CCHCS Care Guide: Anticoagulation

**SUMMARY**

**GOALS**

- Identify patients with indications (diagnosis) present for anticoagulation
- Choose appropriate drug for each patient based on clinical indications, adherence history, bleeding risks and absence of contraindications
- Clearly identify drug, dose, and duration of treatment for each patient on anticoagulation, and ensure proper patient education on diagnosis and treatment plan
- Know how to evaluate bleeding risks and their roles in managing: Venous Thromboembolism (VTE) vs. Atrial Fibrillation (AFib)/flutter
- Identify an International Normalized Ratio (INR) target goal for every patient on warfarin (e.g., target INR range 2.0-3.0) and monitor

**DIAGNOSTIC CRITERIA**

**INDICATIONS FOR ANTICOAGULATION**

**Venous Thromboembolism (VTE) Conditions (See page 4)**
- Proven deep vein thrombosis (DVT)
- Pulmonary embolism (PE)
- Cancer associated DVT or PE
- Unprovoked DVT
- PE Recurrent VTE

**Cardiovascular (CV) Conditions (See page 13)**
- Arterial thrombus
- Mural thrombus
- Valvular heart disease
- Non-valvular AFib/flutter
- Acute myocardial infarction (AMI)
- Left ventricular (LV) dysfunction

**EVALUATION**

1. Confirm indication for anticoagulation is present: VTE, such as DVT/PE, or a CV indication such as AFib/flutter
2. Identify presence (if any) of contraindications to anticoagulation for all patients AND determine the need for a higher level of care (HLOC)
3. Conduct risk/benefit assessment for all patients including bleeding risks (See page 6 for VTE; 15 for CV indications)
4. Review current medications to identify potential DDIs and concurrent use of antiplatelet medications (e.g., aspirin and clopidogrel)
5. Review or order diagnostic studies:
   - Initial labs: complete blood count (CBC), comprehensive metabolic panel (CMP), prothrombin time (PT)/INR, partial thromboplastin time (PTT)
   - Electrocardiogram (EKG), echocardiogram (ECHO), and other imaging may be ordered as clinically indicated
   - Additional labs for inherited causes of hypercoagulability may be ordered as clinically indicated (See page 11)

**TREATMENT**

6. Select the anticoagulant that is most appropriate for the patient and determine duration of therapy.
   - DVT of the lower extremity or PE (See pages 8-9)
   - CV indications for anticoagulation: Arterial thrombus, valvular heart disease, non-valvular AFib/flutter, post acute MI with LV thrombus (See pages 15-17)
   - Perioperative Management of Anticoagulation (See page 33)
   - Warfarin Preferred: End stage renal disease, valvular heart disease, patients with poor adherence
   - Direct Oral Anticoagulant Preferred: non-valvular AFib/flutter
   - Low Molecular Weight Heparin Preferred: Malignancy, pregnancy (See chart on the bottom of page 3 for details)
7. Document the following in the Electronic Health Record System (EHRS):
   - Update Problem List with:
     1. Indication for anticoagulation and
     2. “Long-term (current) use of anticoagulants” (ICD10 Z79.01- to be marked resolved with completion of therapy)
   - Start date with anticipated stop date (if lifelong indicate lifelong)
   - Assessment of bleeding risks and risks/benefits of anticoagulation
   - Target INR (if on warfarin)
   - Next INR check (if on warfarin)
   - Patient Education (See PE1-PE4)
   - Specialty that is co-managing, if any (i.e., cardiology)
   - Evaluate for lower bunk chronic

**FOLLOW-UP AND MONITORING**

8. Follow-up and monitor with an individualized treatment plan. For VTE and CV indications:
   - First year: 3 months, 6 months, and 12 months or more often as clinically indicated
   - Follow-up at least every 6 months thereafter
   - Continue to weigh the risks and benefits of continued anticoagulation at each visit
   - Review medication list for DDIs and use of antiplatelet medications at each visit
   - Conduct medication specific lab monitoring. For short term anticoagulation, re-evaluate need for lower bunk after anticoagulation is stopped.
   - Warfarin: INR at least monthly, more frequent if clinically indicated, CBC, CMP every 6 months
   - *Direct oral anticoagulants (DOACs) and low molecular weight heparin (LMWH) (enoxaparin): CBC, CMP (including Cr) every 6 months, weight check at each visit

Note: Measures will utilize Time in Therapeutic Range (TTR) for patients on warfarin. This will better reflect the patient’s ongoing anticoagulation status and assist the provider in determining efficacy of treatment plan.

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</tbody>
</table>

**NOTES:**

- Significant drug-drug interactions (DDIs)
- High risk of serious bleeding
- INR outside desired range
- Extremity pain or swelling/skin necrosis
- Altered level of consciousness
- Pregnancy/breastfeeding
- Perioperative management
- Provoked VTE due to COVID-19

Information contained in the Care Guide is not a substitute for a health care professional’s clinical judgment. Evaluation and treatment should be tailored to the individual patient and the clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to “Disclaimer Regarding Care Guides” for further clarification. http://cchcs.ca.gov/clinical-resources/
# Anticoagulation Overview Algorithm

## Summary

- **1. Confirm indication is present for anticoagulation.**
  - VTE (DVT/PE): See page 5
  - CV indications (e.g., AFib/flutter, arterial thrombus, LV dysfunction/ LV thrombus, valvular heart disease): See page 14
  - Perioperative Management of Anticoagulation: See page 33

- **2. Identify presence (if any) of contraindications to anticoagulation (absolute vs. relative)**
  - **Absolute:**
    - Major trauma
    - Active/severe bleeding
    - Neurosurgery, ocular surgery, or intracranial bleed within the past 10 days
    - Recent or planned emergent or high risk surgery
    - Intracranial or spinal tumors
  - **Relative:**
    - Pregnancy (co-management with high risk OB required)
    - Large abdominal aortic aneurysm with concurrent severe hypertension
    - Stable aortic dissection
    - Falls/gait instability

- **Determine need to transfer patient to a HLOC or referral to a specialist.** If presence of any of the following (but not limited to), consider transferring patient to HLOC:
  - Signs and/or symptoms of acute heart failure and PE, such as chest pain, palpitations, shortness of breath
  - Tachycardia, hemodynamic instability, or syncope or loss of consciousness
  - Presence of contraindications in the setting of urgent need to anticoagulate (e.g., DVT/PE, mural thrombus)
  - In general, patients with significant comorbid conditions including but not limited to: end stage renal disease (ESRD), advanced chronic kidney disease (CKD), advanced heart failure, and advanced liver disease will require, at minimum, specialty evaluation prior to starting anticoagulation.

- **3. Conduct Risk/Benefit Assessment:**
  - Bleeding risks vs. benefits of anticoagulation (i.e., preventing a recurrent/worsening VTE, or stroke for AFib)
  - For VTE: Patient’s bleeding risk will help determine duration of therapy (beyond 3 months) and need for closer monitoring (See page 6)
  - For AFib: Use HAS-BLED for bleeding risks (See Attachment A)

- **4. Review Medication List for DDI and concurrent use of antiplatelet medications**
  - Encourage use of the DDI Tool available on LifeLine

- **5. Review or Order Diagnostic Studies:**
  - Initial labs: CBC, CMP, PT/INR, PTT
  - Additional labs for inherited causes of hypercoagulability as clinically indicated (See page 11)

- **6. Select most appropriate anticoagulant for patient and determine anticipated duration of therapy** (See pages 7-9 for VTE, and pages 15-17 for CV indications)

- **7. Document in EHRS the following:**
  - Update Problem List
  - Indication
  - Start date
  - Duration of therapy (anticipated stop date)
  - Target INR (if on warfarin)
  - Next INR check (if on warfarin)
  - Assessment of bleeding risks
  - Patient education provided (See PE 1-4)
  - Specialty that is co-managing, if any (i.e., cardiology)
  - Evaluate for lower bunk chrono

- **8. Follow-up and Monitoring on a regular basis to weigh risks/benefits of anticoagulation, review current medication list, modify dosage of medications, and discuss patient concerns.**
  - First year: 3 months, 6 months, and 12 months or more often as clinically indicated
  - Follow-up at least every 6 months thereafter
  - For medication specific monitoring: Warfarin- see pages 21, DOACs- see pages 24, LMWH- see pages 31
The use of anticoagulation therapy is high risk and complex. The decision to start therapy, the choice of specific agent, and the duration of therapy should be carefully and systematically considered. The evaluation and risk assessment of a patient needs to be frequent, as there is risk of recurrence of VTE, in some cases, when patients are not on anticoagulation. The following steps must be performed at initial visit and periodically thereafter (confirming indication still exists).

1. **Confirm indication is present for anticoagulation.**

2. **Identify presence of contraindications (if any) to anticoagulation (absolute vs. relative) and determine need to transfer the patient to a HLOC or refer to specialty.**
   - Absolute contraindications: major trauma, active/severe bleeding (signs/symptoms of hemodynamic instability), neurosurgery, ocular surgery or intracranial bleed within the past 10 days, recent or planned emergent high risk surgery, intracranial or spinal tumors
   - Relative contraindications: pregnancy (co-management with high risk OB required), large abdominal aortic aneurysm with concurrent severe hypertension, stable aortic dissection, falls/gait instability

3. **If no absolute contraindications present, conduct risk/benefit assessment for anticoagulation.** This will help you determine duration of therapy.

4. **Review the patient’s current medication list to identify potential DDIs** with anticoagulants, if starting on warfarin, note concurrent use of antiplatelet medications, i.e., aspirin and clopidogrel. (Recommend use of the DDI Tool available on Lifeline)

5. **Order appropriate diagnostic studies.** (For VTE see page 7; for CV indications see page 15)

6. **Select most appropriate anticoagulant and determine duration of treatment.**
   - Selecting the appropriate anticoagulant is complex and depends on a variety of individual patient factors.
   - Within CCHCS, the following anticoagulants are used: Warfarin, DOACs, and LMWH.
   - Medication selection varies by indication (For VTE see pages 7-9; for CV indications see pages 15-17)
   - See Attachment B for site of action for anticoagulants

7. **Document in EHRS, include indication and anticipated duration of therapy.** (See PE 1-4)

8. **Patients should be re-evaluated on a regular basis to address anticoagulation.** At each appointment related to follow for anticoagulation management, the provider should weigh the risks/benefits of continuing anticoagulation and review the 8 steps which include:
   - Ensure there remains a continued indication (e.g., if DVT and the patient had 3 months of anticoagulation, do they still need continued anticoagulation?)
   - Ensure no new contraindications to anticoagulation, or complication requiring a HLOC, or specialty referral: Review any changes in general health, functional status (recent falls), activity level (avoid contact sports), change in diet, and substance use including alcohol.
   - Reassess risks/benefits of anticoagulation: Does a new medical condition/bleeding risk cause the risk/benefit equation to shift in favor of discontinuation of anticoagulation?
   - Review current medication list: especially for any new medications (including over the counter) pay special attention to addition or discontinuation of antiplatelet agents. Confirm medication adherence.
   - Review any new laboratory results.
   - Confirm current anticoagulant is still most appropriate agent and that the continued use is appropriate.
   - Update EHRS documentation (including the Problem List) and re-evaluate need for lower bunk if anticoagulation is stopped.
   - Schedule clinically appropriate follow-up appointments for monitoring.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Preferred Agent</th>
<th>DOAC</th>
<th>Warfarin</th>
<th>Lovenox</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE (DVT/PE)</td>
<td>Depends on comorbidities</td>
<td>Yes</td>
<td>Yes</td>
<td>Short-term except in Malignancy/Pregnancy</td>
</tr>
<tr>
<td>AFib/Flutter – w/o sign. Valvular Disease</td>
<td>DOACS Preferred</td>
<td>Yes</td>
<td>Used for bridging</td>
<td></td>
</tr>
<tr>
<td>Valvular Heart Disease</td>
<td>Warfarin NO</td>
<td>Yes</td>
<td>Preferred</td>
<td>NO</td>
</tr>
<tr>
<td>ESRD</td>
<td>Warfarin NO*</td>
<td>Preferred</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td>Poor Adherence</td>
<td>Warfarin NO</td>
<td>Preferred</td>
<td>NO</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Lovenox NO</td>
<td>No</td>
<td>No</td>
<td>Preferred</td>
</tr>
<tr>
<td>Active Malignancy</td>
<td>Lovenox NO*</td>
<td>Yes</td>
<td>Preferred</td>
<td></td>
</tr>
<tr>
<td>Cost</td>
<td>$555555</td>
<td>$</td>
<td>$</td>
<td>$555555</td>
</tr>
<tr>
<td>Reversal Agent</td>
<td>Yes**</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

*Limited evidence **Hospital/ER setting only
The most common presentations of VTE are DVT of the lower extremity and PE. Patients can present across the clinical spectrum from asymptomatic incidental finding on imaging to life-threatening saddle embolus.

The goal of treatment for VTEs is the prevention and reduction of adverse outcomes from a VTE event (i.e., death from PE, pulmonary hypertension, heart failure, chronic phlebitis, and venous insufficiency) weighed against the risk of the therapeutic agent (anticoagulant). VTE must be viewed as a chronic and lifelong medical issue and managed with continued regular follow-up.

Management of VTE Algorithm

1. Patient presents with VTE
   1. Confirm Indication
      - Proximal DVT/PE*
      - Distal DVT**

2. Contraindications to anticoagulation present or findings needing HLOC? (see page 2)
   - YES
     - Refer to Higher Level of Care (HLOC)
       - If Inferior Vena Cava (IVC) filter placed, a retrievable filter is preferred
     - Upon return from HLOC, continue anticoagulation as recommended by hospital and see step 8 Follow-up/Monitoring for guidance
   - NO

3. Conduct Risk/Benefit Assessment including bleeding risk evaluation (see page 6)

4. Review Medication List (see page 7)

5. Review or Order Diagnostic Studies (see page 7)

6. Select anticoagulant: may use warfarin, DOAC or LMWH (typically used as bridge to warfarin).
   Determine anticipated duration of treatment-minimum 3 months (see page 7-8)

7. Document in EHRS the following:
   - Next INR check (if on warfarin)
   - Assessment of bleeding risks
   - Patient education provided
   - Specialty that is co-managing, if any
   - Evaluate for lower bunk chrono

8. Follow-up/Monitoring:
   - First year: 3 months, 6 months, and 12 months or more often as clinically indicated
   - Follow-up at least every 6 months thereafter
   - For medication specific monitoring: Warfarin- see pages 21, DOACs- see page 24, LMWH- see pages 31

*Proximal DVT occurs in the popliteal, femoral, or iliac veins.
**Isolated distal DVT has no proximal component, is located below the knee, and is confined to the calf veins (peroneal, posterior, anterior tibial, and muscular veins).

Within CCHCS, patients will likely present to the provider with one of the following circumstances:

- Patient new to the provider, but previously diagnosed with a VTE
- Patient presents with signs/symptoms concerning for a new VTE
- Recent diagnosis of VTE after return from a HLOC

For any patient above, the provider evaluation should consider:

**History:** Obtain historical information to determine provoked vs. unprovoked VTE, determine if the patient needs to be transferred to a HLOC, identify which diagnostic tests to order, identify need for co-management with specialty and to determine duration of therapy.

Note presence of any of the following as potentially life-threatening signs needing a HLOC:

- Dyspnea and orthopnea/pleuritic chest pain/cough and/or hemoptysis
- Pain and/or swelling of the extremity and extent of symptoms
- Syncope/loss of consciousness

To help determine the presence of a provoked vs. unprovoked VTE, look for the following:

- Presence or absence of family history of VTE (i.e., first degree relative? age of onset?)
- Previous personal history of VTE (and age of onset)
- Recent surgery (including neurological and ocular)
- Prolonged travel during transfers

To determine presence of contraindications.

**Physical Exam:** A thorough physical exam including vital signs, level of consciousness, oxygenation, bruises/petechial rashes, presence of swelling/erythema in extremity, presence of venous catheters (e.g., peripherally inserted central catheter, central venous catheters, mediports)

Exam findings concerning for pulmonary embolism include the following:

- Tachycardia and/or tachypnea
- Rales or decreased breath sounds on lung exam
- Presence of right heart strain such as jugular venous distention

The above evaluation will assist the provider in working through the steps of anticoagulation management.

### 1. Confirm Presence of Indication for Anticoagulation

Ensure that an indication for anticoagulation is present by:

- Confirming a previously made diagnosis, or
- If a patient presents with a suspected new DVT or PE, perform a risk assessment for likelihood of DVT and/or PE using the Well’s Criteria to assist in the diagnostic work-up:
  - DVT: [https://www.mdcalc.com/wells-criteria-dvt](https://www.mdcalc.com/wells-criteria-dvt)
- Patients will typically need to be sent out for confirmatory testing.

#### Provoked VTE

Pay attention to the presence of provoking factors and acquired hypercoagulable conditions and if the provoking factor will be temporary or permanent.

