A. Purpose

The purpose of this agreement is to provide guidelines for the outpatient anticoagulation collaborative practice agreement with providers and pharmacists. It is common for novel oral anticoagulants (NOACs) such as dabigatran, rivaroxaban, or apixaban, and warfarin, low-molecular-weight-heparin (LMWH), fondaparinux, and heparin to be prescribed for the prevention or treatment of thrombosis. This protocol serves to optimize these therapies, improve patient outcomes, and ensure patient safety. It is not intended to encompass all aspects of therapy management. Clinical judgment and consideration of individual patient characteristics should always be included when making decisions regarding patient care.

B. Policy Statement

Under the supervision of the Medical Director of the Clinic, and in collaboration with the referring provider, the pharmacist will coordinate most aspects of anticoagulation therapy (order appropriate laboratory tests, adjust anticoagulant medications, schedule return appointments, etc.) in accordance with these guidelines. This will be done in accordance with State of Colorado Board of Pharmacy Rules and Regulations. See Colorado Board of Pharmacy Rule 6.00.00; Pharmaceutical Care, Drug Therapy management, and Practice by Protocol.

C. Supervision

Anticoagulation therapy should be managed by the pharmacist in collaboration with the Medical Director and/or referring provider following a patient-specific referral. The referring provider is ultimately responsible for therapeutic decisions regarding therapy.

Routine management of anticoagulation therapy should be provided by the pharmacist in accordance with this guideline. Consultation with a provider should occur under the following circumstances:

- Occurrence of significant bleeding regardless of INR
- Occurrence of potential thromboembolic complications
- Prior to the discontinuation of anticoagulation therapy
- Occurrence of an INR > 5.0 (or as determined by the referring provider)
- Patients are not compliant with appointments and/or medication
- Patients needing to be bridged for a procedure

D. Guideline

1. Care Management and Coordination

The pharmacist will maintain a patient profile and monitoring registry that lists each patient enrolled in the service. This registry list should be reviewed regularly to enable the pharmacist to:

- Identify all patients actively being managed by the service
- Ensure the scheduling of laboratory appointments for anticoagulation therapy monitoring
- Identify patients who have failed to return for laboratory monitoring as directed

The pharmacist will order and/or conduct point-of-care INR testing by contacting each patient by telephone and/or in person at the patient’s clinic appointment.
2. Communication and Documentation
Communication between pharmacists and patients or caregivers may occur via telephone, electronic mail and/or in person. All communications with patients and caregivers should be documented summarily in the patient’s medical record.

Communication between pharmacists and the Medical Director and/or referring provider may occur via telephone, the patient’s medical record, or in person depending on the acuity of the situation.

All communication with health care professionals should be documented in the patient’s medical record within 24 hours of any drug therapy modification. The Medical Director and/or referring/managing provider may override any action taken by the pharmacist as deemed appropriate.

In addition to the above, the anticoagulation clinic referral or patient’s medical record should contain the following information:
Patient demographic information
- Indication(s) for anticoagulation therapy
- Desired target range of anticoagulation intensity
- Desired length of anticoagulation therapy or date of next review
- Tablet size(s) of warfarin prescribed and used
- Relevant laboratory values
- Dosage and medication adjustments
- Other information pertinent to the patient’s anticoagulation therapy

The pharmacist managing anticoagulation will edit the patient’s active problem list and medical history with all pertinent information. All newly referred patients to the Pharmacy Anticoagulation Clinic should have an indication for anticoagulation on the active problem list. The “Notes” Section of the DX code should include INR goal and duration of therapy.

3. Patient Selection and Assessment
All patients should be referred by the Medical Director or other physician designee. Effective 2015, patients will receive an annual referral from their provider for enrollment in the service. Every January, pharmacy personnel will send a Telephone Encounter to the patient’s PCP for renewal of the referral.

For all patients referred for treatment with warfarin, all of the following should be taken into consideration:
- Relative/absolute contraindications for warfarin therapy (See Appendix A)
- Medical history and medication profile review
- Appropriate baseline laboratory values
- Determination of appropriate target INR and duration of therapy (See Appendix B)
- Monitoring and follow-up plan
- Patient education

4. Initiation of Therapy
Prior to initiation of anticoagulation therapy, an appropriate diagnosis should be objectively confirmed. The referring provider should determine the appropriateness of ongoing anticoagulation therapy for each patient, but the pharmacist should agree on appropriateness of treatment prior to enrollment in the anticoagulation clinic. The therapeutic range (INR) for each patient should be
determined by the Medical Director and/or referring provider in consultation with the pharmacist when appropriate. This will be documented on the patient’s problem list.

