**Guideline: Management of Anticoagulant Medications in the Periprocedural and Surgical Settings**

**Purpose of Guidelines:**
Provide guidance to clinicians at Froedtert and The Medical College of Wisconsin for safely and effectively managing the use of anticoagulant medications during the periprocedural period. **These guidelines are not intended to replace clinical judgment and may not apply to all patients.** Periprocedural management of anticoagulant medications is a collaborative effort of the multidisciplinary healthcare team requiring analysis of individualized, patient specific factors. Given the challenges presented by patients requiring thromboembolic management undergoing surgical and other interventional procedures, strategies to optimally manage oral and parenteral anticoagulant medications were reviewed and are provided in this guideline.

Refer to the Department of Anesthesiology Preoperative Medication Management Guidelines for a more comprehensive list medications (including antiplatelets) and associated management in the perioperative setting.

Refer to table 2 for links to any surgical subspecialty specific guides that exist that can be used in combination or in place of this guideline based on the needs of the patient.

**Background:**
Parenteral and oral anticoagulants have become a standard of care for the treatment and prevention of venous thromboembolism (VTE) in certain surgical procedures (e.g., total hip and knee arthroplasty) and in the management of a variety of clinical disease states (e.g., atrial fibrillation, hereditary coagulopathies, systemic lupus erythematosus.[1-7] The periprocedural management of patients receiving long-term anticoagulant therapy is a common and difficult clinical problem where the risk of bleeding must be carefully weighed against the risk of thromboembolism. Improper management of anticoagulants in the periprocedural setting can result in increased bleeding intra- and postoperatively. Alternatively, too little anticoagulation can lead to severe morbidity, including stroke and death.[8]

**Clinical Assessment:**
*Thrombotic Risk and Bridging:*
Patients on direct anticoagulant therapies (i.e. apixaban, dabigatran, edoxaban and rivaroxaban) do not require bridging due to the quick onset of action and short half-life of these medications.[9]

For patients on warfarin, the need for bridging in the periprocedural setting should be evaluated on a case-by-case basis.[8] **Bridging should be considered in patients at high risk for thrombosis and in some patients at moderate risk for thrombosis**.

Stratification of high, intermediate, and low risk of thrombosis has been described by the American College of Chest Physicians and is summarized in Table 1.

**Atrial fibrillation:** Evidence from a randomized controlled trial recommends against bridging patients on warfarin for atrial fibrillation at low to moderate risk of thrombosis.[23] Patient harm with increased bleeding rates were shown with bridging anticoagulation. [23] Consensus guidelines suggest that a patient's bleeding risk should also be considered to determine if bridging is used.[24]

**Mechanical Heart Valves**: 2017 AHA/ACC Update of the 2014 AHA/ACC Guideline for Management of Patients with Valvular Heart Disease have downgraded the recommendation for bridging in patients with 1) mechanical AVR and any thromboembolic risk factor, 2) ball-cage or tilting disk mechanical AVR, or 3) mechanical MVR from a strong recommendation to a moderate recommendation.[25] The risk of thrombosis must be outweighed by the risk of bleeding to consider bridging.

**VTE**: Retrospective studies of perioperative management of warfarin in patients with VTE have shown increased bleeding in patients who were bridged without a difference in thrombosis between patients treated with and without bridging.[26] 79% of patients in the analysis were low-risk, 18% were moderate risk, and 3% were high risk. Based on retrospective data and extrapolation from randomized studies in atrial fibrillation, in patients with VTE at moderate risk of thrombosis, the harm associated with bridging needs to be outweighed by the thrombosis risk to consider bridging.

*Bleeding Risk and Resuming Anticoagulation Therapy:* Procedural bleeding risk determines how and when postprocedural anticoagulant therapy should be resumed.