- Recent and prolonged transport from other institutions or outside care facilities
- Immobility (bed or wheelchair bound status)
- Recent hospitalization or recent diagnosis of COVID-19
- Trauma or injury to an extremity
- Comorbid conditions: inflammatory bowel disease, myeloproliferative disorders, nephrotic syndrome, malignancy
- Hormone replacement/birth control
- History of central lines

#### Unprovoked VTE

- Lack of a CLEAR provoking factor, consider the possible presence of an inherited hypercoagulable condition see page 11
2. Identify Presence of Contraindications to Anticoagulation and Determine Need for Transfer to a HLOC (Hospital)

Patients in whom anticoagulation is contraindicated or in whom the risk of bleeding is estimated by the clinician to outweigh the risk of VTE should be transferred to a HLOC to have an IVC filter placed promptly. Patients with relative contraindications should be monitored closely and co-managed with a specialist.

**Absolute Contraindications include:**
- Active bleeding
- Severe bleeding diathesis
- Recent, planned or emergent high bleeding risk surgery/procedure
- Major trauma
- Acute intracranial hemorrhage
- Platelets <50,000

**Relative Contraindications include:**
- Large abdominal aortic aneurysm with concurrent severe hypertension
- Stable aortic dissection
- Recent, planned, or emergent low bleeding risk surgery or procedure
- Recurrent bleeding from multiple GI telangiectasias
- Pregnancy

For patients with a newly diagnosed VTE (not yet anticoagulated), determine need to transfer the patient to a HLOC or referral to a specialist.
- Chest pain, palpitations, shortness of breath, and other signs and/or symptoms of acute heart failure.
- In general, patients with significant comorbid conditions such as ESRD, CKD, advanced heart failure and advanced liver disease will require, at minimum, specialty evaluation prior to starting anticoagulation.
- If suspicion of onset of new PE, transfer to a HLOC (hospital).

3. Conduct Risk/Benefit Assessment

**Determine Bleeding Risk**

VTE patients who do not have contraindications to anticoagulation should be started on anticoagulation. The bleeding risk evaluation is used to assist in determining the anticipated duration of therapy and the need for closer monitoring (note the difference between bleeding risk and contraindications).

Patients with high bleeding risks are more likely to have anticoagulation stopped at 3 months and require closer monitoring while on anticoagulation, as compared to patients with low bleeding risks.

**Factors Which May Increase Risk of Bleeding While on Anticoagulants**

- Age > 65 years
- Anemia
- Diabetes
- Cancer
- Frequent falls
- Malignancy
- Hypertension
- Acute or chronic alcohol use
- Liver failure or renal failure
- Comorbidity and reduced functional capacity
- Presence of bleeding lesion or injury (GI, peptic ulcer disease [PUD], etc.)
- Bleeding disorder (coagulation, thrombocytopenia)
- Poor anticoagulant control
- Recent surgery
- Previous bleed
- Previous stroke
- Concomitant use of aspirin, NSAIDs, clopidogrel, antibiotics, amiodarone, statins, or fluoroquinolones

**Risk of Bleeding Based on Risk Factors**

(Determines duration of therapy after the initial 3 months)

<table>
<thead>
<tr>
<th># of Risk Factors</th>
<th>Risk Category</th>
<th>Bleed Risk 0-3 months</th>
<th>Bleed Risk After 3 months</th>
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<tbody>
<tr>
<td>0</td>
<td>Low</td>
<td>1.60%</td>
<td>0.8%/year</td>
</tr>
<tr>
<td>1</td>
<td>Moderate</td>
<td>3.20%</td>
<td>1.6%/year</td>
</tr>
<tr>
<td>≥ 2</td>
<td>High</td>
<td>12.80%</td>
<td>≥ 6.5%/year</td>
</tr>
</tbody>
</table>

1 Lip, Gregory YH, MD, FRCPE.FESC.FACC and Russell D.Hull MBBS, MSc, Overview of treatment of lower extremity DVT, Uptodate, Dec 2019
4. Review Current Medication List

Review current medication list and look for DDIs (recommend use of the DDI Tool available on Lifeline).

Look for concurrent antiplatelet use and confirm indication for use with anticoagulation therapy.

Some patients with coronary artery disease have indications for antiplatelet agents (aspirin or clopidigrel [Plavix®] or both depending on presence of coronary stent) as well as anticoagulation therapy. The risk of thrombosis or bleeding in these patients can be very high and must be taken into account when initiating anticoagulation therapy and in determining the duration of concurrent therapy. Consult specialty as needed.

5. Review or Order Diagnostic Studies

- Initial: CBC, CMP, PT/INR, PTT (if not done within 30 days)
- EKG, ECHO and further imaging as clinically indicated
- Additional labs for hypercoagulability as clinically indicated (see page 11)
- Consider a Medical Hold for any patient with INR above 5.0

6. Anticoagulant Selection and Duration of Therapy

Select most appropriate anticoagulant. Vitamin K Agonist (VKA), DOACs, and LMWH products are used for anticoagulation in patients with VTE. Choice of anticoagulant is based on multiple patient specific factors. (See below)

While warfarin has typically been used for VTE, there is data available supporting the use of DOACS in some patients.

- Some examples of patients with VTE where DOAC would be used over warfarin (VKA) include: Unstable INR despite patient adherence to VKA, warfarin allergy or prohibited DDIs with VKA, documented thrombotic event despite therapeutic INR, unable to obtain monitoring INRs (difficult phlebotomy access) (also see page 23)

When choosing anticoagulant consider the following factors:

- Indications or comorbidities present - see next page for conditions which influence choice of anticoagulant
- Adherence: VKA preferred if adherence is an issue due to being able to monitor INR
- Availability of reversal agents vitamin K widely available, DOAC reversal agents less available in our setting
- DDIs less frequent with DOACs
- Continuity of med: Patient arriving on medication consider switch to formulary agent if no clinical contraindications

Duration of Therapy

Minimum length of anticoagulation for VTE is 3 months. If the optimal length of anticoagulation is not clearly defined and needs to be evaluated on an individual (case by case) basis, consider the following:

Patient’s bleeding risks: The higher the bleeding risk, the shorter the duration of therapy. Please use the table below to assist you when determining whether anticoagulation should continue past the minimum 3 months. The level of evidence presented for the recommendations is included in italicized parenthesis.

<table>
<thead>
<tr>
<th>Thrombotic Recurrence Risk Group</th>
<th>Bleeding Risk Group*</th>
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<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>First VTE provoked by surgery</td>
<td>Discontinue (strong)</td>
</tr>
<tr>
<td>First VTE provoked by non-surgical factor (assuming resolution of provoking factor)</td>
<td>Discontinue (weak)</td>
</tr>
<tr>
<td>First unprovoked proximal DVT or PE</td>
<td>Continue (weak)**</td>
</tr>
<tr>
<td>Second unprovoked VTE</td>
<td>Continue (strong)**</td>
</tr>
</tbody>
</table>

*The 2012 ACCP bleeding risk model assumes risk of major bleeding after the first three months of anticoagulation as 0.8,1.6, and 26.5 % for the low, intermediate, and high risk groups, respectively

**Consider indefinite anticoagulation after 12 months with risk/benefit assessment
6. Anticoagulant Selection and Duration of Therapy Continued

The patient is more likely to be continued on extended therapy if the following factors are present:
- Continuation of provoking factors (i.e., bed bound status, wheelchair bound)
- Presence of risk factors for a recurrent VTE such as:
  - Inherited thrombophilias or Antiphospholipid syndrome (See page 11)
  - Malignancy - more likely to extend anticoagulation until resolution of the malignancy
  - Moderate-to-severe post thrombotic syndrome
  - Elevated D-Dimer within 3 months after stopping anticoagulation
- Patients with poor cardiorespiratory reserve (such as heart failure/chronic obstructive pulmonary disease [COPD]) in whom a recurrent PE may be life-threatening

Overall risks for recurrence - see rate of VTE recurrence table below:

<table>
<thead>
<tr>
<th>VTE Type</th>
<th>First Year</th>
<th>Annual Rate After First Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>First episode of unprovoked VTE</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Second episode of unprovoked VTE</td>
<td>15%</td>
<td>7.5%</td>
</tr>
<tr>
<td>First VTE provoked by surgery</td>
<td>1%</td>
<td>0.5%</td>
</tr>
<tr>
<td>First VTE provoked by non-surgical factor</td>
<td>5%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

Consider stopping anticoagulation if:
- Presence of, or development of, new contraindications
- Patients with limited life-expectancy due to other diseases - less likely to benefit from extended anticoagulation

For VTE scenarios without clear consensus for duration of anticoagulation, referral to specialty is advised.
### Factors That May Influence Which Anticoagulant Is Chosen for Initial and Long-Term Treatment of VTE

<table>
<thead>
<tr>
<th>Factor</th>
<th>Choice of Anticoagulant</th>
<th>Qualifying Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal disease and CrCl &lt;30mL/min</td>
<td>Vitamin K Antagonist (VKA)</td>
<td>DOACs and LMWH contraindicated with severe renal impairment. If mild/moderate renal impairment and DOAC is used, dose adjustment required.</td>
</tr>
<tr>
<td>Poor Adherence</td>
<td>VKA</td>
<td>INR monitoring can help to confirm adherence. However, some patients may be more compliant with a DOAC because no need for monthly INR. A single missed dose of DOAC has greater potential to result in inadequate anticoagulation.</td>
</tr>
<tr>
<td>Once daily oral therapy preferred</td>
<td>VKA; Rivaroxaban; Edoxaban</td>
<td>No remarks</td>
</tr>
<tr>
<td>Reversal agent needed</td>
<td>VKA</td>
<td>Reversal agents for DOACs and LMWH not readily available.</td>
</tr>
<tr>
<td>Dyspepsia or history of GI bleeding</td>
<td>VKA, Apixaban</td>
<td>Dabigatran increases dyspepsia. Dabigatran, rivaroxaban, and edoxaban may be associated with more GI bleeding than VKA.</td>
</tr>
<tr>
<td>Weight &lt; 50 kg</td>
<td>VKA</td>
<td>The pharmacokinetics and pharmacodynamics of factor Xa inhibitors may be affected by weight but the clinical impact of these effects remains unknown. Pending further evidence in patients at extremes of weight (e.g., &lt;50 kg, &gt;120 kg or BMI ≥ 35 kg/m²) it is advisable to limit DOAC use to situations where vitamin K antagonists cannot be used.</td>
</tr>
<tr>
<td>Weight &gt; 120 kg or BMI ≥ 35 kg/m²</td>
<td>VKA</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Avoid Dabigatran</td>
<td>Coronary artery events appear to occur more often with dabigatran than with VKA. This has not been seen with the other DOACs, and they have demonstrated efficacy for coronary artery disease. Antiplatelet therapy should be avoided if possible in patients on an anticoagulant because of increased bleeding risk.</td>
</tr>
<tr>
<td>Need for rapid anticoagulation with oral agent without using initial IV heparin</td>
<td>Rivaroxaban; Apixaban</td>
<td>VKA, dabigatran, and edoxaban require initial parenteral therapy with IV heparin or LMWH when immediate anticoagulation is needed.</td>
</tr>
<tr>
<td>Bleeding risk (Especially if history of intracranial hemorrhage or significant non-GI bleed)</td>
<td>DOAC</td>
<td>A systematic review and meta-analysis of 12 randomized controlled trials including over 100,000 patients with either non-valvular AFib or VTE showed that DOACs are associated with less major bleeding, fatal bleeding, intracranial bleeding, clinically relevant non-major bleeding, and total bleeding compared to warfarin. This provides an argument to favor these agents over conventional therapy in these pts for VTE treatment whenever possible.</td>
</tr>
<tr>
<td>Liver disease and coagulopathy</td>
<td>LMWH</td>
<td>VKA dosing is difficult to control; INR may not reflect antithrombotic effect. Rivaroxaban is contraindicated; other DOACs may require dose adjustment. Recommended involving hematology/hepatology for ongoing anticoagulation.</td>
</tr>
<tr>
<td>Cancer</td>
<td>LMWH</td>
<td>More so if just diagnosed, extensive VTE, metastatic cancer, very symptomatic; vomiting; on cancer chemotherapy. However, for those patients who cannot use long term LMWH, either a DOAC or VKA could be prescribed as a second-line option. DOACs have limited data in cancer patients.</td>
</tr>
<tr>
<td>Pregnancy or pregnancy risk</td>
<td>LMWH</td>
<td>Potential for other agents to cross the placenta. Warfarin &amp; DOACs are contraindicated.</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>VKA, LMWH</td>
<td>DOACs contraindicated. It is unknown whether any of the DOACs are excreted in breast milk. Because of the potential for infant harm, a decision should be made to either avoid breastfeeding or use an alternative anticoagulant, such as warfarin, in these women.</td>
</tr>
</tbody>
</table>

---

# Monitoring of Patients with VTE

## 7. Documentation in EHRS

Document in EHRS the following:
- Update Problem List with:
  1. Indication for Anticoagulation, and
  2. “Long-term (current) use of anticoagulants” (ICD10 Z79.01) - which should be marked resolved upon completion of therapy.
- Anticoagulation start date and anticipated stop date (indicate if lifelong)
- Assessment of bleeding risks and risks/benefits of anticoagulation
- Target INR (if on warfarin); next INR check (if on warfarin)
- Patient Education (See PE 1-4)
- Specialty that is co-managing, if any (i.e., cardiology)
- Evaluate for lower bunk chrono

## 8. VTE Follow-Up and Monitoring

Monitoring should be ongoing:
- First Year: 3 months, 6 months and 12 months or more often as clinically indicated
- Follow-up at least every 6 months thereafter
- Note: follow the patient periodically after anticoagulation is stopped and be alert that the patient maintains a lifelong increased risk of recurrent VTE
- At periodic follow-up visits address the 8 steps outlined in this care guide:
  - Ensure there remains a continued indication (e.g., if DVT and the patient had 3 months of anticoagulation, do they still need continued anticoagulation?)
  - Ensure no new contraindications to anticoagulation, or complication requiring a HLOC, or specialty referral:
    - Review any changes in general health, functional status (recent falls), activity level (avoid contact sports), change in diet, and substance use including alcohol.
  - Reassess risks/benefits of anticoagulation: Does a new medical condition/bleeding risk cause the risk/benefit equation to shift in favor of discontinuation of anticoagulation?
  - Review current medication list: especially for any new medications (including OTC) pay special attention to addition or discontinuation of antiplatelet agents. Confirm medication adherence
  - Review any new laboratory results
  - Confirm current anticoagulant is still most appropriate agent and that the continued use is appropriate
  - Confirm documentation (including the Problem List) is up to date in EHRS
  - Schedule appropriate follow-up and monitoring
  - If stopping anticoagulation, re-evaluate need for lower bunk chrono
In general, treatment is similar to patients with proximal lower extremity DVTs.

- Evidence for DOAC use is limited and not routinely recommended.
- Routine removal of the catheter is not recommended. Continue anticoagulation as long as the central venous catheter remains in place.
- If the catheter needs to be removed, specialty consultation is advised.
- For catheter-related thrombosis confined to the brachial vein, there is uncertainty about the need to anticoagulate. Consider anticoagulation for up to 3 months if the thrombosis is symptomatic, is associated with cancer, or the catheter remains in place. Specialty consultation advised.

### Temporary Inferior Vena Cava (IVC) Filter Placement

A majority of the indications for a temporary IVC filter placement are for patients with a contraindication to anticoagulation in the setting of an immediate life-threatening thromboembolic event.

The presence of an IVC filter is itself thrombogenic and therefore arrangement for IVC filter removal should be made when the contraindication to anticoagulation is anticipated to resolve.

### VTE in Malignancy

- LMWH is the drug of choice for initial therapy. If LMWH is contraindicated and renal insufficiency is present, consult with specialty.
- DOACs are being used more frequently, however, data is limited.
- Avoid use of DOACs in patients with GI malignancy.

### Inherited Thrombophilias

Patients with inherited thrombophilias are likely to present with an unprovoked or recurrent VTE. Therefore, depending on the ongoing risk/benefit evaluation, the duration of anticoagulation will likely be lifelong. History is key to help determine if a VTE is provoked or unprovoked. Referral to specialty services is advised if uncertain.

#### When to Test for Inherited Thrombophilias:

1. Routine evaluation for hypercoagulable disorders in patients with a diagnosis of VTE is not recommended.
2. Patients with a family history of VTE (at least one first degree relative with documented VTE before the age of 45) should be tested for all five inherited thrombophilias: Levels of Protein S, Protein C, antithrombin, factor V Leiden, and prothrombin gene mutations.
3. Patients without a family history of VTE who have unprovoked or recurrent VTE:
   - Young patients (<45) - test for inherited thrombophilias and antiphospholipid syndrome (APS)
   - Recurrent thrombosis - test for inherited thrombophilias and APS
   - Multiple venous sites or unusual vascular beds (portal, hepatic, mesenteric or cerebral veins) - test for inherited thrombophilias and APS
   - History of warfarin induced skin necrosis - test for protein C deficiency

### Labs to Order

<table>
<thead>
<tr>
<th>Labs to Order</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden Gene Mutation</td>
<td>Factor V Leiden is the most common clotting factor mutation in the United States, most frequent in Caucasians</td>
</tr>
<tr>
<td>Prothrombin Mutation</td>
<td>Prothrombin mutation most common after Factor V Leiden</td>
</tr>
<tr>
<td>Antithrombin Level</td>
<td>Antithrombin function and quantity are measured to determine deficiency. The test should <strong>not be performed in presence of thrombosis or during treatment for thrombosis</strong></td>
</tr>
<tr>
<td>Protein C / Protein S Levels</td>
<td>Protein C and Protein S should <strong>not be measured while the patient is on warfarin or within 10 days of thrombotic event</strong></td>
</tr>
</tbody>
</table>

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1 Anticoagulation therapy for venous thromboembolism (lower extremity venous thrombosis and pulmonary embolism) in adult patients with malignancy; Kenneth A. Bauer, MD, UpToDate. May 31st, 2019.
APS is a systemic autoimmune disease characterized by venous or arterial thrombosis and/or pregnancy loss. It can occur as a primary condition or in the presence of systemic lupus erythematosus (SLE) or another systemic autoimmune disease.

