Anticoagulation Therapy Care Guide

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CALIFORNIA CORRECTIONAL
HEALTH CARE SERVICES

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.

https://cchcs.ca.gov/clinical-resources/

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GOALS

- ✓ **Identify patients with indications for anticoagulation**
- ✓ **Choose the appropriate medication 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**
- ✓ **Ensure appropriate patient education on diagnostic and therapeutic plan is shared with patients**
- ✓ **Evaluate bleeding risks and the implications on managing venous thromboembolism (VTE) and atrial fibrillation/flutter (AF/AFL)**
- ✓ **Identify the International Normalized Ratio (INR) target goal for every patient on warfarin and monitor Time in Therapeutic Range (TTR)**

ALERTS

- **Significant drug-drug interactions (DDIs)**
- **High risk of serious bleeding**
- **INR outside desired range**
- **Red Flag Physical Findings: Extremity pain or swelling, and skin necrosis**
- **Pregnancy and breastfeeding**
- **Periprocedural management**

DIAGNOSTIC CRITERIA

Indications for Anticoagulation

Thromboembolic Conditions	Cardiovascular Conditions
Deep vein thrombosis (DVT)	Nonvalvular AF/AFL
Pulmonary embolism (PE)	Valvular heart disease
Cancer-associated thrombosis (CAT)	Periprocedural parenteral anticoagulation during percutaneous coronary intervention (PCI)
Upper extremity DVT (UEDVT)	Acute coronary syndromes (ACS)
Recurrent VTE	Arterial thrombus, (e.g., myocardial infarction (MI), stroke, mesenteric arterial thrombosis, acute limb ischemia, etc.)
Chronic thromboembolic pulmonary hypertension (CTEPH)	Left ventricular (LV) thrombus
Hepatic vein thrombosis	Secondary prevention in patients with higher thrombotic risk
Splanchnic vein thrombosis	Specific cardiomyopathies, (e.g., peripartum cardiomyopathy with LVEF < 35%, cardiac amyloidosis, etc.)
Cerebral venous thrombosis (CVT)	Ventricular assist device (VAD)/total artificial heart (TAH)
Superficial venous thrombosis of lower limb with increased risk of clot progression to VTE	
Heparin-induced thrombocytopenia (HIT)	
Note: This care guide does not address the use of anticoagulants for VTE primary prophylaxis	

EVALUATION

1. Confirm the indication for anticoagulation is present
2. Identify the presence of any contraindications to anticoagulation AND determine the need for higher level of care (HLOC)
3. Conduct risks/benefits/alternatives assessment for all patients, including bleeding risks (See page 13 for VTE; see page 24 for cardiovascular)
4. Review current medications to identify potential DDIs and concurrent use of antiplatelet medications (e.g., aspirin, P2Y12 inhibitors like clopidogrel, etc.) or NSAIDs (e.g., ibuprofen, naproxen, etc.)
5. Review or order diagnostic studies
   - Initial labs: CBC, CrCl/eGFR, AST, ALT, prothrombin time (PT/INR), partial thromboplastin time (aPTT)
   - Electrocardiogram (EKG), echocardiogram (echo), and other imaging studies as clinically indicated
   - Additional labs for inherited causes of hypercoagulability may be ordered as clinically indicated (See page 20)

TREATMENT

6. Select the anticoagulant that is most appropriate for the patient and determine duration of therapy
   - Warfarin preferred[1,17]
     - Advanced CKD or end-stage renal disease (ESRD), valvular heart disease, patients with poor adherence, antiphospholipid syndrome (APS), LV thrombus, post-bariatric surgery requiring anticoagulation
   - Direct oral anticoagulant (DOAC*) preferred
     - VTE
     - Nonvalvular AF/AFL
   - Low molecular weight heparin (LMWH) preferred: pregnancy, malignancy
   - Perioperative management of anticoagulation

DOCUMENTATION

7. Document the following in the Electronic Health Record System (EHRS):
   - Update **Problem List**
     - Indication for anticoagulation
     - "Long-term (current) use of anticoagulant" (ICD-10 Z79.01) to be marked resolved upon completion of therapy
   - Start date with anticipated stop date, indicate if anticoagulation is needed lifelong
   - Assessment of bleeding risks, as well as risks/benefits/alternatives of anticoagulation
   - Target INR, if on warfarin
   - Next scheduled INR check, if on warfarin
   - Patient Education (see PE1 - PE4)
   - Specialty that is comanaging, if any, (e.g., cardiology, hematology, etc.)
   - Evaluate for lower bunk Chrono

*Direct Factor Xa Inhibitors and Direct Thrombin Inhibitors may also be called NOACs for non-vitamin K antagonist oral anticoagulant or TOACs/TSOACs for target-specific oral anticoagulant. (Throughout this care guide, we will call these agents DOACs)

FOLLOW-UP AND MONITORING

8. Follow-up and monitor with individualized treatment plan. For VTE and cardiovascular indications:
   - First year: 3 months, 6 months, and 12 months, or more frequently as clinically indicated
   - Follow-up at least every 6 months thereafter
   - Continue to weigh the risks/benefits/alternatives of continued anticoagulation at each visit
   - Review medication list for DDIs, as well as use of antiplatelets/NSAIDs 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 frequently if clinically indicated, CBC and CMP every 6 months
     - Measures will utilize TTR to better reflect the patient's ongoing anticoagulation status and assist in determining efficacy of treatment plan
   - DOACs and LMWH: CBC and CMP every 6 months, weight check at each visit

DECISION SUPPORT

Anticoagulation Overview Algorithm

The use of anticoagulation therapy is high-risk and complex. Carefully and systematically consider the decision to start therapy, the choice of specific agent, and the duration of therapy. The evaluation and risk assessment of a patient needs to be frequent, as there is a risk of recurrence of VTE in some cases when patients are not on appropriate anticoagulation. Consider using the following steps at the initial visit and periodically thereafter if the indication for anticoagulation still exists.

1. Confirm an indication for anticoagulation

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2. Identify presence, if any, of contraindications to anticoagulation. Determine need to transfer patient to HLOC or referral to a specialist. If presence of acute life-threatening or limb-threatening condition, transfer patient to HLOC.

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3. Conduct risk/benefit/alternative assessment, as well as need for HLOC.
   - Bleeding risks vs. benefits of anticoagulation
     - VTE: Use American College of Chest Physicians (ACCP) Bleeding Risk Model to determine duration of therapy and need for closer monitoring.
     - AF/AFL: Use HAS-BLED to assess modifiable bleeding risks. (See Appendix A).

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4. Review medication list for DDIs and concurrent use of antiplatelets and NSAIDs. Use DDI Tool on **Lifeline**.

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5. Review or order diagnostic studies.

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6. Select the most appropriate anticoagulant for clinical presentation of patient, determine appropriate dose and duration of therapy (See page 14 for VTE and page 26 for cardiovascular indications).

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7. Document the following in the EHRS:
   - Update **Problem List**
   - Indication and "Long-term (current) use of anticoagulant" (ICD-10 Z79.01) – marked resolved upon therapy completion
   - Start date
   - Duration of therapy with anticipated end date
   - Target INR, if on warfarin
   - Next INR check, if on warfarin
   - Hemoglobin and platelets
   - Creatinine and CrCl/eGFR
   - Assessment of bleeding risks
   - Patient education provided
   - Co-managing specialty, (e.g., cardiology, etc.)
   - Evaluate for lower bunk Chrono

↓

8. Follow-up and monitoring on a regular basis to weigh risks/benefits/alternatives of anticoagulation, review current medication list, modify dosage, 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 39-44)
     - DOACs. (See pages 32-39)
     - LMWH. (See pages 45-49)

Decision Support Cont'd

1. **TREATMENT INDICATION**: Confirm indication for anticoagulation.
   - **Thromboembolic conditions**[2,3,5,7,8,9]

VTE (DVT/PE)	CAT
UEDVT	Recurrent VTE
CTEPH	Hepatic vein thrombosis
Splanchnic vein thrombosis, which includes portal vein thrombosis, mesenteric thrombosis, and splenic vein thrombosis	CVT, associated intracranial hemorrhage is not a contraindication to anticoagulation
Superficial venous thrombosis	HIT

   - **Cardiovascular conditions**[33,34,35]

Nonvalvular AF/AFL	Valvular heart disease, (e.g., moderate-to-severe mitral stenosis (MS) or presence of mechanical heart valve)
Parenteral anticoagulation for PCI	Arterial thrombus, (e.g., MI, stroke, mesenteric arterial, acute limb ischemia, etc.)
Initial management of ACS, (e.g., STEMI or NSTE-ACS)	LV thrombus prophylaxis after MI for high-risk patient (e.g., anteroapical wall motion abnormality and/or LVEF < 30%)
LV thrombus treatment due to acute MI or nonischemic/dilated cardiomyopathy LVEF < 30%	Secondary prevention in high thrombotic risk patients with symptomatic lower extremity peripheral artery disease (PAD)
Secondary prevention in high thrombotic risk patient with coronary artery disease (CAD) or after initial ACS management*	Mechanical circulatory support (MCS) ‡
Specific cardiomyopathies†	

* Low dose rivaroxaban may be considered for patients who are at high risk of cardiovascular events and low risk of bleeding if therapeutic anticoagulation is not required for another indication. Patient preference and shared-decision making should be taken into consideration, especially in the setting of adding low dose rivaroxaban to dual antiplatelet therapy (DAPT).
† e.g., peripartum cardiomyopathy with LVEF < 35%, cardiac amyloidosis, left ventricular noncompaction, etc.
‡ Ventricular assist device (VAD) or total artificial heart (TAH)

2. **CONTRAINDICATIONS AND REASONS TO TRANSFER TO HIGHER LEVEL OF CARE**: Identify presence of any contraindications[2,3,9,10,24] to anticoagulation for all patients and determine the need for HLOC.

Absolute	Relative
Major trauma with bleeding that occurred in at least one critical site (e.g., intracranial, intraspinal, intraocular, pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal)	Intracranial or spinal tumors
	Recent intracranial bleeding (within 4 weeks)
	Active, but not life threatening, bleeding
	Active GI ulceration at high risk of bleeding
Major active, severe, or potentially life-threatening bleeding with hemodynamic instability or decrease in hemoglobin ≥ 2 g/dL that is not reversible with medical or surgical intervention (e.g., active gastrointestinal or retroperitoneal bleeding)	Recurrent bleeding from multiple gastrointestinal telangiectasias
	Recent surgery or invasive procedure that had hemorrhagic complications
Active ischemic stroke within 2-14 days	Recent, planned, or emergent low bleeding risk surgery or invasive procedure
Recent intracranial bleeding or neurosurgery within 2 weeks	
Upcoming planned or emergent high-risk surgery or invasive procedure (e.g., epidural or spinal procedure)	

Decision Support Cont'd

Consider Higher Level of Care Transfer or Specialty Consultation*[13,15,16,30,31,32]
Signs/symptoms of acute heart failure and PE, such as chest pain, palpitations, shortness of breath
Tachycardia, hemodynamic instability, syncope/loss of consciousness
Uncontrolled severe hypertension
Presence of contraindications in the setting of urgent need to anticoagulated, (e.g., VTE, LV thrombus)

Patients with significant comorbid conditions will require specialty consultation prior to starting anticoagulation
• Advanced CKD or ESRD
• Advanced liver disease (Child-Pugh score B and C)
• Platelets < 25,000/mL or platelets < 50,000/mL in patients with cancer
• Bleeding disorder
  ○ Acquire, (e.g., hepatic dysfunction with coagulopathy, antiphospholipid syndrome (APS))
  ○ Inherited, (e.g., hemophilia, von Willebrand disease)
• Advanced heart failure
• History of gastric cancer or major GI bleed
• Presence of intracranial tumor or brain metastases without evidence of active bleeding
• Infective endocarditis (IE)
• History of HIT
• Pregnancy, co-management with high-risk obstetrician required
• Perioperative management of anticoagulation

* Determine need to transfer patient to HLOC or refer to a specialist. The following clinical scenarios are not an exhaustive list of conditions when one considers transferring to HLOC or referring to a specialist.

3. **RISKS/BENEFITS/ALTERNATIVES**: Conduct a risks/benefits/alternatives assessment for all patients, including bleeding risks (See page 13 for VTE; see page 25 for cardiovascular). This will help determine the duration of therapy.

4. **DRUG-DRUG INTERACTIONS**: Review current medications to identify potential DDIs and concurrent use of antiplatelet medications (e.g., aspirin, P2Y12 inhibitors like clopidogrel, etc.) or NSAIDs (e.g., ibuprofen, naproxen, etc.). Recommend use of DDI Tool available on Lifeline.

5. **DIAGNOSTIC STUDIES**: Review or order diagnostic studies (See page 13 for VTE; see page 26 for cardiovascular).
   - Initial labs: CBC, eGFR, AST, ALT, prothrombin time (PT/INR), partial thromboplastin time (aPTT)
     - Consider a Medical Hold for any patient with INR above 5.0.
   - Electrocardiogram (EKG), echocardiogram (echo), and other imaging studies as clinically indicated
   - Additional labs for inherited causes of hypercoagulability may be ordered as clinically indicated (See page 20 for hypercoagulable workup)

6. **DURATION OF TREATMENT**: 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 (See Appendix B for mechanism of action):
     - DOACs: apixaban, rivaroxaban, dabigatran (NF)
     - VKA: warfarin
     - Unfractionated heparin (UFH)
     - LMWH: enoxaparin
     - Fondaparinux (NF)
   - Medication selection varies by indication (See page 14 for VTE; see pages 26-30 for cardiovascular).

