Clinical Directive for Warfarin Management in Adult Ambulatory Patients

Author: Anne Rose, Pharm.D.
Coordination: Lee Vermeulen, MS, RPh, FCCP, Director of CDP
Reviewed by: Anticoagulation Task Force
Approved by: Pharmacy and Therapeutics Committee
Next Scheduled Review Date: 2011

I. PURPOSE
To establish a consistent standard for the management of warfarin therapy in adult ambulatory patients using a clinical guideline and an individualized approach.

II. POLICY
Warfarin is the oral anticoagulant of choice for treatment and prophylaxis of venous thrombosis and pulmonary embolism. It is also used to prevent complications of embolism in high-risk patients including but not limited to those with chronic atrial fibrillation, prosthetic heart valves, and those undergoing major orthopedic surgery. Warfarin falls into a category of medications with a narrow therapeutic index which relies on a specific range for benefit and reduction of complications. Because of this narrow therapeutic index, warfarin has been associated with bleeding complications, longer lengths of stay, and higher hospitalization costs.

III. PROCEDURE FOR INITIATION OF ANTICOAGULATION DURING CLINIC VISIT
A. Physician Evaluation
   1. The provider will evaluate the patient’s need for anticoagulation during the clinic visit

B. Patient Assessment
   1. Initial warfarin dosing should be tailored based on patient bleed risk, potential sensitivity to warfarin, indication, goal INR range, and potential for existing drug interactions (See Guidelines for Ambulatory Warfarin Management in Adults)
   2. If appropriate, patients should receive another form of anticoagulation such as LMWH for at least 5 days and until they are therapeutic on warfarin for 24-48 hours

C. Prior to initiating warfarin
   1. A baseline INR must be resulted within the previous 30 days
   2. CBC with platelets, ALT, total bilirubin, and creatinine must be resulted within the past 90 days
   3. If no baseline of above is available the patient must be sent to lab to get an INR drawn prior to prescribing warfarin
   4. For women of child bearing age a pregnancy test is recommended

D. Initial warfarin dosing
   1. Table 1 should be utilized to identify patients who may be potentially sensitive to warfarin
   2. Table 2 should be utilized for initial dose and time to next INR follow up.
   3. A dose larger than the anticipated maintenance dose (loading dose) of warfarin is inappropriate and should not be used.
   4. The provider must prescribe the initial warfarin dose and schedule the next INR check before delegating warfarin management to pharmacist or nurse.

E. Maintenance warfarin management
   1. The provider may choose to manage warfarin therapy, utilize nursing staff resources, or refer the patient to an anticoagulation clinic.
   2. If outsourcing warfarin management to nursing staff or anticoagulation clinic the ordering provider must personally communicate the following:
      i. Indication for anticoagulation
      ii. Target INR range
      iii. Anticipated duration of anticoagulation and/or review date
iv. Initial warfarin starting dose  
v. Time for next INR draw  
vi. Need for bridge therapy  
vii. Concurrent drug therapy  
viii. Bleeding risk, if applicable  
ix. Any medical or social issue which may influence compliance or outcomes

IV. PROCEDURE FOR ANTICOAGULATION FOLLOW-UP AFTER HOSPITAL DISCHARGE  
A. Physician Evaluation  
   1. The provider will evaluate discharge recommendations for anticoagulation
B. Maintenance warfarin management  
   1. The provider may choose to manage warfarin therapy, utilize nursing staff resources, or refer the patient to an anticoagulation clinic
   2. If outsourcing warfarin management to nursing staff or anticoagulation clinic the provider must personally communicate the following:  
      i. Indication for anticoagulation  
      ii. Target INR range  
      iii. Anticipated duration of anticoagulation and/or review date  
      iv. Warfarin dose at discharge  
      v. Start date of warfarin therapy  
      vi. Time for next INR draw  
      vii. Concurrent drug therapy  
      viii. Bleeding risk, if applicable  
      ix. Any medical or social issue which may influence compliance or outcomes