The recommended starting dose for most patients is 10 mg po daily for the first two days, then dosing based on INRs. However, starting at 2.5 mg po daily may be appropriate for patients with any of the following:

- Age > 60 years
- Untreated hyperthyroidism
- Malnourished patient
- Severe liver disease
- Decompensated Heart Failure
- Elevated baseline INR
- Low body weight
- Drug interactions (Appendix C)

Initial dose adjustments will be made using the Warfarin Initiation Nomogram. Some patients may require higher-than-expected doses of warfarin to get their INR into the therapeutic range. The cause for warfarin resistance can be either acquired (poor compliance, drug interactions, dietary interactions) or hereditary and should be taken into consideration when using higher-than-expected doses.

Following initiation of warfarin therapy, an INR should be checked after 2 to 3 days and every 2 to 7 days thereafter until the dose of warfarin stabilizes. More frequent monitoring may be necessary for patients being treated concurrently with injectable anticoagulants as well as those with an unexpected response to therapy, medical instability, or within 2 weeks of heart valve replace surgery. During initial titration, warfarin dosage increases should not exceed doubling the previous total weekly (or total daily) dose. Omitting or decreasing warfarin doses may be necessary in the setting of excessive INR response.

Low molecular weight heparin (LMWH, i.e. enoxaparin 1 mg/kg BID or 1.5mg/kg once daily) or fondaparinux should be administered concurrently with warfarin for the outpatient treatment of acute Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE). See Appendix D, Tables 1 and 2. Patients should receive an overlap of a parenteral agent with warfarin for at least 5 days and until the INR is therapeutic for 24 hours. The parenteral agent may be discontinued early for significant bleeding or supratherapeutic INR.

Patients being initiated on warfarin for atrial fibrillation may be started on LMWH plus warfarin if they are at a moderate to high risk for an embolic stroke. (See AHA Atrial fibrillation guidelines) LMWH does not need to be administered concurrently when the treatment is not urgent (eg, stable atrial fibrillation).

5. Maintenance and Management of Therapy

Pharmacists should utilize a standardized procedure for evaluating each anticoagulation laboratory result (see Appendix D, Figures 1 and 2). Patients with anticoagulation laboratory values outside the established therapeutic range should be questioned in an attempt to identify precipitating factors that, if corrected, would eliminate the need for dose adjustment (e.g. changes in medications, diet, health status, failure to adhere to prior dosage instructions, etc.). Identified precipitating factors should be appropriately documented. If no precipitating factors are documented, it is assumed that no precipitating factors were identified.
If no responsible factor can be identified, anticoagulant therapy should be adjusted and return laboratory visits scheduled in accordance with past dose-response data, pharmacokinetic principles, consultation with the patient’s healthcare provider if necessary, and the judgment of the pharmacist.

The Medical Director and/or referring provider should review the appropriateness of ongoing anticoagulation therapy annually. The pharmacist should contact the Medical Director and/or referring provider whenever clarification of the duration of anticoagulation therapy is required. Pharmacy personnel will send an annual Telephone Encounter to the provider requesting review of appropriateness of ongoing anticoagulation.

6. Laboratory Monitoring
   See “Initiation of therapy”
   Once a patient’s INR has been stabilized, INR values should be rechecked every 2-4 weeks unless one of the following conditions apply:
   - Changes in the patient’s other medications warrant re-checking the INR more frequently
   - When making a change in the patient’s maintenance dose
   - Changes in a patient’s diet, activity level, or health status
   If a patient’s INR has been checked every 3-4 weeks and has been in therapeutic range for 6 months on the same weekly dose of warfarin, then follow up INR checks can be scheduled every 6-8 weeks.

7. Patient Education
   Each patient enrolled in the anticoagulation service should receive verbal and/or written education regarding the appropriate use of anticoagulation therapy. Verbal and/or written educational material should be provided to each new patient from the pharmacist and/or other appropriate medical staff.