Decision Support Cont'd

7. **DOCUMENTATION**: Document in the EHRS
   - Updated **Problem List**
     - Indication for anticoagulation
     - "Long-term (current) use of anticoagulant" *ICD-10 Z79.01* - marked **Resolved** upon therapy completion
   - Start date
   - Duration of therapy with an anticipated end date, indicate if lifelong anticoagulation is indicated
   - Target INR, if on warfarin
   - Next INR check, if on warfarin
   - Hemoglobin and platelets
   - Creatinine and CrCl/eGFR
   - Assessment of bleeding risks
   - Patient education provided
   - Comanaging specialty (e.g., cardiology, hematology, oncology, etc.)
   - Evaluated for lower bunk Chrono

8. **EVALUATION INTERVALS**: Patient should be re-evaluated on a regular basis to address anticoagulation. At each appointment related to anticoagulation management, the provider should assess risk/benefit/alternative of continuing anticoagulation and review these steps.
   - Is there still an indication for anticoagulation?
   - Are there any new contraindications for anticoagulation, or are there any complications requiring HLOC or specialty referral? Review any changes in general health, functional status, recent falls, activity level, participation in contact sports, change in diet, and substance use including alcohol.
   - Does a new medical condition or bleeding risk cause a shift in favor of discontinuation of anticoagulation?
   - Update medication list and inquire about any new medications, including over-the-counter medications. Pay special attention to concurrent use of antiplatelets and NSAIDs. Confirm medication adherence.
   - Review any new laboratory results.
   - Confirm the current anticoagulant is still the most appropriate agent and that the dose is appropriate.
   - Update the EHRS and re-evaluate need for lower bunk Chrono.

Summary of Anticoagulants by Indication

Indication	Preferred Agent	DOAC	Warfarin	LMWH
VTE[3,4,5,6]	Depends on comorbidities	Preferred	Yes	Short-term/bridge
Breakthrough VTE on therapeutic anticoagulation[3,4,5,6]	LMWH	Yes	Yes	Preferred
Active malignancy with VTE[5,6,9,10]	DOACs	Preferred	Yes	Yes
UEDVT[26,27]	LMWH	Yes	Yes	Preferred
CVT with or without intracranial hemorrhage[2,4]	Depends on acuity and comorbidities	Yes	Yes	Short-term/bridge
Mesenteric venous thrombosis[2,4]	Depends on acuity and comorbidities	Yes	Yes	Short-term/bridge
Superficial venous thrombosis[2,4,7,8]	Fondaparinux or low dose rivaroxaban	Yes, if parenteral anticoagulation with fondaparinux refused	No	No
HIT[32]	Depends on comorbidities or fondaparinux	Yes	No	No

Decision Support Cont'd

Indication	Preferred Agent	DOAC	Warfarin	LMWH
APL with history of clot[28,29,30,31]	Warfarin	No	Preferred	Short-term/bridge
Nonvalvular AF/AFL[33,34,35,36]	DOAC	Preferred	Yes	Short-term/bridge
Valvular heart disease[41,42]	Warfarin	No	Yes	Short-term/bridge
LV thrombus after MI[43]	Depends on comorbidities	Yes	Preferred	Short-term/bridge
LV thrombus with DCM[43]	Depends on comorbidities	Yes	Preferred	Short-term/bridge
LV thrombus prophylaxis in high-risk patient after MI[43,45]	Shared decision making	Yes	Preferred	Short-term/bridge
Secondary prevention for CAD or ACS[45,46,47]	Rivaroxaban 2.5mg BID with aspirin	Preferred	No	No
Secondary prevention for symptomatic PAD[48,49,50]	Rivaroxaban 2.5mg BID with aspirin	Preferred	No	No
Specific cardiomyopathies[43]	Depends on comorbidities	Yes	Yes	Yes
MCS with VAD or TAH[43]	Warfarin	No	Preferred	No
Poor adherence	Warfarin	No	Preferred	No
Pregnancy*	Enoxaparin	No	Mechanical heart valve	Preferred
Cost	--------	$$$$	$	$$$$
Reversal agent	--------	Yes, but limited to hospital/ED setting	Yes	Yes

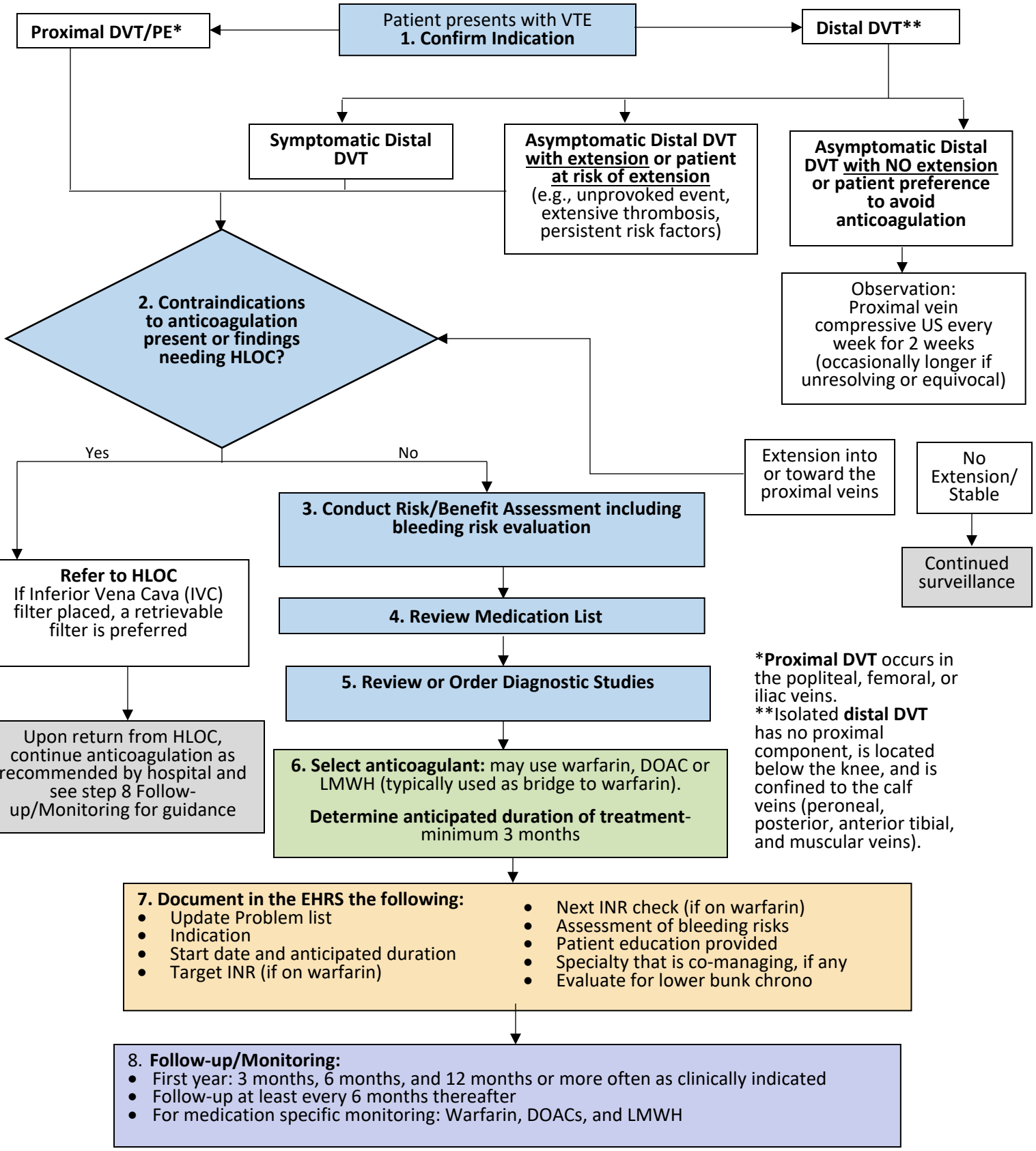
*If the patient has a mechanical heart valve, use shared decision-making to choose an anticoagulation strategy for pregnancy. Discuss with patient the risks and benefits of anticoagulation to both patient and fetus.[41]

VENOUS THROMBOEMBOLISM (VTE) GOALS

The most common presentation 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 post thrombotic syndrome) weighed against the risk of anticoagulation. VTE is a chronic and lifelong medical issue that is managed with continued regular follow-up, even after completion of anticoagulation therapy.

VENOUS THROMBOEMBOLISM (VTE) MANAGEMENT ALGORITHM[1]



*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).

VENOUS THROMBOEMBOLISM (VTE) EVALUATION[2,3,4,5,6,7,8,9,10]

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

- Patient is new to provider but was previously diagnosed with VTE
- Patient presents with signs or symptoms concerning for a new VTE
- Patient returned from HLOC with a recently diagnosed VTE

For any patient above, the provider evaluation should consider:

History: Obtain historical information to determine the pretest probability of VTE by using a validated scoring model, such as Wells Criteria. Next, determine if the patient needs to be transferred to HLOC by noting the presence of any of the following potentially life-threatening or limb-threatening symptoms:

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

Also identify which diagnostic tests to order, identify the need for co-management with specialty consultation, and determine the duration of therapy.

Finally, determine the presence of any contraindications to anticoagulation.

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
- Prolonged travel
- Recent acute illness or leg injury associated with limited mobility
- Pregnancy

Determine presence of contraindications.

Physical exam: A thorough physical exam includes vital signs, oxygenation, level of consciousness, bruises, petechiae, presence of swelling and/or erythema of an extremity, presence of venous catheters such as peripherally inserted central catheters (PICC), central venous catheters, and Mediports/Port-A-Cath.

Exam findings concerning for pulmonary embolism include the following:

- Tachycardia and/or tachypnea, possibly with O2 sat < 94%
- Decreased breath sounds on lung exam
- Presence of right heart strain such as jugular venous distention
- Systolic BP < 90 mmHg

1. TREATMENT INDICATION[2,3,4,5,6]

Ensure that an indication for anticoagulation is present by:

- Confirming a previously made diagnosis
- If the patient presents with a suspected new VTE, use Wells score to assist in the diagnostic work-up
  - DVT: https://www.mdcalc.com/wells-criteria-dvt
  - PE: https://www.mdcalc.com/wells-criteria-pulmonary-embolism
- Patients will typically need to be sent out for confirmatory testing

VTE Evaluation Cont'd

Provoked VTE	**Pay attention to the presence of provoking factors and acquired hypercoagulable conditions. Determine if the provoking factor is temporary or permanent.**
	Recent and prolonged transport from another institution or outside care facility
	Immobility, (e.g., bedbound or wheelchair-bound)
	Recent hospitalization
	Trauma or injury to an extremity causing immobilization
	Comorbid conditions, such as inflammatory bowel disease, myeloproliferative disorder, nephrotic syndrome, malignancy
	Presence of venous catheter
	Hormone therapy, such as birth control
	Pregnancy
Unprovoked VTE	**Lack of clear provoking factor, consider the possible presence of an inherited hypercoagulable condition**

2. CONTRAINDICATIONS TO ANTICOAGULATION AND REASONS TO TRANSFER TO HLOC[11,12,13,14,15,16,17,18]

Patients in whom anticoagulation is absolutely contraindicated or in whom the risk of bleeding is estimated by the clinician to outweigh the risk of VTE, should be transferred to HLOC to have an IVC filter placed promptly. Patients with relative contraindications or patients with significant comorbid conditions should be monitored closely and comanaged with a specialist.

For patients with newly diagnosed VTE who are not yet anticoagulated, determine the need to transfer the patient to HLOC or refer to a specialist, for the above relative contraindications. Also consider transfer to HLOC if patient complains of chest pain, palpitations, shortness of breath, or other signs/symptoms of acute heart failure. If there is a clinical suspicion of new onset PE, transfer to HLOC.

Absolute Contraindications	**Relative Contraindications** (not limited to the following)
Acute major trauma	Active, but not life-threatening, bleeding
Major active, severe, or potentially life-threatening bleeding that is not reversible with medical or surgical intervention	Intracranial or spinal tumors. The presence of an intracranial tumor or brain metastases without evidence of active intracranial bleeding is not an absolute contraindication to anticoagulation.
Recent intracranial bleeding or neurosurgery within the past 2 weeks	Recent intracranial bleeding within the past 4 weeks. Intracranial hemorrhage in the setting of CVT is not a contraindication to anticoagulation.
Upcoming plans or emergent high-risk surgery or invasive procedure	Active GI ulceration at high risk of bleeding or recurrent bleeding from multiple gastrointestinal telangiectasias
Acute ischemic stroke within 2-14 days	Recent surgery or procedure that had hemorrhagic complications
	Perioperative management of anticoagulation of recent/plans for/emergent low bleeding risk surgery/procedure
	Uncontrolled severe hypertension
	Advanced CKD or ESRD
	Advanced heart failure
	Advanced liver disease (Child-Pugh score B and C)
	History of gastric cancer or major GI bleed
	Platelets < 25,000/mL or platelets < 50,000/mL in patients with cancer
	Bleeding disorder, such as hepatic dysfunction with coagulopathy, hemophilia or von Willebrand disease (vWD)
	Infective endocarditis (IE)
	History of HIT
	Pregnancy

VTE Evaluation Cont'd

3. RISKS/BENEFITS/ALTERNATIVES[2,3,4]

VTE patients who do not have absolute 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. Patients with high bleeding risks are more likely to have anticoagulation therapy stopped after 3 months without offering extended-phase therapy, compared to patients with lower bleeding risks. Additionally, patients with high bleeding risks may also require closer monitoring while on anticoagulation. Extended-phase anticoagulation therapy is continued anticoagulant use at full or reduced dose for the goal of secondary prevention of VTE beyond the 3 months of full anticoagulation therapy.