- Procedures and their associated bleeding risk have also been identified and are described in Table 2

Table 1. Thrombotic Risk Stratification for the Perioperative Period[10,24]

| Thrombosis Risk Category | Mechanical Heart Valve | Atrial Fibrillation | Venous Thromboembolism |
|---|---|---|---|
| **High** | • Any mitral valve prosthesis<br>• Any caged-ball or tilting disc aortic valve prosthesis<br>• Recent (within 6 months) stroke or TIA | • $CHADS_2$ Score 5-6; $CHA_2DS_2$-VASc Score 7-9<br>• Recent (within 3 months) stroke, TIA, or systemic embolism<br>• Rheumatic valvular heart disease | • Recent (within 3 months) VTE<br>• Severe thrombophilia (e.g., protein C, protein S or antithrombin deficiency; APLA, multiple abnormalities) |
| **Moderate** | • Bileaflet aortic valve prosthesis and 1 or more of the following:<br>o Atrial fibrillation<br>o Prior stroke or TIA<br>o Hypertension<br>o Diabetes mellitus<br>o Congestive heart failure<br>o Age > 75 years old | • $CHADS_2$ Score 3-4; $CHA_2DS_2$-VASc Score 5-6<br>• History of stroke, TIA or systemic embolism | • VTE within the past 3 to 12 months<br>• Non-severe thrombophilia (e.g., heterozygous factor V Leiden or prothrombin gene mutation)<br>• Recurrent VTE<br>• Active cancer (treated within 6 months or palliative patients) |
| **Low** | • Bileaflet aortic valve prosthesis without AF and no other risk factors for stroke | • $CHADS_2$ Score 0-2<br>• $CHA_2DS_2$-VASc Score 0-4<br>• No history of stroke, TIA or systemic embolism | • VTE events > 12 months previous and no other risk factors |

Abbreviations: AF = Atrial Fibrillation; APLA = Antiphospholipid Antibodies; $CHADS_2$ = Congestive Heart Failure, Hypertension, Age > 75 years, Diabetes Mellitus, and Stroke or Transient Ischemic Attack; $CHA_2DS_2$-VASc = Congestive Heart Failure, Hypertension, Age > 75 years, Diabetes Mellitus, Stroke or Transient Ischemic Attack, Vascular Disease and Sex; TIA= Transient Ischemic Attack; VTE = Venous Thromboembolism

As a reminder, this guideline is **not** intended to replace clinical judgment and may not apply to all patients. Please **double-check with the proceduralist** regarding the risk of bleeding related to the procedure.

A procedure list has been created as part of the "2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation."[24] This is intended as reference material for discussion with providers related to risk categories.

Table 2. Procedures and Associated Bleeding Risk[10,11]

| Procedure | High Risk[a] of Major Bleeding (2-day risk of major bleeding 2 to 4%) | Low Risk of Major Bleeding (2-day risk of major bleeding 0 to 2%) | Low Bleeding Risk |
|---|---|---|---|
| **Cardiac** | • Abdominal aortic aneurysm repair<br>Coronary artery bypass<br>• Heart valve replacement | • VAD removal<br>• Pacemaker or defibrillator insertion, EP testing<br>• Noncoronary angiography | -- |
| **Dental** | • Multiple tooth extractions | -- | • Dental cleaning<br>• Single tooth extraction<br>• Root canal |
| **Dermatologic** | -- | -- | • Basal and squamous cell cancer removal |
| **Gastrointestinal** | • Biliary sphincterectomy<br>• Bowel resection<br>• PEG placement<br>• Polypectomy/Colonic polyp resection (i.e. Sessile polyps > 1-2 cm)<br>• Refer to GI Peri-procedure guidelines (under review) | • Bronchoscopy +/- biopsy<br>• Cholecystectomy<br>• GI endoscopy procedures<br>• Refer to GI Peri-procedure guidelines (under review) | -- |
| **General (Other)** | • Abdominal surgery[b]<br>• Endoscopic fine needle aspiration<br>• Cancer surgery (e.g., breast cancer)<br>• Reconstructive plastic surgery | • Abdominal hernia repair<br>• Axillary node dissection<br>• Biopsy procedures: bladder, breast, prostate, lymph node, thyroid | -- |
| **Gynecologic** | -- | • Abdominal hysterectomy<br>• Dilation and curettage | -- |
| **Nephrology** | • Kidney biopsy<br>• Nephrectomy | -- | -- |
| **Neurosurgical/ Spinal** | • Any intracranial or spinal surgery (e.g. laminectomy)<br>• Refer to Guideline for Use of Antithrombotic Medications in the Presence of Neuraxial Anesthesia for management of spinal or epidural anesthesia | -- | -- |
| **Ophthalmologic** | • Refer to Ophthalmology Antithrombotic Management Protocol for management | | |
| **Orthopedic** | • Bilateral knee replacement | • Carpal tunnel repair<br>Single joint arthroscopy | -- |
| **Urologic** | • Bladder resection<br>• Transurethral prostate resection<br>• Tumor ablative procedures | • Hemorrhoid surgery<br>Hydrocele repair | -- |
| **Vascular** | • All procedures | -- | -- |

