Choosing an Anticoagulant

This CPM presents a model of care based on scientific evidence available at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative.

Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base.

If you have questions or concerns regarding this information, contact:

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This CPM is part of Presbyterian's Clinical Care Model, a broad, enterprise-wide body of documentation covering PHS' functions, programs, and care pathways, intended to build organizational acumen, facilitate cross-system collaboration, and accelerate our implementation of clinical initiatives.

Find all of PHS’ Care Model at www.PHSCareModel.org.

This Clinical Practice Model (CPM) summarizes evidence-based guidelines for:

- Adults over the age of 18
- With indications for anticoagulant therapy, including:
  - Prevention and treatment of venous thromboembolism (VTE)
  - Stroke prevention in the setting of atrial fibrillation
  - Prevention of valve thrombosis and arterial thromboembolism in patients with prosthetic heart valve

Based on recommendations from Presbyterian's Anticoagulation Subcommittee, this CPM offers Providers and Pharmacist Clinicians guidance for initiating anticoagulation.

Why Focus on Anticoagulants?

Management of anticoagulants is challenging. Although warfarin remains an inexpensive and useful agent in the treatment and prevention of thromboembolic disorders, it is not without its drawbacks. The anticoagulated patient requires regular monitoring. Warfarin is the second most commonly implicated drug in emergency department visits for adverse drug events (ADEs) in the US. Moreover, anticoagulants are the most common drug class associated with an inpatient adverse event and have been shown to be the cause of 41% of deaths attributed to an ADE. Newer oral anticoagulants provide a more predictable dose-response, thus, eliminating the need for routine laboratory monitoring, along with the added benefit of fewer drug–drug and drug–nutrient interactions. However, these newer medications have challenges: clinical experience is lacking; there are no reliable coagulation monitoring assays to measure the anticoagulant effect of these agents; and some antidotes to reverse bleeding (in cases of overdose or when an urgent surgical procedure) are still pending. Finally, the number of patients receiving anticoagulants is substantial and is expected to grow with time.

Care Pathway Roles and Responsibilities

<table>
<thead>
<tr>
<th>Responsibility</th>
<th>Clinician</th>
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<tbody>
<tr>
<td>Initiate orders for anticoagulant medication, authorize refills, adjust dosages, and discontinue therapy</td>
<td>Provider or Pharmacist Clinician*</td>
</tr>
<tr>
<td>Manage patient intake, evaluation (including INR testing), and education</td>
<td>Nurse Care Manager (RNCM) or Pharmacist Clinician</td>
</tr>
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*In the State of New Mexico, Pharmacist Clinicians have prescriptive authority; they can independently prescribe any medication used in the scope of a primary care visit, as well as manage a spectrum of common chronic disease states, including anticoagulant therapy.

Evidence/Resources

Notes:

1. DOACs have much higher co-pays compared to warfarin and may cause the Medicare patient to fall into the coverage gap (donut hole) phase earlier.
2. In clinical trials, few patients had CrCl less than 30. DOACs are either contraindicated or to be used cautiously in patients with significant hepatic disease or mechanical valves.
3. Warfarin is affected by diet and general health status, has many medication interactions, and may be complicated to manage peri-procedurally.
4. Each DOAC is only approved for certain indications and may have warnings about use in specific populations and with certain concurrent medications. Review the Quick Reference for Direct Oral Anticoagulants to ensure a DOAC is appropriate. For more drug interactions, refer to Drug-Drug Interactions with Target Specific Oral Anticoagulants.
5. DOACs are recommended over warfarin or LMWH in treatment of DVT of leg or PE in patients without active cancer (CHEST Guidelines).
6. LMWH is recommended over warfarin or DOACs in treatment of DVT of leg or PE in patients with active cancer (CHEST Guidelines).
Indications and Dosing

**Warfarin**

Warfarin is indicated for use in many different clinical settings including the following: 1) Prophylaxis and treatment of VTE and its extension, PE; 2) Prophylaxis and treatment of thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement; 3) Reduction of risk of death, myocardial infarction (MI), and thromboembolic events such as stroke or embolization after MI.

The international normalized ratio (INR) is used to monitor warfarin therapy because it allows for a more accurate and standardized comparison of PT values between reference laboratories. The normal range for the INR for most patients not receiving anticoagulants is 0.9 to 1.2. For most patients, including those with atrial fibrillation, a therapeutic INR range is within 2.0 to 3.0.

Generally, a starting dose of 5 mg is typically initiated on day 1. A lower starting dose may be indicated in patients who are likely to be more sensitive to warfarin (e.g., the elderly, patients with hepatic disease, patients at high risk for bleeding, patients taking medications that can cause bleeding or increase the sensitivity to warfarin). For patients who were stabilized on warfarin prior to hospital admission, it is recommended to maintain the current warfarin dose and monitor the INR accordingly; this depends on the admission INR and any new drug interactions or disease states that affect the INR, as well as patient status as determined by the clinician.