Bleeding Risk Factors with Anticoagulant Therapy
Age > 65 y
Age > 75 y
Previous bleeding event
Cancer
Metastatic cancer
Renal failure
Liver failure
Thrombocytopenia
Previous stroke
Diabetes
Anemia
Antiplatelet use
NSAID use
Poor anticoagulant control
Comorbidity and reduced functional capacity
Recent surgery
Frequent falls
Alcohol use disorder

Categorization of Risk of Bleeding			
	Estimated Absolute Risk of Major Bleeding		
	Low 0 Risk Factors	Moderate 1 Risk Factors	High ≥ 2 Risk Factors
Anticoagulation 0-3 months			
Baseline risk (%)	0.6	1.2	4.8
Increased risk (%)	1.0	2.0	8.0
Total risk (%)	1.6	3.2	12.8
Anticoagulation after first 3 months			
Baseline risk (%/y)	0.3	0.6	≥ 2.5
Increased risk (%/y)	0.5	1.0	≥ 4.0
Total risk (%/y)	0.8	1.6	≥ 6.5

4. DRUG-DRUG INTERACTIONS

Review current medication list and look for DDIs. In particular, look for concurrent antiplatelet and/or NSAID use. Recommend use of DDI Tool available on Lifeline.

Some patients with coronary artery disease (CAD) have indications for antiplatelet agents (aspirin or P2Y12 inhibitors like clopidogrel [Plavix®]/prasugrel [Effient®]/ticagrelor [Brilinta®] or both depending on the presence of coronary stent) as well as anticoagulation therapy.[41,42] The risk of thrombosis or bleeding in these patients can be very high, so account for this when initiating anticoagulation therapy and in determining the duration of concurrent therapy. Specialty consultation is advised, as needed.

5. DIAGNOSTIC STUDIES

- Initial: CBC, CMP, PT/INR, aPTT, if not done within 30 days
  - Consider medical hold for any patient with INR above 5.0.
- EKG, echo, further imaging as clinically indicated
- Additional labs for hypercoagulability as clinically indicated (See page 20)

VTE Evaluation Cont'd

6. DURATION OF TREATMENT

Select the most appropriate anticoagulant based on clinical presentation and patient factors. DOACs, warfarin, and LMWH are used for anticoagulation in patients with VTE.

In patients with DVT of the leg and PE without cancer, DOACs (apixaban, rivaroxaban, edoxaban, or dabigatran) are preferred over warfarin in the treatment phase (first 3 months). Initial parenteral anticoagulation is given before edoxaban, dabigatran, and warfarin but is not necessary for initiating therapy on apixaban or rivaroxaban.[2,3,4,5,6,7,8]

In patients with acute VTE in the setting of cancer (cancer-associated thrombosis, CAT), Factor Xa inhibitor DOACs such as apixaban, rivaroxaban, and edoxaban are preferred over LMWH for initiation and treatment phase of therapy. Rivaroxaban and edoxaban appear to be associated with a higher risk of major GI bleeding than LMWH in patients with CAT and a luminal GI malignancy, while apixaban does not. Therefore, apixaban or LMWH may be the preferred option in patients with luminal GI malignancy.[5,6,9,10,11]

In patients with confirmed APS treated with anticoagulation, warfarin is preferred with target INR 2.5 (range 2.0-3.0) for lifelong therapy.[2,3,5,6]

When making the choice for a specific anticoagulant, consider the following factors:

- Indication
- Comorbidities
- Patient adherence: Warfarin is preferred if adherence is an issue because INR can be monitored. Additionally, warfarin has a longer half-life in the event of patient missing occasional doses.
- DDIs are less frequent with DOACs.
- For patients arriving on a nonformulary medication, consider switching to a formulary agent, if there is no clinical contraindication.

The minimum length of anticoagulation for VTE is 3 months. If the optimal length of anticoagulation is not clearly defined, then the duration of therapy needs to be evaluated on an individual, case-by-case, basis. If the patient has higher bleeding risks, then the patient should be kept on the shortest duration of anticoagulation therapy.

VTE Recurrence Risk Stratification[7]		
High Risk	Moderate Risk	Low Risk
VTE within past 3 months	VTE within past 3-12 months	VTE > 12 months ago with no other risk factors
Deficiency of protein C, protein S, or antithrombin	Heterozygous factor V Leiden	
Antiphospholipid syndrome	Prothrombin 20210 mutation	
Multiple thrombophilic abnormalities	Recurrent VTE	
	Active cancer	

VTE Recurrence Risk Group[2,4]	**Bleeding Risk Group ***		
	Low	Moderate	High
First VTE provoked by surgery	Discontinue (strong)	Discontinue (strong)	Discontinue (strong)
First VTE provoked by non-surgical factor assuming resolution of provoking factor	Discontinue (weak)	Discontinue (weak)	Discontinue (strong)
First unprovoked proximal VTE	Continue (weak) †	Continue (weak) †	Discontinue (strong)
Second unprovoked VTE	Continue (strong) †	Continue (weak) †	Discontinue (weak)

* 2012 ACCP bleeding risk model assumes risk of major bleeding after the first 3 months of anticoagulation as 0.8, 1.6, and ≥ 6.5% for the low, intermediate, and high-risk groups, respectively

† Consider indefinite anticoagulation after 12 months with risk/benefits/alternative assessment

VTE Evaluation Cont'd

The patient is more likely to continue extended-phase therapy if the following factors are present:

- Continuation of provoking factors (e.g., chronic immobility, such as bedbound status or wheelchair-bound status)
- Presence of risk factors for recurrent VTE such as:[18]
  - Malignancy
  - Inherited thrombophilias
  - APS
  - Elevated D-dimer a month after stopping anticoagulation
  - Chronic infections or chronic inflammatory conditions[19]
  - Inflammatory bowel disease[19]
  - Obesity[18,19,20]

Consider stopping anticoagulation if:

- Presence of or development of contraindications
- Patient has limited life expectancy due to other disease factors and are less likely to benefit from extended-phase anticoagulation
- VTE scenarios without clear consensus for duration of anticoagulation, then specialty consultation is advised

Factors that may influence which anticoagulant is chosen for initial and long-term treatment of VTE.

Factor	Choice of anticoagulant	Remarks [40, 13, 12, 52, 53, 17, 19, 20, 21, 22, 16, 4, 29, 14, 15, 11, 37, 39, 38, 10, 8, 18]
CKD with CrCl < 30 mL/min	Dose adjusted DOAC Warfarin	Some DOACs and LMWH are contraindicated with severe renal impairment. If patient has mild to moderate renal impairment and DOAC is used, dose adjustment is required. Dose adjusted apixaban 2.5 mg twice daily can be used for severe renal disease.
Poor adherence	Warfarin	INR monitoring can help confirm adherence. However, some patients may be more adherent with DOAC therapy because there is no need for monthly INR checks.[51,52] A single missed dose of DOAC has greater potential to result in inadequate anticoagulation because DOACs have a shorter half-life than warfarin.
Once daily oral therapy preferred	Rivaroxaban Edoxaban Warfarin	No remarks.
Need for rapid anticoagulation with oral agent without using initial parenteral therapy	Apixaban Rivaroxaban	Warfarin, edoxaban, and dabigatran require initial parenteral therapy with UFH or LMWH when immediate anticoagulation is needed.
Reversal agent needed	Warfarin	Reversal agents for DOACs and LMWH are not readily available at CCHCS.
Weight ≤ 60 kg	Dose adjusted apixaban Warfarin	If patient meets 2 of the following 3 criteria, then apixaban dose should be reduced to 2.5 mg twice daily: serum creatinine < 1.5 mg/dL, age ≥ 80 years of age, body weight ≤ 60 kg.
Weight ≥ 120 kg or BMI ≥ 40 kg/m^2	Apixaban Rivaroxaban Warfarin	Avoid edoxaban and dabigatran.[18,20,21,22]
History of bariatric surgery	Warfarin	DOAC absorption may be reduced after bariatric surgery.[17,23]

VTE Evaluation Cont'd

Antiphospholipid syndrome	Warfarin	DOACs should be avoided in patients with antiphospholipid syndrome, especially if positive for lupus anticoagulant, anticardiolipin, and anti-β-glycoprotein-I antibodies (i.e., "triple-positive" antiphospholipid syndrome). DOACs should also be avoided in patients with antiphospholipid syndrome who had arterial thrombosis.[5]
Inherited thrombophilia	Warfarin	Studies have suggested that DOACs may be an appropriate treatment option for some thrombophilia's, but this has not been recommended in national guidelines because of limited data in specific subgroups.[29]
Advanced liver disease with coagulopathy	LMWH	DOACs are contraindicated if the INR is raised because of liver disease. Warfarin is difficult to control, and INR may not accurately reflect the antithrombotic effects of warfarin therapy.[15,16]
Increased bleeding risk, especially if history of intracranial hemorrhage or significant non-GI bleed	DOAC	A systematic review and meta-analysis of 12 randomized control trials, including over 100,000 patients with either nonvalvular AF/AFL or VTE, showed that DOACs are associated with less major bleeding, fatal bleeding, intracranial bleeding, clinically relevant and on major bleeding, and total bleeding compared to warfarin. [12]
Dyspepsia or history of GI bleeding	Apixaban Warfarin	Dabigatran increases dyspepsia. Dabigatran, rivaroxaban, and edoxaban may be associated with more GI bleeding than warfarin. [37,38,39] A systematic review and meta-analysis of 28 randomized control trials, including over 100,000 patients, compared major GI bleeding risk among DOACs. Apixaban had a lower rate of major GI bleed compared to rivaroxaban and dabigatran.[11]
Cancer	DOACs Factor Xa inhibitor LMWH	Suggest DOAC (apixaban and rivaroxaban) or LMWH for initial treatment and short-term treatment of VTE. Edoxaban can also be used for short-term treatment of VTE. [9] Factor Xa inhibitor DOACs are recommended over LMWH. Edoxaban and rivaroxaban appear to be associated with higher risk of major GI bleeding. Apixaban or LMWH may be the preferred option in patients with luminal GI malignancy.[5,6]
Pregnancy	LMWH	Potential for other agents to cross the placenta. DOACs and warfarin are contraindicated.
Breastfeeding	Warfarin LMWH	DOACs are contraindicated.

7. DOCUMENTATION

Document the following in the EHRS:

- Updated **Problem List**
  - Indication
  - "Long-term (current) use of anticoagulant" (ICD-10 Z79.01) to be marked resolved upon completion of therapy
- Start date
- Duration of therapy with an anticipated end date, include if lifelong anticoagulation is indicated
- Target INR, if on warfarin

VTE Evaluation Cont'd

- Next INR check, if on warfarin
- Hemoglobin and platelets
- Creatinine and CrCl/eGFR
- Assessment of bleeding risks
- Patient education provided
- Comanaging specialty, (e.g., cardiology, hematology, oncology, etc.)
- Evaluated for lower bunk Chrono

8. EVALUATION INTERVALS

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 anticoagulation, do they still need continued anticoagulation?)."
  - Ensure no new contraindications to anticoagulation, complication requiring HLOC, or specialty referral. Review any changes in general health, functional status, recent falls, activity level and engagement in contact sports, change in diet, and substance use including alcohol.
  - Reassess risks/benefits/alternatives of anticoagulation (e.g., does a new medical condition or bleeding risk cause the risks/benefits/alternatives assessment shift in favor of discontinuation of anticoagulation?).
  - Review current medication list, especially for any new medications, including over-the-counter medications. Pay special attention to addition or discontinuation of antiplatelet agents or NSAIDs. Confirm medication adherence.
  - Review any new laboratory results.
  - Confirm current anticoagulant is still most appropriate agent and that the continued dose is still appropriate.
  - Confirm documentation, including **Problem List**, is up to date in the EHRS.
  - Schedule appropriate follow-up and monitoring.
  - If stopping anticoagulation, re-evaluate need for lower bunk Chrono.

SPECIFIC VTE CLINCIAL SCENARIOS

Cancer-associated Thrombosis[5,6,9,10]

- In patients with acute VTE in the setting of cancer-associated thrombosis (CAT), start a Factor Xa inhibitor (apixaban, rivaroxaban, or edoxaban) over LMWH.
  - Edoxaban and rivaroxaban appear to be associated with a higher risk of GI major bleeding than LMWH in patients with CAT and a luminal gastrointestinal malignancy, while apixaban does not.
  - Apixaban or LMWH may be the preferred option in patients with luminal GI cancer. However, LMWH has the potential advantages of bypassing the GI system in patients with nausea or mucositis and may be more easily dose-adjusted in patients with thrombocytopenia due to cancer therapy.[5,6,9,10,11]
- For patients with active cancer and VTEs, long-term anticoagulation for secondary prophylaxis indefinitely rather than short-term treatment along is recommended.[9,10]
- Indefinite anticoagulation can be discontinued when the patient is no longer at high risk of recurrent VTE or if the patient is entering the last weeks of life.[9,10]
- For patients with primary or metastatic intracranial malignancies and established VTE, anticoagulation as described for other patients with cancer should be offered, although uncertainties remain about choice of agents and selection of patients most likely to benefit.
  - Limited safety data exists for DOAC use in patients requiring cancer surgery and in those with primary intracranial malignancies or untreated brain metastases.