[a] Any operation with procedure duration greater than 45 minutes
[b] Highly vascularized organs include: kidney, liver, and spleen

**Appendix A. Planned Elective Procedures**

- **Warfarin (Coumadin)**
- **Dabigatran (Pradaxa)**
  - **High Risk Bleeding Procedures**
  - **Standard (Low) Risk Bleeding Procedures**
- **Factor Xa Inhibitors: Rivaroxaban (Xarelto), Apixaban (Eliquis) and Edoxaban (Savaysa)**
  - **High Risk Bleeding Procedures**
  - **Standard (Low) Risk Bleeding Procedures**
- **Unfractionated Heparin, Enoxaparin (Lovenox), Dalteparin (Fragmin), and Fondaparinux (Arixtra)**

**Appendix B. Emergent Procedures**

**Refer to Guideline: Management of Anticoagulation-Associated Bleeding and Anticoagulation Reversal**

**Appendix C. Pharmacokinetic Considerations for Anticoagulant Medications**

## Appendix A. Planned Elective Procedures

### Warfarin (Coumadin)

A. **Refer to Table 1 for risk stratification based on indication for warfarin therapy and review the clinical assessment (from pages 1 and 2) to make final decision.**
B. Table 3 provides guidance for management of warfarin in the perioperative and postoperative period for planned procedures
C. If platelet count is less than 100 and bridging therapy is considered, recommend discussion with proceduralist about if bridging therapy should be done.
D. For patient requiring bridging anticoagulation, recommended enoxaparin dosing is as follows:

| Creatinine Clearance | Enoxaparin Dose (subcutaneous injection) |
|---|---|
| Greater than 50 ml/min | 1 mg/kg twice daily |
| 31-50 ml/min | 1 mg/kg twice daily<br>75 year and over: round down to nearest syringe size (e.g. if patient 77 years old and weights 72 kg with CrCl of 35 mL per min use 60 mg subcutaneously twice daily) |
| 15-30 ml/min | 1 mg/kg once daily |
| Less than 15 ml/min or on dialysis | **DO NOT** use; consult with proceduralist for bridging plan if indicated |

E. See Table 8 for additional information about medications that can be used for bridging therapy, heparin, LMWH and fondaparinux