For more warfarin dosing information, protocols, and guidelines, see [warfarin procedures](#). [PHS login required]

**Direct oral anticoagulants (DOAC)**

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Mechanism</th>
<th>FDA-approved indications</th>
<th>Off-label uses</th>
<th>PHP Formulary</th>
<th>Strength</th>
<th>Cost*</th>
</tr>
</thead>
</table>
| apixaban (Eliquis) | factor Xa inhibitor | • Thromboembolism/stroke prevention in non-valvular afib  
• VTE prevention post hip or knee repl.  
• DVT/PE treatment; prevention of recurrence |                                                                                   | Centennial Care: NF  
Commercial: NF  
Metal Level Plans: NF  
Senior Care/Medicare: Tier 4, PA, QL (2 EA per day) | tablets: 2.5mg, 5mg | $503.00 |
| betrixaban (Bevyxxa) | factor Xa inhibitor | • VTE prophylaxis in medical patients during and post hospitalization |                                                                                   | Centennial Care: NF  
Commercial: NF  
Metal Level Plans: NF  
Senior Care/Medicare: NF | capsules: 40 mg, 80 mg | $540.00 |
| dabigatran (Pradaxa) | thrombin inhibitor | • Thromboembolism/stroke prevention in non-valvular afib  
• VTE prevention post hip or knee repl.  
• DVT/PE treatment; prevention of recurrence |                                                                                   | Centennial Care: NF  
Commercial: NF  
Metal Level Plans: Tier 4, PA, QL (2 EA per day)  
Senior Care/Medicare: Tier 4, PA, QL (2 EA per day)*  
*75mg and 150mg strengths only | capsules: 75mg, 110mg, 150mg | $481.00 |
| edoxaban (Savaysa) | factor Xa inhibitor | • Systemic embolism/stroke prevention in non-valvular afib  
• DVT/PE treatment following 5-10 days of initial therapy with parenteral anticoagulant  
• VTE prevention post knee replacement |                                                                                   | Centennial Care: NF  
Commercial: NF  
Metal Level Plans: NF  
Senior Care/Medicare: NF | tablets: 15mg, 30mg, 60mg | $404.00 |
| rivaroxaban (Xarelto) | factor Xa inhibitor | • Thromboembolism/stroke prevention in non-valvular afib  
• VTE prevention post hip or knee repl.  
• DVT/PE treatment; prevention of recurrence  
• VTE (DVT) prophylaxis in hospitalized medical patients  
• Stroke prevention in cardiac ablation |                                                                                   | Centennial Care: PA, QL (10mg = 35 per 365 days)  
Commercial: Tier 2, QL (10mg = 35 per 365; 15 mg and 20 mg: 1 EA per day)  
Metal Level Plans: Tier 3, QL (1 EA per day)  
Senior Care/Medicare: Tier 3 | tablets: 10mg, 15mg, 20mg | $503.00 |

F=Formulary  
NF=Non-Formulary  
T=Tier  
PA=Prior Authorization  
QL=Quantity Limit  
ST=Step Edit

*Cost is based on a 30-day supply and is subject to change.
Early in their development, an obstacle to using DOACs was that there were no specific antidotes to reverse bleeding in cases of overdose or when an urgent surgical procedure was required. At this time, Dabigatran has an antidote, idarucizumab (Praxbind), and we anticipate the approval of an antidote for the other four, Andexanet Alpha, by February, 2018.

For dosing recommendations, see Quick Reference for Direct Oral Anticoagulants. [PHS login required]

**Low molecular weight heparin (LMWH)**

LMWH may also be used for the treatment of acute venous thromboembolism (VTE), prevention of VTE, and acute coronary syndrome (ACS). These agents (e.g., enoxaparin, dalteparin) are administered subcutaneously, although an intravenous bolus may be given initially in selected patients with ACS. The dose is based on weight and differs depending on the indication.