For diagnostic criteria for APS: Please see UpToDate article titled: Diagnosis of antiphospholipid syndrome. Revised classification criteria for the antiphospholipid syndrome table.

Phlegmasia Cerelea Dolens (PCD)
Although uncommon, patients with PCD should be identified and considered for more aggressive management due to the high degree of morbidity and mortality. Immediate transfer to a HLOC (hospital) is required.

1. PCD is part of a clinical spectrum that ranges from phlegmasia alba dolens to venous gangrene. It usually results from acute massive venous thrombosis that causes an obstruction of the venous drainage of an extremity, venous gangrene, compartment syndrome, impaired arterial supply, circulatory collapse and shock.

2. Usually presents with sudden severe pain, swelling, cyanosis and edema.

3. Malignancy is the most common triggering factor. Inherited thrombophilias, surgery, IVC filter insertion, pregnancy and heparin-induced thrombocytopenia (HIT) are other triggering factors.

4. PCD is the only accepted indication for thrombolysis and/or thrombectomy in patients with DVT.

Portal Vein Thrombosis (PVT) Chronic and Acute
- Typically diagnosed by abdominal imaging (US, CT, or MRI)
- The risk for bleeding or other complications is high; referral to specialty services is advised when diagnosed
- Consider testing for JAK2 mutations for myeloproliferative syndromes as clinically indicated

1. Acute PVT: Patients with acute PVT have the sudden onset of portal venous occlusion due to thrombus, and have not yet developed features of chronic PVT, such as collateral circulation or portal hypertension.
- The primary management of acute PVT is anticoagulation to allow for recanalization so that intestinal infarction or portal hypertension does not occur. In addition, treatment of predisposing conditions when possible is advised.

<table>
<thead>
<tr>
<th>Common Causes of Portal Vein Thrombosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal sepsis</td>
</tr>
<tr>
<td>Abdominal surgery</td>
</tr>
<tr>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Compression or invasion of the portal vein by tumor (e.g., pancreatic cancer)</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td>Inherited thrombophilias</td>
</tr>
<tr>
<td>Myeloproliferative syndromes</td>
</tr>
<tr>
<td>Pancreatitis</td>
</tr>
</tbody>
</table>

- Screen for esophageal varices prior to initiating anticoagulation
- Referral to specialty services for input is advised to help differentiate between chronic and acute PVT and determine duration of therapy (typically 6 months)

2. Chronic PVT: Usually discovered incidentally, patients with chronic PVT, even if asymptomatic, frequently will have esophageal or gastric varices, and the most common clinical presentation is GI bleeding. Basic management includes screening for esophageal varices and treating complications of portal hypertension and portal cholangiopathy (aka Portal Biliopathy)
- The goal of anticoagulation in patients with chronic PVT is unclear and must be made on a case by case basis. In addition, it is often difficult to distinguish an acute PVT from chronic PVT; therefore referral for specialty evaluation is recommended for patients diagnosed with PVT.

Recurrent or Worsening VTE While on Anticoagulation
- Evaluate for compliance with anticoagulation; consider change in anticoagulant
- Consider an undiagnosed underlying disease such as:
  - Malignancy (See Page 11)  
  - Hypercoagulable state (See page 11)  
  - APS (See top of page)
- Consider temporary IVC filter placement which requires transfer to a HLOC (hospital)
- Referral for specialty evaluation is often indicated
The goal of anticoagulation for CV indications is to prevent the cardiac source of embolic event leading to ischemia at a distant site such as brain or intestines. Traditionally, choices were limited to VKA. Over the last few years, DOACs have been used more widely. CV indications require lifelong anticoagulation and, in general, patients tend to have more comorbidities and higher bleeding risks.

Management of Cardiovascular Indications for Anticoagulation Algorithm

- **Arterial thrombus**
- **Symptomatic new onset AFib/flutter**
- **Symptomatic valvular heart disease**
- **Post acute MI with LV thrombus** (See page 17)
  - In general, anticoagulation is initiated at a hospital setting requiring co-management with cardiology and other specialty as needed.

**Patient presents with cardiovascular indications**

1. **Confirm Indication**
   - **Valvular Heart Disease** (Asymptomatic)
   - **Biprosthetic valve** (See page 16)
   - **Mechanical valve** (See page 17)
   - **Mitrvalc Valve Disease** (See page 16)

2. **New Contraindications to anticoagulation present or findings needing HLOC on follow-up?** (see page 2)
   - YES
     - Refer to HLOC and/or urgent specialty evaluation to address contraindications and acute medical issues
   - NO
     - **3. Conduct Risk/Benefit Assessment including bleeding risks** (see page 15)

3. **Conduct Bleeding Risk Assessment using HAS-BLED** (see Attachment A)
   - Should not be interpreted as absolute recommendations and provider should correct modifiable risk factors

4. **Review Medication List** (see page 15)

5. **Review or Order Diagnostic Studies** (see page 15)

6. **Select anticoagulant**: DOACs can be used in nonvalvular AFib, warfarin for most valvular disease and LV thrombus.
   - **Determine duration of therapy**: Duration is typically lifelong. (See details pages 15-17)

7. **Document in EHRS the following**:
   - **Update Problem list**
   - **Indication**
   - **Start date, anticipated duration**
   - **Target INR (if on warfarin)**
   - **Next INR check (if on warfarin)**
   - **Assessment of bleeding risks**
   - **Patient education provided**
   - **Specialty (if any) is co-managing**
   - **Evaluate for lower bunk chrono**

8. **Follow-up/Monitoring**: See decision support on page 18
   - For medication specific monitoring: Warfarin: See page 21, DOACs: See page 24; LMWH: See page 31

**NOTE**: For patients with atrial flutter, anticoagulation therapy is recommended according to the same profile used for AFib (American College of Cardiology [ACC]). Limited data evidence level C. Selection of anticoagulant therapy should be based on the risk of thromboembolism, irrespective of whether the AFib pattern is paroxysmal, persistent, or permanent. [ACC]
The most commonly seen sequela of an embolic event is a stroke leading to disability. Patients with CV diseases tend to be older with multiple comorbidities. It can be difficult to know when to recommend antiplatelet agents such as aspirin or clopidogrel, anticoagulants or both. Think of using antiplatelet agents for clots in the arteries due to platelet aggregation, used to prevent ischemic events. Anticoagulants are used to treat clots in the veins or atria due to fibrin meshes of red blood cells.

The options for anticoagulation for CV indications have been expanding over the last several years. Risks and benefits of choosing to anticoagulate, or the choice of drug is based on drug characteristics as well as the patient’s disease process, comorbidities, risk of stroke, and risk of bleed.

### CV Indications Overview

The most commonly seen sequela of an embolic event is a stroke leading to disability. Patients with CV diseases tend to be older with multiple comorbidities. It can be difficult to know when to recommend antiplatelet agents such as aspirin or clopidogrel, anticoagulants or both. Think of using antiplatelet agents for clots in the arteries due to platelet aggregation, used to prevent ischemic events. Anticoagulants are used to treat clots in the veins or atria due to fibrin meshes of red blood cells.

### Evaluation of Patients with CV Indications

An appropriate history and physical will provide information to help determine the indication for anticoagulation, bleeding risk, duration of treatment, choice of anticoagulant, as well as diagnostic tests to be ordered.

#### History:

- Symptoms of chest pain/shortness of breath and palpitations can indicate symptomatic AFib/flutter and would need consideration for evaluation at a HLOC (hospital)
- History of heart failure (HF), hypertension, diabetes mellitus, cerebrovascular accident/transient ischemic attack (TIA) and vascular disease (coronary and peripheral) along with age and sex will help determine the stroke risk in a patient with AFib/flutter using CHA\textsubscript{2}DS\textsubscript{2}-VASc score (See Attachment A)
- Recent hospitalizations for HF, myocardial infarction and history of coronary/vascular stent placement with associated mural thrombus will help determine the need and duration of combined antiplatelet and anticoagulant therapy
- Last ECHO, EKG (obtain if not done)

#### Physical Exam:

A comprehensive exam looking at hemodynamic stability, cardiovascular exam including presence of, and location of, heart murmurs (type of valvular disease) and acute neurological deficits.

### 1. Confirm Presence of Indication for Anticoagulation

For all CV indications, the provider should:

- Confirm that an indication for anticoagulation is present by review of documents (e.g., old records, EKG, ECHO’s/catheter reports, imaging results, consultant’s notes) or order new diagnostic tests if there is evidence of a new indication.

Patients with Afib should have CHA\textsubscript{2}DS\textsubscript{2}-VASc score calculated and used in step 3.

### 2. Identify Presence of any Contraindications and Determine Need for Transfer to a HLOC (Hospital)

CV indications usually require lifelong anticoagulation. Many times, anticoagulation is initiated in the hospital. If you are initiating anticoagulation while a patient is in an institution, please rule out any of the following contraindications:

#### Absolute Contraindications Include:

- Active bleeding
- Severe bleeding diathesis
- Recent, planned or emergent high bleeding risk surgery/procedure
- Major trauma
- Acute intracranial hemorrhage
- Platelets <50,000

#### Relative Contraindications Include:

- Large abdominal aortic aneurysm with concurrent severe hypertension
- Stable aortic dissection
- Recent, planned, or emergent low bleeding risk surgery or procedure
- Recurrent bleeding from multiple gastrointestinal telangiectasias

If any contraindications present, refer to specialty co-management is recommended.

Patients with CV indications for anticoagulation commonly have comorbidities and can have signs and symptoms of hemodynamic instability. Consider transfer to a HLOC if any of the following are present, or consult specialty:

- Shortness of breath
- Hemodynamic instability
- Heart failure
- Loss of consciousness or syncope
- Uncontrolled AFib/flutter
- Signs and symptoms of stroke
- Chest pain or palpitations
- Pregnancy
3. Conduct Risk/Benefit Assessment

If no contraindications exist, look at the possible benefit patient would receive from anticoagulation (usually most important benefit is decrease in stroke risk) and then look at patient’s comorbidities, fall risk, medications and recent surgeries as potential factors that may increase risk of bleed.

For patients with AFib, first determine the risk of embolic stroke by utilizing CHA₂DS₂-VASc calculator. Points are assigned for the factors below – max score is 9. Annual adjusted stroke risk varies from 0% for patients with zero points, to 3.2% with patients with 3 points and 15.2% for patients with 9 points. (For details, see Attachment A)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive Heart Failure (CHF)</td>
<td>1</td>
<td>Stroke or TIA</td>
<td>2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>Vascular disease (Coronary Artery Disease, Peripheral Vascular Disease, Aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>2</td>
<td>Age 65-74</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1</td>
<td>Sex (female)</td>
<td>1</td>
</tr>
</tbody>
</table>

Determine Bleeding Risk – consider risk of bleeding for all patients considering comorbidities and medications or dietary factors that may increase risk of bleed by altering drug metabolism.

For AFib ONLY- to determine bleeding risk, utilize HAS-BLED table. The HAS-BLED score was developed as a practical risk assessment tool used to estimate the 1 year risk for major bleeding in patients with AFib by stratifying patients as low, moderate, or high bleed risk. This should not automatically exclude patients from receiving anticoagulation if clinically indicated, but instead should be used to identify modifiable risk factors that can be corrected (e.g., uncontrollable hypertension). (See Attachment A)

4. Review Current Medication List

- Review of medications and DDIs is crucial prior to initiation of anticoagulants, as these agents are considered high risk medications due to their narrow therapeutic window.
- Patients with CV indications for anticoagulation can frequently be on antiplatelet agents as well.
- In patients who are on concurrent antiplatelet agents, co-management with cardiology is recommended.

5. Review or Order Diagnostic Studies

- Initial Labs: CBC, CMP, PT/INR, PTT
- EKG and ECHO if needed
- Consider a Medical Hold for any patient with INR above 5.0

6. Anticoagulant Selection and Duration of Therapy

Choice of anticoagulant is complex and depends on many factors including:

- Specific indication for anticoagulation examples below – details on pages 16-17:
  - VKA is drug of choice for prosthetic, mechanical valves or moderate-to-severe mitral valve stenosis
  - If weight < 50 kg or > 120 kg or BMI ≥ 35 kg/m², DOACS are contraindicated
  - DOACs are preferred for non-valvular AFib/flutter
  - NOTE: use of aspirin as alternative anti-thrombotic strategy for patients with AFib/flutter has been eliminated
  - Comorbidities including renal function, pregnancy, or severe liver disease
  - Adherence: VKA preferred if adherence is an issue due to being able to monitor INR
  - Availability of reversal agents: VKA has readily available reversal agents while DOACs do not
  - DDIs less frequent with DOACs
  - Continuity of medication: Patient arriving on med consider switch to formulary agent if no clinical contraindications

Duration of Therapy

Duration of therapy is typically lifelong for CV indications except in bio prosthetic valves and LV thrombus.

See pages 16-17 for duration of therapy and INR goals based on specific indication.
In general, for patients treated with warfarin, the target INR is 2.5 (Therapeutic Range 2–3). Important exceptions are for patients with a specific valvular heart disease. Consultation with specialty is recommended when managing anticoagulation in all patients with valvular heart diseases. DOACs are not recommended for patients with valvular heart disease.

While INR gives the status of anticoagulation in a short window of time, TTR provides a measure of quality and success of anticoagulation, with the goal being >70% time within therapeutic range. There are various ways of calculating TTR, usually dependent on interval of time between blood draws as well as INR itself. If TTR is not at goal, more frequent INR checks are recommended.

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>INR GOAL (IF ON WARFARIN)</th>
<th>DURATION OF THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Valvular, Chronic or Paroxysmal, AFib/flutter (DOACs or warfarin, DOACs recommended over warfarin)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOACs are recommended over warfarin in DOAC eligible patients with AFib/flutter (except with moderate-to-severe mitral stenosis or a mechanical heart valve)</td>
<td>INR 2.5 (range 2.0-3.0)</td>
<td>Lifelong</td>
</tr>
<tr>
<td>For patients with AFib/flutter who have mechanical heart valves, warfarin is recommended</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke prevention (see Attachment A for CHA₂DS₂-VASc)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Valvular Heart Disease, Mitral Stenosis (DOACs NOT recommended)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatic mitral stenosis (moderate-to-severe)</td>
<td>INR 2.5 (range 2.0 to 3.0)</td>
<td>Lifelong</td>
</tr>
<tr>
<td>With one or more:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- AFib/flutter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Previous systemic embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Left atrial thrombus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In a patient with moderate-to-severe mitral stenosis due to rheumatic heart disease, with normal sinus rhythm and left atrium diameter &gt;55mm and no other risk factors, there is no supporting evidence to anticoagulate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rheumatic mitral valve disease with AFib/flutter who suffer systemic embolism or have left atrial thrombus</td>
<td>INR of 2.5 (range 2.0 to 3.0) Add low dose aspirin (50–100 mg po/daily) or INR of 3.0 (range 2.5 to 3.5)</td>
<td></td>
</tr>
<tr>
<td>Calcified mitral stenosis with AFib/flutter: For elderly patients with calcified mitral stenosis, treat for AFib using the standard approach based on CHA₂DS₂-VASc score (see Attachment A)</td>
<td>INR 2.5</td>
<td></td>
</tr>
<tr>
<td><strong>Valvular Heart Disease, Bioprosthetic Valves (DOACs NOT recommended)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral or aortic position</td>
<td>INR 2.5 (range 2.0 to 3.0) + low dose aspirin if low risk for bleeding</td>
<td>3-6 months post surgery followed by lifelong low dose aspirin</td>
</tr>
<tr>
<td>Mitral or aortic in patients with a prior history of systemic embolism</td>
<td>INR 2.5 (range 2.0-3.0) + low dose aspirin if low risk for bleeding</td>
<td>3-6 months post surgery then clinical reassessment; followed by lifelong low dose aspirin</td>
</tr>
<tr>
<td>Bioprosthetic valves either mitral or aortic in patients who have additional risk factors for thromboembolism, including AFib, hypercoagulable state, or low ejection fraction</td>
<td>INR 2.5 (range 2.0-3.0)</td>
<td>Lifelong</td>
</tr>
</tbody>
</table>

Table continues on next page.
### Valvular Heart Disease, Mechanical Prosthetic Valves