   The following learning objectives should be covered during educational efforts:
   - The reason for anticoagulation therapy and how it relates to clot formation
   - Name of anticoagulant medication(s)
   - How anticoagulant medication(s) works
   - The potential implications of too much or too little anticoagulation
   - The reasons behind the need for regular blood tests
   - The meaning of the INR and the desired INR range appropriate for the patient’s treatment
   - The importance of close monitoring and compliance with the therapeutic plan
   - Common symptoms and signs of bleeding
   - Common symptoms and signs of thromboembolism (e.g. stroke, deep venous thrombosis, pulmonary embolism, etc.)
   - Precautionary measures to decrease trauma and bleeding
   - Diet, drug, and alcohol use patterns that might cause complications with anticoagulation therapy
   - The effect of disease processes (e.g. fever, diarrhea) on the response to anticoagulation therapy
   - The importance of informing health care providers about ongoing anticoagulation therapy when dental, surgical, or invasive procedures and hospitalizations are scheduled or occur unexpectedly
   - What to do in case of an emergency
   - How INR monitoring will occur

   Provision of education should be documented in the patient’s medical record. The pharmacist should reinforce education regarding anticoagulation during subsequent interactions with the patient.
8. **Management of Therapy-Related Problems**

All complications related to anticoagulation therapy will be documented in the patient’s medical record.

### A. Bleeding Complications

A major bleeding episode should be defined as the occurrence of any of the following:

- Intraocular bleeding
- Retroperitoneal bleeding
- Central nervous system (CNS) bleeding
- Any bleeding into an enclosed anatomical space that threatens adjacent structures
- Bleeding resulting in a decrease in hemoglobin concentration of ≥2 gm/dl
- Any bleeding requiring transfusion of ≥2 units of packed red blood cells

The Medical Director and/or referring provider will be notified of patients experiencing major bleeding. These patients should be referred to an appropriate medical facility for medical attention. Pharmacists should assist health care personnel in determining proper management of the bleeding patient (e.g. method of anticoagulation therapy reversal) when necessary.

A minor bleeding episode is defined as any bleeding not satisfying the definition of major bleeding (e.g. increased bleeding from minor trauma sites, increased bruising, epistaxis controlled by home therapy, etc.)

Patients experiencing minor bleeding should be managed by the pharmacist based on the severity of the bleeding, the patient’s indication for anticoagulation therapy, and in consultation with the patient’s healthcare provider if appropriate. Referral for appropriate medical attention should be arranged if necessary. If possible, anticoagulation therapy should be maintained at the lower end of the target range until minor bleeding is resolved.

### B. Thromboembolic Complications

Patients experiencing symptoms of thromboembolic complications should be referred for appropriate medical attention. Thromboembolic complications include, but are not limited to:

- Venous thromboembolism (DVT and PE)
  - Arterial thromboembolism
  - Transient ischemic attack
  - Ischemic or embolic stroke
  - Prosthetic cardiac valve thrombosis

### C. Excessive Anticoagulation

Patients with an INR ≥ 5.0 utilizing point-of-care INR machine should have a confirmatory sample using a venous blood draw due to inaccuracy of point-of-care INR above INR of 5.0. The lab ordered should be a prothrombin time (PT).

Patients with excessively high INR values (≥5.0) who are not actively bleeding should be communicated to the Medical Director or other appropriate provider and managed according to the guidelines in Appendix E. Management should be facilitated and coordinated by the pharmacist in consultation with the referring provider when necessary.
Patients who are having an active major bleeding episode (see Section 8.A., above) should be referred to the Medical Director or other appropriate provider for medical attention. Pharmacists should facilitate and assist in the coordination of emergency services when necessary.

D. Subtherapeutic Anticoagulation
The following factors should be taken into consideration when determining the therapeutic plan for patients with subtherapeutic anticoagulation:

- The degree to which the INR is subtherapeutic,
- The estimated time that the patient’s INR may have been subtherapeutic,
- The individual’s risk of thromboembolism, and
- The estimated time required to reestablish therapeutic anticoagulation.

Based on the above factors, the pharmacist should identify and remedy the cause of the low INR if possible (e.g. medication noncompliance, interfering medications, dosage confusion, etc.), and promptly reestablish therapeutic anticoagulation. When appropriate, the pharmacist should also consult with the Medical Director and/or referring provider when determining the best therapeutic plan.

Critical values are defined as the following:

- INR <1.8 for the following patients:
  - First 6 to 8 weeks of therapy following acute DVT
  - First 3 months of treatment following PE or intracardiac thrombus
  - First 6 months of treatment for Aortic Value Replacement, and anytime during treatment for Mitral Valve Replacement

The medical director and/or referring provider will be notified of any critical values within 24 hours. These patients will be referred when appropriate to a health care provider for evaluation.