V. DOCUMENTATION FOR INITIAL ANTICOAGULATION VISIT  
A. Upon initiation of warfarin or agreement to follow a patient’s anticoagulation the following information must be documented in the patient’s electronic medical record:  
   1. Indication for anticoagulation  
   2. Target INR range  
   3. Anticipated duration of anticoagulation or review date  
   4. Medication dose and tablet strength  
   5. Telephone contacts for the patient and the patient’s pharmacy  
   6. Completion of warfarin patient education that highlights the importance of the following:  
      i. Follow-up  
      ii. Monitoring  
      iii. Compliance  
      iv. Dietary restrictions  
      v. Potential for drug interactions  
      vi. Potential adverse reactions
B. This initial note may be placed by the following provider, nursing staff, or anticoagulation clinic

VI. PROCEDURE FOR FOLLOW-UP ANTICOAGULATION VISITS  
A. Patient follow up will occur within 24 hours of the reported INR level  
B. Follow up may be completed via telephone conversation or scheduled clinic visit  
C. At each patient encounter (clinic appointment or telephone conversation, etc.) for INR monitoring patients must be assessed for any missed doses, changes in diet or activity and any other changes that may affect INR level  
D. Refer to Appendix A for the complete list of assessment questions that should be addressed at each patient encounter for INR management  
E. Maintenance warfarin dosing
1. Missed doses, recent INR trends, changes in diet and/or activity, or changes to medications should be taken into account before making a dosing change.
4. Warfarin doses must not be adjusted without a resulted INR.
5. If the patient is within the first 7 days of therapy table 2 should be utilized for dose adjustments and time to next INR draws.
6. If the patient is greater than 7 days after initiating warfarin therapy tables 3 or 4 should be utilized for dose adjustments depending on target INR range.
7. If the reported INR is above the specified range for accuracy per point of care testing machine, a repeat venipuncture is required to verify INR result. Use the repeated venipuncture INR to determine if a dose change is needed.

D. Management of elevated INR
1. INR 5.1-9.0 requires a physician notification and approval of adjusted dose.
   i. Refer to table 3 or 4 for treatment options for elevated INR.
   ii. Consider checking a hematocrit level.
2. INR > 9.0 requires urgent evaluation by a physician.
   i. Refer to table 3 or 4 for treatment options for elevated INR.

E. Follow up
1. The health care provider managing warfarin therapy will instruct the patient on when to have the next INR level checked.
2. For newly initiated patients who have not achieved a stable warfarin dose refer to table 5 for follow up recommendations.
3. Refer to table 6 for follow up recommendations for maintenance warfarin patients.

F. Documentation
1. After each patient encounter for INR monitoring a note must be placed in the patient’s medical record.
2. Each note should include
   i. Patient assessment questions (- See appendix A)
   ii. Previous warfarin dose
   iii. Most recent INR
   iv. Recommended warfarin dose based on the most recent INR
   v. Date of next INR check

IV. Patient Education
A. Education must be provided to all patients receiving anticoagulation at their initial visit for initiating anticoagulation and thereafter if reinforcement is needed.
   1. Anticoagulation is defined as warfarin, unfractionated heparin and low molecular weight heparin.
B. Anticoagulation education must include information on the importance of:
   1. Follow up
   2. Monitoring
   3. Compliance
   4. Dietary restrictions
   5. Potential adverse drug reactions
   6. Potential drug interactions
C. The following patient education material has been designed to encompass the above information.
   1. Health Facts For You #6900: Warfarin Information Booklet
   2. Health Facts For You #6915: Unfractionated Heparin/Low Molecular Weight Heparin Drug Information Sheet
D. Completion of education must be documented within the patient’s medical record.

V. PROCEDURE FOR REFERAL ANTICOAGULATION CLINICS
A. Prior to referring patients to an anticoagulation clinic the provider must first
   1. Verbally communicate with the clinic regarding patient referral.
2. After verbal confirmation of acceptance to clinic the provider must send an official consult
3. If anticoagulation clinic discharges the patient from the clinic based on poor compliance, follow up the referring provider must be contacted
   i. The referring provider will be responsible for identifying additional follow up for the patient
B. UW affiliated anticoagulation clinics will follow the same above procedures for documentation of initial and follow up appointments, management of INRs and patient education.