Specific VTE Clinical Scenarios Cont'd

- Observational data suggest that patients with intracranial metastases have a lower risk of intracranial bleeding on pharmacologic anticoagulation than patients with primary intracranial malignancy.
- Although patients with intracranial tumors are at increased risk for thrombotic complications and intracranial hemorrhage, the presence of a stable or active primary intracranial malignancy or brain metastases is NOT an absolute contraindication to anticoagulation.
- Preliminary data from a retrospective cohort of patients with metastatic brain disease and venous thrombosis suggest that DOACs may be associated with a lower risk of intracranial hemorrhage than LMWH in this population.[9,10]

Contraindications to Anticoagulation in Patients with Cancer[10]
Absolute Contraindications
Non-DOACs and DOACs
Active major, serious, or potentially life-threatening bleeding not reversible with medical or surgical intervention, including but not limited to any active bleeding in a critical site (e.g., intracranial, pericardial, retroperitoneal, intraocular, intra-articular, intraspinal)
Severe, uncontrolled malignant hypertension
Severe, uncompensated coagulopathy (e.g., liver failure)
Severe platelet dysfunction or inherited bleeding disorder
Persistent, severe thrombocytopenia < 20,000 mL
High-risk invasive procedure and critical site, including but not limited to lumbar puncture, spinal anesthesia, epidural catheter placement
DOAC specific
Concurrent use of potent P-glycoprotein or CYP 3A4 inhibitors or inducers
Relative Contraindications
Non-DOACs and DOACs
Intracranial or spinal lesion at high risk for bleeding
Active GI ulceration at high risk of bleeding
Active but non-life-threatening bleeding (e.g., trace hematuria)
Intracranial or CNS bleeding within the past 4 weeks
Recent high-risk surgery or bleeding events
Persistent thrombocytopenia < 50,000 mL
Patients for whom anticoagulation is of uncertain benefit
Patient receiving end-of-life or hospice care
Very limited life expectancy with no palliative or symptom reduction benefit
Asymptomatic thrombosis with concomitant high risk of serious bleeding
Patient characteristics and values
Preference or refusal
Nonadherence to dosing schedule, follow-up, or monitoring

Upper Extremity DVT (Primary or Catheter-induced)[1,2,8, 25, 26]

Upper extremity DVTs (UEDVT) can be primary or secondary. Primary UEDVT are unprovoked with or without thrombophilia, effort-related (dominant arm more often affected), or thoracic outlet syndrome. Secondary UEDVT, which account for ~75% of cases, are provoked by central venous catheters (CVC), pacemakers, or cancer. In general, treatment is similar to patients with proximal lower extremity DVT.

- Although evidence for DOAC use in the setting of UEDVT is scarce, they are more frequently prescribed.
- Initial treatment for acute UEDVT that involves the axillary and more proximal veins should be treated with LMWH or fondaparinux over UFH. If UEDVT is associated with a CVC, catheter should not be removed if it is functioning and there is an ongoing need for the catheter.
- Anticoagulation should be continued for at least 3 months with either LMWH, warfarin, or DOACs. For UEDVT associated with CVC that is not removed, continue anticoagulation as long as the CVC remains.[2,9,26,27] If CVC needs to be removed, specialty consultation is advised.
- LMWH is the preferred anticoagulant for cancer with UEDVT with therapy continuing beyond 3 months.

Specific VTE Clinical Scenarios Cont'd

- Uncertainty exists about the need to prescribe anticoagulation to patients with thrombosis confined to the brachial vein. Anticoagulation can be considered if isolated brachial vein thrombosis is symptomatic, associated with a CVC that will remain in place, or associated with cancer in the absence of CVC. Specialty consultation is advised.

Progressive VTE on Appropriate Anticoagulation[2,3]

- Progressive VTE should prompt the following assessments:
  - Reevaluation of whether there truly is progressive VTE
  - Evaluation of patient adherence to anticoagulation
  - Consideration of an underlying malignancy or thrombophilia
- For progressive VTE on therapeutic dose of non-LMWH anticoagulant, recommend switching therapy to LMWH for at least 1 month.
- For progressive VTE on therapeutic dose of LMWH, recommend increasing LMWH dose by about one-quarter or one-third.
- Specialty consultation is advised.

Recurrent VTE After Stopping Anticoagulation[4,5,6]

- Recurrent VTE should prompt the following assessments:
  - Reevaluation of whether there truly is a recurrent VTE
  - Evaluation of transient risk factors that may have provoked the recurrent VTE
  - Consideration of an underlying malignancy or thrombophilia if the recurrent VTE is unprovoked
- In the event of a recurrent VTE in a patient who is not on secondary prevention, restart therapeutic anticoagulation, then offer extended-phase anticoagulation in the setting of unprovoked VTE, recurrent VTE with chronic risk factors, or recurrent VTE with transient risk factors that have not yet resolved.
- After 6 months of full-dose anticoagulation treatment of recurrent VTE, extended-phase anticoagulation should be given as reduced-dose apixaban or rivaroxaban, if there are no contraindications to using these DOACs (considering age, BMI, renal function, adherence, cost, etc.) and if there is no indication for full-dose anticoagulation for another indication.
  - Apixaban 2.5 mg BID
  - Rivaroxaban 10mg daily
  - Other DOACs or warfarin are also acceptable for VTE secondary prevention (extended-phase therapy)
- In patients using extended-phase anticoagulation, reduced-dose DOAC is preferred over aspirin or no therapy.
  - Rivaroxaban is the only DOAC to be directly compared to aspirin for secondary prevention of VTE.
  - Aspirin is much less effective at preventing recurrent VTE than anticoagulants and confers a similar risk of bleeding, so aspirin is not a reasonable alternative to anticoagulation.
  - However, if the patient decides to stop anticoagulation after shared decision-making, aspirin may be suggested to prevent recurrent VTE.
- Specialty consultation is advised.

Chronic Thromboembolic Pulmonary Hypertension[2,3,4]

Prospective studies suggest that chronic thromboembolic pulmonary hypertension (CTEPH) occurs in ~3% of patients who are treated for PE. About one third of patients have a history of VTE, whereas two thirds have had single or recurrent episodes of PE that were not diagnosed and may have been asymptomatic.

Patients with CTEPH are likely to have high risk of recurrent VTE because they have had previous VTE and have cardiopulmonary impairment. Recurrent VTE may be fatal more often in patients with severe cardiopulmonary impairment. Extended-phase anticoagulation is recommended. Specialty consultation by an experienced pulmonary hypertension team is advised.

Hepatic Vein Thrombosis[2,4]

Hepatic vein thrombosis, particularly Budd-Chiari syndrome with occlusion of the main hepatic vein, can result in impairment of liver function and associated coagulopathy.

- In patients with symptomatic hepatic vein thrombosis, anticoagulation is recommended.
  - Coagulopathy due to liver dysfunction caused by hepatic vein thrombosis is not a contraindication to anticoagulation because anticoagulant therapy may improve hepatic function.

Specific VTE Clinical Scenarios Cont'd

- The presence of reversible provoking risk factors for hepatic vein thrombosis, such as oral contraceptive therapy, supports a time-limited course of anticoagulation.
- In the absence of reversible risk factors, extended-phase anticoagulation may be considered.

- In patients with incidentally detected hepatic vein thrombosis, surveillance without anticoagulation is recommended.

Splanchnic Vein Thrombosis[2,3,4]

Thrombosis in the portal venous system, which includes the superior mesenteric, inferior mesenteric, splenic, and portal veins, is collectively termed splanchnic vein thrombosis, which may result in bowel or splenic infarction in the setting of sudden venous occlusion due to thrombus or portal hypertension. Consider testing for Janus kinase 2 mutations for myeloproliferative syndromes or solid-organ malignancy, such as pancreatic cancer or hepatocellular carcinoma, as clinically indicated.

- In patients with symptomatic splanchnic vein thrombosis, anticoagulation is recommended.
  - Esophageal varices secondary to acute portal vein thrombosis are not necessarily a contraindication to anticoagulation because treatment may improve portal hypertension, but screening of esophageal varices should be done when splanchnic vein thrombosis is diagnosed.
  - The presence of a reversible provoking factor for splanchnic vein thrombosis, such as intra-abdominal sepsis or recent intra-abdominal surgery, supports stopping anticoagulation after 3 months.
  - In the absence of risk factors and a low risk of bleeding, extended-phase anticoagulation may be considered.
  - Specialty consultation is advised to help differentiate between acute and chronic splanchnic vein thrombosis and to determine the duration of therapy.
- In patients with incidentally detected splanchnic vein thrombosis, surveillance without anticoagulation is recommended.
  - Acute and chronic splanchnic vein thrombosis may be symptomatic, but many episodes are detected incidentally in imaging studies performed for other indications.
  - Chronic splanchnic vein thrombosis, even if asymptomatic, frequently presents with esophageal and/or gastric varices, so screening of varices should be done when splanchnic vein thrombosis is diagnosed.
  - Specialty consultation is advised to help treat complications of portal hypertension and portal cholangiopathy.

Cerebral Venous Thrombosis[5,6]

Cerebral vein thrombosis (CVT)/dural sinus thrombosis is uncommon and accounts for less than 0.5% of all strokes. This can make diagnosis challenging. Some risk factors for CVT include head injury or mechanical precipitants, infection, hormone therapy, pregnancy, malignancy, and thrombophilia.

- In patients with CVT, treat with anticoagulation for at least 3 months.
- Although anticoagulation is suggested even in the presence of intracranial hemorrhage and/or venous infarction, patients with CVT causing venous infarcts and large parenchymal hematomas may be at unacceptably high risk of hemorrhage extension and the benefits of anticoagulation may not outweigh the potential for harm in these cases.
- Patients who have clinically stabilized with either heparin or LMWH as initial therapy may be switched to oral anticoagulation.
- Extended-phase anticoagulation may be considered in the absence of hormonal or other provocation or in the presence of persisting risk factors for recurrent VTE.
- Immediate transfer to HLOC and specialty consultation is required, especially if CVT is complicated by intracranial hemorrhage and/or venous infarction.

Superficial Venous Thrombosis[2,3,5,6]

Superficial venous thrombosis has been less well studied than DVT but is estimated to occur more often. It usually affects the lower limbs, often involves a varicose vein, and may be unprovoked. Note that the "superficial femoral vein" (SFV) is a deep vein, not a superficial one, and is now termed the femoral vein (FV) to avoid confusion with superficial veins.

- In patients with superficial vein thrombosis of the lower limb at increased risk of clot progression to VTE, consider anticoagulation for 45 days.
  - Fondaparinux 2.5 mg daily is recommended over other anticoagulant therapy.

Specific VTE Clinical Scenarios Cont'd

  - Patients who refuse or are unable to use parenteral anticoagulation may use rivaroxaban 10 mg daily.
- Factors that favor anticoagulant therapy in patients with superficial vein thrombosis include:
  - Extensive superficial vein thrombosis
  - Involvement above the knee, particularly if close to the saphenofemoral junction
  - Severe symptoms
  - Involvement of the greater saphenous vein
  - History of VTE or superficial vein thrombosis
  - Active cancer
  - Recent surgery
- Anticoagulation is generally not used to treat superficial vein thrombosis associated with IV infusion (i.e., infusion thrombophlebitis).

Antiphospholipid Syndrome[4, 5,6]

Antiphospholipid syndrome (APS) is an acquired thrombophilia that is defined by vascular thromboses and/or pregnancy loss with persistently positive antiphospholipid antibodies (aPL). It can occur as a primary condition or in the presence of an autoimmune disease such as systemic lupus erythematosus (SLE).

- In patients with confirmed APS treated with anticoagulation, warfarin is preferred and should be dose adjusted to INR 2.5.
- DOACs should be avoided in patients with antiphospholipid syndrome, especially if positive for lupus anticoagulant, anticardiolipin, and anti-β-glycoprotein-I antibodies (i.e., "triple-positive" antiphospholipid syndrome). DOACs should also be avoided in patients with antiphospholipid syndrome who had arterial thrombosis.
- Periprocedural bridging during warfarin interruption in patients with APS is recommended.
- Among patients who experience new or progressive thrombosis while receiving standard intensity VKA, it is not recommended to transition to a DOAC. For these patients' other treatment options may include increasing the target INR range, standard treatment dose low-molecular-weight heparin, transitioning to fondaparinux, or the addition of antiplatelet therapy.

Inherited Thrombophilias[1,2, 28, 30, 31]

- Patients with inherited thrombophilias are likely to present with an unprovoked or recurrent VTE. Depending on the ongoing risks/benefits/alternatives evaluation, the duration of anticoagulation will be lifelong. Specialty consultation is advised, as needed.
- In persons with asymptomatic thrombophilia (i.e., without a previous history of VTE), do not use long-term daily anticoagulation for thromboprophylaxis to prevent VTE.
- Negative thrombophilia testing does not specifically indicate low VTE risk since there can be other persistent risk factors that increase VTE risk such as malignancy or chronic immobility.

When to Test for Inherited Thrombophilias[28, 30]

- Routine evaluation for hypercoagulable disorders in patients with a diagnosis of VTE is not recommended.
- Patients being treated for VTE, who have 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.
- Patients without a family history of VTE who have an unprovoked or recurrent VTE:
  - Young patients (< 45 years old) – test for inherited thrombophilias and antiphospholipid syndrome (APS)
  - Recurrent, unexplained thromboses while on appropriate antithrombotic therapy – test for inherited thrombophilias and APS
  - Multiple venous sites or unusual vascular beds (splanchnic and cerebral veins) without provoking risk factors – test for inherited thrombophilias and APS
  - History of warfarin-induced skin necrosis – test for Protein C deficiency
- Do not offer thrombophilia testing to patients who are already treated with lifelong anticoagulation.
- Do not offer thrombophilia testing at the time of acute VTE event because acute phase reactants can affect the results. In general, thrombophilia testing should be delayed for at least 6 weeks after an acute VTE.

Specific VTE Clinical Scenarios Cont'd

- When assessing ongoing anticoagulation or assuming management of a patient with a known thrombophilia, ensure that confirmatory testing was appropriately performed and interpreted (i.e., performed off anticoagulation, not at the time of acute VTE event, no interfering medical conditions such as coagulopathy of liver disease or DIC).

Labs to Order [31]	Comments
Factor V Leiden gene mutation	Factor V Leiden is the most common clotting factor mutation in the US, most frequent in white patients
Prothrombin mutation	Prothrombin mutation is the second most common after Factor V Leiden
Antithrombin level	Antithrombin function and quantity are measured to determine deficiency, so the test should not be performed in the presence of thrombosis or during treatment of thrombosis
Protein C and Protein S levels	Protein C and Protein S should not be measured while the patient is on warfarin or within 10 days of a thrombotic event

Temporary Inferior Vena Cava Filter Placement[2,3, 23, 24]

Inferior vena cava (IVC) filter placement is not a treatment for DVT and does not eliminate the need for anticoagulation therapy. An IVC filter may reasonably reduce the risk of PE until anticoagulation can be started.

- The majority of the indications for temporary IVC filter placement are for patients with an absolute contraindication to anticoagulation.
- The presence of an IVC filter is itself thrombogenic and is associated with increased risk of proximal extension of DVT. Therefore, arrangement for IVC filter removal should be made when the contraindication to anticoagulation is anticipated to resolve.
- In patients with acute VTE who are already treated with anticoagulation, IVC filter placement is not recommended.

Phlegmasia Cerulea Dolens[2,4]

Although uncommon, patients with phlegmasia cerulea dolens (PCD) should be identified and considered for more aggressive management due to the high degree of morbidity and mortality. Immediate transfer to HLOC is required.

- 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.
- Usually presents with sudden severe pain, swelling, cyanosis, and edema.
- Malignancy is the most common triggering factor. Inherited thrombophilias, surgery, IVC filter insertion, pregnancy, and HIT or other triggering factors.
- PCD is the only accepted indication for thrombolysis and/or thrombectomy in patients with DVT.

CARDIOVASCULAR GOALS

The goal of anticoagulation for cardiovascular indications is to prevent cardiac source of embolic events leading to ischemia at a distal site such as the brain, the intestines, etc. Traditionally, choices were limited to warfarin, but over the last decade, DOACs have been used more widely. Cardiovascular indications require lifelong anticoagulation and, in general, patients tend to have more comorbidities and higher bleeding risks.

Most commonly seen sequelae of an embolic event is stroke leading to disability. Patients with cardiovascular diseases tend to be older and have multiple comorbidities. It can be difficult to know when to recommend antiplatelet agents, such as aspirin or P2Y12 inhibitors like clopidogrel, anticoagulants, or both.

CARDIOVASCULAR MANAGEMENT ALGORITHM

Management of Cardiovascular Indications for Anticoagulation Algorithm[33,34,35,41,42,44]

- Arterial thrombus
- Symptomatic new onset AF/AFL*
- Symptomatic valvular heart disease
- Post acute MI with LV thrombus
- 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

Non-valvular AFib (Asymptomatic)

Calculate CHA_2DS_2-VASc Score

Valvular Heart Disease (Asymptomatic)

- Bioprosthetic valve
- Mechanical valve
- Mitral Valve Disease

MALE

- If score= 0, no anticoagulation needed, follow up as chronic care for changes in CHA_2DS_2-VASc score
- If score= 1: Consider anticoagulation treatment
- If score ≥2: Treat with anticoagulant unless risk of bleeding outweighs benefit

FEMALE

- If score= 0-1, no anticoagulation needed, follow up as chronic care for changes in CHA_2DS_2-VASc score
- If score= 2: Consider anticoagulation treatment
- If score ≥3: Treat with anticoagulant unless risk of bleeding outweighs benefit

2. New Contraindications to anticoagulation present or findings needing HLOC on follow-up?

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**

3. Conduct Bleeding Risk Assessment using HAS-BLED
Should not be interpreted as absolute recommendations, provider should correct modifiable risk factors

4. Review Medication List

5. Review or Order Diagnostic Studies

Benefit > Risk

Risk > Benefit

2. Contraindications to anticoagulation present or findings needing HLOC?

NO

Confirm and coordinate follow-up with specialty. Hold anticoagulation if care team and patient

Hold anticoagulation and consult specialty

6. Select anticoagulant: DOACs can be used in nonvalvular AF/AFL, warfarin for most valvular disease and LV thrombus.
- **Determine duration of therapy:** Duration is typically lifelong.

7. Document in the 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
- For medication specific monitoring: See Warfarin, DOACs, and LMWH

***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

CARDIOVASCULAR EVALUATION

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

History: Investigate past medical history and past procedures, review relevant data and diagnostics, and gather new information to help make an accurate assessment.

- Note the presence of any of the following potentially life-threatening symptoms, which may need HLOC: chest pain, palpitations, shortness of breath, acute neurologic deficits, and presyncope/syncope can indicate symptomatic atrial fibrillation/flutter (AF/AFL), heart failure, and/or cardiac ischemia.
- History of heart failure, hypertension, diabetes, stroke, or transient ischemic attack (TIA), coronary artery disease (CAD), and peripheral artery disease (PAD) along with age and sex will help determine stroke risk in a patient with AF/AFL using CHA_2DS_2-VASc score. (See Appendix A).
- Recent hospitalization for heart failure, acute coronary syndrome (ACS), left ventricular (LV) thrombus, or stent placement will help determine the need and duration of combined antiplatelet and anticoagulant therapy.
- Last EKG and echo. Order the studies, if not yet done.

Determine presence of contraindications.

Physical exam: A comprehensive physical exam includes vital signs, oxygenation, level of consciousness, cardiovascular exam, pulmonary exam, and neurologic exam.

- Tachycardia and/or tachypnea
- Hypotension or severe hypertension (i.e., hypertensive urgency, hypertensive emergency)
- Presence and location of heart murmurs
- Decreased breath sounds and/or rales on lung exam
- Presence of right heart strain such as elevated jugular venous distention and bilateral lower extremity edema
- Peripheral pulses
- Acute neurologic deficits

1. TREATMENT INDICATION[33,34,35,41,42,44]

Ensure that an indication for anticoagulation is present by:

- Confirming the previously made diagnosis that an indication for anticoagulation is present by reviewing prior documentation (e.g., outside medical records, prior EHRS encounters, discharge paperwork from HLOC, consultants' notes, EKG, echo, catheterization reports, radiology reports).
- Ordering new diagnostic tests as clinically indicated.

2. CONTRAINDICATIONS TO ANTICOAGULATION AND REASONS TO TRANSFER TO HLOC[34,35,36,37]

Cardiovascular indications usually require lifelong anticoagulation. Many times, anticoagulation is initiated in hospital. If anticoagulation is initiated in clinic, please assess for contraindications and risk of bleeding. Patients with relative contraindications and/or patients with significant comorbid conditions should be monitored closely and comanaged with a specialist.

Cardiovascular Evaluation Cont'd

Absolute Contraindications	**Relative Contraindications** (not limited to the following)
Acute major trauma	Active, but not life-threatening, bleeding
Major active, severe, or potentially life-threatening bleeding that is not reversible with medical or surgical intervention	Intracranial or spinal tumors The presence of an intracranial tumor or brain metastases without evidence of active intracranial bleeding is not an absolute contraindication to anticoagulation.
Recent intracranial bleeding or neurosurgery within the past 2 weeks	Recent intracranial bleeding within the past 4 weeks Intracranial hemorrhage in the setting of CVT is not a contraindication to anticoagulation.
Upcoming plans or emergent high-risk surgery or invasive procedure	Active GI ulceration at high risk of bleeding or recurrent bleeding from multiple gastrointestinal telangiectasias
Acute ischemic stroke within the past 2-14 days	Recent surgery or invasive procedure that had hemorrhagic complications
	Recent, plans for, or emergent low bleeding risk surgery or invasive procedure
	Uncontrolled severe hypertension
	Advanced CKD or ESRD
	Advanced heart failure
	Advanced liver disease (Child-Pugh score B and C)
	History of gastric cancer or major GI bleed
	Platelets < 25,000/mL or platelets < 50,000/mL in patients with cancer
	Bleeding disorder, such as hepatic dysfunction with coagulopathy, hemophilia, vWD
	Infective endocarditis (IE)
	History of HIT
	Pregnancy
	Perioperative management of anticoagulation

For patients who would benefit from anticoagulation but have a relative contraindication, specialty consultation is advised. Also consider transfer to HLOC if patient complains of chest pain, palpitations, shortness of breath, or other signs/symptoms of acute heart failure, cardiac ischemia, or limb-threatening ischemia.

3. RISKS/BENEFITS/ALTERNATIVES[33,34,35,36]

If no contraindications exist, look at the possible benefit the patient would receive from anticoagulation, such as reduced risk of stroke or other embolism. Then look at the patient's comorbidities, fall risk, medications, and recent or upcoming surgeries as potential factors that may increase the risk of bleeding.

For patients with AF/AFL, determine the risk of embolic stroke by utilizing CHA_2DS_2-VASc score. Points are assigned for the factors below with a maximum score of 9. Annual adjusted stroke risk varies from 0% for patients with 0 points, 3.2% for patients with 3 points, and 15.2% for patients with 9 points (See Appendix A).

CHA_2DS_2 VASc Score			
Condition	**Points**	**Condition**	**Points**
Congestive Heart Failure (CHF) LVEF < 40%	1	Vascular disease (coronary artery disease, peripheral vascular disease, aortic plaque)	1
Hypertension	1		
Age ≥ 75	2	Female Sex	1
Age 65-74	1	Recommend anticoagulation for nonvalvular AF/AFL: Men with CHA_2DS_2-VASc score ≥ 2 Women CHA_2DS_2-VASc score ≥ 3	
Diabetes mellitus	1		
Stroke or transient ischemia attack (TIA)	2		

Cardiovascular Evaluation Cont'd

Determine patient's bleeding risk by considering their comorbidities, medications, and dietary factors.

For patients with AF/AFL, determine bleeding risk by utilizing HAS-BLED score. HAS-BLED was developed as a practical risk assessment tool using the estimated 1-year risk for major bleeding in patients with AF/AFL by stratifying patients as low, moderate, or high bleed risk. This does not automatically exclude patients from receiving anticoagulation, if clinically indicated. HAS-BLED score should be used to identify modifiable risk factors that can be corrected to minimize bleeding risk in patients receiving anticoagulation.

HAS BLED* Score

Condition	Points
Hypertension	1
Abnormal renal or liver function (1 point each)	1 or 2
Stroke	1
Bleeding	1
Labile INR	1
Elderly (age > 65)	1
Drugs or alcohol (1 point each)	1 or 2

HAS-BLED Score	Bleeds per 100 patient years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.5

HAS-BLED is validated for warfarin, not DOACs

4. DRUG-DRUG INTERACTIONS

Review current medication list and look for DDIs. In particular, look for concurrent antiplatelet and/or NSAID use. Recommend use of DDI Tool available on Lifeline.

Some patients with coronary artery disease (CAD) have indications for antiplatelet agents (aspirin or P2Y12 inhibitors like clopidogrel [Plavix®]/prasugrel [Effient®]/ticagrelor [Brilinta®] or both depending on the presence of coronary stent) as well as anticoagulation therapy. The risk of thrombosis or bleeding in these patients can be very high, so account for this when initiating anticoagulation therapy and in determining the duration of concurrent therapy. Specialty consultation is advised.

5. DIAGNOSTIC STUDIES

- Initial: CBC, CMP,PT/INR, aPTT, if not done within 30 days
  - Consider medical hold for any patient with INR above 5.0
- EKG, echo, further imaging as clinically indicated

6. DURATION OF TREATMENT[33,34]

Select the most appropriate anticoagulant based on clinical presentation and patient factors.

- Specific indication for anticoagulation examples below:
  - DOACs are preferred for nonvalvular AF/AFL, depending on CHA_2DS_2-VASc score.
  - Warfarin is preferred and DOACs are not recommended for mechanical prosthetic heart valves and moderate to severe mitral stenosis (MS).
  - Specialty consultation is recommended when managing anticoagulation for all patients with valvular heart disease.
- Comorbidities
- Patient adherence: Warfarin is preferred if adherence is an issue because INR can be monitored. Additionally, warfarin has a longer half-life in the event of patient missing occasional doses.
- DDIs are less frequent with DOACs.
- For patient arriving on a nonformulary medication consider switching to a formulary agent, if there is no clinical contraindication.

The length of anticoagulation for cardiovascular indications is typically lifelong, except for bioprosthetic heart valves and LV thrombus (See pages 27-29 for duration of therapy and INR goals based on specific indication). While INR gives the status of anticoagulation for a short window of time, Time within Therapeutic Range (TTR) provides a measure of quality and success of anticoagulation with the goal being >70%. There are various ways of calculating TTR, usually dependent on time interval between blood draws as well as INR. If TTR is not at goal, more frequent INR checks are recommended.

Cardiovascular Evaluation Cont'd

Indication for Anticoagulation	INR Goal (if on warfarin)	Duration of Therapy
Nonvalvular, chronic or paroxysmal, atrial fibrillation/atrial flutter[33,34]		
• DOACs are recommended over warfarin in patients with AF/AFL, who do not have moderate-to-severe MS or a mechanical prosthetic heart valve • Prevention of thromboembolic events (See Appendix A)	DOACs preferred INR 2.5 (Range 2.0-3.0)	Lifelong
Chronic or paroxysmal, atrial fibrillation/atrial flutter with native valvular heart disease excluding rheumatic mitral stenosis[33,34,42]		
• DOACs are recommended over warfarin in patients with AF/AFL with negative valvular heart disease, who do not have moderate-to-severe MS or a mechanical prosthetic heart valve • Prevention of thromboembolic events (See Appendix A)	DOACs preferred INR 2.5 (Range 2.0-3.0)	Lifelong
Valvular heart disease, moderate-to-severe mitral stenosis[42]		

• Rheumatic moderate-to-severe MS with one of the following:
  ○ Atrial fibrillation
  ○ Prior embolic event
  ○ Left atrial thrombus
• Warfarin is indicated
• It is controversial whether long-term anticoagulation should be given to patients with rheumatic MS normal sinus rhythm on the basis of left atrial enlargement or spontaneous contrast on TEE
	INR 2.5
	(Range 2.0-3.0)
		Lifelong

Valvular heart disease, mechanical prosthetic heart valve[42]		
• Patients with mechanical bileaflet or current-generation single-tilting disc AVR and no risk factors for thromboembolism should be anticoagulated with warfarin	INR 2.5 (Range 2.0-3.0)	Lifelong
• Patients with mechanical MVR • Patients with mechanical AVR and additional risk factors for thromboembolism (e.g., AF, previous thromboembolism, LV dysfunction, hypercoagulable state) • Patients with an older generation prosthesis (e.g., ball-in-cage)	INR 3.0 (Range 2.5-3.5)	Lifelong
• Patient with mechanical MVR, who had a TIA or ischemic stroke prior to valve replacement, anticoagulate with warfarin and add aspirin 75-100 mg daily	INR 3.0 (Range 2.5-3.5) Add aspirin 75-100 mg daily	Lifelong
• If patient with mechanical AVR has a thromboembolic event while within appropriate INR range, increase warfarin to higher INR goal or add aspirin 75-100 mg daily.	INR 3.0 (Range 2.5-3.5) or INR 2.5 (Range 2.0-3.0) Add aspirin 75-100 mg daily	Lifetime
• If patient with mechanical MVR has a thromboembolic event while within appropriate INR range, increase warfarin to higher INR goal or add aspirin 75-100 mg daily.	INR 4.0 (Range 3.5-4.5) or INR 3.0 (Range 2.5-3.5) Add aspirin 75-100 mg daily	Lifetime

Cardiovascular Evaluation Cont'd

Indication for Anticoagulation	INR Goal (if on warfarin)	Duration of Therapy
Valvular heart disease, mechanical On-X aortic valve replacement[42]		
• For patients < 3 months after On-X aortic valve replacement, anticoagulate with warfarin and add aspirin 75-100 mg daily	INR 2.5 (Range 2.0-3.0) Add aspirin 75-100 mg daily	Initial 3 months
• For patients without another indication for anticoagulation ≥ 3 months after On-X aortic valve replacement, anticoagulate with warfarin targeted at the lower INR and add aspirin 75-100 mg daily	INR 1.5-2.0 Add aspirin 75-100 mg daily	Lifelong
Valvular heart disease, bioprosthetic heart valve[42]		
• For patients with new onset AF ≤ 3 months after surgical or transcatheter bioprosthetic valve replacement, anticoagulate with warfarin	INR 2.5 (Range 2.0-3.0)	Lifelong
• DOACs are an alternative to warfarin in patients with a bioprosthetic heart valve and AF > 3 months after implantation		
• For patients with bioprosthetic SAVR or bioprosthetic MVR who have a low bleeding risk, anticoagulate with warfarin for 3-6 months after valve replacement	INR 2.5 (Range 2.0-3.0)	Initial 3-6 months
• After 3-6 months of initial therapy with warfarin, patients with bioprosthetic SAVR or bioprosthetic MVR without another indication for anticoagulation should be prescribed aspirin 75-100 mg daily		
• If patient with bioprosthetic heart valve has a thromboembolic event while on antiplatelet therapy, start warfarin	INR 2.5 (Range 2.0-3.0)	Lifetime
Valvular heart disease, bioprosthetic TAVI[42]		
• For patients who have a low bleeding risk without another indication for anticoagulation, prescribe aspirin 75-100 mg daily and clopidogrel 75 mg for 3-6 months after valve implantation		
• Alternatively, for patients who have a low bleeding risk, anticoagulate with warfarin for 3-6 months after valve implantation	INR 2.5 (Range 2.0-3.0)	3-6 months
• After 3-6 months of initial therapy with dual antiplatelet therapy (DAPT) or warfarin, patients without another indication for anticoagulation should be prescribed aspirin 75-100 mg daily		
• If patient with bioprosthetic heart valve has a thromboembolic event while on antiplatelet therapy, start warfarin	INR 2.5 (Range 2.0-3.0)	Lifetime
Left ventricular thrombus[43]		
• Anticoagulate with warfarin for the following diagnoses: ○ TIA or stroke with confirmed left ventricular (LV) thrombus ○ TIA or stroke after acute anterior myocardial infarction (MI) with reduced ejection fraction (LVEF < 50%) without evidence of LV thrombus ○ Dilated cardiomyopathy due to specific cardiomyopathies (e.g., takotsubo syndrome, LV noncompaction, eosinophilic myocarditis, peripartum cardiomyopathy, and cardiac amyloidosis) with associated factors that increase risk of LV thrombus formation (AHA Scientific Statement, but not ACC/AHA Guidelines) ○ Nonischemic cardiomyopathy with LV thrombus anticoagulation for at least 3-6 months with discontinuation of therapy if LV thrombus resolves and LVEF improves > 35% (AHA Scientific Statement, but not ACC/AHA Guidelines) ○ LV thrombus persists beyond 3 months, then trial of an alternative anticoagulant (AHA Scientific Statement, but not ACC/AHA Guidelines)	INR 2.5 (Range 2.0-3.0) DOAC use uncertain	≥ 3 months

Cardiovascular Evaluation Cont'd

Indication for Anticoagulation	INR Goal (if on warfarin)	Duration of Therapy
○ Discontinue anticoagulation if persistent LV thrombus becomes organized or calcified (AHA Scientific Statement, but not ACC/AHA Guidelines) • For patients with an indication for anticoagulation, the addition of mono- or dual antiplatelet therapy (DAPT) can be prescribed with caution, and bleeding should be monitored • If antiplatelet therapy is indicated in a patient with low bleeding risk, add P2Y12 inhibitor like clopidogrel or aspirin 75-100 mg daily ○ When anticoagulation is added to antiplatelet therapy after PCI, dual therapy of an anticoagulant with a P2Y12 inhibitor, preferably clopidogrel, after 1-4 weeks of "triple therapy" is preferred over long-term "triple therapy" consisting of anticoagulation with DAPT • Specialty consultation is advised		

Indication for Anticoagulation	Acute Event	Anticoagulation Timing [45, 46, 47, 48, 49, 50]
Atrial fibrillation/atrial flutter, cardioversion[33,34]	< 48 hours	DOAC or heparin as soon as possible before cardioversion, followed by long term anticoagulation if CHA_2DS_2-VASc ≥ 2 in men, ≥ 3 in women
	≥ 48 hours hemodynamically stable	DOAC or warfarin (INR 2.0-3.0) for at least 3 weeks, then at least 4 weeks after cardioversion, followed by long term anticoagulation if CHA_2DS_2-VASc ≥ 2 in men, ≥ 3 in women
	≥ 48 hours requiring immediate cardioversion	DOAC or heparin as soon as possible before cardioversion, then DOAC or warfarin (INR 2.0-3.0) at least 4 weeks after cardioversion, followed by long term anticoagulation if CHA_2DS_2-VASc ≥ 2 in men, ≥ 3 in women
Atrial fibrillation/atrial flutter, acute neurologic event[33,34,35,36,44]	TIA in patients with nonvalvular AF/AFL	DOAC immediately after index event
	Ischemic stroke, low risk of hemorrhagic transformation	DOAC (for nonvalvular AF/AFL) or warfarin (for AF/AFL with moderate-to-severe mitral stenosis or with mechanical heart valve) between 2-14 days of ischemic stroke
	Ischemic stroke, high risk of hemorrhagic transformation	DOAC (for nonvalvular AF/AFL) or warfarin (for AF/AFL with moderate-to-severe mitral stenosis or with mechanical heart valve) beyond 14 days of ischemic stroke
	Hemorrhagic stroke	Delay anticoagulation and consult with appropriate specialists to determine the appropriate timing to restart anticoagulation after hemorrhagic stroke has stabilized
Moderate-to-severe mitral stenosis, acute neurologic event[35,36,42]	TIA or ischemic stroke	Aspirin 75-100 mg daily added to warfarin INR 3.0 (Range 2.5-3.5) after mechanical mitral valve replacement

Cardiovascular Evaluation Cont'd

Indication for Anticoagulation	Acute Event	Anticoagulation Timing [45, 46, 47, 48, 49, 50]
Mechanical aortic valve replacement, acute neurologic event[35,36,42,44]	TIA or ischemic stroke	Higher-intensity warfarin INR 3.0 (Range 2.5-3.5) or aspirin 75-100 mg daily added to standard-dose warfarin INR 2.5 (Range 2.0-3.0)
Indications for antiplatelet therapy and anticoagulation[45,46,47] **Indications for antiplatelet therapy and anticoagulation, Cont'd**	Recent PCI Recent ACS Recent PCI Recent ACS	For patients with an indication for anticoagulation, the addition of mono- or dual antiplatelet therapy (DAPT) can be prescribed with caution. Monitor for bleeding. If antiplatelet therapy is indicated in a patient with low bleeding risk, add P2Y12 inhibitor like clopidogrel or aspirin 75-100 mg daily for 6-12 months, then reassess if anticoagulation, antiplatelet, or combination should be continued long term. When anticoagulation is added to antiplatelet therapy after PCI, dual therapy of an anticoagulant with a P2Y12 inhibitor, preferably clopidogrel, after 1-4 weeks of "triple therapy" is preferred over long-term "triple therapy" consisting of anticoagulation with DAPT. Specialty consultation is advised.
Coronary artery disease (CAD)[45,46,47]	Recent ACS Stable CAD	After stabilization with initial management of ACS, start rivaroxaban 2.5 mg twice daily as add-on therapy to clopidogrel (not approved for add-on therapy to prasugrel or ticagrelor) and aspirin therapy in patients, who are not at high risk of bleeding and do not require chronic therapeutic anticoagulation for another indication. Continue rivaroxaban for approximately one year. Among DOACs, only rivaroxaban has been shown to reduce the risk of recurrent ischemic events, including mortality, when added to dual antiplatelet therapy (DAPT) in patients with ACS, who have not undergone PCI with stenting. In stable CAD, consider adding rivaroxaban 2.5 mg twice daily to aspirin therapy in patients who are at high risk of cardiovascular events and low risk of bleeding if chronic therapeutic anticoagulation is not required for another indication.
Peripheral artery disease (PAD)[48,49,50,51]	Lower extremity revascularization Stable PAD	In stable symptomatic PAD, consider adding rivaroxaban 2.5 mg twice daily to aspirin therapy in patients, who are at high risk of major thrombotic vascular events and low risk of bleeding if chronic therapeutic anticoagulation is not required for another indication. When starting rivaroxaban after lower extremity revascularization, initiate when hemostasis is achieved. Do not use if DAPT is planned.