Cross-coverage is generally indicated in patients with an INR of <1.8 and any of the above “critical values.” See Appendix F, Table 1.

E. Interruption of Anticoagulation Therapy for Invasive Procedures
When appropriate, the pharmacist will consult with the Medical Director and/or referring provider to assist in determining the management of oral anticoagulation therapy in individuals requiring surgery or other invasive procedures.

The discussion should include the following questions:

- Based on the type of procedure, what is the risk of bleeding associated with continued anticoagulation?
- If anticoagulation therapy is temporarily stopped, what is the risk of thromboembolism?
- Is the thromboembolic risk associated with stopping warfarin sufficient to warrant cross-coverage with unfractionated heparin or LMWH?

Designing a peri-procedural plan for anticoagulation therapy should involve an individualized risk-benefit assessment. See Appendix F, Table 2 and Figure 1 for possible options.

Anticoagulation therapy should generally not be interrupted for routine dental procedures. Dentists, referring providers, and pharmacists should collaborate to ensure the INR is within acceptable limits prior to dental surgery for patients on warfarin.
F. Variable INR Response
For patients receiving warfarin therapy with a variable INR responses due to known and/or unknown causes for instability, the pharmacist should consult with the Medical Director and/or referring provider.

9. Management of warfarin drug interactions
Warfarin is metabolized by the cytochrome P450 system (2C9, 3A4, and 1A isoenzymes). Drugs that are either hepatic enzyme inducers or inhibitors may affect the INR. When a potential warfarin drug interaction is detected, the pharmacist should determine the management of oral anticoagulation therapy, in consultation with the Medical Director and/or referring provider, as appropriate. (See Appendix C)

Management of warfarin-aspirin combination
Pharmacists should ask patients about the use of aspirin therapy at least annually. Aspirin therapy should be stopped if the patient meets all the following criteria:
   1. No mechanical valves
   2. No history of warfarin failure
      a. No stroke/MI/PE/DVT history while taking warfarin monotherapy
   3. No documented coronary artery disease (CAD)
   4. No vascular disease requiring vessel reconstruction with stent, bypass, or grafting
   5. No anticardiolipin antibody syndrome
Aspirin discontinuation should be documented in medical record and a discontinuation notification should be sent to the patient’s primary care provider. Patient refusal should also be documented.

10. Non-compliance
Anticoagulation therapy requires a combination of healthcare provider and patient responsibility. Some patients who require anticoagulation therapy may lack the personal and social resources to comply safely with their prescribed anticoagulation regimen.

Patients who do not return for INR monitoring as directed will be managed as follows:
   ▪ Upon determination that the patient has missed their appointment for INR monitoring, they should be contacted by phone three times and reminded to return as soon as possible
   ▪ Patients who do not return for INR monitoring following three reminder calls should receive a letter requesting them to schedule an appointment.
   ▪ Pharmacists should contact the Medical Director and/or referring provider for the appropriateness of continuing therapy in patients who habitually fail to follow warfarin dosing.
Approval:

[Name of Medical Director or Collaborating Provider] [Date]
### Appendix A: Relative and Absolute Contraindication to Warfarin Therapy

<table>
<thead>
<tr>
<th>Relative Contraindications</th>
<th>Absolute Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senility</td>
<td>Blood dyscrasias (prone to bleeding)</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>Recent or planned neuro, ocular, or traumatic surgery</td>
</tr>
<tr>
<td>2\textsuperscript{nd} and 3\textsuperscript{rd} Trimester of Pregnancy</td>
<td>Malignant HTN</td>
</tr>
<tr>
<td>Poor patient reliability/compliance</td>
<td>Overt bleeding or active ulcerations</td>
</tr>
<tr>
<td></td>
<td>Current or recent cerebrovascular hemorrhage</td>
</tr>
<tr>
<td></td>
<td>Pericarditis or pericardial effusion</td>
</tr>
<tr>
<td></td>
<td>Eclampsia or pre-eclampsia</td>
</tr>
<tr>
<td></td>
<td>Spinal puncture</td>
</tr>
<tr>
<td></td>
<td>1\textsuperscript{st} Trimester of Pregnancy (esp. weeks 6-12)</td>
</tr>
<tr>
<td></td>
<td>Threatened abortion</td>
</tr>
</tbody>
</table>