Table 1. Factors for Identifying Warfarin Sensitive Patients

<table>
<thead>
<tr>
<th>High Sensitivity Warfarin</th>
<th>Low Sensitivity Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline INR ≥ 1.5</td>
<td>Baseline INR &lt; 1.5</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>Age ≤ 65</td>
</tr>
<tr>
<td>Actual body weight &lt; 45 kg or actual &lt; ideal</td>
<td>No other risk factors</td>
</tr>
<tr>
<td>Malnourished/ NPO &gt;3 days</td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia &lt;2 g/dl</td>
<td></td>
</tr>
<tr>
<td>Chronic diarrhea</td>
<td></td>
</tr>
<tr>
<td>Significant drug interactions (see Table 7)</td>
<td></td>
</tr>
<tr>
<td>Decompensated heart failure</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
</tr>
<tr>
<td>Current antiplatelet therapy</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia: platelet &lt;75 K/uL</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse history</td>
<td></td>
</tr>
<tr>
<td>Significant hepatic disease: cirrhosis or total bilirubin &gt;2.4 mg/dl</td>
<td></td>
</tr>
<tr>
<td>End stage renal disease</td>
<td></td>
</tr>
<tr>
<td>GI bleed within past 30 days</td>
<td></td>
</tr>
<tr>
<td>Surgery within past 2 weeks</td>
<td></td>
</tr>
<tr>
<td>Intracranial bleed within past 30 days</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Warfarin Initiation Dosing Protocol (Week 1) with INR Goal 2-3

<table>
<thead>
<tr>
<th>Day Therapy</th>
<th>INR Value</th>
<th>Dose Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
<td>5 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2.5 mg daily if high sensitivity to warfarin identified)</td>
</tr>
<tr>
<td>In 2-3 days after initiation</td>
<td>&lt; 1.5</td>
<td>5 – 7.5 mg daily</td>
</tr>
<tr>
<td></td>
<td>1.5-1.9</td>
<td>2.5 - 5 mg daily</td>
</tr>
<tr>
<td></td>
<td>2.0-2.5</td>
<td>2.5 mg daily</td>
</tr>
<tr>
<td></td>
<td>2.5-3.0</td>
<td>0-2.5 mg daily</td>
</tr>
<tr>
<td></td>
<td>&gt; 3.0</td>
<td>Hold and recheck INR next day</td>
</tr>
<tr>
<td>In additional 2-3 days after last INR check</td>
<td>&lt; 1.5</td>
<td>7.5 – 10 mg daily</td>
</tr>
<tr>
<td></td>
<td>1.5-1.9</td>
<td>5 – 10 mg daily</td>
</tr>
<tr>
<td></td>
<td>2.0-3.0</td>
<td>2.5 – 5 mg daily</td>
</tr>
<tr>
<td></td>
<td>&gt; 3.0</td>
<td>Hold warfarin, recheck in 1-2 days</td>
</tr>
</tbody>
</table>
Table 3. Warfarin Maintenance Dosing Protocol with INR Goal 2-3

<table>
<thead>
<tr>
<th>INR &lt; 1.5</th>
<th>INR 1.5 - 1.9</th>
<th>INR 2.0 - 3.0</th>
<th>INR 3.1- 4.0*</th>
<th>INR 4.1-5.0*</th>
<th>INR 5.1- 9.0*</th>
<th>INR &gt; 9.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extra Dose Increase weekly dose 10-20%</td>
<td>Increase weekly dose 5-10%</td>
<td>No change</td>
<td>Decrease weekly dose 5-10%</td>
<td>Hold 1 dose Decrease weekly dose 10%</td>
<td>MD order required</td>
<td>Contact MD for urgent patient evaluation</td>
</tr>
<tr>
<td><strong>See Treatment Recommendations for Elevated INR (Guidelines for Ambulatory Warfarin Management)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* If the INR is above the specified range for accuracy per POC device, a repeat venipuncture is required to verify INR

Table 4. Warfarin Maintenance Dosing Protocol with INR Goal 2.5-3.5

<table>
<thead>
<tr>
<th>INR &lt; 1.9</th>
<th>INR 1.9 - 2.4</th>
<th>INR 2.5 - 3.5</th>
<th>INR 3.6 - 4.5*</th>
<th>INR 4.6-5.0*</th>
<th>INR 5.1- 9.0*</th>
<th>INR &gt; 9.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extra Dose Increase weekly dose 10-20%</td>
<td>Increase weekly dose 5-10%</td>
<td>No change</td>
<td>Decrease weekly dose 5-10%</td>
<td>Hold 1 dose Decrease weekly dose 10%</td>
<td>MD order required</td>
<td>Contact MD for urgent patient evaluation</td>
</tr>
<tr>
<td><strong>See Treatment Recommendations for Elevated INR (Guidelines for Ambulatory Warfarin Management)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* If the INR is above the specified range for accuracy per POC device, a repeat venipuncture is required to verify INR