Cardiovascular Evaluation Cont'd

7. DOCUMENTATION

Document the following in the EHRS:

- Updated **Problem List**
  - Indication
  - "Long-term (current) use of anticoagulant" (ICD-10 Z79.01) to be marked resolved upon completion of therapy
- Start date
- Duration of therapy with an anticipated end date, include if lifelong anticoagulation is indicated
- Target INR, if on warfarin
- Next INR check, if on warfarin
- Hemoglobin and platelets
- Creatinine and CrCl/eGFR
- Assessment of bleeding risks
- Patient education provided (See PE1 - PE4)
- Comanaging specialty, (e.g., cardiology, hematology, oncology, etc.)
- Evaluated for lower bunk Chrono

8. EVALUATION INTERVALS

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 anticoagulation, do they still need continued anticoagulation?).
  - Ensure no new contraindications to anticoagulation, complication requiring HLOC, or specialty referral. Review any changes in general health, functional status, recent falls, activity level and engagement in contact sports, change in diet, and substance use including alcohol.
  - Reassess risks/benefits/alternatives of anticoagulation (e.g., does a new medical condition or bleeding risk cause the risks/benefits/alternatives assessment shift in favor of discontinuation of anticoagulation?).
  - Review current medication list, especially for any new medications, including over-the-counter medications. Pay special attention to addition or discontinuation of antiplatelet agents or NSAIDs. Confirm medication adherence.
  - Review any new laboratory results.
  - Confirm current anticoagulant is still most appropriate agent and that the continued dose is still appropriate.
  - Confirm documentation, including **Problem List**, is up to date in the EHRS.
  - Schedule appropriate follow-up and monitoring.
  - If stopping anticoagulation, re-evaluate need for lower bunk Chrono.

ANTICOAGULATION MEDICATION'S INTRODUCTION

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

- DOACs pages 32-39
- Warfarin pages 39-44
- LMWH pages 45-49

Please see the following Specific Clinical Scenario Sections:

- Periprocedural Management of Anticoagulation page 50
- Antiplatelet Therapy with Anticoagulation page 54
- Bleeding Complications page 54
- Heparin-induced Thrombocytopenia pages 54-55

DIRECT-ACTING ORAL ANTICOAGULANT (DOAC)[51,52]

There are two classes of DOACs. (See Appendix B for Site of Action)

1. Factor Xa inhibitor: apixaban, rivaroxaban, and edoxaban
2. Direct thrombin inhibitor: dabigatran

A single missed dose of DOAC has greater potential to result in inadequate anticoagulation because DOACs have a short half-life, so patients being considered to take these anticoagulants should be highly adherent. Consider prescribing DOACs as NA or DOT for monitoring of adherence.

Dose adjustments are dependent on indication for anticoagulation, age, weight, and renal function. Recommend verifying dose with pharmacist, especially for patients with CrCl < 30 mL/min. Apixaban can be renally dosed for advanced CKD and ESRD.

Indications for DOACs

Apixaban and rivaroxaban are formulary anticoagulants. Edoxaban and dabigatran remain nonformulary.

- DOACs are first-line therapy for VTE
- DOACs are first-line therapy for nonvalvular AF/AFL
- DOACs are one of the first-line therapy options for CAT
- Apixaban is the preferred DOAC for patients with a history of gastrointestinal bleed

Consider DOACs over warfarin in the following clinical situations:

- Unstable INR despite patient adherence to warfarin
- Progressive VTE or recurrent VTE despite therapeutic INR on warfarin
- Inability to obtain monitoring INR (e.g., difficult phlebotomy access)
- Warfarin allergy
- Prohibitive DDIs with warfarin

Contraindications for DOACs

For the following contraindications to DOACs, warfarin is the suggested alternative anticoagulant:

- Antiphospholipid syndrome
- AF/AFL in the setting of moderate-to-severe mitral stenosis
- Mechanical prosthetic heart valve
- Nonadherent patients: A single missed dose of DOAC has greater potential to result in inadequate anticoagulation because DOACs have a short half-life

For the following contraindications to DOACs, LMWH is the suggested alternative anticoagulant:

- Progressive or recurrent thrombosis on DOAC for CAT
- Significant liver disease, Child-Pugh score B and C
- Pregnancy
- Breastfeeding

DOAC Cont'd

Potential Advantages and Disadvantages of DOACs Compared to VKA[1]	
Advantages of DOACs	**Disadvantages of DOACs**
• No routine monitoring • Improved safety profile • Rapid onset (may preclude the need for induction or bridging therapy) • Short half-life (advantageous for invasive procedures or active bleed) • Fixed dosing • Greater convenience, patient satisfaction • Fewer drug, disease, and diet interactions	• No reliable, readily available measurement assay • Dose reduction or avoidance in renal impairment and avoidance in moderate or severe hepatic impairment • Short half-life (mandates strict adherence) • Less flexibility in dosing • Fewer studies and approved indications (e.g., contraindicated in mechanical valve replacement) • Potentially higher drug acquisition costs for patients • DOAC drug interactions do exist that may preclude use

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.

Select the hyperlink below:
http://qmtools/Reports/report/QM/Tools/DrugDrugInterationSearch

Dosing and Dose Adjustment

Please see the 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.

DOAC Cont'd

MEDICATION	DOSING	ADVERSE EFFECTS / INTERACTIONS*	COMMENTS*
DIRECT THROMBIN INHIBITOR			
APIXABAN ELIQUIS® **Formulary** Strengths: 5 mg 2.5 mg Administer NA **$$$$$** May order as KOP in select cases where the patient would benefit from self-administration	**Stroke prevention and systemic embolism prophylaxis in patients with non-valvular Afib**: 5 mg orally twice daily Consider 2.5 mg orally twice daily if patient has at least 2 of the following: • Age ≥ 80 years • Body weight of ≤ 132 lb. (60 kg) • Serum CREAT level of ≥ 1.5 mg/dL **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) 10 mg orally twice daily for 7 days, then 5 mg orally twice daily for at least 6 months **Prophylaxis for reduction in the risk of recurrent DVT and/or PE** 2.5 mg orally twice daily after at least 6 months of standard anticoagulation therapy **Post-surgical DVT and PE prophylaxis:** 2.5 mg orally twice daily Administer initial dose 12 to 24 hours after surgery. Duration: 12 days (knee replacement), 35 days (hip replacement) 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 **Hepatic Impairment:** • Mild impairment: No dosage adjustments needed • Moderate impairment: Limited experience in this population, dosing recommendations not available • Severe impairment: Not recommended **Monitoring**: None recommended Converting from apixaban to another DOAC	• **Adverse reactions:** Bleeding rash, anemia, nausea, hematuria, epistaxis • Increased risk of epidural spinal hematoma with neuraxial anesthesia or spinal puncture • **Drug Interactions:** Avoid concurrent use with strong dual inducers of CYP3A4 and P-glycoprotein (e.g., rifampin, phenytoin, carbamazepine) • Increased bleeding risk with antiplatelets, anticoagulants, and thrombolytics	• **Contraindications:** 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 • Use caution in patients with moderate hepatic impairment, renal impairment Half-Life: 12 hours Antidote: Andexxa® (recombinant Factor Xa)

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.

DOAC Cont'd

MEDICATION	DOSING	ADVERSE EFFECTS / INTERACTIONS*	COMMENTS*
DIRECT FACTOR XA INHIBITORS			
RIVAROXABAN XARELTO® **Formulary** Strengths: 2.5 mg 10 mg 15 mg 20 mg Administer NA May order as KOP in select cases where the patient would benefit from self-administration **$$$$$**	**Post-surgical DVT and PE prophylaxis:** 10 mg orally once daily Duration: 12 days (knee replacement), 35 days (hip replacement) **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 **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 **Prevent stroke in patients with non-valvular AFib:** 20 mg orally once daily in the evening with food **Renal Impairment:** VTE prophylaxis and treatment: CrCl < 15 mL/min: avoid use Prevent stroke in patients with non-valvular AFib: CrCl ≤ 50 mL/min: 15 mg orally once daily **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 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. Convert from warfarin to rivaroxaban: Discontinue warfarin and start rivaroxaban when INR < 3.0. Converting from rivaroxaban to another DOAC	• **Adverse Reactions:** Bleeding, muscle cramps, abdominal pain, back pain, dyspepsia, fatigue, pruritus, sinusitis, syncope • Increased risk of epidural spinal hematoma with neuroaxial anesthesia or spinal puncture • **Drug Interactions:** Avoid with combined P-glycoprotein inhibitor and CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, ritonavir, conivaptan [Vaprisol]) • Increased bleeding risk with anti-platelets, anticoagulants, and thrombolytics	• **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 • Use caution in patients with hepatic impairment, renal impairment • **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 Half-Life: 5-9 hours Monitoring: Renal function prior to initiation of therapy, periodically throughout treatment and more frequently in clinical situations where renal function may decline. Antidote: Andexxa® (recombinant Factor Xa)

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.

DOAC Cont'd

MEDICATION	DOSING	ADVERSE EFFECTS / INTERACTIONS*	COMMENTS*
DIRECT FACTOR XA INHIBITORS			
EDOXABAN SAVAYSA® Nonformulary Tablet Strengths: 15 mg 30 mg 60 mg Administer DOT Only Consider NA **$$$$$**	**Stroke and Systemic Embolism Prevention in patients with non-valvular AFib:** (dosing based on CrCl) CrCl ≥ 95 mL/min: Use not recommended CrCl 51-94 mL/min: 60 mg orally once daily CrCl 15-50 mL/min: 30 mg orally once daily CrCl < 15 mL/min: Use not recommended **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: • CrCl 15-50 mL/min; or • Body weight ≤ 60 kg; or • Concomitant use of P-gp inhibitors (e.g., verapamil, quinidine, azithromycin, clarithromycin, erythromycin, itraconazole, ketoconazole) • CrCl < 15 mL/min: Use not recommended **Moderate or severe hepatic impairment (Child-Pugh Class B and C):** Use not recommended 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. Convert from warfarin to edoxaban: Discontinue warfarin and start edoxaban when INR ≤ 2.5. Converting from edoxaban to another DOAC When converting from edoxaban to another DOAC	• **Adverse Reactions**: Bleeding, anemia, elevated hepatic enzymes, rash • Increased risk of epidural spinal hematoma with neuraxial anesthesia or spinal puncture • **Drug Interactions:** Avoid concurrent use with rifampin. Avoid long term concomitant treatment with other anticoagulants.	**Black Box Warning**: Do not use in non-valvular Afib patients with CrCl ≥ 95 mL/min due to reduced efficacy. • **Contraindications**: Active pathological bleeding, mechanical heart valves, moderate to severe mitral stenosis, severe hypersensitivity reaction to edoxaban or any component of the formulation • Use caution in patients with hepatic impairment, renal impairment. Half-Life: 10-14 hours Monitoring: Renal function prior to initiation of therapy, periodically throughout treatment and more frequently in clinical situations where renal function may decline. Antidote: none available

Bold = Formulary *See prescribing information for complete description of contraindications/precautions, adverse effects and drug interactions.
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DOAC Cont'd

MEDICATION	DOSING	ADVERSE EFFECTS / INTERACTIONS*	COMMENTS*
DIRECT THROMBIN INHIBITOR			
DABIGATRAN PRADAXA® Nonformulary Strengths: 75 mg 110 mg 150 mg Administer NA **$$$$$** May order as KOP in select cases where the patient would benefit from self-administration	**Stroke 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. **Renal Impairment:** • Non-valvular Afib ○ CrCl >30 mL/min: No dose adjustment needed ○ CrCl 15-30 mL/min: 75 mg orally twice daily ○ CrCl <15 mL/min: No data, avoid use ○ CrCl 30-50 mL/min and concurrent use of dronedarone ○ or systemic ketoconazole: 75 mg orally twice daily ○ CrCl <30 mL/min and concurrent use of P-glycoprotein ○ Inhibitor: Avoid co-administration • VTE ○ CrCl >30 mL/min: No dose adjustment needed ○ CrCl ≤30 mL/min: No data, avoid use ○ CrCl <50 mL/min and concurrent use of P-glycoprotein ○ Inhibitor: Avoid co-administration **Monitoring**: Renal function prior to initiation of therapy, periodically throughout treatment and more frequently in clinical situations where renal function may decline. **Hepatic Impairment:** Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed. Converting from dabigatran to another DOAC.	• **Adverse reactions:** Bleeding, dyspepsia, edema, rash, pruritus, urticaria, abdominal pain, gastritis • Increased risk of epidural spinal hematoma with neuraxial anesthesia or spinal puncture • **Drug Interactions:** Avoid concurrent use with P-glycoprotein inducers (e.g., rifampin). Evaluate P-glycoprotein. inhibitors individually • Increased bleeding risk with anti-platelets, anticoagulants, and thrombolytics	• **Contraindications:** Active pathological bleeding, prosthetic heart valves (mechanical/bio prosthetic), pregnancy or breastfeeding, CrCl < 15 mL/min, moderate to severe mitral stenosis, serious hypersensitivity reaction to dabigatran or any component of the formulation • Use caution in patients with hepatic impairment, renal impairment. • Do not chew, break, or open capsules. Dispense capsules in original container, **not repackaged due to sensitivity to moisture.** Half-Life: 12-17 hours Antidote: Praxbind® (Idarucizumab)

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DOAC Cont'd

	Apixaban (Eliquis®) (formulary)	**Rivaroxaban (Xarelto®) (formulary)**	Edoxaban (Savaysa®) (nonformulary)	Dabigatran (Pradaxa®) (nonformulary)
Mechanism of Action	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitor	Thrombin Inhibitor
Half-Life	12 hours	5-9 hours	10-14 hours	12-17 hours
Special Considerations	Avoid use with dual strong CYP3A4 and P-gp inducers. If patient is taking strong CYP3A4 and P-gp inhibitor: • If dose > 2.5 mg BID, decrease dose by 50%. • If already taking 2.5 mg BID, avoid use.	Avoid use with dual strong CYP3A4 and P-gp inhibitors or inducers.	CrCl ≥95 mL/min, increased rate of thrombosis seen Use dose of 30 mg once daily if any of the following: • CrCl 15-50 mL/min • Weight ≤ 60 kg • Use with P-gp inhibitor	Avoid concurrent use with any P-gp inducer. Avoid concurrent use with any P-gp inhibitor IF CrCl < 50 mL/min. Avoid in patients with history of GI bleed, severe hepatic/ renal disease.
Dosing Interval	Twice daily	Once daily with food	Once daily	Twice daily
Renal Elimination	Dose adjustment needed. Is dependent on indication, age, weight, and Serum CREAT. • For stroke prevention in AFib/flutter: 2.5 mg PO BID if at least two of the following (age ≥80 years, body weight of ≤ 132 lb. (60 kg) or Serum CREAT level of ≥ 1.5 mg/dL). Off label use for other indications	Dose adjustment needed. Is dependent on indication and CrCl. Off Label use for ESRD patients on HD	Dose adjustment needed. Is dependent on indication and CrCl. • CrCl < 15 mL/min: Use not recommended Off label use for ESRD patients on HD	Dose adjustment needed. Is dependent on indication and CrCl. Contraindicated in ESRD.
Convert TO Warfarin	Discontinue apixaban and start warfarin plus parenteral anticoagulant at time of next apixaban dose. Discontinue parenteral anticoagulant when INR is therapeutic.	Discontinue rivaroxaban and start warfarin plus parenteral anticoagulant at time of next rivaroxaban dose. Discontinue parenteral anticoagulant when INR is therapeutic.	Discontinue edoxaban and start warfarin plus parenteral anticoagulant at time of next edoxaban dose. Discontinue parenteral anticoagulant when INR ≥ 2.0.	Based on CrCl start warfarin 3 days (> 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 <15 mL/min.
Convert FROM Warfarin	Discontinue warfarin, start apixaban when INR < 2.0.	Discontinue warfarin, start rivaroxaban when INR <3.0.	Discontinue warfarin, start edoxaban when INR < 2.5.	Discontinue warfarin, start dabigatran when INR < 2.0.