**(DOACs NOT recommended)**

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>INR GOAL (IF ON WARFARIN)</th>
<th>DURATION OF THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve replacement (AVR) in normal sinus rhythm with normal left atrial size</td>
<td>INR 2.5 (range 2.0 to 3.0)</td>
<td>Lifelong + low dose aspirin if low risk for bleeding</td>
</tr>
<tr>
<td>For mechanical aortic valves:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Patients with risk factors for thromboembolism such as: AFib/flutter, hypercoagulable state</td>
<td>INR 3.0 (range 2.5 to 3.5)</td>
<td></td>
</tr>
<tr>
<td>• Starr-Edwards or disc valve (other than Medtronic Hall)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral valve replacement any mechanical mitral valve</td>
<td>INR 3.0 (range 2.5 to 3.5)</td>
<td></td>
</tr>
<tr>
<td>Patients with a caged ball or caged disk valve any position</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Post Acute MI with LV Thrombus

**(DOACs NOT recommended)**

- Patients are at a high risk of systemic embolization. Evaluation and initiation of anticoagulation should be started in a hospital-based setting and continue as an outpatient. Transfer patient to a HLOC (hospital).
- Antiplatelet medications are often used in addition to anticoagulation.
- Co-management with specialty is recommended.
- Duration of triple therapy (anticoagulant and 2 antiplatelet agents) is dependent on whether an intracoronary stent has been placed and by the type of stent:

<table>
<thead>
<tr>
<th>For patients who did not undergo percutaneous coronary intervention (PCI)/stent placement:</th>
<th>Warfarin plus low dose aspirin (75-81 mg) QD x 3 months (can consider clopidogrel 75 mg QD instead of aspirin)</th>
<th>INR 2.5 (range 2.0 to 3.0)</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients who underwent PCI and bare metal stent placement:</td>
<td>Triple therapy with warfarin, plus low dose aspirin (75-100 mg) QD plus clopidogrel 75 mg QD x 1 month. Then warfarin plus a single antiplatelet agent (aspirin or clopidogrel) x 2 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For patients who underwent PCI and drug-eluding stent placement:</td>
<td>Triple therapy with warfarin, plus low dose aspirin (75-100 mg) plus clopidogrel 75 mg x 3 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- After termination of warfarin, low dose aspirin 75-100 mg plus clopidogrel 75 mg for up to one year

---

2. Gaasch, William H. M.D., UpToDate. Overview of the management of mitral stenosis.
### Monitoring of Patients with CV Indications

#### 7. Documentation in EHRS

Document in EHRS the following:

- Update the Problem List with:
  1. Indication for anticoagulation and
  2. “Long-term (current) use of anticoagulants” (ICD 10 Z79.01) – which should be marked resolved upon completion of therapy.
- Anticoagulation start date and anticipated stop date (indicate if lifelong)
- Assessment of bleeding risks and risks/benefits of anticoagulation
- If on Warfarin: Target INR; next INR check
- Patient Education (See PE 1-4)
- Specialty that is co-managing, if any (i.e., cardiology)
- Evaluate for lower bunk chrono

#### 8. Follow-Up and Monitoring

Monitoring should be ongoing:

- First Year: 3 months, 6 months and 12 months or more often as clinically indicated
- Follow-up at least every 6 months thereafter
- At periodic follow-up visits address the 8 steps outlined in this care guide
  - Ensure there remains a continued indication (e.g., if DVT and patient had 3 months of anticoagulation do they still need continued anticoagulation?)
  - Ensure no new contraindications to anticoagulation, or complication requiring a HLOC, or specialty referral: Review any changes in general health, functional status (recent falls), activity level (avoid contact sports), change in diet and substance use including alcohol.
  - Reassess risks/benefits of anticoagulation: Does a new medical condition/bleeding risk cause the risk/benefit equation to shift in favor of discontinuation of anticoagulation?
  - Review current medication list: especially for any new medications (including OTC) pay special attention to addition or discontinuation of antiplatelet agents. Confirm medication adherence
  - Review any new laboratory results
  - Confirm current anticoagulant is still most appropriate agent and that the continued use is appropriate
  - Confirm documentation (including the Problem List) is up to date in EHRS
  - Schedule appropriate follow-up and monitoring
  - If stopping anticoagulation, re-evaluate need for lower bunk chrono

### Medications

Please see the following Medication Sections for discussion of advantages, disadvantages, drug-drug interactions and dosing with relevant medication tables.

- Warfarin pages 19-22
- DOACs pages 23-28
- LMWH pages 29-31

### Specific Clinical Scenarios and Perioperative Management of Anticoagulation

The medication sections are followed by:

- Specific Clinical Scenarios: Anticoagulant-related page (page 32)
  - Antiplatelets and Anticoagulation
  - Heparin-Induced Thrombocytopenia (HIT)
- Perioperative Management of Anticoagulation (page 33)
- References (page 34)
Summary

Warfarin is an oral anticoagulant that acts by inhibiting vitamin K-dependent coagulation factors II, VII, IX and X. (See Attachment B) It increases clotting time as measured by INR, a standardized measure of a prothrombin time. Warfarin is the oldest and most studied anticoagulant and has a readily available reversal agent (Vitamin K).

Decision Support

Indications

Warfarin is the drug of choice for mechanical mitral, aortic or tricuspid valves as DOACs are contraindicated.

It is a reasonable choice for the vast majority of clinical indications requiring anticoagulation (e.g., AFib, acute coronary syndrome, prosthetic heart valve, heart failure, DVT/PE and anti-phospholipid syndrome).

Contraindications

- Cancer patients with VTE (use LMWH)
- Hemorrhagic tendencies (e.g., active GI bleed, CNS hemorrhage, dissecting aortic aneurysm, severe thrombocytopenia, large esophageal varices, within 72 hours of major surgery); anticoagulation contraindicated
- Spinal puncture or other diagnostic procedures with potential for significant bleeding
- Recent or potential surgery of the eye or CNS; major regional lumbar block anesthesia
- Pregnancy (except in women with mechanical heart valves at high risk for thromboembolism) (use LMWH)

Advantages vs. Disadvantages

Advantages:
- Can be monitored
- Reversal agent readily available
- Less GI bleeding
- Once daily dosing

Disadvantages:
- Many interactions (drug-drug, drug-food, and with endogenous factors)
- Frequent INRs and dose changes
- Delayed onset of action
- May require bridging around procedures and when initiating therapy
- More intracranial bleeds

Drug-Drug Interactions

Numerous drugs have the potential for interfering with warfarin, especially when the interacting substance is started, stopped, or changed in dose. Below is a very limited number of drugs that can have interaction with warfarin.

<table>
<thead>
<tr>
<th>Interaction Potentiates PT/INR ↑</th>
<th>Reduce Warfarin Dose By</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone (Cordarone®, Pacerone®)</td>
<td>20-50%</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole (Septra®, Bactrim®)</td>
<td>20-30%</td>
</tr>
<tr>
<td>Ciprofloxacin (Cipro®)</td>
<td>10%</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>15-30%</td>
</tr>
<tr>
<td>Metronidazole (Flagyl®)</td>
<td>20-30%</td>
</tr>
<tr>
<td>Azole antifungals (Fluconazole)</td>
<td>50%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interaction Blunts PT/INR Response ↓</th>
<th>Increase Warfarin Dose By</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine (Tegretol®)</td>
<td>100%</td>
</tr>
<tr>
<td>Nafcillin or Dicloxacillin</td>
<td>100-400%</td>
</tr>
</tbody>
</table>

Clinicians are encouraged to use the DDI Tool on Lifeline whenever a new medication is added to patient profile.

1. Go to Lifeline (http://lifeline/Pages/Home.aspx)
2. Under Divisions/Programs on the left, and subheading Health Care Operations, select Quality Management
4. Under Care Team Tools, select All Care Team Tools
5. Under Pharmacy/Medication Management, select Drug-Drug Interaction Checker or hyperlink below:

### Dosing, Therapeutic Range and Dose Adjustment

- In general, starting dose is 5 mg orally every evening. Higher “loading” doses are not recommended.
- Heparin therapy (LWMH or unfractionated) along with warfarin is recommended if there is an emergent/urgent need to anticoagulate the patient. (Typically the heparin is discontinued when INR is therapeutic)
- Evening dosing is strongly recommended. Allows time for same day dose adjustment for out of range INRs.
- Vitamin K is the reversal agent for warfarin. Use oral dosing only on outpatient basis and avoid subQ or IM injections due to unpredictable absorption.
- Note: The decision whether to hold warfarin and monitor, give vitamin K, or transfer the patient to a HLOC will largely depend on the patient’s INR, presence of active bleeding, patient’s bleeding risk and indication for anticoagulation.

### Summary

The cost scale $-$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.

### Decision Support

#### Warfarin (VKA) Continued

### Patient Education/Self Management

### Warfarin

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects / Interactions*</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Warfarin</strong>&lt;br&gt;Jantoven®&lt;br&gt;Tablet: 1 mg -pink&lt;br&gt;2 mg -lavender&lt;br&gt;2.5 mg -green&lt;br&gt;3 mg -tan&lt;br&gt;4 mg -blue&lt;br&gt;5 mg -peach&lt;br&gt;6 mg -teal&lt;br&gt;7.5 mg -yellow&lt;br&gt;10 mg -white</td>
<td>Usual initial dose: 5 mg orally every evening. Avoid loading doses&lt;br&gt;Consider lower starting dose: 2.5 mg every evening if: Age &gt; 75 yrs Multiple comorbidities Hypoalbuminemia Elevated pretreatment INR Elevated liver function tests Changing thyroid status&lt;br&gt;Consider higher starting dose: 7.5 mg orally every evening for patients weighing &gt; 80 kg&lt;br&gt;Patients restarting warfarin can usually start at their previous dose. If stopped due to bleeding, assess risk of thrombosis vs. risk of re-bleeding&lt;br&gt;Recheck INR on day 3 after first two doses, if INR &gt; 2.0, consider reducing dose by 1/2. Evaluate for cause of rapid rise in INR (See page 21-22) Steady-state INR will take up to 3 weeks&lt;br&gt;Dose adjustments at steady state (See page 22)&lt;br&gt;Assess variables affecting the INR before changing dose (e.g., patient adherence, medication interactions, dietary changes)&lt;br&gt;10% warfarin dose adjustment changes INR approximately 0.7-0.8</td>
<td>Adverse reactions: Bleeding (Patients treated with usual doses of warfarin have a 2%-4% risk per year of bleeding episodes requiring transfusion, and a 0.2% risk per year of fatal hemorrhage), skin necrosis (rare but serious, typically occurs on the 3rd to 8th day of therapy; four times as common in women as in men), Purple toe syndrome or other manifestations of peripheral emboli (rare, usually occurs 3-10 weeks after initiation of therapy), abdominal pain, bloating, diarrhea, flatulence, nausea or vomiting&lt;br&gt;Interactions: Multiple drug and food interactions</td>
<td>Contraindications: Pregnancy (teratogenic), active hemorrhage or hemorrhagic tendencies, aortic dissection, unsupervised patients with conditions associated with increased potential for non-adherence, recent or potential surgery of the eye or central nervous system, lumbar puncture, hypersensitivity to warfarin or any component of the formulation&lt;br&gt;Use with caution in patients with dietary insufficiency, HIT, hepatic impairment, renal impairment, thyroid disease&lt;br&gt;Risk of bleeding is highest in first month of therapy&lt;br&gt;GI bleeding in a patient on warfarin must be evaluated.&lt;br&gt;A baseline INR value is helpful to rule out underlying coagulopathy&lt;br&gt;NOTE: Do not cut pills</td>
</tr>
</tbody>
</table>

| **Vitamin K Antagonist (VKA) (oral) / VKA Reversing Agent (Vitamin K)**<br>Vitamin K Phytodiolone<br>Mephyton®<br>Tablet: 5 mg Injectable: 1 mg/0.5ml 10 mg/ml | Supratherapeutic INR (anticoagulant induced)<br>Outpatient setting: 2.5 to 5 mg orally as a single dose then re-evaluate before repeat administration<br>Hospital setting (patient NPO): IV vitamin K should be given over 30 minutes in a mixture of D5W 50 mL under monitored conditions<br>Avoid subQ or IM injections due to unpredictable absorption, which can lead to erratic correction of INR and resistance to warfarin | Adverse reactions: Chest pain, dizziness, flushing, hypotension, rash, urticaria, dyspnea<br>Note: Most people do not experience side effects taking small doses of vitamin K<br>Drug interactions: warfarin, cloestipol, cholestyramine, castor oil, mineral oil | **Contraindications:** Hypersensitivity to vitamin K or any component of the formulation<br>Use caution with parenteral administration. Severe hypersensitivity reactions, including anaphylactoid reactions and deaths have been reported following parenteral administration |

**BOLD=Formulary**

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.
March 2021

CCHCS Care Guide: Anticoagulation

Dosing, Therapeutic Range and Dose Adjustment Continued

- The narrow therapeutic index of warfarin and the complex number of factors that influence INR response makes consistent optimization of warfarin challenging.
- Several factors can affect an individual's response to warfarin including drug interactions (OTC and herbal supplements included), disease states, age, pregnancy, diet, and alcohol consumption.
- Vitamin K containing foods such as broccoli and leafy greens will blunt the PT/INR response. Encourage patients to maintain stable intake of these foods as available on CDCR Heart Healthy Diet. (See PE pages 1-4 for guidance)
- Significant increases in exercise and mobility can decrease the INR.
- Patients should be counseled to report any changes in diet, medications, exercise habits, or health status to their health care team.

Monitoring

When initiating therapy:
1. PT/INR, PTT, CBC and CMP first day of treatment, repeat INR morning of day 3 (after 2nd warfarin dose)
2. Schedule of subsequent INR checks is dependent on INR results and stability of warfarin dosing (in general follow table below):

<table>
<thead>
<tr>
<th>When to Check INR</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initially every 2-3 days</td>
<td>Until INR is in therapeutic range on 2 consecutive INR checks with stable warfarin dose</td>
</tr>
<tr>
<td>Then every 1-2 weeks</td>
<td>Until INR within therapeutic range on 2 consecutive INR checks with stable warfarin dose</td>
</tr>
<tr>
<td>Then every 4 weeks</td>
<td>When dose is stable, check monthly</td>
</tr>
</tbody>
</table>

3. CBC, CMP every 6 months, for the first year, and more frequent as clinically indicated.
4. If INR is unexpectedly out of therapeutic range, a repeat stat INR should be ordered. Subsequent warfarin dose adjustment as clinically indicated.
5. After any change in warfarin dosing, monitor INR closely until stable on new dose.

To manage increased INR see page 22.

**INR checks should be ordered for the first morning blood draw and warfarin should be given in the evening before bedtime (to allow time for dose adjustments if needed)**

- Consider causes of rapid INR rise (See page 19 for drug interactions), poor nutritional status, infection, systemic disease process)

NOTE: Some institutions may have a statewide, standardized Pharmacist Managed Anticoagulation Clinic for INR monitoring. Providers are encouraged to check with their institution. These clinics will more likely utilize Time in Therapeutic range (TTR) to measure the efficacy of anticoagulation with standard goal of TTR >70% within a given time range.

Special Circumstances

<table>
<thead>
<tr>
<th>Endogenous Factors That May DECREASE INR</th>
<th>Endogenous Factors That May INCREASE INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema</td>
<td>Blood dyscrasias</td>
</tr>
<tr>
<td>Hereditary factors</td>
<td>Cancer</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Collagen vascular disease</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>Diarrhea</td>
</tr>
<tr>
<td></td>
<td>Elevated temperature</td>
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<td></td>
</tr>
</tbody>
</table>
### Warfarin Dose Adjustment

The following table should be used only when maintenance dose adjustment is necessary after a stable INR has been achieved.

#### Goal INR 2.5 (Range 2.0–3.0)

<table>
<thead>
<tr>
<th>If INR Result Is:</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1.5*</td>
<td>Increase weekly dose by 15%</td>
</tr>
</tbody>
</table>
| 1.51–1.99*        | Continue same dose warfarin  
If INR still 1.5-1.99,  
increase weekly dose by 10% |
| 2.00–3.00         | Continue same dose warfarin |

#### Goal INR 3.0 (Range 2.5–3.5)

<table>
<thead>
<tr>
<th>If INR Result Is:</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1.5*</td>
<td>Increase weekly dose by 20%</td>
</tr>
<tr>
<td>1.51–1.99*</td>
<td>Increase weekly dose by 15%</td>
</tr>
</tbody>
</table>
| 2.00–2.49*        | Continue same dose warfarin  
If INR still 2.0-2.49, increase weekly dose by 10% |
| 2.50–3.50         | Continue same dose warfarin |

#### Dose Adjustment for Supratherapeutic INR Results

<table>
<thead>
<tr>
<th>If INR Result is:</th>
<th>Action</th>
</tr>
</thead>
</table>
| Greater than goal INR, but < 4.5 (between 3.0-4.5 and no bleeding) | • Option 1: Decrease or hold dosage, increase frequency of monitoring, and resume at lower dosage once INR is within therapeutic range  
• Option 2: May continue current dosage if INR is minimally elevated (0.5 or less above therapeutic range in a previously stable patient) |
| 4.5–10 and no bleeding (Consider medical hold for any patient with INR above 5.0) | • Consider possible cause (new medication, acute illness, etc.)  
• Hold next 1-2 warfarin doses  
• Increase frequency of INR monitoring (every 24 hr as long as INR ≥ 5)  
• Resume warfarin when INR is within therapeutic range; restart at a dosage that reflects a 10% decrease in the total weekly warfarin dose  
• Vitamin K is not recommended |
| > 10 and no bleeding (Consider medical hold for any patient with INR above 5.0) | • Consider possible cause (new medication, acute illness, etc.)  
• Hold warfarin  
• Administer vitamin K 2.5 - 5 mg orally* once  
• Increase frequency of INR monitoring (every 24 hr as long as INR ≥ 5)  
• If INR remains > 10, repeat vitamin K 2.5 - 5 mg orally* once  
• Resume warfarin when INR reaches < 3.0; restart at a dosage that reflects a 15% decrease in the total weekly warfarin dose |
| Serious bleeding regardless of INR | • Hold warfarin and transfer to a HLOC (hospital)  
• If elevated INR, hold warfarin, give vitamin K 2.5-5 mg orally*, and transfer to a HLOC (hospital) |

*Oral vitamin K administration is preferred in non-emergency situations. Avoid subcutaneous or intramuscular administration of vitamin K.