Table 3. Perioperative and Postoperative Recommendations – Warfarin[10,12]

| | Pre-Operative Period | | | | | | Procedure | Post-Operative Period | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Day** | **Day -6** | **Day -5** | **Day -4** | **Day -3** | **Day -2** | **Day -1** | **Day 0** | **Day +1** | **Day +2** | **Day +3 and beyond** |
| Warfarin Dosing | Last Dose Warfarin | No warfarin[a] | No warfarin[a] | No warfarin[a] | No warfarin[a] | No warfarin[a]<br><br>Consider obtaining INR in patients with a high bleeding risk procedure<br><br>If INR >1.5, consider 1 to 2.5 mg PO Vitamin K | Consider restarting warfarin the night of surgery if taking PO liquids. | Restart/continue warfarin | Continue warfarin +/- therapeutic LMWH (if bridging is being done) | Continue warfarin +/- therapeutic LMWH (if bridging is being done) |
| Procedure risk and need for bridging | | | | | | | | | | |
| High Thrombosis Risk | Consider consult with proceduralist if you feel bridging therapy is warranted<br><br>Refer to the Thrombotic Risk Stratification for further guidance | | | Start bridging with therapeutic dose parenteral anticoagulant if indicated | Continue LMWH in patients being bridged | For once daily LMWH dosing, no dose given<br><br>For twice daily LMWH dosing, last dose is in the AM (omit PM dose)<br><br>Last dose 24 hours prior to neuraxial anesthesia | Inpatient procedures: Collaboration with proceduralist is **REQUIRED** before restarting therapy | If bridging indicated:<br><br>High Risk Bleeding Procedure:<br>Mechanical prophylaxis; Consider initiation of **prophylactic** LMWH 24 to 48 hours (day +1 or day +2) post-op<br><br>Low Risk Bleeding Procedure:<br>Resume therapeutic LMWH 24 hours post-op with PM dose | If bridging indicate:<br><br>High Risk Bleeding Procedure:<br>Resume **therapeutic** LMWH 48 to 72 hours (day +2 or day +3) post-op | Stop LMWH when INR is therapeutic |
| Moderate Thrombosis Risk | Consider consult with proceduralist if you feel bridging therapy is warranted<br><br>The risk of thrombosis must be outweighed by the risk of bleeding to consider bridging | | | Start bridging with therapeutic dose parenteral anticoagulant if indicated | Continue LMWH in patients being bridged | For once daily LMWH dosing, no dose given<br><br>For twice daily LMWH dosing, last dose is in the AM (omit PM dose)<br><br>Last dose 24 hours prior to neuraxial anesthesia | Inpatient procedures: Collaboration with proceduralist is **REQUIRED** before restarting therapy<br><br>Outpatient procedures: Resume warfarin, unless specific instruction given by proceduralist for later restart date | If bridging indicated:<br><br>High Risk Bleeding Procedure:<br>Mechanical prophylaxis; Consider initiation of **prophylactic** LMWH 24 to 48 hours (day +1 or day +2) post-op<br><br>Low Risk Bleeding Procedure:<br>Resume therapeutic LMWH 24 hours post-op with PM dose | If bridging indicated:<br><br>High Risk Bleeding Procedure:<br>Resume **therapeutic** LMWH 48 to 72 hours (day +2 or day +3) post-op | Stop LMWH when INR is therapeutic |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Low Thrombosis Risk | No bridging | | | | | | | | | |

Note: All recommendations for bridging and restarting anticoagulation therapy do not account for regional anesthesia. LMWH does not need to be used for bridging therapy; UFH is an appropriate option.
Abbreviations: INR = International Normalized Ratio; LMWH = low molecular weight heparin (eg, enoxaparin); UFH = unfractionated heparin
[a] May consider continuing warfarin in patients undergoing a procedure with a low risk of bleeding

Back to Appendix Guide

## Dabigatran (Pradaxa)

A. Tables 4 and 5 provide guidance for management of dabigatran in the perioperative and postoperative period for planned procedures
B. Note that patients on targeted anticoagulant therapies (i.e., apixaban, dabigatran, rivaroxaban and edoxaban) do not require bridging due to the relatively quick onset of action and short half-life of these medications
C. Holding dabigatran prior to a procedure is based on renal function and the risk of bleeding associated with the procedure
D. **Inpatient Procedures REQUIRE** approval by proceduralist is before restarting therapy
E. **Outpatient Procedures RECOMMEND** restarting post-operative day +1 or 2 based on risk as in table 4 and 5 (below) unless otherwise specified by proceduralist

Table 4. **High Bleeding Risk Procedures**: Perioperative and Postoperative Recommendations for Dabigatran[2,14]

| | **Pre-Operative Period** | | | | | | | **Procedure** | **Post-Operative Period** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Renal Function** | **Day -7** | **Day -6** | **Day -5** | **Day -4** | **Day -3** | **Day -2** | **Day -1** | **Day 0** | **Day +1** | **Day +2** | **Day +3** |
| **>50 mL/min** | Continue dabigatran | Continue dabigatran | Continue dabigatran | Last dabigatran dose if neuraxial anesthesia, otherwise continue dabigatran | Last dabigatran dose before procedure (i.e., dabigatran-free period of 2 days before procedure) | No dabigatran | No dabigatran | No dabigatran | No dabigatran | May consider restarting dabigatran | Restart dabigatran if not already done |
| **30 to 50 mL/min** | Continue dabigatran | Last dabigatran dose if neuraxial anesthesia, otherwise continue dabigatran | Last dabigatran dose before procedure (i.e., dabigatran-free period of 4 days before procedure) | No dabigatran | No dabigatran | No dabigatran | No dabigatran | No dabigatran | No dabigatran | May consider restarting dabigatran | Restart dabigatran if not already done |
| **< 30 mL/min** | Last dabigatran dose if neuraxial anesthesia, otherwise continue dabigatran | Last dabigatran dose before procedure (i.e. dabigatran-free period 5 days before procedure) | No dabigatran | No dabigatran | No dabigatran | No dabigatran | No dabigatran | • Consider a hematology consult [2]<br>• Dabigatran is not recommended in patients with a CrCl < 30 mL/min [2] | | | |

Note: Recommendations for bridging and restarting anticoagulation therapy do not account for regional anesthesia. May consider longer times for patients undergoing major surgery, spinal puncture, or placement of a spinal or epidural catheter or port.

Back to Appendix Guide

Table 5. **Standard (Low) Bleeding Risk Procedures**: Perioperative and Postoperative Recommendations for Dabigatran[2,14]

| | Pre-Operative Period | | | | | Procedure | Post-Operative Period | |
|---|---|---|---|---|---|---|---|---|
| **Renal Function** | **Day -5** | **Day -4** | **Day -3** | **Day -2** | **Day -1** | **Day 0** | **Day +1** | **Day +2** |
| **>50 mL/min** | Continue dabigatran | Continue dabigatran | Continue dabigatran | Last dabigatran dose before procedure | No dabigatran | No dabigatran | Resume dabigatran 24 hours post-op | Resume dabigatran if not already done |
| **30 to 50 mL/min** | Continue dabigatran | Continue dabigatran | Last dabigatran dose before procedure | No dabigatran | No dabigatran | No dabigatran | Resume dabigatran 24 hours post-op | Resume dabigatran if not already done |
| **< 30 mL/min** | Last dabigatran dose before procedure if CrCl <15 mL/min | Last dabigatran dose before procedure if CrCl 15-29 mL/min | No dabigatran | No dabigatran | No dabigatran | • Consider a hematology consult [2]<br>• Dabigatran is not recommended in patients with a CrCl < 30 mL/min [2] | | |

Note: Recommendations for bridging and restarting anticoagulation therapy do not account for regional anesthesia. May consider longer times for patients undergoing major surgery, spinal puncture, or placement of a spinal or epidural catheter or port.

Back to Appendix Guide

## Factor Xa Inhibitors: Rivaroxaban(Xarelto), Apixaban (Eliquis) and Edoxaban (Savaysa)

**Tables 6 and 7 provide guidance for management of factor Xa inhibitors in the perioperative and postoperative period for planned procedures**

A. Note that patients on targeted anticoagulant therapies (i.e., apixaban, dabigatran, rivaroxaban and edoxaban) usually do not require bridging due to the relatively quick onset of action and short half-life of these medications.
B. Holding factor Xa inhibitors prior to a procedure is based on renal function and the risk of bleeding associated with the procedure
C. **Inpatient Procedures REQUIRE** approval by proceduralist is before restarting therapy
D. **Outpatient Procedures RECOMMEND** restarting post-operative day +1 or 2 based on risk as in table 6 and 7 (below) unless otherwise specified by proceduralist

Table 6. **High Bleeding Risk Procedures**: Perioperative and Postoperative Recommendations for Factor Xa Inhibitors[3,6,10]

| | Pre-Operative Period | | | | Procedure | Post-Operative Period | | |
|---|---|---|---|---|---|---|---|---|
| **Renal Function** | **Day -4** | **Day -3** | **Day -2** | **Day -1** | **Day 0** | **Day +1** | **Day +2** | **Day +3** |
| **>50 mL/min** | Continue apixaban, edoxaban or rivaroxaban | Last apixaban, edoxaban or rivaroxaban dose before procedure including neuraxial anesthesia (i.e. apixaban, edoxaban or rivaroxaban-free period of 2 days before procedure) | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | May consider restarting apixaban, edoxaban or rivaroxaban | Restart apixaban, edoxaban or rivaroxaban if not already done |
| **< 50 mL/min** | Last apixaban, edoxaban or rivaroxaban dose before procedure including neuraxial anesthesia | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | May consider restarting apixaban, edoxaban or rivaroxaban | Restart apixaban, edoxaban or rivaroxaban if not already done |

Note: Recommendations for bridging and restarting anticoagulation therapy do not account for regional anesthesia. May consider longer times for patients undergoing major surgery, spinal puncture, or placement of a spinal or epidural catheter or port.

Back to Appendix Guide

Table 7. **Standard (Low) Bleeding Risk Procedures**: Perioperative and Postoperative Recommendations for Factor Xa Inhibitors[3,6,10]

| | **Pre-Operative Period** | | | **Procedure** | **Post-Operative Period** | | |
|---|---|---|---|---|---|---|---|
| **Renal Function** | **Day -3** | **Day -2** | **Day -1** | **Day 0** | **Day +1** | **Day +2** | **Day +3** |
| **>50 mL/min** | Continue apixaban, edoxaban or rivaroxaban | Last apixaban, edoxaban or rivaroxaban dose before procedure | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | May consider restarting apixaban, edoxaban or rivaroxaban | May consider restarting apixaban, edoxaban or rivaroxaban | Restart apixaban, edoxaban or rivaroxaban if not already done |
| **< 50 mL/min** | Last apixaban, edoxaban or rivaroxaban dose before procedure | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | No apixaban, edoxaban or rivaroxaban | May consider restarting apixaban, edoxaban or rivaroxaban | Restart apixaban, edoxaban or rivaroxaban if not already done<br><br>For restarting see recommendations above |

Note: All recommendations for bridging and restarting anticoagulation therapy do not account for regional anesthesia. May consider longer times for patients undergoing major surgery, spinal puncture, or placement of a spinal or epidural catheter or port.

Back to Appendix Guide

## Unfractionated Heparin, Enoxaparin (Lovenox), Dalteparin (Fragmin), and Fondaparinux (Arixtra)

Table 8. Recommendations for Anticoagulant Management Prior to Planned Surgical and Interventional Procedures – Parenteral Anticoagulants

| Anticoagulant Medication | Pre-Operative Recommendation | Post-Operative Recommendation | Additional Considerations Dosing add |
|---|---|---|---|
| **Unfractionated Heparin (UFH)** | • Continuous IV infusion: Stop Infusion 4 to 6 hours prior to the procedure[10]<br>• Intermittent, Subcutaneous Dosing (VTE Prophylaxis): No holding required for doses of 7,500 or less, can consider holding one dose prior to procedure in patients with high bleed risk procedures | • Collaboration with proceduralist is **REQUIRED** before restarting therapy<br>• High risk bleeding surgical procedures: Re-initiate therapy 48 to 72 hours after the procedure[10]<br>• Low risk bleeding risk surgical procedures: Re-initiate therapy 24 hours after the procedure[10] | • Continuous IV infusion: Restart IV infusion at the same infusion rate (if therapeutic) without a bolus[10]<br>• Intermittent, Subcutaneous Dosing: Start at the same dose prior to surgery.<br>• Refer to the Thrombotic Risk Stratification for the full classifications of low, moderate, and high thrombotic risk |
| **Enoxaparin (Lovenox)**<br>**-OR-**<br>**Dalteparin (Fragmin)** | • Bridging Therapy Prior to the Procedure (BID Dosing): Administer the last dose 1 days (24 hours) prior to the procedure[10]<br>• Bridging Therapy Prior to the Procedure (Daily Dosing): Administer the last dose 2 days (36-48 hours) prior to the procedure<br>• General VTE Prophylaxis – Medical Patients: Last dose greater than 12 hours prior to procedure<br>• Treatment of DVT with or without PE: Last dose 24 hours prior to procedure<br>• Unstable Angina (UA) and Non-Q-Wave MI: Last dose 1 day (24 hours) prior to procedure<br>• Acute ST-Segment Elevated MI:<br>o Fibrinolytic therapy intervention: Administer between 15 minutes before and 30 minutes after the start of fibrinolytic therapy[7]<br>o PCI intervention: Do not administer enoxaparin if patient has received a SC dose within the last 8 hours before balloon inflation. If the last enoxaparin SC dose was greater than 8 hours ago, administer a 0.3 mg/kg by IV bolus[7] | • Collaboration with proceduralist is **REQUIRED** before restarting therapy<br>• Bridging Therapy Prior to the Procedure:<br>o High risk bleeding surgical procedures: Re-initiate therapy 48 to 72 hours after the procedure[10]<br>o Low bleeding risk surgical procedures: Re-initiate therapy 24 hours after the procedure[10]<br>• Prophylactic Dosing: Consider following the same recommendations above that are used for patients who are receiving bridging therapy before the procedure | • Restart patients at the same doses that were being used prior to the procedure<br>• Refer to the Thrombotic Risk Stratification for the full classifications of low, moderate, and high thrombotic risk |
| **Fondaparinux (Arixtra)** | • Give the Last dose 3 days (72 hours) prior to procedure based on product half-life and in patients with a normal renal function<br>• Patients with impaired renal function (CrCl 30-50 mL/min) may require holding therapy longer last dose 5-7 days before procedure<br>o May consider an Anti-Xa level in patients where there is a concern of residual fondaparinux impacting coagulation (eg, obesity, renal dysfunction) | • Collaboration with proceduralist is **REQUIRED** before restarting therapy<br>• VTE prophylaxis following hip fracture, hip replacement, knee arthroplasty, or abdominal surgery: initiate no sooner than 6 to 8 hours after surgery[5] | • Fondaparinux is contraindicated in patients with a CrCl < 30 mL/min and for VTE prophylaxis in patients weighing less than 50 kg who are undergoing hip fracture surgery, knee arthroplasty, or abdominal surgery[5]<br>o Fondaparinux may be used for acute symptomatic DVT and PE in patients who weigh < 50 kg[5]<br>• Refer to the Thrombotic Risk Stratification for the full classifications of low, moderate, and high thrombotic risk |

Note: All recommendations for bridging and restarting anticoagulation therapy do not account for regional anesthesia

Back to Appendix Guide

## Appendix B. Emergent Procedures – Managing Anticoagulant Medications

Refer to Guideline: Management of Anticoagulation-Associated Bleeding and Anticoagulation Reversal

## Appendix C. Pharmacokinetic Considerations for Anticoagulant Medications

Table 9. Oral and Parenteral Anticoagulant Pharmacokinetic Considerations[1-7,13, 22]

| Pharmacokinetic Property | Mechanism of Action | Bioavailability | Protein Binding | Time to Peak | Metabolism | Excretion | Half-Life |
|---|---|---|---|---|---|---|---|
| **Oral Anticoagulant Medications** | | | | | | | |
| **Warfarin (Coumadin)** | Inhibits the synthesis of vitamin K-dependent clotting factors II, VII, IX, and X and the anticoagulant proteins C and S | 100% | 99% | 4 hours | Hepatic (CYP2C9 and CYP3A4) | Renal 92% | 20 to 60 hours (mean ~ 40 hours) |
| **Dabigatran (Pradaxa)** | • Selective, direct reversible factor IIa (thrombin) inhibitor<br>• Inhibits free and clot-bound thrombin and thrombin induced-platelet aggregation | 3 to 7% | 35% | 1 hours | Hepatic (glucuronidation and P-glycoprotein) | Renal (~66%) | CrCl > 30 mL/min: 12 to 17 hours<br>CrCl < 30 mL/min: 27 hours |
| **Rivaroxaban (Xarelto)** | Direct, reversible inhibitor of factor Xa | 80 to 100% | 92 to 95% | 2 to 4 hours | Hepatic (CYP3A4) | Renal (~33% unchanged) | 5 to 9 hours (healthy adults 20 to 45 years old)<br>11 to 13 hours (elderly) |
| **Apixaban (Eliquis)** | Direct, reversible inhibitor of factor Xa Apixaban also indirectly inhibits platelet aggregation induced by thrombin | 50% | 87% | 3 to 4 hours | Hepatic (CYP3A4 and P-glycoprotein) | Renal (~27%) | 12 hours |
| **Edoxaban (Savaysa)** | A selective factor Xa inhibitor, inhibits free factor Xa and prothrombinase activity and inhibits thrombin-induced platelet aggregation | 62% | 55% | 1 to 2 hours | Hepatic (CYP3A4) | Renal 50% | 10-14 Hours |
| **Parenteral Anticoagulant Medications** | | | | | | | |
| **Enoxaparin (Lovenox)** | Strongly inhibits factor Xa and also inhibits antifactor IIa (antifactor thrombin) | 100% | None | 3 to 5 hours | Hepatic desulfation or depolymerization | Renal (10% unchanged) | 4.5 hours after a single subcutaneous dose and about 7 hours after repeated dosing |
| **Fondaparinux (Arixtra)** | • Selectively binds to antithrombin resulting in inhibition of Factor Xa<br>• It does not inactivate Factor II (thrombin) and has no known effect on platelet function | 100% | None | 2 hours | Has not been evaluated since the majority of drug is eliminated unchanged | Renal (77% unchanged) | 17 to 21 hours |
| **Heparin** | • Potentiates the action of antithrombin causing inactivation of thrombin and activated coagulation factors IX, X, XI, XII, and plasmin | Unknown<br>IV: immediate onset of action | Unknown | IV: 15 to 30 minutes<br>SQ: 2 to 4 hours | Hepatic and partial reticuloendothelial system | Renal (small amounts as unchanged drug) | Dose-dependent<br>Mean: 1.5 hours<br>(range, 1 to 2 hours) |

| Pharmacokinetic Property | Mechanism of Action | Bioavailability | Protein Binding | Time to Peak | Metabolism | Excretion | Half-Life |
|---|---|---|---|---|---|---|---|
| | • Also prevents the conversion of fibrinogen to fibrin | SQ: 20 to 30 minute onset of action | | | | | |

Abbreviations: IV = Intravenous; SQ = subcutaneous

Back to Appendix Guide

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**Approval and Revision Dates:** 12/2015 [System P&T]; 6/2014 [System P&T]; 8/2017 [System P&T] 11/2018 [System P&T]; 03/2019 [System P&T, electronic vote]

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