# Appendix B: Recommended Intensity and Duration of Warfarin Therapy

<table>
<thead>
<tr>
<th>Target INR</th>
<th>Length of Therapy (level of Evidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0-3.0</td>
<td>3 months (1B)</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>at least 3 months (1B) then reevaluate</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>extended (1B)</td>
</tr>
<tr>
<td>LMWH x 3 – 6 months then Warfarin or LMWH</td>
<td>Long term (or until cancer resolves)</td>
</tr>
<tr>
<td>fondaparinux (2.5 mg daily, preferred) OR LMWH (enoxaparin 40mg daily)</td>
<td>4 weeks</td>
</tr>
<tr>
<td>N/A</td>
<td>no therapy (2B) or ASA 75-325mg (2B)</td>
</tr>
<tr>
<td>2.0-3.0 or dabigatran</td>
<td>long-term</td>
</tr>
<tr>
<td>2.0-3.0 or dabigatran</td>
<td>long-term</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>long-term (1B)</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>long-term (2C)</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>3 weeks/4weeks (1B)</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>long-term (1B)</td>
</tr>
<tr>
<td>2.5-3.5</td>
<td>Long term</td>
</tr>
<tr>
<td>2.5 – 3.5</td>
<td>Long term</td>
</tr>
<tr>
<td>2.5-3.5</td>
<td>long-term (2C)</td>
</tr>
<tr>
<td>N/A</td>
<td>aspirin 50-100mg (2C)</td>
</tr>
<tr>
<td>2.5 – 3.5</td>
<td>Long term</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>3 months then switch to ASA (2C)</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>3 months then reassess</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>Until thrombus resolves</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>Long term</td>
</tr>
<tr>
<td>2.0-3.0</td>
<td>indefinite (2B)</td>
</tr>
</tbody>
</table>

*CHADS2 C=Congestive Heart failure-1 point; H=Hypertension-1 point; A=Age >75 years-1 point; D=Diabetes-1 point; S2=Stroke or TIA- 2 points

**Chest. 2012;141(2_suppl):e1S-e801S**

http://health.ucsd.edu/specialties/anticoagulation/providers/warfarin/Pages/indications-duration.aspx
APPENDIX C: Clinically Significant Drug-Drug Interactions

<table>
<thead>
<tr>
<th>Clinically Significant Drug-Drug Interactions</th>
<th>DECREASED effect of Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCREASED effect of Warfarin</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Barbiturates</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Azole Antifungals</td>
<td>Cholestyramine</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Dicloxacillin</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Mesalamine</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Nafcillin</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Phenytion</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Ribavirin</td>
</tr>
<tr>
<td>Macrolide antibiotics</td>
<td>Rifampin</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Ritonavir</td>
</tr>
<tr>
<td>Propafenone</td>
<td>Sucralfate</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td></td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td></td>
</tr>
<tr>
<td>Sulfinpyrazone-Trihexoprim</td>
<td></td>
</tr>
</tbody>
</table>

This is not a complete list of interactions with warfarin. It is recommended to consult the latest edition of Micromedex, Lexi-Comp or other appropriate references for further information on drug interactions.

### Table 1: Appropriate starting dose of enoxaparin for patients with VTE (DVT or PE)

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Enoxaparin Dose* (doses based on estimated CrCl ≥ 30 ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35 – 45 kg</td>
<td>60 mg SC once daily</td>
</tr>
<tr>
<td>46 – 60 kg</td>
<td>80 mg SC once daily</td>
</tr>
<tr>
<td>61 – 75 kg</td>
<td>100mg SC once daily</td>
</tr>
<tr>
<td>76 – 90 kg</td>
<td>120mg SC once daily</td>
</tr>
<tr>
<td>91 – 110 kg</td>
<td>150mg SC once daily</td>
</tr>
<tr>
<td>111 – 135 kg</td>
<td>120mg SC twice daily</td>
</tr>
<tr>
<td>136 – 165 kg</td>
<td>150mg SC twice daily</td>
</tr>
<tr>
<td>&gt;165 kg</td>
<td>Consult with pharmacist</td>
</tr>
</tbody>
</table>

*Consult pharmacist for patients with CrCl <30ml/min

### Table 2: Appropriate starting dose of Fondaparinux for patients with VTE (DVT or PE)

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Fondaparinux Dose* (doses based on estimated CrCl ≥ 30 ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 kg</td>
<td>5 mg SC once daily</td>
</tr>
<tr>
<td>50-100 kg</td>
<td>7.5 mg SC once daily</td>
</tr>
<tr>
<td>&gt;100 kg</td>
<td>10 mg SC once daily</td>
</tr>
</tbody>
</table>