Note: Clinical and professional judgment may allow variation in the application of the algorithm.

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1 Adapted from: Holbrook, A et al. Evidence-Based Management of Anticoagulant Therapy. Chest 2012; 141(2) (Suppl):e152s-e184s, e326s-e350s.  
Hull, Russell D, MBBS, MSc and Valentine, Karen A, MD, PhD, “Correcting excess anticoagulation after warfarin” - UpToDate. 11/10/2014.  
Hull, Russell D, MBBS, MSc and Valentine, Karen A, MD, PhD, “Outpatient management of anticoagulation with warfarin” - UpToDate. 10/16/2013.  
Hull, Russell D, MBBS, MSc and Valentine, Karen A, MD, PhD, “Therapeutic use of warfarin and other vitamin K antagonists” - UpToDate. 10/16/2013.
There are two classes of DOACs:
1. Direct Thrombin Inhibitor (dabigatran)
2. Factor Xa Inhibitors (apixaban, edoxaban, and rivaroxaban)

Due to the short half-life of DOACs, patients being considered to take these drugs should be highly adherent, as there is increased risk of thrombosis even if only one dose is missed.

- Dose adjustments are dependent on CrCl and indication for anticoagulation. Recommend verifying dose with local pharmacist especially for patients with CrCl <30 or on hemodialysis

### Indications for DOACs (Nonformulary Use Considerations)

All DOACs remain nonformulary. **Dabigatran is the preferred non-formulary agent.**

- DOACs should be considered if a patient has a thromboembolic event while on warfarin, especially if the patient’s INR was in therapeutic range at time of event
- National Guidelines favor DOACs over VKA for non-valvular AFib due to decreased risk of bleed and greater convenience
- FDA approval: Apixaban (Eliquis®) for stroke prevention in AFib/flutter with dose adjustment
- Patients who come to CCHCS on one of these direct acting agents should be evaluated to see if they qualify for continued DOAC use or should be converted to VKA
- If a patient comes to CCHCS on a non-preferred nonformulary DOAC, they should be transitioned to the preferred agent unless contraindications exist

VKA treatment remains an appropriate treatment of choice in our setting for the majority of patients, except in the following patients when a DOAC should be considered over VKA:

- Patients with non-cancer related VTE or AFib/flutter and history of intracranial hemorrhage
- History of major non-GI bleed
  - For patients with history of GI bleed, VKA is preferred over DOACs due to increased risk of GI bleed with dabigatran, rivaroxaban, edoxaban
- Unstable INR despite patient adherence to VKA
- Warfarin allergy or prohibited DDIs with VKA
- Documented thrombotic event despite therapeutic INR
- Unable to obtain monitoring INRs (difficult phlebotomy access)
- New patients entering CCHCS system can be maintained on DOACs for up to 60 days until patient is evaluated for continued use versus switch to VKA
- DOACS may be given on a case-by-case basis for other indication
- In CCHCS, must be given NA or DOT for monitoring of adherence

### Contraindications for DOACs

In the following contraindications to DOACs, **VKA is the suggested alternative to use:**

- Patients with prosthetic heart valve or severe mitral stenosis
- Patients with antiphospholipid antibody or other strongly thrombophilic condition
- Severe renal impairment CrCl <30 mL/min (dabigatran and rivaroxaban); <15 mL/min (edoxaban)
- Non-adherent patients. Due to short half-life of these drugs, there is increased risk of thrombosis even if only one dose is missed
- Patients with BMI >35, weight >120 kg or weight <50 kg due to potential of pharmacokinetics and pharmacodynamics of DOAC being affected by weight

In the following contraindications to DOACs, **LMWH is recommended:**

- Patients with VTE in setting of active cancer
- Pregnancy or breastfeeding
- Known significant liver disease: LFT > 2-3X upper limit of normal Child-Pugh B/C (if absolutely necessary)

For patients with active bleeding, refer to a HLOC for non pharmacological IVC filter for VTE or AFib ablation as clinically indicated.
### Direct Oral Anticoagulants Continued

#### Potential Advantages and Disadvantages of DOACs Compared to VKA

<table>
<thead>
<tr>
<th>Advantages of DOACs</th>
<th>Disadvantages of DOACs</th>
</tr>
</thead>
<tbody>
<tr>
<td>No routine monitoring</td>
<td>No reliable, readily available measurement assay</td>
</tr>
<tr>
<td>Improved safety profile</td>
<td>Dose reduction or avoidance in renal impairment and avoidance in moderate or severe hepatic impairment</td>
</tr>
<tr>
<td>Rapid onset (may preclude the need for induction or bridging therapy)</td>
<td>Short half-life (mandates strict adherence)</td>
</tr>
<tr>
<td>Short half-life (advantageous for invasive procedures or active bleed)</td>
<td>Less flexibility in dosing</td>
</tr>
<tr>
<td>Fixed dosing</td>
<td>Fewer studies and approved indications (e.g., contraindicated in mechanical valve replacement)</td>
</tr>
<tr>
<td>Greater convenience, patient satisfaction</td>
<td>Potentially higher drug acquisition costs for patients</td>
</tr>
<tr>
<td>Fewer drug, disease, and diet interactions</td>
<td>DOAC drug interactions do exist that may preclude use</td>
</tr>
</tbody>
</table>

#### Drug-Drug Interactions

- DDIs include P-glycoprotein and CYP3A4 inducers and inhibitors, which changes blood concentration of the drug
- The only food-related drug concern with DOACs is that rivaroxaban should be taken with food

Clinicians are encouraged to use the DDI Tool on Lifeline whenever a new medication is added to patient profile:

1. Go to Lifeline [http://lifeline/Pages/Home.aspx](http://lifeline/Pages/Home.aspx)
2. Under Divisions/Programs on the left, and subheading Health Care Operations, select Quality Management
4. Under Care Team Tools, select All Care Team Tools
5. Under Pharmacy/Medication Management, select Drug-Drug Interaction Checker

Or select the hyperlink below:

#### Dosing and Dose Adjustment

Please see pages 25-27 (next 3 pages) for DOAC dosing and dose adjustment guidelines.

#### Monitoring for Patients on DOACs

When initiating therapy:

- Record patient’s weight, CBC, CMP on first day of treatment, PT/INR, PTT
- Repeat every 6 months thereafter and more frequently as clinically indicated

Close monitoring of renal function is recommended for patients at increased risk of renal insufficiency (i.e., dehydration) or underlying CKD. Dose adjustments may be required.

---

### SUMMARY

**DABIGATRAN PRADAXA®**

- **Nonformulary Preferred**
- **Strengths:** 75 mg, 110 mg, 150 mg
- **Administer NA**
- **$$$$$**

May order as KOP in select cases where the patient would benefit from self-administration.

### DECISION SUPPORT

#### Direct Thrombin Inhibitor

**DABIGATRAN PRADAXA®**

- **Stoke prevention and systemic embolism prophylaxis in patients with non-valvular AFib:** 150 mg orally twice daily
- **Treatment of acute DVT or PE:** 150 mg orally twice daily after 5 to 10 days of IV or subQ anticoagulation
- **DVT or PE prophylaxis in patients who have been previously treated:** 150 mg orally twice daily
- **DVT and PE prophylaxis after Hip Replacement Surgery:** 110 mg orally on first day beginning 1 to 4 hours after surgery and after hemostasis achieved, then 220 mg orally once daily for 28 to 35 days. If not started on the day of surgery, after hemostasis achieved, initiate with 220 mg orally once daily.

### PATIENT EDUCATION/Self Management

#### Direct Oral Anticoagulants continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects / Interactions*</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DABIGATRAN PRADAXA®</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke prevention and systemic embolism prophylaxis in patients with non-valvular AFib:</td>
<td>150 mg orally twice daily</td>
<td>- Adverse reactions: Bleeding, dyspepsia, edema, rash, pruritus, urticaria, abdominal pain, gastritis</td>
<td></td>
</tr>
<tr>
<td>Treatment of acute DVT or PE:</td>
<td>150 mg orally twice daily after 5 to 10 days of IV or subQ anticoagulation</td>
<td>- Increased risk of epidural spinal hematoma with neuroaxial anesthesia or spinal puncture</td>
<td></td>
</tr>
<tr>
<td>DVT or PE prophylaxis in patients who have been previously treated:</td>
<td>150 mg orally twice daily</td>
<td>- Drug Interactions: Avoid concurrent use with P-glycoprotein inducers (e.g., rifampin). Evaluate P-glycoprotein inhibitors individually</td>
<td></td>
</tr>
<tr>
<td>DVT and PE prophylaxis after Hip Replacement Surgery:</td>
<td>110 mg orally on first day beginning 1 to 4 hours after surgery and after hemostasis achieved, then 220 mg orally once daily for 28 to 35 days. If not started on the day of surgery, after hemostasis achieved, initiate with 220 mg orally once daily.</td>
<td>- Increased bleeding risk with anti-platelets, anticoagulants, and thrombolytics</td>
<td></td>
</tr>
<tr>
<td>Renal Impairment:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Non-valvular AFib</td>
<td></td>
<td><strong>Contraindications:</strong> Active pathological bleeding, prosthetic heart valves (mechanical/bio prosthetic), pregnancy or breastfeeding, CrCl &lt; 15 mL/min, moderate to severe mitral stenosis, serious hypersensitivity reaction to dabigatran or any component of the formulation</td>
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<tr>
<td></td>
<td>- CrCl &gt;30 mL/min: No dose adjustment needed</td>
<td>- Use caution in patients with hepatic impairment, renal impairment</td>
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<tr>
<td></td>
<td>- CrCl 15-30 mL/min: 75 mg orally twice daily</td>
<td>- Do not chew, break, or open capsules. Capsules must be dispensed in original container and not repackaged due to sensitivity to moisture.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- CrCl &lt;15 mL/min: No data, avoid use</td>
<td>- Indications: reduce risk of stroke and systemic embolism in patients with non-valvular AFib, prevention and management of VTE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- CrCl 30-50 mL/min and concurrent use of dronedarone or systemic ketoconazole: 75 mg orally twice daily</td>
<td>Half-Life: 12-17 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- CrCl &lt;30 mL/min and concurrent use of P-glycoprotein Inhibitor: Avoid co-administration</td>
<td>Antidote: Praxbind® (Idarucizumab)</td>
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<td></td>
<td>- VTE</td>
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<tr>
<td></td>
<td></td>
<td>- Adverse reactions: Bleeding, dyspepsia, edema, rash, pruritus, urticaria, abdominal pain, gastritis</td>
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<td></td>
<td></td>
<td>- Increased risk of epidural spinal hematoma with neuroaxial anesthesia or spinal puncture</td>
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<tr>
<td></td>
<td></td>
<td>- Drug Interactions: Avoid concurrent use with P-glycoprotein inducers (e.g., rifampin). Evaluate P-glycoprotein inhibitors individually</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Increased bleeding risk with anti-platelets, anticoagulants, and thrombolytics</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Contraindications: Active pathological bleeding, prosthetic heart valves (mechanical/bio prosthetic), pregnancy or breastfeeding, CrCl &lt; 15 mL/min, moderate to severe mitral stenosis, serious hypersensitivity reaction to dabigatran or any component of the formulation</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Use caution in patients with hepatic impairment, renal impairment</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Do not chew, break, or open capsules. Capsules must be dispensed in original container and not repackaged due to sensitivity to moisture.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Indications: reduce risk of stroke and systemic embolism in patients with non-valvular AFib, prevention and management of VTE</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Half-Life: 12-17 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antidote: Praxbind® (Idarucizumab)</td>
<td></td>
</tr>
</tbody>
</table>

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.

**Bold = Formulary**
# CCHCS Care Guide: Anticoagulation

## Summary

### Decision Support

### Patient Education/Self Management

## Direct Oral Anticoagulants Continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects / Interactions*</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Apixaban Eliquis®</strong>&lt;br&gt;Nonformulary&lt;br&gt;Strengths: 5 mg 2.5 mg&lt;br&gt;Administer NA&lt;br&gt;$$$$$$&lt;br&gt;May order as KOP in select cases where the patient would benefit from self-administration</td>
<td><strong>Stroke prevention and systemic embolism prophylaxis in patients with non-valvular Afib</strong>: 5 mg orally twice daily&lt;br&gt;Consider 2.5 mg orally twice daily if patient has at least 2 of the following:&lt;br&gt;• Age ≥ 80 years&lt;br&gt;• Body weight of ≤ 132 lb (60 kg)&lt;br&gt;• Serum CREAT level of ≥ 1.5 mg/dL</td>
<td><strong>Adverse reactions</strong>: Bleeding rash, anemia, nausea, hematuria, epistaxis&lt;br&gt;• Increased risk of epidural spinal hematoma with neuroaxial anesthesia or spinal puncture&lt;br&gt;<strong>Drug Interactions</strong>: Avoid concurrent use with strong dual inducers of CYP3A4 and P-glycoprotein (e.g., rifampin, phenytoin, carbamazepine)&lt;br&gt;• Increased bleeding risk with antiplatelets, anticoagulants, and thrombolytics</td>
<td><strong>Contraindications</strong>: Active pathological bleeding, prosthetic heart valves, severe hepatic impairment, pregnancy or breastfeeding, moderate to severe mitral stenosis, severe hypersensitivity reaction to apixaban or any component of the formulation&lt;br&gt;• Use caution in patients with moderate hepatic impairment, renal impairment&lt;br&gt;• Indications: reduce risk of stroke in patients with non-valvular AFib and prevention and management of VTE&lt;br&gt;Half-Life: 12 hours&lt;br&gt;Antidote: Andexxa® (recombinant Factor Xa)</td>
</tr>
<tr>
<td><strong>Direct Thrombin Inhibitor</strong>&lt;br&gt;<strong>Treatment of acute DVT or PE</strong>: (NOT recommended acutely in place of unfractionated heparin in patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy) 10 mg orally twice daily for 7 days then 5 mg orally twice daily for at least 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prophylaxis for reduction in the risk of recurrent DVT and/or PE</strong>: 2.5 mg orally twice daily after at least 6 months of standard anticoagulation therapy</td>
<td></td>
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</tr>
<tr>
<td><strong>Post-surgical DVT and PE prophylaxis</strong>: 2.5 mg orally twice daily. Administer initial dose 12 to 24 hours after surgery.&lt;br&gt;Duration: 12 days (knee replacement), 35 days (hip replacement)</td>
<td></td>
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<tr>
<td>Combined P-glycoprotein and strong CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, ritonavir): Decrease dosage by 50% for patients receiving apixaban doses greater than 2.5 mg orally twice daily; avoid coadministration in patients already receiving apixaban 2.5 mg twice daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hepatic Impairment</strong>:&lt;br&gt;Mild impairment: No dosage adjustments needed&lt;br&gt;Moderate impairment: Limited experience in this population, dosing recommendations not available&lt;br&gt;Severe impairment: Not recommended</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring: None recommended&lt;br&gt;Converting from apixaban to another DOAC see page 28</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Bold = Formulary<br>*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.<br>The cost scale $$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.
# CCHCS Care Guide: Anticoagulation

## Direct Oral Anticoagulants Continued

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing</th>
<th>Adverse Effects / Interactions*</th>
<th>Comments*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Direct Factor Xa Inhibitors</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>Rivaroxaban</strong> (Xarelto®)</td>
<td>Post-surgical DVT and PE prophylaxis: 10 mg orally once daily (12 days) (knee replacement), 35 days (hip replacement)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment of acute DVT or PE: (NOT recommended acutely in place of unfractionated heparin in patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy) 15 mg orally twice daily with food for 21 days then 20 mg orally once daily with food for a total of 6 months</td>
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<tr>
<td></td>
<td>Prophylaxis for reduction in the risk of recurrent DVT and/or PE: 10 mg orally once daily after at least 6 months of standard anticoagulation therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonformulary</td>
<td>Prevent stroke in patients with non-valvular AFib: 20 mg orally once daily in the evening with food</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strengths:</td>
<td>Renal Impairment:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 mg</td>
<td>VTE prophylaxis and treatment: CrCI &lt; 15 mL/min: avoid use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mg</td>
<td>Prevent stroke in patients with non-valvular AFib: CrCI ≤ 50 mL/min: 15 mg orally once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 mg</td>
<td>Hepatic Impairment: Mild impairment (Child-Pugh Class A): No dose adjustment needed, but avoidance of rivaroxaban is recommended for any degree of hepatic disease associated with coagulopathy. Moderate/Severe impairment (Child-Pugh Class B/C): Avoid use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administer</td>
<td>Convert from rivaroxaban to warfarin: Discontinue rivaroxaban and begin warfarin plus parenteral anticoagulant at time of next rivaroxaban dose. Discontinue parenteral anticoagulant when INR is therapeutic.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA</td>
<td>Convert from warfarin to rivaroxaban: Discontinue warfarin and start rivaroxaban at INR &lt; 3.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>May order as KOP in select cases where the patient would benefit from self-administration</td>
<td>Converting from rivaroxaban to another DOAC see page 28</td>
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<td>$$$$$</td>
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<tr>
<td><strong>Edoxaban</strong> (Savaysa®)</td>
<td>Stroke and Systemic Embolism Prevention in patients with non-valvular AFib: (dosing based on CrCI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonformulary</td>
<td>CrCI ≥ 95 mL/min: Use not recommended</td>
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<tr>
<td>Tablet</td>
<td>CrCI 51-94 mL/min: 60 mg orally once daily</td>
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<tr>
<td>Strengths:</td>
<td>CrCI 15-50 mL/min: 20 mg orally once daily</td>
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<tr>
<td>15 mg</td>
<td>CrCI &lt; 15 mL/min: Use not recommended</td>
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<tr>
<td>30 mg</td>
<td>Treatment of DVT and PE: 60 mg orally once daily following 5-10 days of initial therapy with parenteral anticoagulant. Dose reduction to 30 mg once daily recommended if:</td>
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<tr>
<td>60 mg</td>
<td>• CrCI 15-50 mL/min; or</td>
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</tr>
<tr>
<td>Administer</td>
<td>• Body weight ≤ 60 kg; or</td>
<td></td>
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<tr>
<td>DOT Only</td>
<td>• Concomitant use of P-gp inhibitors (e.g., verapamil, quinidine, azithromycin, clarithromycin, erythromycin, itraconazole, ketoconazole)</td>
<td></td>
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<tr>
<td>Consider NA</td>
<td>• CrCI &lt; 15 mL/min: Use not recommended</td>
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<tr>
<td>$$$</td>
<td>Moderate or severe hepatic impairment (Child-Pugh Class B and C): Use not recommended</td>
<td></td>
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<tr>
<td></td>
<td>Convert from edoxaban to warfarin: Discontinue edoxaban and administer parenteral anticoagulant and warfarin at same time of next scheduled edoxaban dose. Discontinue parenteral anticoagulant when INR ≥ 2.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Convert from warfarin to edoxaban: Discontinue warfarin and start edoxaban when INR ≤ 2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Converting from edoxaban to another DOAC see page 28</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>When converting from edoxaban to another DOAC see page 28</td>
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<td></td>
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<tr>
<td></td>
<td>Adverse Reactions: Bleeding, muscle cramps, abdominal pain, back pain, dyspepsia, fatigue, pruritus, sinusitis, syncope</td>
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<td></td>
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<tr>
<td></td>
<td>Increased risk of epidural spinal hematoma with neuroaxial anesthesia or spinal puncture</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Drug Interactions: Avoid concurrent use with rifampin, Avoid long term concomitant treatment with other anticoagulants</td>
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<tr>
<td></td>
<td>Contraindications: Active pathological bleeding, pregnancy or breastfeeding, prosthetic heart valves, moderate-severe hepatic impairment, severe hypersensitivity reaction to rivaroxaban or any component of the formulation</td>
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<td></td>
<td>Use caution in patients with hepatic impairment, renal impairment</td>
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<tr>
<td></td>
<td>Indications: FDA approved for the prevention of DVT and PE in patients undergoing knee or hip replacement surgery, treatment of DVT and PE and stroke prevention in non-valvular AFib; prevention and management of VTE</td>
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<td></td>
<td>Half-Life: 5-9 hours</td>
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<tr>
<td></td>
<td>Monitoring: Renal function prior to initiation of therapy, periodically throughout treatment and more frequently in clinical situations where renal function may decline.</td>
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<td></td>
<td>Antidote: Andexxa® (recombinant Factor Xa)</td>
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<tr>
<td></td>
<td>Black Box Warning: Do not use in non-valvular AFib patients with CrCI ≥ 95 mL/min due to reduced efficacy</td>
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</tr>
<tr>
<td></td>
<td>Contraindications: Active pathological bleeding, mechanical heart valves, moderate to severe mitral stenosis, severe hypersensitivity reaction to edoxaban or any component of the formulation</td>
<td></td>
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<tr>
<td></td>
<td>Use caution in patients with hepatic impairment, renal impairment</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Indications: reduction in risk of stroke and systemic embolism in non-valvular AFib; treatment of DVT and PE</td>
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<tr>
<td></td>
<td>Half-Life: 10-14 hours</td>
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<tr>
<td></td>
<td>Monitoring: Renal function prior to initiation of therapy, periodically throughout treatment and more frequently in clinical situations where renal function may decline.</td>
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<tr>
<td></td>
<td>Antidote: none available</td>
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</tr>
</tbody>
</table>

**Bold = Formulary**

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

The cost scale $$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.
### Summary of Dosing and Conversion to/from Warfarin

<table>
<thead>
<tr>
<th>Mechanism of Action</th>
<th>Dabigatran (Pradaxa&lt;sup&gt;®&lt;/sup&gt; (nonformulary, preferred)</th>
<th>Apixaban (Eliquis&lt;sup&gt;®&lt;/sup&gt;) (nonformulary)</th>
<th>Rivaroxaban (Xarelto&lt;sup&gt;®&lt;/sup&gt;) (nonformulary)</th>
<th>Edoxaban (Savaysa&lt;sup&gt;®&lt;/sup&gt;) (nonformulary)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half-Life</td>
<td>12-17 hours</td>
<td>12 hours</td>
<td>5-9 hours</td>
<td>10-14 hours</td>
</tr>
<tr>
<td>Special Considerations</td>
<td>Avoid concurrent use with any P-gp inducer</td>
<td>Avoid concurrent use with any P-gp inhibitor IF CrCl &lt; 50 mL/min</td>
<td>Avoid in patients with history of GI bleed, severe hepatic/renal disease</td>
<td>Discontinue dabigatran and initiate the preferred agent at the time that the next dabigatran dose would have been administered</td>
</tr>
<tr>
<td>Dosing Interval</td>
<td>BID See page 25 for details</td>
<td>BID See page 26 for details</td>
<td>Once daily with food See page 27 for details</td>
<td>Once daily See page 27 for dose adjustments</td>
</tr>
<tr>
<td>Renal Elimination</td>
<td>Dose adjustment needed. Is dependent on indication and CrCl. Contraindicated in ESRD</td>
<td>Dose adjustment needed. Is dependent on indication, age, weight, and Serum CREAT</td>
<td>Dose adjustment needed. Is dependent on indication and CrCl. Off Label use for ESRD patients on HD</td>
<td>Dose adjustment needed. Is dependent on indication and CrCl. CrCl &lt; 15 mL/min: Use not recommended Off label use for ESRD patients on HD</td>
</tr>
<tr>
<td>Convert TO Warfarin</td>
<td>Based on CrCl start warfarin 3 days (&gt; 50 mL/min), 2 days (31-50 mL/min) or 1 day (15-30 mL/min) before discontinuation of dabigatran. Manufacturer provides no recommendations for CrCl &lt; 15 mL/min</td>
<td>Discontinue apixaban and start warfarin plus parenteral anticoagulant at time of next apixaban dose. Discontinue parenteral anticoagulant when INR is therapeutic</td>
<td>Discontinue rivaroxaban and start warfarin plus parenteral anticoagulant at time of next rivaroxaban dose. Discontinue parenteral anticoagulant when INR is therapeutic</td>
<td>Discontinue edoxaban and start warfarin plus parenteral anticoagulant at time of next edoxaban dose. Discontinue parenteral anticoagulant when INR ≥ 2.0</td>
</tr>
<tr>
<td>Convert FROM Warfarin</td>
<td>Discontinue dabigatran when INR &lt; 2.0</td>
<td>Discontinue warfarin, start apixaban when INR &lt; 2.0</td>
<td>Discontinue warfarin, start rivaroxaban when INR &lt; 3.0</td>
<td>Discontinue warfarin, start edoxaban when INR &lt; 2.5</td>
</tr>
<tr>
<td>Convert FROM one DOAC TO another DOAC</td>
<td>Discontinue dabigatran and initiate the preferred agent at the time that the next dabigatran dose would have been administered</td>
<td>Discontinue apixaban and initiate the preferred agent at the time that the next apixaban dose would have been administered</td>
<td>Discontinue rivaroxaban and initiate the preferred agent at the time that the next rivaroxaban dose would have been administered</td>
<td>Discontinue edoxaban and initiate the preferred agent at the time that the next edoxaban dose would have been administered</td>
</tr>
<tr>
<td>Storage</td>
<td>• Must be used w/in 4 months after opening</td>
<td>Store between 20-25 °C (68 to 77 °F); excursions permitted between 15-30°C (59-86°F)</td>
<td>Store at 25 °C (77 °F); excursions permitted between 15-30 °C (59-86 °F)</td>
<td>Store at 25 °C (77 °F); excursions permitted between 15-30 °C (59-86 °F)</td>
</tr>
</tbody>
</table>

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In the acute setting, enoxaparin is used for the treatment of VTE, CV events, and for DVT prophylaxis.

In the outpatient setting, enoxaparin is indicated for:
- The initial management of DVT patients who do not require hospitalization
- Long term treatment in patient with active cancer and VTE

- Baseline Data: Patient weight, CBC, serum CREAT, PT/INR, PTT, albumin and liver enzymes (ALT, AST)
- Renal function and a CBC should be monitored at least every 3 months or more frequently as the clinical situation dictates
- Close monitoring of renal function is recommended for patients at increased risk of renal insufficiency (i.e., dehydration) or underlying CKD. Dose adjustments may be required for worsening renal function

**Indications for LMWH Use**

**Acute VTE Treatment**
- Initiate concurrent warfarin (usually within 72 hours of enoxaparin treatment)
- Continue treatment for at least 5 days and until INR is in therapeutic range x 2 daily INR checks (INR 2-3)

**Long-term treatment of VTE in patients with active cancer (recommended over warfarin or DOACs)**
- VTE Prophylaxis for patient at risk for VTE (not covered in this care guide)

**Contraindications for LMWH Use**
- Active major bleeding (anticoagulation contraindicated)
- Presence or history of HIT (refer to a HLOC)
- Thrombocytopenia (Platelet < 100,000/mm³) (use VKA or DOAC)
- Hypersensitivity to enoxaparin sodium (use VKA or DOAC)
- Hypersensitivity to heparin or pork products (use VKA or DOAC)
- Hypersensitivity to benzyl alcohol (only in multi-dose formulation) (use VKA or DOAC if no other contraindication)
- ESRD (use heparin for HD flush, VKA/DOAC for other)

**Precautions for LMWH Use**
- Conditions with increased risk of hemorrhage; bleeding diathesis; uncontrolled arterial hypertension; history of recent GI ulcer, diabetic retinopathy or hemorrhage
- Indwelling epidural catheters and spinal punctures
- Pregnant women with mechanical prosthetic heart valves
- Obesity and Anorexia
- Renal and Hepatic impairment

**Advantages for LMWH Use**
- More predictable anticoagulant effect over conventional unfractionated heparin
- No regular blood monitoring required
- Reduced incidence of thrombocytopenia
- Reduced incidence of osteoporosis

**Disadvantages for LMWH Use**
- SubQ administration can be uncomfortable
- Prolonged anticoagulation effect in patients with renal failure
- Requirement of special assays to measure anti-Xa activity
- Longer activity can complicate reversal, if necessary

**Drug-Drug Interactions**

DDIs include aspirin, alteplase, ibuprofen, rivaroxaban, and warfarin

Clinicians are encouraged to use the DDI Tool on Lifeline whenever a new medication is added to patient profile

1. Go to Lifeline ([http://lifeline/Pages/Home.aspx](http://lifeline/Pages/Home.aspx))
2. Under Divisions/Programs on the left, and subheading Health Care Operations, select Quality Management
4. Under Care Team Tools, select All Care Team Tools
5. Under Pharmacy/Medication Management, select Drug-Drug Interaction Checker

Or select the hyperlink below: 
### Dosing and Dose Adjustments

- **Usual treatment dose for patients of average weight and normal renal function is 1 mg/kg BID**
- **Dose adjustment is required based on weight and renal function**
- Monitoring first 2 weeks of therapy (extend beyond 2 weeks as clinically indicated, especially for suspected bleeding, thrombocytopenia and change in renal function):
  - CBC (for platelets and hematocrit) every 2-3 days
  - CREAT every week x 2

### Medication | Dosing | Adverse Effects / Interactions* | Comments*
--- | --- | --- | ---
**ENOXAPARIN**
Lovenox® (LMWH)

**Injectable pre-filled syringe:**
- 30 mg/0.3 mL
- 40 mg/0.4 mL
- 60 mg/0.6 mL
- 80 mg/0.8 mL
- 100 mg/L
- 120 mg/0.8 mL
- 150 mg/mL

**Multiple dose vial (MDV):**
- 300 mg/3 mL

$$$$$

| **DVT treatment (acute):**
| **Inpatient treatment (with or without pulmonary embolism):** 1 mg/kg/dose subQ every 12 hours or 1.5 mg/kg subQ once daily
| **Outpatient treatment (without pulmonary embolism):** 1 mg/kg/dose subQ every 12 hours
| **Note:** Start warfarin on first treatment day and continue enoxaparin until INR is between 2-3 for 2 consecutive days (usually 5-7 days).
| **DVT treatment (acute) in pregnant patients:** 1 mg/kg/dose subQ every 12 hours throughout pregnancy
| **DVT prophylaxis after knee or hip replacement surgery:** 30 mg subQ every 12 hours, start within 12-24 hours after surgery
| **Duration of treatment:** 10 days or until risk of DVT has diminished or the patient has therapeutic INR on warfarin
| **DVT prophylaxis for acute illness:** 40 mg subQ once daily (usually 6-11 days)
| **DVT prophylaxis for abdominal surgery:** 40 mg subQ once daily starting 2 hours prior to surgery (usually 7-10 days)
| **Unstable angina and non-Q-wave MI:** 1 mg/kg subQ every 12 hours with ASA (100-325 mg once daily) for 2-8 days
| **Geriatric:** dose alteration may be required due to increased incidence of bleeding

| **Renal Impairment:** CrCl < 30 mL/min
| **DVT prophylaxis during acute illness, after abdominal or hip/knee replacement surgery:** 30 mg subQ once daily
| **DVT treatment (during warfarin initiation) or acute STEMI (<75 yo):** 1 mg/kg subQ once daily
| **Acute STEMI (<75 yo):** 30 mg IV bolus plus 1 mg/kg subQ then 1 mg/kg subQ once daily

| **Hepatic impairment:** Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.

**Adverse reactions:**
- Bleeding, anemia, confusion, diarrhea, dyspnea, edema, elevated hepatic enzymes, injection site reactions, fever, nausea
- HIT is a rare complication of heparin exposure due to a HIT antibody which activates platelets and can cause life-threatening arterial and venous thrombosis. Suspect HIT in patients who:
  - Develop necrosis at the injection site
  - Have a systemic reaction (fever, chills, dyspnea, etc.) to a bolus administration of heparin
  - Develop a greater than 50% decrease in platelet count from base line labs while on heparin
  - Experience a new thrombotic event within 5 to 14 days of initiating heparin therapy, even if the heparin has been discontinued
- HIT can occur in patients getting ≥ 1 dose of unfractionated heparin (including heparin IV flushes) within the past 100 days

**Drug Interactions:**
- Avoid long term concomitant treatment with other anticoagulants, aspirin
- Increased bleeding risk with antiplatelets, anticoagulants, and thrombolytics

**Absolute Contraindications:**
- Active major bleeding, including intracerebral hemorrhage within past 2 weeks, subarachnoid hemorrhage until definitively treated
- Thrombocytopenia, with positive antiplatelet test in presence of enoxaparin
- Hypersensitivity to enoxaparin, heparin or pork products, or any component of the formulation (including benzyl alcohol in MDVs)

**Use with caution in elderly, low weight patients, obesity**

**Other Contraindications:**
- Recent thrombolytic therapy
- History of HIT

**Reversal of Enoxaparin:**
- No agent is effective for complete reversal in the event of supra-therapeutic anticoagulation (e.g., fresh frozen plasma, vitamin K, protamine).