For dosing recommendations, see PHS’ Heparin Protocols and Guidelines. [PHS login required]

**Patient Education and Support**

<table>
<thead>
<tr>
<th>Patient Goal</th>
<th>Key Messages for the Patient</th>
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<tbody>
<tr>
<td>Understand what “blood thinners” do.</td>
<td>• Anticoagulation therapy is medication taken to treat or prevent harmful blood clots from forming. Clots can cause a stroke, heart attack, or other serious problems. Anticoagulants are often called “blood thinners,” but these medications don’t actually thin your blood.</td>
</tr>
</tbody>
</table>
| Take medication as prescribed. | • Compliance with anticoagulation therapy is important to your safety.  
• Take this medication at the same time/times each day to keep the blood level of medication consistent. If you forget or miss a dose, do not take a double dose to make up for a missed dose.  
• Be sure to refill your prescription so you do not run out. |
| Make key lifestyle changes. | • You may bleed more easily while on anticoagulants: Stay away from contact sports or other situations where you could be bruised, cut, or injured; Brush and floss your teeth gently; Be careful when using sharp objects, including razors and fingernail clippers; Avoid picking your nose, if you need to blow your nose, blow it gently.  
• Alcohol interacts with your liver and may affect anticoagulant medications. Talk to your healthcare provider before using alcohol while on anticoagulants.  
• Carry an ID card or wear a medical alert bracelet to let any emergency caregivers know you are taking anticoagulant medications. |
| Monitor. | • Your physician or healthcare provider may need to check your blood at regular intervals while you are using anticoagulant therapy. Be sure to keep all appointments and always bring your current medication list.  
• If you take warfarin, you will have regular blood tests called international normalized ratio (INR) tests. The results help your doctor decide if the medication is at the right level in your body. |
| Communicate with your provider. | • Make sure all your physicians and healthcare providers know you are on anticoagulant therapy.  
• Immediately inform your physician and healthcare providers if you become pregnant or are breast feeding.  
• Call your physician and consider emergency medical care if you notice any side effects; for uncontrolled bleeding seek immediate medical attention.  
• Inform your physician or healthcare provider if you plan on having surgery or certain dental procedures. These may put you at risk of bleeding that is difficult to stop.  
• Ask your physician(s), healthcare provider or pharmacist before stopping or starting any other medication, including over-the-counter (OTC) medicines, vitamins, and herbal products, as many of these may interact with anticoagulant medications. |

**Educational Materials**

- Staying Active and Healthy with Blood Thinners. Video. AHRQ 2015.
- Manténgase activo y saludable con los diluyentes de la sangre. Video. AHRQ 2015.
- Pastillas que diluyen la sangre: Guía para su uso seguro
Clinical Definitions

**direct oral anticoagulant (DOAC)**
DOACs are oral medications that inhibit a specific enzyme in the coagulation cascade. DOACs are associated with a low overall risk of major bleeding. Routine coagulation tests cannot be used to determine the degree of anticoagulation, making it more challenging to determine when the anticoagulant effect has resolved.

The medication that is covered by PHP is rivaroxaban (Xarelto). Other DOACs appearing in the discharge orders may be: apixaban (Eliquis); dabigatran (Pradaxa); edoxaban (Savaysa); or betrixaban (Bevyxxa).

**low-molecular-weight heparin (LMHW)**
LMWH is a class of medication (including enoxaparin, dalteparin) used as an anticoagulant in diseases that feature thrombosis, as well as for prophylaxis in situations that lead to a high risk of thrombosis. Because it can be taken subcutaneously and does not require aPTT or INR monitoring, LMWH permits outpatient treatment of conditions such as deep vein thrombosis (DVT) or pulmonary embolism (PE). Because LMWH has more predictable pharmacokinetics and anticoagulant effect, LMWH is recommended over unfractionated heparin (UFH) for patients with massive pulmonary embolism and for initial treatment of deep vein thrombosis.

**warfarin**
A widely-used synthetic anticoagulant, warfarin inhibits the hepatic synthesis of vitamin K-dependent clotting factors (Factors II, VII, IX and X) and the natural anticoagulant proteins C and S. Warfarin acts to inhibit the reduction of oxidized vitamin K, resulting in a depletion of active vitamin K that is required for carboxylation of the clotting factors. Although therapeutic doses of warfarin only inhibit up to 50% of clotting factor synthesis, it is enough to weaken the biologic activity of the clotting factors and produce a therapeutic anticoagulant effect.

The PT test (Prothrombin Time) can be used to monitor patients being treated with warfarin. Brand names include: Athrombin-K, Compound 42, Co-Rax, Coumadin, Panwarfin, Rodex, and WARF Compound 42. It is also used as a rodenticide, causing fatal hemorrhaging in any mammal consuming a sufficient dose.

Additional References

**Related Care Model Topics**
- Anticoagulation Management

**Clinical Practice Guidelines** [PHS login required]
- Drug-Drug Interactions with Target Specific Oral Anticoagulants
- First Choice of Long-Term Anticoagulant
- Presbyterian Anticoagulation Services PresNet site
- Quick Reference for Direct Oral Anticoagulants

**Policies and Procedures** [PHS login required]
- Baseline and Ongoing Laboratory Values for Anticoagulant Therapy

**Other Resources**
- Compendium of Resources: Discharge Instructions / Education Materials for Venous Thromboembolism (VTE): A Comprehensive Approach to Medication Management (Joint Commission)