Contraindicated in patients with CrCl <30ml/min
Appendix D: Suggested Dose Adjustment and Monitoring of Warfarin Therapy

Figure 1: Suggested Dose Adjustment and Monitoring of Warfarin Therapy (Goal INR 2.5, Range 2 – 3)

***ADJUSTMENTS SHOULD BE MADE ACCORDING TO PATIENT CHARACTERISTICS AND CLINICAL JUDGEMENT***

Clinical Assessment
- compliance
- medication changes
- changes in diet
- lifestyle changes
- bruising/bleeding
- sign or symptoms of disease

Subtherapeutic
INR < 1.3
Increase weekly dose by 15 – 20 %
Labs in 5 – 7 day
Labs 2 weeks

INR 1.3 - 1.5
Increase weekly dose by 10 – 15%
Labs in 1 week
Labs 2 weeks

INR 1.5 - 1.8
Increase weekly dose by 5 – 10%
Labs in 2 weeks
Labs 2 weeks

INR 1.8 - 2.0
No change
Labs 2 weeks

INR 3.0 – 3.2
No change
Labs in 2 weeks

INR 3.2 – 4.0
Decrease weekly dose by 5 – 10%
Labs 2 weeks

INR 4.0 – 5.0
Decrease weekly by dose 10 – 15%
(Optional: Vitamin K 2.5 mg PO)
Labs in 1 week

Suprathapeutic
INR 5.0 – 9.0
Hold 1 - 2 doses
Decrease weekly dose by 15 – 20%
(Optional: Vitamin K 2.5 mg PO)
Labs 2 weeks

INR > 9.0
Hold dose until INR < 3
Decrease weekly dose by 15 – 20%
(Optional: Vitamin K 2.5 - 5 mg PO)

Yes
INR within therapeutic range?
Stable INR on same warfarin dose for 6 months?

No
Correctable factors?
(change in medications, compliance, illness, diet, ETOH, etc.)

Yes
Use clinical judgment; consider temporary adjustment and recheck in 1 – 2 wks

No
Recheck within 6-8 weeks

Recheck within 4 weeks
Figure 2: Suggested Dose Adjustment and Monitoring of Warfarin Therapy (Goal INR 3.0, Range 2.5 – 3.5)
***ADJUSTMENTS SHOULD BE MADE ACCORDING TO PATIENT CHARACTERISTICS AND CLINICAL JUDGEMENT***

**Clinical Assessment**
- compliance
- medication changes
- changes in diet
- lifestyle changes
- bruising/bleeding
- sign or symptoms of disease

**INR within therapeutic range?**
- Yes
  - Stable INR on same warfarin dose for 6 months?
    - Yes
      - Recheck within 6-8 weeks
    - No
      - Recheck within 4 weeks
- No
  - Correctable factors?
    - Yes
      - Use clinical judgment; consider temporary adjustment and recheck in 1 – 2 wks
    - No
      - Recheck within 6 weeks

**Subtherapeutic**
- INR < 1.8
  - Increase weekly dose by 15 – 20%
  - Labs in 5 – 7 day
  - Labs 2 weeks
- INR 1.8-2
  - Increase weekly dose by 10 – 15%
  - Labs in 1 week
  - Labs 2 weeks
- INR 2-2.3
  - Increase weekly dose by 5 – 10%
  - Labs in 2 weeks
  - Labs 2 weeks
- INR 2.3-2.5
  - No change
  - Labs 2 weeks

**Supratherapeutic**
- INR 3.5 – 3.7
  - No change
  - Labs in 2 weeks
- INR 3.7-4.5
  - Decrease weekly dose by 5 – 10%
  - Labs 2 weeks
- INR 4.5-5.0
  - Decrease weekly dose by 10 – 15%
  - Labs in 1 week
- INR 5.0 – 9.0
  - Decrease weekly dose by 15 – 20%
  - Labs in 3 days
  - (Optional: Vitamin K 2.5 mg PO)
- INR 5.0 – 9.0
  - Hold 1 - 2 doses
  - Decrease weekly dose by 15 – 20%
  - (Optional: Vitamin K 2.5 - 5 mg PO)
- INR > 9.0
  - Hold dose until INR < 3
  - Decrease weekly dose by 15 – 20%
  - Labs in 3 days
  - (Optional: Vitamin K 2.5 - 5 mg PO)
Appendix E: Management of Supratherapeutic INR and/or Bleeding Complications

Any INR >5 on the CoaguChek machine should be confirmed with a venous blood draw. A prothrombin time (PT) should be ordered. An aPTT will not deliver appropriate results.