Table 5. Frequency of INR Monitoring After Initiation of Warfarin

<table>
<thead>
<tr>
<th>INR Check</th>
<th>INR Monitoring Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every 2 – 3 days</td>
<td>Until INR within therapeutic range on 2 consecutive INR checks</td>
</tr>
<tr>
<td>Then every week</td>
<td>Until INR within therapeutic range on 2 consecutive INR checks</td>
</tr>
<tr>
<td>Then every 2 weeks</td>
<td>Until INR within therapeutic range on 2 consecutive INR checks</td>
</tr>
<tr>
<td>Then every 4 weeks</td>
<td>When dose is stable check monthly</td>
</tr>
</tbody>
</table>

Table 6. Frequency of INR Monitoring for Maintenance of Warfarin

<table>
<thead>
<tr>
<th>INR Check</th>
<th>INR Monitoring Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>In 1 week</td>
<td>If dose adjusted by 10-20%, starting or stopping an interacting medication, change in diet, change in activity level or other change that could affect INR</td>
</tr>
<tr>
<td>Every 1-2 weeks</td>
<td>If dose adjusted by 5-10%</td>
</tr>
<tr>
<td>Every 4 weeks</td>
<td>If patient maintained on same stable dose</td>
</tr>
</tbody>
</table>
Table 7. Common Drug Interactions

<table>
<thead>
<tr>
<th>Interactions that increase INR*</th>
<th>Drug</th>
<th>Time to Effect</th>
<th>Suggested Dose Change</th>
<th>Time to Recheck INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoroquinolones</td>
<td>Within 3-5 days</td>
<td>Decrease warfarin dose 30%</td>
<td>After 5-7 days of starting or discontinuing therapy</td>
<td></td>
</tr>
<tr>
<td>Macrolides</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMP/Sulfa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Within 3-5 days</td>
<td>Decrease warfarin dose 30%</td>
<td>After 5-7 days of starting or discontinuing therapy</td>
<td></td>
</tr>
<tr>
<td>Itraconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Within 7-14 days</td>
<td>Decrease warfarin dose 50%</td>
<td>Every 7 days for 1 month after starting or discontinuing therapy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interactions that decrease INR*</th>
<th>Drug</th>
<th>Time to Effect</th>
<th>Suggested Dose Change</th>
<th>Time to Recheck INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dicloxacillin</td>
<td>Within 4-7 days</td>
<td>Increase warfarin dose 30%</td>
<td>After 5-7 days of starting or discontinuing therapy</td>
<td></td>
</tr>
<tr>
<td>Nafcillin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rifampin</td>
<td>Within 7-14 days</td>
<td>Increase warfarin dose 50-60%</td>
<td>Every 7 days for 1 month after starting or discontinuing therapy</td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Within 14 days</td>
<td>Increase warfarin dose 30%</td>
<td>Every 7 days for 1 month after starting or discontinuing therapy</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX A.

Patient Assessment Tool

1. Verify patient dose (patient repeats what dose they have been taking)
2. Missed doses: Y/N
3. Medication Changes Y/N
4. Diet Changes: Y/N
5. Alcohol Use: Y/N
6. Activity Change: Y/N
7. Diarrhea: Y/N
8. Nausea: Y/N
9. Fever: Y/N
10. Nose Bleeds: Y/N
11. Bloody Sputum: Y/N
12. Bloody Emesis: Y/N
13. Bloody Stool: Y/N
14. Bloody Urine: Y/N
15. Falls/Injuries Y/N
16. Abnormal Bleeding: Y/N
17. Abnormal bruising: Y/N
18. Chest Pain: Y/N
19. Shortness of Breath: Y/N
20. Dizziness: Y/N
21. Headache: Y/N
22. Numbness: Y/N
23. Vision Changes: Y/N
24. Confusion/Slurred Speech: Y/N
25. New Pain/Swelling: Y/N
26. Upcoming surgery or procedures: Y/N
27. Change in medical condition: Y/N
   (ie. Cancer dx/liver disease)

If YES is answered to any of the above, explain details in note section.

References: