with intact hepatic and renal function. Impairments can alter the metabolism and excretion. For patients with renal impairment please refer to the guidelines “Guidance for the management of DOACs and LMWHs in kidney disease” and “Guidelines for the Peri-procedural Management of Adults Taking DOACs”.

### **Cytochrome P450 Metabolism**

Many of these drugs are metabolized through the CYP450 metabolism pathway. Be aware of interactions with other substances (e.g., grapefruit juice, herbals, drugs). If unclear, please refer to the package insert of a medication.

### **Combination of Factors**

This table does not identify the risk associated with combinations of antithrombotic etiologies. Therefore, when a patient has multiple factors, this must be assessed on a case by case basis. Examples include combinations of drugs with herbal supplements, von Willebrand disease, etc.

### **Traumatic or “Bloody” Tap**

Inform the Acute Pain Service (APS) if there is traumatic placement of a neuraxial regional anesthetic. There is a ~10-fold increased risk of epidural hematoma with traumatic placement.

## **APPENDIX**

See attached file: Appendix I: Antithrombotic agents in neuraxial procedures

Reference #	Citation
1	Horlocker TT 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. <b>ASRA</b>
2	Bateman BT et al. The Risk and Outcomes of Epidural Hematomas After Perioperative and Obstetric Epidural Catheterization: A Report from the Multicenter Perioperative Outcomes Group Research Consortium. Anesthesia & Analgesia. June 2013; 116 (6): 1380-1385. <b>MPOG</b>

Revision History	
Revision Date	Update(s)
July, 2019 Version 4.0	Recommendations in revised guideline were aligned with the updated ASRA guideline (published in April 2018)
May 2015 Version 3.0	




GUIDELINES FOR THE USE OF ANTITHROMBOTIC AGENTS IN THE SETTING OF NEURAXIAL PROCEDURES

  		Minimum time between the last dose and when neuraxial shot/ catheter placement can occur	Minimum time after catheter placement to drug start.	Minimum time between last dose of drug and catheter removal	Minimum time between neuraxial shot/ catheter removal and when next dose can be given
<b>ANTICOAGULANTS FOR VENOUS THROMBOEMBOLISM PROPHYLAXIS</b>					
	dalteparin (Fragmin) 5000 units SQ daily	12 hours	Wait 6 hrs after catheter placement before next dose. No additional anticoagulants.	12 hours	4 hours
★	enoxaparin (Lovenox) 40mg SQ daily	12 hours	Wait 12 hrs after catheter placement before next dose. No additional anticoagulants.	12 hours, check platelet count after 4 days of enoxaparin	4 hours
★	enoxaparin (Lovenox) 30mg SQ bid or 40mg SQ bid	12 hours	CONTRAINDICATED while catheter in place		4 hours
	fondaparinux (Arixtra) ≤2.5mg SQ daily	48 hours	CONTRAINDICATED while catheter in place		4 hours
	heparin 5000 Units SQ bid and tid	4 hours, check platelet count after 4 days of heparin	immediately	4 hours, check platelet count after 4 days of heparin	immediately
	heparin 7500-10,000 Units SQ bid or total daily dose ≤20,000 Units SQ	12 hours, check platelet count after 4 days of heparin	Safety has not been established for doses >5000 Units SQ or total daily dose >15,000 Units SQ. Use caution		1 hour
★★	rivaroxaban (Xarelto) 10mg PO daily	72 hours	6 hours	24 hours	6 hours
★	betrixaban (Bevyxxa) 80mg PO daily	5 days (limited data)	CONTRAINDICATED while catheter in place		5 hours
<b>ANTICOAGULANTS AT THERAPEUTIC DOSES</b>					
★★	apixaban (Eliquis) 2.5, 5, 10mg PO bid	72 hours	CONTRAINDICATED while catheter in place		6 hours
★★	dabigatran (Pradaxa) 75, 150mg PO bid	3 days & TT or aPTT is normal	CONTRAINDICATED while catheter in place		6 hours
	dalteparin (Fragmin) 100-120 units/kg SQ q12h	24 hours	CONTRAINDICATED while catheter in place		4 hours
	dalteparin (Fragmin) 150-200 units/kg SQ daily	36 hours	CONTRAINDICATED while catheter in place		4 hours
★★	edoxaban (Savaysa) 30, 60mg PO daily	72 hours	CONTRAINDICATED while catheter in place		6 hours
★	enoxaparin (Lovenox) 1mg/kg SQ bid	24 hours	CONTRAINDICATED while catheter in place		4 hours
★	enoxaparin (Lovenox) 1.5mg/kg SQ daily	36 hours	CONTRAINDICATED while catheter in place		4 hours
	fondaparinux (Arixtra) 5-10mg SQ daily	72 hours	CONTRAINDICATED while catheter in place		6 hours
	heparin >10,000 Units SQ bid or total daily dose >20,000 Units SQ	12 hours, check platelet count after 4 days of heparin	Safety has not been established for doses >5000 Units SQ or total daily dose >15,000 Units SQ.		1 hour
	heparin full dose IV (In emergent situations, may have to be used. Recommend neuro checks q2h)	4 hours & coagulation status is normal	Not contraindicated, but should be avoided and used only in emergent situations. Wait at least 1 hour.	4 hours & coagulation status is normal. Check platelet count after 4 days of heparin	1 hour
★★	rivaroxaban (Xarelto) 15 mg PO daily to bid, 20mg PO daily	72 hours	CONTRAINDICATED while catheter in place		6 hours
★	warfarin (Coumadin)	5 days & INR < 1.5	CONTRAINDICATED while catheter in place		immediately

★ Thrombosis risk is increased when these anticoagulants are held. Although parenteral bridging is not generally needed for target specific oral anticoagulants (dabigatran, rivaroxaban, apixaban, edoxaban) it may be considered in some situations. Consult Anticoagulation Clinic or Hematology if additional input is desired.

★ In patients with renal impairment taking enoxaparin, apixaban, rivaroxaban, edoxaban or dabigatran, please refer to the guidelines “Guidance for the management of DOACs and LMWHs in kidney disease” and “Guidelines for the Peri-procedural Management of Adults Taking DOACs” or Consult Anticoagulation Clinic.

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  University of California San Francisco	 SF HEALTH NETWORK <small>AN INTEGRAL PARTNER OF UCSF</small>	Minimum time between the last dose and when neuraxial shot/ catheter placement can occur	Minimum time after catheter placement to drug start.	Minimum time between last dose of drug and catheter removal	Minimum time between neuraxial shot/ catheter removal and when next dose can be given
<b>ORAL ANTIPLATELET AGENTS</b>					
<b>aspirin/NSAIDS/COX inhibitors/pentoxifylline</b>		May be given, but can increase risk of bleeding; No time restrictions for catheter placement or removal			
<b>dipyridamole</b>		24 hours	CONTRAINDICATED while catheter in place		6 hours
<b>clopidogrel (Plavix)</b>		7 days	CONTRAINDICATED while catheter in place		2 hours
<b>prasugrel (Effient)</b>		10 days	CONTRAINDICATED while catheter in place		6 hours
<b>ticagrelor (Brilinta)</b>		5 days	CONTRAINDICATED while catheter in place		6 hours
<b>ticlopidine (Ticlid)</b>		10 days	CONTRAINDICATED while catheter in place		2 hours
<b>cangrelor (Kengreal)</b>		3 hours	CONTRAINDICATED while catheter in place		8 hours
<b>anagrelide (Agrylin)</b>		24 hours	CONTRAINDICATED while catheter in place		8 hours
<b>DIRECT THROMBIN INHIBITORS</b>					
<b>argatroban / bivalirudin (Angiomax)</b>		When TT or aPTT is normal	CONTRAINDICATED while catheter in place		2 hours
<b>GP IIB/IIIa INHIBITORS</b>					
<b>abciximab (Reopro)</b>		48 hours	CONTRAINDICATED while catheter in place		2 hours (ACS)
<b>eptifibatide (Integrilin) / tirofiban (Aggrastat)</b>		8 hours	CONTRAINDICATED while catheter in place		2 hours (ACS)
<b>THROMBOLYTIC AGENTS</b>					
<b>alteplase (TPA) Full dose for stroke, MI, etc</b>		10 days	CONTRAINDICATED while catheter in place		10 days
<b>alteplase (TPA) 2mg dose for catheter clearance</b>		May be given; No time restrictions for catheter placement or removal			
<b>MISCELLANEOUS AGENTS</b>					
<b>bevacizumab (Avastin)</b>		Caution			
<b>cilostazol (Pletal)</b>		2 days	CONTRAINDICATED while catheter in place		6 hours
<b>sulodexide</b>		5 days	CONTRAINDICATED while catheter in place		6 hours
<b>voropaxar (Zontivity) Limited data, consider expert consultation</b>		40-50 days	CONTRAINDICATED while catheter in place		24 hours
<b>VITAMINS</b>					
<b>Vitamin C</b>		May be given; No time restrictions for catheter placement or removal			
<b>Vitamin E</b>		May be given; No time restrictions for catheter placement or removal			

★ There is an increased risk of thrombosis when antiplatelets are held for patients with vascular stents (e.g. cardiac, intracranial, etc.). Consult cardiology.

### Antineoplastic Agents

This group of medications may have an impact on coagulation and should be evaluated on a case by case basis.

### Herbals & Supplements

This group of medications may have an impact on coagulation and should be evaluated on a case by case basis. Examples include ginkgo, garlic, ginseng, omega-3 fish oil, or turmeric. In general, the UCSF PREPARE clinic advises that these medications be discontinued at least 1 week prior to surgery. No time restrictions for catheter placement or removal.

### References

- Horlocker TT 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. **ASRA**
- Bateman BT et al. The Risk and Outcomes of Epidural Hematomas After Perioperative and Obstetric Epidural Catheterization: A Report from the Multicenter Perioperative Outcomes Group Research Consortium. Anesthesia & Analgesia. June 2013; 116 (6): 1380-1385. **MPOG**

*The contents of these clinical practice guidelines are to be used as a guide, and not a substitute for medical judgment. Healthcare professionals should exercise sound clinical judgment and individualize patient care based upon the patient's condition.*