Table 1. Guideline for the management of excessive anticoagulation in the absence of bleeding

<table>
<thead>
<tr>
<th>INR Value</th>
<th>Suggested Management</th>
<th>Next INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.5 to 10</td>
<td>Temporarily discontinue warfarin administration; instruct the patient to monitor for symptoms of bleeding and to notify the anticoagulation service immediately if symptoms occur</td>
<td>24 to 72 hours</td>
</tr>
<tr>
<td>&gt;10</td>
<td>When possible, administer vitamin K (2.5 mg orally, 1 mg intravenously, or 1 mg subcutaneously [only if oral or intravenous unavailable]); Alternative forms of oral vitamin K such as V8® juice, Ensure®, green tea, etc. should also be considered when other forms of vitamin K are unavailable</td>
<td>12 to 24 hours</td>
</tr>
</tbody>
</table>

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# Appendix F: Managing Complications of Anticoagulant Therapy

Table 1: Options for unfractionated heparin and low-molecular-weight heparin cross-coverage

<table>
<thead>
<tr>
<th>Agent</th>
<th>Therapeutic dose</th>
<th>Prophylactic dose</th>
</tr>
</thead>
</table>
| Unfractionated heparin (UH)| **Pre-procedure**
Begin intravenous UH 2 days pre-procedure, titrate to therapeutic aPTT; stop infusion 4 to 6 hours prior to procedure

**Post-procedure**
Restart UH infusion without a loading dose 12 to 24 hours post-procedure when risk of bleeding determined to be safe
Continue until INR is within therapeutic range

|                                | **Pre-procedure**
Rarely indicated                                                                | **Post-procedure**
Begin 24 hours post-procedure when risk of bleeding determined to be safe; dose is 5,000 to 7,500 units subcutaneously every 8 to 12 hours
Continue until INR is within therapeutic range                                      |

| Low-molecular-weight heparin (LMWH) | **Pre-procedure**
Begin 2 days prior to procedure in the morning
Dose: enoxaparin 1 mg/kg every 12 hours subcutaneously or 1.5 mg/kg every day subcutaneously
Last dose in the morning on the day prior to the procedure |

**Post-procedure**
Begin 24 to 72 hours post-procedure when risk of bleeding determined to be safe
Continue until INR is within therapeutic range |

|                                | **Pre-procedure**
Rarely indicated                                                                | **Post-procedure**
Begin 24 hours post-procedure when risk of bleeding determined to be safe
Dose: enoxaparin 30 mg every 12 hours or 40 mg every day subcutaneously
Continue until INR is within therapeutic range                                      |
### Table 2. Risk profiles for bleeding and thromboembolic complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Low risk</th>
<th>Medium risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bleeding</strong></td>
<td>Cutaneous biopsy</td>
<td>Acute venous thromboembolic event within past 2 to 3 months</td>
<td>Central Nervous System surgery</td>
</tr>
<tr>
<td></td>
<td>Potentially bloodless surgery (e.g. cataract)</td>
<td>Recurrent venous thromboembolic disease (last episode at least 3 months ago)</td>
<td>Major thoracic, abdominal or pelvic surgery</td>
</tr>
<tr>
<td></td>
<td>Other open procedures</td>
<td>History of thromboembolic event with active cancer</td>
<td>Polypectomy via colonoscopy</td>
</tr>
<tr>
<td></td>
<td>Dental procedures</td>
<td>History of thromboembolic event with diagnosis of heterozygous factor V leiden mutation, elevated factor VIII or PT2010A mutation</td>
<td>Other closed procedures</td>
</tr>
<tr>
<td><strong>Thromboembolism</strong></td>
<td>Acute venous thromboembolic event &gt;3 month ago</td>
<td>急性静脉血栓事件在3个月内</td>
<td>Acute venous thromboembolic event within past month</td>
</tr>
<tr>
<td></td>
<td>Uncomplicated nonvalvular atrial fibrillation with CHADS2 score 1-2)</td>
<td>History of thromboembolic event with active cancer</td>
<td>History of thromboembolic event while on warfarin or during warfarin interruption</td>
</tr>
<tr>
<td></td>
<td>Bileaflet mechanical heart valve in the aortic position without additional risk factors*</td>
<td>History of thromboembolic event with diagnosis of heterozygous factor V leiden mutation, elevated factor VIII or PT2010A mutation</td>
<td>History of thromboembolic event with diagnosis of protein C, protein S or ATIII deficiency, APLA or multiple hypercoagulable traits</td>
</tr>
<tr>
<td></td>
<td></td>
<td>History of thromboembolic event undergoing surgery with high risk of DVT (ie. THA, TKA)</td>
<td>Atrial fibrillation with acute arterial thromboembolic event within past 3 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonvalvular atrial fibrillation with CHADS2 score 3-4</td>
<td>Atrial fibrillation with CHADS2 score 4-6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mechanical heart valve implanted &gt;6 weeks ago with 1 additional risk factor*</td>
<td>Mechanical heart valve implanted &gt;6 weeks ago with &gt;1 additional risk factor*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Apical wall motion abnormality without mural thrombus</td>
<td>Atrial fibrillation with rheumatic mitral valve disease (moderate to severe stenosis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fixed mural thrombus without presence of symptoms (e.g. TIA)</td>
<td>Mobile mural thrombus in the presence of symptoms (e.g. TIA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fixed mural thrombus without presence of symptoms (e.g. TIA)</td>
<td>Mechanical or bioprosthetic heart valve implanted &lt;6 weeks ago</td>
</tr>
</tbody>
</table>