If life-threatening bleeding, consider protamine. Do not exceed 50 mg in 10 minutes.
- First dose: 1 mg for each 1 mg enoxaparin; give by slow IV over 10 minutes
- Second dose: 0.5 mg protamine for each 1 mg enoxaparin; give by slow IV infusion over 10 minutes

*See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.

*Bold = Formulary

The cost scale $$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment.
### Enoxaparin (Lovenox®) Continued

#### Laboratory Monitoring

When initiating therapy:
- CBC, CMP and weight check on first day of treatment, PT/INR, PTT
- For the first 2 weeks of therapy (extend beyond 2 weeks as clinically indicated):
  - CBC every 2-3 days
  - Serum creatinine every week
- Record the patient’s weight at each clinic visit (LMWH dosing is weight based)
- Dose adjustment as clinically indicated based on renal function (CrCl) and weight

Ongoing Monitoring:
- Weight check, CBC, CMP every 3 months or more frequently if clinically indicated
- Even with dose adjustment for weight and CrCl, obtaining anti-factor Xa levels with closer monitoring should be considered for the following:
  - Patients with renal impairment (CrCl < 60 mL/min)
  - Obese patients and patients > 150 kg
  - Anorexic patients
  - Pregnant patients (co-management with high risk OB is required)

#### Anti-Factor Xa Levels

Dosing for LMWH is primarily weight-based and monitoring with anti-factor Xa levels is recommended only under certain clinical scenarios.

Monitoring anti-factor Xa levels: indicated only when appropriate dosing is difficult to determine – such as in:
- Acute changes in renal function (especially CrCl < 60 mL/min)
- Acute decompensation of a chronic disease (i.e., acute worsening of kidney or heart failure)
- Pregnancy (co-management with OB is required)
- Anorexia and obesity (BMI <18 or >30 kg/m²)
- When unable to determine the patient’s dry weight (e.g., anasarca, ascites or significant peripheral edema)

Dose adjustments based on anti-Xa levels are in general performed in a hospital setting.
Specific Clinical Scenarios: Anticoagulant-related

Anticoagulation

Occasionally, you will come across patients who are on single or dual antiplatelet agents and also need anticoagulation, such as:

- Patients already on anticoagulation for AFib or VTE who develop an acute coronary event requiring stent placement
- Patients with a mechanical heart valve

These individuals present a challenge and specialty involvement is recommended. If the patient needs lifelong anticoagulation, need for antiplatelet agents should be re-evaluated at 12 months.

If an antiplatelet medication (such as aspirin and/or clopidogrel) and an anticoagulant is used without above indications, clarify the need for dual therapy with specialty input, and document on the Problem List the reason for dual therapy.

Heparin-Induced Thrombocytopenia (HIT)

HIT is typically seen in a hospital setting. However, it can occur in any setting where a patient is being treated with heparin products. Thrombocytopenia is the most common manifestation of HIT and typically occurs 5-10 days after exposure to heparin. HIT should be considered in a patient with new or worsening thrombocytopenia, and a detailed review of ALL possible heparin (unfractionated or LMWH) exposure should be done. Thrombosis (venous or arterial) occurs in up to 50% of patients with HIT who are not treated with a non-heparin anticoagulant.

Heparin cessation alone is not sufficient since patients with HIT remain at risk for subsequent thrombosis.

The treatment plan should include:

1. Immediate/acute management (occurs in inpatient setting)
   - **Stop all heparin exposure:** Individuals with suspected or diagnosis of HIT should have immediate discontinuation of ALL sources of heparin (LMWH and Unfractionated Heparin), heparin flushes, heparin exposure during hemodialysis, heparin-bound catheters, and heparin-containing medications. Diagnosis **MUST** be clearly documented and relayed to ALL individuals (including providers outside of CCHCS) involved in the care of the patient.
   - **Immediate referral to a specialty provider is required** and transfer to a HLOC (hospital) should be considered depending on the severity of thrombocytopenia, presence of thrombosis, presence of bleeding, and comorbid conditions.

2. Post acute and long-term management
   - Decisions on choice and duration of anticoagulant must be done in coordination with specialty input. It must take into account all factors one needs to consider for anticoagulation.

3. Clear documentation of the management plan
   - Documentation including diagnosis, choice of anticoagulant, and duration of anticoagulation after evaluation at a HLOC or with specialty provider is required.
Determine risk of bleeding vs. thrombosis in perioperative period and adjust anticoagulant therapy accordingly. For those surgeries not listed below, follow recommendations from surgery consultants.

### LOW BLEEDING RISK PROCEDURES THAT CAN BE PERFORMED WITHOUT DISCONTINUING OR CHANGING WARFARIN/VKA

<table>
<thead>
<tr>
<th>Dental</th>
<th>Endodontics</th>
<th>Prosthetics</th>
<th>Restorations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teeth cleaning</td>
<td>Endodontics</td>
<td>Prosthetics</td>
<td>Restorations</td>
</tr>
<tr>
<td>Uncomplicated extractions</td>
<td>Prosthetics</td>
<td>Restorations</td>
<td></td>
</tr>
<tr>
<td>Periodontal therapy</td>
<td>Restorations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For most dental procedures no change in anticoagulant dosing is needed. It may be reasonable to allow the patient to “drift” to the low end of his/her therapeutic INR prior to a dental procedure with a higher risk of bleeding.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Dermatologic                   | Skin Biopsy  | Simple excisions |
| Mohs surgery                   | Skin Biopsy  | Simple excisions |
| Simple excisions               | Skin Biopsy  | Simple excisions |
| Continue anticoagulant around the time of the procedure and optimize local hemostasis. |

| Ophthalmic                     | Cataract surgery | Trabeculectomy |
| Cataract surgery               | Cataract surgery | Trabeculectomy |
| Trabeculectomy                 | Cataract surgery | Trabeculectomy |
| Continue anticoagulant around the time of surgery. |

| Gastrointestinal               | Diagnostic esophagastroduodenoscopy (EGD) | Colonoscopy without biopsy | Endoscopic ultrasonography without biopsy | Diagnostic endoscopic retrograde cholangiopancreatography | Biliary stent without sphincterotomy |
| Diagnostic esophagastroduodenoscopy (EGD) | Colonoscopy without biopsy | Endoscopic ultrasonography without biopsy | Diagnostic endoscopic retrograde cholangiopancreatography | Biliary stent without sphincterotomy |
| For procedures with intermediate and high risk of bleed (not listed here), follow recommendations from the surgeon regarding perioperative management of anticoagulation. Generally, DOACs are stopped 2-3 days before surgery depending on CrCl (earlier if CrCl <30-50 ml/min)
- Restart DOAC 24 hours after procedure in patients who are at low risk of bleed
- In patients with high risk of bleed, resume DOACs 2-3 days after the procedure, after hemostasis has occurred
- Bridging decision based on Thromboembolic Risk of Underlying Condition – See table below |

### ACCP’s Perioperative Thromboembolism Risk Stratification

<table>
<thead>
<tr>
<th>Low Thrombosis Risk</th>
<th>Moderate Thrombosis Risk</th>
<th>High Thrombosis Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5%/year risk of Arterial Thromboembolism (ATE)</td>
<td>5% -10%/year risk of ATE</td>
<td>10%/year risk of ATE</td>
</tr>
<tr>
<td>Bileaflet aortic valve w/o AFib and no other risk factors for stroke</td>
<td>Bileaflet aortic valve and one of the following: AFib, prior stroke/TIA, HTN, DM, CHF, age &gt;75 year</td>
<td>Any mechanical mitral valve</td>
</tr>
<tr>
<td>AFib and CHA-D-S-VASc score of 0-2 (and no prior stroke or TIA) (See Attachment A)</td>
<td>AFib and CHA-D-S-VASc score of 3 or 4 (See Attachment A)</td>
<td>Older aortic valve</td>
</tr>
<tr>
<td>Single VTE more than 12 months ago and no other risk factors</td>
<td>VTE within past 3-12 months</td>
<td>Mechanical heart valve and recent (&lt;6 months) stroke or TIA</td>
</tr>
<tr>
<td>Consider no bridging anticoagulation during anticoagulation interruption</td>
<td>Recurrent VTE</td>
<td>AFib and CHA-D-S-VASc score of 5 or 6 (See Attachment A), recent (&lt;3 months) stroke or TIA, or rheumatic valvular heart disease</td>
</tr>
<tr>
<td>Bridging or no bridging decision needs to be individualized based on the surgical risk of bleeding and patient risk factors</td>
<td>Non-severe thrombophilic conditions-such as heterozygous factor V Leiden or prothrombin gene mutation</td>
<td>Recent (&lt;3 months) VTE</td>
</tr>
<tr>
<td>Active cancer</td>
<td>Severe thrombophilia such as protein C, protein S or anti-thrombin deficiency, antiphospholipid antibodies or more than one defect</td>
<td>Consider bridging anticoagulation with LMWH; stop VKA 5 days prior to surgery.</td>
</tr>
</tbody>
</table>

### REFERENCES


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Blood clotting, or coagulation, is an important process that prevents too much bleeding when a blood vessel is injured. Blood cells and proteins in your blood work together to stop the bleeding by forming a clot over the injury.

Typically your body will naturally dissolve the blood clot after the injury has healed. Sometimes, clots form on the inside of blood vessels without an obvious injury or do not dissolve naturally. This can be dangerous and require accurate diagnosis and treatment.

Clots can occur in veins or arteries, which are vessels that are part of your body’s circulatory system. Clots in your arteries, veins, and heart can cause heart attacks, strokes and blockages.

The following factors increase your risk for developing a blood clot:
- Obesity
- Pregnancy
- Sitting in one position for long periods of time
- Smoking
- Birth control pills
- Some cancers
- Trauma
- Some surgeries
- Age (especially if over age 60)
- A family history of blood clots
- Diabetes
- High blood pressure
- High cholesterol

People who may have a blood clot in a vein might feel or see:
- Leg cramping or skin that is tender to a light touch
- Swelling
- Warm skin
- Redness of the skin
- Pain near the vein
- A vein that looks blue

In addition to knowing your risk factors, and signs of a blood clot, it is also important to be aware of the symptoms of blood clots, which are different depending on where the clot is located.

**HEART**
Chest heaviness or pain, shortness of breath, sweating, nausea, lightheadedness

**BRAIN**
Weakness of the face, arms or legs, trouble speaking, vision problems, sudden and severe headache, dizziness. Can lead to stroke and death.

**ARM OR LEG**
Sudden or gradual pain, swelling, tenderness and warmth

**LUNG**
Sharp chest pain, racing heart, shortness of breath, sweating, fever, coughing up blood
Anticoagulants (also known as blood thinners) are medicines that prevent blood clots from forming. They also keep existing blood clots from getting larger, helping to keep you from having a stroke or other life-threatening problems.

You may be prescribed a blood thinner if you have:
- Certain heart or blood vessel diseases
- An abnormal heart rhythm called atrial fibrillation
- A heart valve replacement
- A risk of blood clots after surgery

When you take a blood thinner, follow directions carefully. Blood thinners may interact with certain foods, medicines, vitamins, and alcohol.

**Make sure that your health care provider knows all of the medicines and supplements you are taking.**

With some blood thinners you may need regular blood tests to check how well your blood is clotting. It is important to make sure that you’re taking enough medicine to prevent clots, but not so much that it causes bleeding.

**Could blood thinners cause problems?**

If you follow your health care team’s guidance, you shouldn’t have any problems taking blood thinners. Reach out to your health care team right away if:

- Your urine turns red or dark brown. This could be a sign of urinary tract bleeding.
- Your stools turn red, dark brown or black. This could be a sign of intestinal bleeding.
- You are a woman and you bleed more than normal when you are on your period.
- Your gums bleed.
- You have a bad headache or stomach pain that doesn’t go away.
- You get sick or feel weak, faint or dizzy.
- You are a woman and you think you’re pregnant.
- You often find bruises or blood blisters.
- You have an accident of any kind.

**When are blood thinners used?**

Blood thinners are used with a number of diseases when there is an increased risk of blood clots. It is used to best prevent blood clots seen in:

- Irregular or fast heartbeat
- Heart valve replacement
- Heart chamber dysfunctions
- Deep vein thrombosis
- Blood clots in lungs
- Stroke
- After some surgeries
**BLOOD THINNERS: WHAT YOU SHOULD KNOW**

**HOW LONG WILL I TAKE THIS MEDICATION?**

It depends on why you take the blood thinner and what other health problems you have. Some people take a blood thinner for only a few months, but many people take it for the rest of their life.

**HOW SHOULD I TAKE THE MEDICATION?**

Always follow your doctor’s or nurse’s instructions and take the pills exactly as prescribed.

- Go to the pill line every day to get your pill. A blood thinner is rarely given as a “carry med”
- Take your blood thinner at about the same time every day
- Never take extra pills or skip a day. If you forget your pills one day, tell a health care team member
- Never stop taking your blood thinner unless your health care team tells you to stop. If you have any trouble with taking blood thinners or getting refills, send a CDCR 7362 request to the triage nurse

**WHAT TESTS WILL I NEED IF I TAKE A BLOOD THINNER?**

It depends on the type of blood thinner. A simple blood test called “INR” needs to be done regularly when taking warfarin. Your doctor will adjust your dose to get to a certain “INR.”

When you first start warfarin, you may need your blood checked often. Once your dose is adjusted, you only need blood tests about once a month.

**WHAT DO I NEED TO KNOW ABOUT USING OTHER MEDICATIONS WHEN I AM TAKING BLOOD THINNERS?**

- When blood thinners are taken with other medicines, they can change the way other medicines work, and other medicines can change the way certain blood thinners work, and your blood can get thinner than needed
- Tell your health care team if you are taking other medications, including over-the-counter medicines, vitamins or other supplements
- Some common medications also raise the risk of bleeding like aspirin, ibuprofen, naproxen, or Motrin®-like medications (Naprosyn®, Advil®, Aleve®)
- Some “cough and cold medicines,” herbal medications, and Pepto-Bismol may have aspirin

**WHAT ARE THE SIDE EFFECTS OF BLOOD THINNERS?**

Side effects with blood thinners are uncommon but can include bleeding or bruising. A little bleeding that stops after a few minutes is okay, such as bleeding gums when brushing your teeth or a small nosebleed.

Tell your doctor or nurse right away if you have more serious bleeding, such as:

- Red, dark, coffee or cola–colored urine
- Stools that are black, bloody, or look like tar
- Bad nosebleeds, bleeding gums, or coughing up blood
- Throwing up coffee-colored or bright red vomit
- New bruises that come for no reason
- A cut that will not stop bleeding within 10 minutes
- Stomach, back or side pain that won’t go away
- New or bad headache, problems with vision or speech, numbness or weakness, or confusion
- Too much menstrual bleeding
**BLOOD THINNERS: MORE INFORMATION ON WARFARIN**

### Know your dose and the color of your pills

The color of warfarin/Jantoven® pills tells you how strong the pill is. CDCR uses:

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pink</td>
</tr>
<tr>
<td>2</td>
<td>Light purple</td>
</tr>
<tr>
<td>2.5</td>
<td>Green</td>
</tr>
<tr>
<td>3</td>
<td>Tan</td>
</tr>
<tr>
<td>4</td>
<td>Blue</td>
</tr>
<tr>
<td>5</td>
<td>Orange</td>
</tr>
<tr>
<td>6</td>
<td>Blue-green</td>
</tr>
<tr>
<td>7.5</td>
<td>Yellow</td>
</tr>
<tr>
<td>10</td>
<td>White</td>
</tr>
</tbody>
</table>

### Why do I need regular blood tests?

**What does the INR number mean?**

The INR number is the way of measuring how fast your blood clots. The higher your INR, the longer it takes for your blood to clot. You need regular INR blood tests to make sure your warfarin dose is correct.

- **If your INR number is too high:** You have more risk of bleeding, and your warfarin dose may need to be lowered.
- **If your INR number drops too low:** Blood clots could form, so your warfarin dose may need to be increased.

It is very important that your INR number stay within a safe range.

### What things can affect my INR?

**DIET:**
- Foods high in vitamin K “work against” warfarin because vitamin K helps the blood clot.
- These lower your INR and increase your risk for blood clots.
- Vitamin K rich foods include: spinach, broccoli, collard greens, turnip greens, green leaf lettuce, kale (and many other dark-green leafy vegetables).
- Green tea, margarine, mayonnaise, and many oils (canola, soybean, olive) can also affect your INR levels.
- Do not drink alcohol (Pruno), which can cause serious side effects with warfarin.
- Let your provider know if you are fasting or doing a hunger strike, this can affect your medication level.
- Do not change your diet too much if you are taking warfarin.

**HEALTH:**
- Fever, nausea, vomiting, or diarrhea for more than 2 days in a row can increase your risk for blood clots and should be reported to your health care provider immediately.

**MEDICATIONS:**
- Many medications can affect your INR number. Always talk to your health care provider before taking any new medication, including canteen items.

The medicines below can change your INR and increase your risk for bleeding or blood clots:

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspirin</strong></td>
<td>Be aware that Alka-Seltzer and Pepto-Bismol contain aspirin. Avoid using ointments or gels that have aspirin.</td>
</tr>
<tr>
<td><strong>Anti-inflammatories</strong></td>
<td>Includes Ibuprofen (Motrin, Advil), naproxen (Aleve), also known as NSAIDs.</td>
</tr>
<tr>
<td><strong>Cold medicines and over the counter medications</strong></td>
<td>Always talk to your health care team before taking any over the counter medications. Check the label on all cold medications as they might have aspirin or anti-inflammatories.</td>
</tr>
<tr>
<td><strong>Herbs/Supplements</strong></td>
<td>Always talk to your health care team before taking any herbs/supplements. Some of the more common ones that may affect your anticoagulation therapy include: Aloe, capsicum, celery, chamomile, Coenzyme Q10, fenugreek, fish oil supplements, garlic, ginger, green tea, melatonin, Omega-3 fatty acids, St. John’s Wort, Turmeric.</td>
</tr>
</tbody>
</table>
COÁGULOS SANGUÍNEOS

La coagulación de la sangre o anticoagulación es un proceso importante que evita el sangrado excesivo cuando se lesionan vasos sanguíneos. Las células y proteínas sanguíneas de la sangre trabajan juntas para detener la hemorragia formando un coágulo sobre la lesión.

Normalmente, el cuerpo disolverá naturalmente el coágulo de sangre después de que la lesión haya sanado. A veces, los coágulos se forman en el interior de los vasos sanguíneos sin una lesión evidente o no se disuelven de forma natural. Estas situaciones pueden ser peligrosas y requieren un diagnóstico y tratamiento precisos.

Los coágulos pueden producirse en venas o arterias, que son vasos que forman parte del sistema circulatorio del cuerpo. Los coágulos en las arterias, las venas y el corazón pueden causar ataques cardíacos, derrames cerebrales y obstrucciones.

RIESGOS DE COÁGULOS SANGUÍNEOS

Los siguientes factores aumentan el riesgo de desarrollar un coágulo sanguíneo:
- Obesidad
- Embarazo
- Sentarse en una posición durante largos períodos
- Fumar
- Píldoras anticonceptivas
- Algunos cánceres
- Traumatismos
- Algunas cirugías
- Edad (especialmente si es mayor de 60 años)
- Historial familiar de coágulos sanguíneos
- Diabetes
- Presión arterial alta
- Colesterol alto

ÍNDICIOS DE COÁGULOS SANGUÍNEOS

Las personas que pueden tener un coágulo en una vena pueden sentir o ver:
- Calambres en las piernas o la piel que son sensibles a un ligero toque
- Inflamación
- Piel caliente
- Enrojecimiento de la piel
- Dolor cerca de la vena
- Una vena que se ve azul

SÍNTOMAS DE LOS COÁGULOS SANGUÍNEOS

Además de conocer los factores de riesgo y los indicios de un coágulo sanguíneo, también es importante conocer sus síntomas, los cuales son diferentes según el lugar donde se encuentre el coágulo.

CORAZÓN

Pesadez o dolor en el pecho, dificultad para respirar, sudoración, náuseas, mareos.

CEREBRO

Debilidad de la cara, brazos o piernas, problemas para hablar, problemas de la visión, dolor de cabeza repentino y grave, mareos. Puede causar un derrame cerebral y la muerte.

BRAZO O PIerna

Dolor repentino o gradual, inflamación, sensibilidad y calor.

PULMÓN

Dolor agudo en el pecho, ritmo cardíaco acelerado, dificultad para respirar, sudoración, fiebre, tos que produce sangre.
TRATAR LOS COÁGULOS SANGUÍNEOS CON ANTICOAGULANTES

¿QUÉ SON LOS ANTICOAGULANTES?
Los anticoagulantes (también conocidos como diluyentes de la sangre) son medicamentos que evitan la formación de coágulos sanguíneos. También evitan que los coágulos sanguíneos existentes se agranden, lo que ayuda a evitar que se produzca un derrame cerebral u otros problemas que pongan en peligro la vida.

Se le puede recetar un anticoagulante si tiene:
- Ciertas enfermedades del corazón o de los vasos sanguíneos.
- Ritmo cardíaco anormal llamado fibrilación auricular.
- Reemplazo de una válvula del corazón.
- Riesgo de coágulos sanguíneos después de una cirugía.

Cuando tome un anticoagulante, siga las instrucciones cuidadosamente. Los anticoagulantes pueden interactuar con ciertos alimentos, medicamentos, vitaminas y alcohol.

Asegúrese de que su proveedor de atención médica conozca todos los medicamentos y suplementos que está tomando.

Con algunos anticoagulantes posiblemente necesite realizarse análisis de sangre regulares para comprobar la eficacia de la coagulación de la sangre. Es importante asegurarse de tomar una cantidad suficiente de medicamento para evitar los coágulos, pero no tanto como para causar hemorragias.

¿PUEDEN LOS ANTICOAGULANTES CAUSAR PROBLEMAS?
Si sigue las indicaciones del equipo médico, no debería tener problemas para tomar anticoagulantes. Acuda al equipo médico de inmediato si:
- La orina se vuelve roja o marrón oscuro. Esto podría ser un indicio de hemorragia del tracto urinario.
- Las heces se vuelven rojas, marrón oscuro o negras. Esto podría ser un indicio de hemorragia intestinal.
- Es mujer y sangra más de lo normal durante el período.
- Las encías sangran.
- Tiene fuerte dolor de cabeza o de estómago que no desaparece.
- Se enferma o se siente débil, se desmaya o se marea.
- Es mujer y cree que está embarazada.
- A menudo se encuentra moretones o ampollas de sangre.
- Tuvo un accidente de cualquier tipo.

¿CUÁNDO SE USAN LOS ANTICOAGULANTES?
Los anticoagulantes se utilizan con una serie de enfermedades cuando hay un mayor riesgo de coágulos sanguíneos. Se usan para prevenir mejor los coágulos que se ven en:
- Ritmo cardíaco irregular o rápido.
- Reemplazo de una válvula del corazón.
- Disfunciones de las cámaras del corazón.
- Trombosis venosa profunda.
- Coágulos en los pulmones.
- Derrame cerebral.
- Después de algunas cirugías.
ANTICOAGULANTES: QUÉ DEBE SABER

¿POR CUÁNTO TIEMPO TOMARÉ ESTE MEDICAMENTO?
Depende de la razón por la cual está tomando anticoagulantes y qué otros problemas de salud tiene. Algunas personas toman anticoagulantes solo durante unos meses, pero muchas personas los toman por el resto de su vida.

¿CÓMO DEBO TOMAR EL MEDICAMENTO?
Siga siempre las instrucciones del médico o enfermera y tome las píldoras exactamente como se lo recetaron.

- Diríjase a la fila de las píldoras todos los días para conseguir la suya. Un anticoagulante rara vez se administra como "medicamento para llevar".
- Tome el anticoagulante aproximadamente a la misma hora todos los días.
- Nunca tome píldoras extras o las omita un día. Si se le olvida tomarlas un día, infórmelo a un miembro del equipo de atención médica.
- Nunca deje de tomar el anticoagulante a menos que el equipo médico se lo indique. Si tiene algún problema para tomar o para resurtirlos, envíe una solicitud 7362 a la enfermera de triaje.

¿QUÉ PRUEBAS NECESITARÉ SI TOMO ANTICOAGULANTES?
Depende del tipo de anticoagulante. Un simple análisis de sangre llamado “índice internacional normalizado” (international normalized ratio, INR) debe hacerse regularmente cuando se toma warfarina.

Su médico ajustará su dosis para llegar a un cierto “INR”.

Cuento comienza a tomar warfarina, es posible que necesite un análisis de sangre con frecuencia. Una vez que se ajuste la dosis, solo necesitará análisis de sangre aproximadamente una vez al mes.

¿QUÉ NECESITO SABER SOBRE EL USO DE OTROS MEDICAMENTOS CUANDO ÉSTOY TOMANDO ANTICOAGULANTES?

- Cuando se toman anticoagulantes junto con otros medicamentos, puede cambiar la forma en que funcionan otros medicamentos, y otros medicamentos pueden cambiar la forma en que funcionan ciertos anticoagulantes y la sangre puede diluirse más de lo necesario.
- Dígale al equipo médico si está tomando otros medicamentos, incluidos los de venta libre, vitaminas u otros suplementos.
- Algunos medicamentos comunes también aumentan el riesgo de sangrado como la aspirina, el ibuprofeno, el naproxeno o los medicamentos similares al Motrin® (Naprosyn®, Advil®, Aleve®).
- Algunos “medicamentos para la tos y el resfriado”, medicamentos a base de hierbas y el Pepto-Bismol pueden contener aspirina.

¿CUÁLES SON LOS EFECTOS SECUNDARIOS DE LOS ANTICOAGULANTES?
Los efectos secundarios de los anticoagulantes son poco comunes, pero pueden incluir hemorragias o moretones. Un poco de sangrado que se detiene después de unos minutos está bien, como el sangrado de las encías cuando se cepilla los dientes o una pequeña hemorragia nasal.

Dígale al médico o enfermera de inmediato si tiene una hemorragia más grave, como, por ejemplo:

- Orina roja, oscura, de color café o de gaseosa
- Heces negras, sangrientas o que parecen alquitran
- Hemorragias nasales graves, encías sangrantes o tos con sangre
- Vómito de color café o rojo brillante
- Nuevos moretones que aparecen sin razón
- Un corte que no deja de sangrar en 10 minutos
- Dolor de estómago, de espalda o de costado que no desaparece
- Dolor de cabeza nuevo o fuerte, problemas con la visión o el habla, entumecimiento o debilidad, o confusión
- Demasiado sangrado menstrual
**ANTICOAGULANTES: MÁS INFORMACIÓN SOBRE LA WARFARINA**

**CONOZCA SU DOSIS Y EL COLOR DE LAS PÍLDORAS**

El color de las píldoras de warfarina/Jantoven® le indica cuán fuerte es la píldora. El Departamento de Correccionales y Rehabilitación de California (CDCR) utiliza:

- 1 mg: rosa
- 2 mg: lila
- 2.5 mg: verde
- 3 mg: tan
- 4 mg: azul
- 5 mg: naranja
- 6 mg: verde azulado
- 7.5 mg: amarillo
- 10 mg: blanco

**¿POR QUÉ NECESITO ANÁLISIS DE SANGRE REGULARES?**

**¿QUÉ SIGNIFICA EL NÚMERO DE INR?**

El número de INR es la forma de medir la velocidad de coagulación de la sangre. Cuanto más alto es el INR, más tiempo tarda la sangre en coagularse. Necesita análisis regulares de INR para asegurarse de que su dosis de warfarina es correcta.

- **Si su número de INR es demasiado alto**: tiene más riesgo de sangrado y posiblemente sea necesario reducir su dosis de warfarina.
- **Si su número de INR es demasiado bajo**: podrían formarse coágulos, por lo que podría ser necesario aumentar la dosis de warfarina.

Es muy importante que su número de INR se mantenga dentro de un rango seguro.

**¿QUÉ PUEDE AFECTAR MI INR?**

**DIETA:**

- Los alimentos ricos en vitamina K "trabajan contra" la warfarina, porque la vitamina K ayuda a la coagulación de la sangre.
- Esto reduce el INR y aumenta el riesgo de coágulos sanguíneos.
- Los alimentos ricos en vitamina K incluyen: espinacas, brócoli, coles, col rizada (y muchas otras verduras de hoja verde oscura).
- El té verde, la margarina, la mayonesa y muchos aceites (canola, soya, oliva) también pueden afectar sus niveles de INR.
- No beba alcohol manufacturado en la prisión (Pruno), que puede causar graves efectos secundarios con la warfarina.
- Hágale saber a su proveedor si está en ayunas o en huelga de hambre, esto puede afectar su nivel de medicamento.
- No cambie demasiado su dieta si está tomando warfarina.

**SALUD:** fiebre, náuseas, vómitos o diarrea durante más de dos días seguidos pueden aumentar el riesgo de que se formen coágulos sanguíneos, por lo que debe informar inmediatamente a su médico.

**MEDICAMENTOS:** muchos medicamentos pueden afectar su número de INR. Siempre consulte con su proveedor de atención médica antes de tomar cualquier medicamento nuevo, incluidos los artículos de la cantina. Los siguientes medicamentos pueden cambiar su INR y aumentar el riesgo de hemorragias o coágulos sanguíneos:

- **Aspirina**
  - Tenga en cuenta que el Alka-Seltzer y Pepto-Bismol contienen aspirina.
  - Evite el uso de ungüentos o geles que contengan aspirina.

- **Antiinflamatorios**
  - Incluye el ibuprofeno (Motrin, Advil), el naproxeno (Aleve), también conocido como antiinflamatorios no esteroides (AINEs).

- **Medicamentos para el resfriado y de venta libre**
  - Siempre hable con el equipo médico antes de tomar cualquier medicamento sin receta.
  - Revise la etiqueta de todos los medicamentos para el resfriado, ya que pueden contener aspirina o antiinflamatorios.

- **Hierbas/ suplementos**
  - Siempre hable con el equipo médico antes de tomar cualquier hierba o suplemento. Algunas de las más comunes que pueden afectar su terapia de anticoagulación incluyen: aloe, pimiento, apio, manzanilla, coenzima Q10, fenogreco, suplementos de aceite de pescado, ajo, jengibre, té verde, melatonina, ácidos grasos de omega-3, hierba de San Juan, cúrcuma.
The CHA₂DS₂-VASc score has been shown to improve stratification of ischemic stroke risk among lower-risk individuals who may not be appropriate for anticoagulation therapy.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive Heart Failure (CHF)</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (Coronary Artery Disease, Peripheral Vascular Disease, Aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Age 65-74</td>
<td>1</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>1</td>
</tr>
</tbody>
</table>

Maximum score = 9

<table>
<thead>
<tr>
<th>CHA₂DS₂-VASc Total Score</th>
<th>Adjusted Stroke Rate (At 1 year follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>1.3%</td>
</tr>
<tr>
<td>2</td>
<td>2.2%</td>
</tr>
<tr>
<td>3</td>
<td>3.2%</td>
</tr>
<tr>
<td>4</td>
<td>4.0%</td>
</tr>
<tr>
<td>5</td>
<td>6.7%</td>
</tr>
<tr>
<td>6</td>
<td>9.8%</td>
</tr>
<tr>
<td>7</td>
<td>9.6%</td>
</tr>
<tr>
<td>8</td>
<td>6.7%</td>
</tr>
<tr>
<td>9</td>
<td>15.2%</td>
</tr>
</tbody>
</table>

Clinical factors that contribute to stroke risk and support anticoagulation in patients with AFib are frequently risk factors for bleeding as well. The HAS-BLED score was developed as a practical risk assessment tool used to estimate the 1 year risk for major bleeding in patients with AFib by stratifying patients as low, moderate, or high bleed risk.

HAS-BLED score only applies to patients with AFib and should not automatically exclude patients from receiving anticoagulation if clinically indicted, but instead should be used to identify modifiable risk factors that can be corrected (e.g., uncontrollable hypertension).

<table>
<thead>
<tr>
<th>Condition</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>H Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A Abnormal renal/liver function (1 pt each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>S Stroke</td>
<td>1</td>
</tr>
<tr>
<td>B Bleeding history or Pre-disposition</td>
<td>1</td>
</tr>
<tr>
<td>L Labile INRs</td>
<td>1</td>
</tr>
<tr>
<td>E Elderly</td>
<td>1</td>
</tr>
<tr>
<td>D Current drugs (medication) or alcohol use (1 pt each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

**Total Points**

<table>
<thead>
<tr>
<th>Total Points</th>
<th>Annual Major Bleed Risk %*</th>
<th>Intracranial Bleeds Per 100-pt-yrs</th>
<th>Major Bleed Risk Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.13</td>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>1</td>
<td>1.02</td>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>2</td>
<td>1.88</td>
<td>0.6</td>
<td>Moderate</td>
</tr>
<tr>
<td>3</td>
<td>3.74</td>
<td>0.7</td>
<td>High</td>
</tr>
<tr>
<td>4</td>
<td>8.7</td>
<td>1</td>
<td>High</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>1.2</td>
<td>High</td>
</tr>
</tbody>
</table>

*Major bleed = Intracerebral hemorrhage or bleeding resulting in a hospitalization, a hemoglobin drop > 2 g/dL, or a blood transfusion
CCHCS Care Guide: Anticoagulation

Attachment B

Site of Action for Oral Anticoagulants

The site of action helps demonstrate the laboratory tests to order for therapeutic monitoring. PT/INR measures the extrinsic and common pathways of the clotting cascade for Vitamin K antagonists (warfarin) Anti-Factor Xa levels for Heparin (LMWH and Unfractionated Heparin). There is limited data determining the therapeutic range for DOACs (Direct thrombin inhibitor and Oral factor Xa inhibitors).

*Warfarin Mechanism of Action: Warfarin competitively inhibits the subunit 1 of the multi-unit VKOR complex, depleting functional vitamin K reserves and hence reduces synthesis of active clotting factors.

1Leung, Lawrence LK, Direct oral anticoagulants and parenteral direct thrombin inhibitors: Dosing and adverse effects, upToDate.com, April 2017.