*Risk factors for arterial thromboembolism in mechanical heart valve: prior thromboembolism, atrial fibrillation, caged ball or caged disk valve, more than one mechanical valve, valve in mitral position, severe left ventricular dysfunction (last ejection fraction <30%), age >65 years.
Figure 1: Options for interrupting warfarin for invasive procedures

- **Low TE risk without anticoagulation**
  - **Bleeding risk**
    - Low
      - Perform procedure under full or reduced anticoagulation
        - **Before procedure:**
          - No change in warfarin dose, or
          - Reduce warfarin dose 2-3 days before procedure to allow INR to decline to subtherapeutic range
        - **After procedure:**
          - Resume/continue previous warfarin dose
    - High
      - Perform procedure under normal hemostasis
        - **Before procedure:**
          - Stop warfarin 3-5 days prior to procedure
          - Check INR day prior to procedure
          - Consider vitamin K 2.5 mg orally if INR >1.7
        - **After procedure:**
          - Restart warfarin as soon as possible
- **Medium TE risk without anticoagulation**
  - **Bleeding risk**
    - Low
      - Perform procedure under full or reduced anticoagulation
        - **Before procedure:**
          - No change in warfarin dose, or
          - Reduce warfarin dose 2-3 days before procedure to allow INR to decline to subtherapeutic range
        - **After procedure:**
          - Resume/continue previous warfarin dose
    - High
      - Perform procedure under normal hemostasis
        - **Before procedure:**
          - Stop warfarin 3-5 days prior to procedure
          - Check INR day prior to procedure
          - Consider vitamin K 2.5 mg orally if INR >1.7
        - **After procedure:**
          - Restart warfarin as soon as possible
          - Therapeutic dose cross-coverage not typically indicated
          - Consider prophylactic cross-coverage for VTE history and multiple medium risk factors
- **High TE risk without anticoagulation**
  - **Bleeding risk**
    - Low
      - Perform procedure under full or reduced anticoagulation
        - **Before procedure:**
          - No change in warfarin dose, or
          - Reduce warfarin dose 2-3 days before procedure to allow INR to decline to subtherapeutic range
        - **After procedure:**
          - Resume/continue previous warfarin dose
    - High
      - Perform procedure under normal hemostasis
        - **Before procedure:**
          - Stop warfarin 3-5 days prior to procedure
          - Check INR day prior to procedure
          - Consider vitamin K 2.5 mg orally if INR >1.7
        - **OR**
          - Stop warfarin 2 days prior to procedure
          - Check INR day prior to procedure
          - Give vitamin K 2.5 mg orally unless INR <1.7
        - **After procedure:**
          - Restart warfarin as soon as possible
          - Start therapeutic dose cross-coverage 24-72 hours after procedure
References


   http://health.ucsd.edu/specialties/anticoagulation/providers/warfarin/Pages/indications-duration.aspx