DOAC Cont'd

	Apixaban (Eliquis®) (formulary)	Rivaroxaban (Xarelto®) (formulary)	Edoxaban (Savaysa®) (nonformulary)	Dabigatran (Pradaxa®) (nonformulary)
Convert FROM one DOAC TO another DOAC	Discontinue apixaban and initiate the preferred agent at the time that the next apixaban dose would have been administered.	Discontinue rivaroxaban and initiate the preferred agent at the time that the next rivaroxaban dose would have been administered.	Discontinue edoxaban and initiate the preferred agent at the time that the next edoxaban dose would have been administered.	Discontinue dabigatran and initiate the preferred agent at the time that the next dabigatran dose would have been administered.
Storage	Store between 20-25 °C (68 to 77 °F); excursions permitted between 15-30°C (59-86°F).	Store at 25 °C (77 °F); excursions permitted between 15-30 °C (59-86 °F).	Store between 20-25 °C (68 to 77 °F); excursions permitted between 15-30 °C (59-86°F).	• Use within 4 months after opening. • Protect from moisture. • Store at 25 °C (77 °F); excursions permitted between 15-30°C (59-86°F). • Store in original package until time of use. • Do not crush or chew. • Not recommended for splitting.

WARFARIN[1,51,52]

Warfarin is an oral anticoagulant that inhibits vitamin K dependent clotting factors II, VII, IX, and X. (See Appendix B) It increases clotting time as measured by INR; a standardized measurement of prothrombin time. Warfarin is the oldest and most studied anticoagulant and has a readily available reversal agent, which is vitamin K.

Indications for Warfarin

Warfarin is a formulary anticoagulant.

- Antiphospholipid syndrome and some inherited thrombophilias
- AF/AFL in the setting of moderate-to-severe mitral stenosis
- Mechanical prosthetic heart valve
- Nonadherent patients
- LV thrombus treatment and prophylaxis
- MCS with VAD or TAH
- Anticoagulation in the setting of CKD with CrCl < 30 mL/min
- Anticoagulation needed in the patient with a history of bariatric surgery

Consider warfarin over DOACs in the following clinical situations:

- Progressive VTE or recurrent VTE despite patient adherence to DOAC therapy
- Persistent LV thrombus that is not organized or calcified after 3 months of DOAC therapy
- DOAC allergy
- Prohibitive DDIs with DOACs

Contraindications for Warfarin

For the following contraindications to warfarin, DOACs are the suggested alternative anticoagulant:

- History of intracranial hemorrhage

For the following contraindications to warfarin, LMWH is the suggested alternative anticoagulant:

- Pregnancy, except in patients with mechanical prosthetic heart valve

Warfarin Cont'd

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.

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

Interaction Blunts PT/INR Response ↓	Increase Warfarin Dose By
Carbamazepine (Tegretol®)	100%
Nafcillin or Dicloxacillin	100-400%

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

http://qmtools/Reports/report/QM/Tools/DrugDrugInterationSearch

Warfarin Cont'd

WARFARIN			
MEDICATION	**DOSING**	**ADVERSE EFFECTS / INTERACTIONS***	**COMMENTS***
VITAMIN K ANTAGONIST (VKA) (ORAL) / VKA REVERSING AGENT (VITAMIN K)			
WARFARIN Jantoven® **Formulary** **Tablet:** **1 mg** -pink **2 mg** -lavender **2.5 mg** -green **3 mg** -tan **4 mg** -blue **5 mg** -peach **6 mg** -teal **7.5 mg** -yellow **10 mg** -white **$**	**Usual initial dose**: 5 mg orally every evening. **Avoid loading doses.** **Consider lower starting dose**: 2.5 mg every evening if: • Age > 75 yrs • Multiple comorbidities • Hypoalbuminemia • Elevated pretreatment INR • Elevated liver function tests • Changing thyroid status **Consider higher starting dose**: 7.5 mg orally every evening for patients weighing > 80 kg Patients restarting warfarin can usually start at their previous dose. If stopped due to bleeding, assess risk of thrombosis vs. risk of re-bleeding. Recheck INR on day 3 after first two doses, if INR > 2.0, consider reducing dose by 1/2. Evaluate for cause of rapid rise in INR. Steady-state INR will take up to 3 weeks. Dose adjustments at steady state • Assess variables affecting the INR before changing dose (e.g., patient adherence, medication interactions, dietary changes). • 10% warfarin dose adjustment changes INR approximately 0.7-0.8.	• **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 • **Interactions:** Multiple drug and food interactions	• **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 • Use with caution in patients with dietary insufficiency, HIT, hepatic impairment, renal impairment, thyroid disease. • Risk of bleeding is highest in first month of therapy. • Consider evaluation if a patient on warfarin presents with GI bleeding. • A baseline INR value is helpful to rule out underlying coagulopathy. • NOTE: Do not cut pills.

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Warfarin Cont'd

WARFARIN			
MEDICATION	**DOSING**	**ADVERSE EFFECTS / INTERACTIONS***	**COMMENTS***
VITAMIN K ANTAGONIST (VKA) (ORAL) / VKA REVERSING AGENT (VITAMIN K)			
VITAMIN K PHYTONADIONE Mephyton® **Tablet: 5 mg** Injectable: 1 mg/0.5ml **10 mg/ml** **$$ - $$$$$**	Supratherapeutic INR (anticoagulant induced) Outpatient setting: 2.5 to 5 mg orally as a single dose then re-evaluate before repeat administration Hospital setting (patient NPO): IV vitamin K should be given over 30 minutes in a mixture of D5W 50 mL under monitored conditions 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 • NOTE: Most people do not experience side effects taking small doses of vitamin K. • **Drug interactions:** Warfarin, colestipol, cholestyramine, castor oil, mineral oil	• **Contraindications:** Hypersensitivity to vitamin K or any component of the formulation • Use caution with parenteral administration. Severe hypersensitivity reactions, including anaphylactoid reactions and deaths have been reported following parenteral administration.

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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.
- 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.

Warfarin Cont'd

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):

When to Check INR	Comments
Initially every 2-3 days	Until INR is in therapeutic range on 2 consecutive INR checks with stable warfarin
Then every 1-2 weeks	Until INR is in therapeutic range on 2 consecutive INR checks with stable warfarin
Then every 4 weeks	When dose is stable, check monthly

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.

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 (e.g., 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

Endogenous Factors That May DECREASE INR	Endogenous Factors That May INCREASE INR	
• Edema • Hereditary factors • Hyperlipidemia • Hypothyroidism • Nephrotic syndrome	• Blood dyscrasias • Cancer • Collagen vascular disease • Congestive heart failure • Diarrhea • Elevated temperature	• Hepatic disorders (infectious hepatitis, jaundice) • Hyperthyroidism • Poor nutritional state • Steatorrhea • Vitamin K deficiency • Hereditary factors: CYP2CP and/or VKORC1 genotype

Warfarin Cont'd

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

Warfarin Dose Adjustment[1]

Goal INR 2.5 (Range 2.0–3.0)		Goal INR 3.0 (Range 2.5–3.5)	
If INR Result Is:	**Action**	**If INR Result Is:**	**Action**
≤1.5	Increase weekly dose by 15%	**≤1.5**	Increase weekly dose by 20%
1.51–1.99	Continue same dose warfarin If INR still 1.5-1.99, increase weekly dose by 10%	**1.51–1.99**	Increase weekly dose by 15%
		2.00–2.49	Continue same dose warfarin If INR still 2.0-2.49, increase weekly dose by 10%
2.00–3.00	Continue same dose warfarin	**2.50–3.50**	Continue same dose warfarin

Dose Adjustment for Supratherapeutic INR Results

If INR Result is:	Action:
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.

LOW MOLECULAR WEIGHT HEPARIN (LMWH)[2,4,5,6,42,43,56]

There are two low molecular weight heparins available for use in the US. Enoxaparin is on formulary; dalteparin is nonformulary. LMWH administration is via subcutaneous injection, which has long-term implications on the choice of chronic anticoagulation.

- Baseline data prior to administration of LMWH: weight, CBC, creatinine, AST/ALT, PT/INR, PTT, albumin
- Renal function and CBC should be monitored at least every 3 months or more frequently as the clinical situation necessitates.
- Close monitoring of renal function is recommended for patients at increased risk of renal insufficiency (i.e., dehydration) or underlying CKD since dose adjustments may be required for worsening renal function.

Indications for LMWH

Acute setting

- May be indicated for newly diagnosed VTE if first line therapy with DOAC is not used and warfarin is prescribed for long-term treatment.
  - Initiate concurrently with warfarin, usually within 72 hours of enoxaparin treatment.
  - Continue enoxaparin for at least 5 days until INR is in therapeutic range for 2 days (Range INR 2-3).
- Patients with STEMI undergoing fibrinolytic therapy for reperfusion should receive enoxaparin for minimum of 48 hours, and preferably for the duration of the index hospitalization, up to 8 days or until revascularization with PCI is performed.
- In the setting of NSTE-ACS, anticoagulation treatment option in addition to antiplatelet therapy for the duration of hospitalization or until PCI is performed.
- May be used as an alternative to unfractionated heparin in patients undergoing PCI.
- Indicated for newly diagnosed LV thrombus:
  - Initiate concurrently with warfarin, usually within 72 hours of enoxaparin treatment.
  - Continue enoxaparin for at least 5 days until INR is in therapeutic range for 2 days (Range INR 2-3).

Outpatient setting

- May be indicated for newly diagnosed CAT if first line therapy with DOAC is not used and LMWH is prescribed for long-term treatment.
- VTE prophylaxis (not covered in this care guide)

LMWH Cont'd

Contraindications for LMWH Use	Precautions for LMWH Use
• Active major bleeding *(anticoagulation contraindicated)* • Presence or history of HIT *(refer to a HLOC)* • Thrombocytopenia (Platelet < 100,000/mm^3) *(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)*	• 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

Select the hyperlink below:
https://qmtools.accounts.cdcr.ca.gov/Reports/report/QM/Tools/DrugDrugInterationSearch

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

LMWH Cont'd

Medication	Dosing		Comments*
Indirect Thrombin Inhibitor (parenteral) LMWH			
Enoxaparin Lovenox® (LMWH) Injectable pre-filled syringe: **30 mg/0.3 mL** **40 mg/0.4 mL** **60 mg/0.6 mL** **80 mg/0.8mL** **100 mg/mL** 120 mg/0.8mL 150 mg/mL Multiple dose vial (MDV): 300 mg/3 mL **$$$$$**	Do not administer IM; administer by subQ injection **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	**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 HITantibody 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 theheparin has been discontinued • HIT can occur in patients getting ≥ 1 dose of unfractionated heparin (including heparin IV flushes) within the past 100 days	**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 porkproducts, or any component of the formulation (including benzyl alcohol in MDVs)

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LMWH Cont'd

Enoxaparin (Cont'd)	DVT prophylaxis for acute illness: 40 mg subQ once daily(usually 6-11 days) DVT prophylaxis for abdominal surgery: 40 mg subQ oncedaily starting 2 hours prior to surgery (usually 7-10 days) Unstable angina and non-Q-wave MI: 1 mg/kg subQ every 12hours 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 orhip/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.	**Drug Interactions:** • Avoid long-term concomitant treatment with other anticoagulants, aspirin • Increased bleeding risk with antiplatelets, anticoagulants, and thrombolytics	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 supratherapeutic 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

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.

LMWH Cont'd

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.

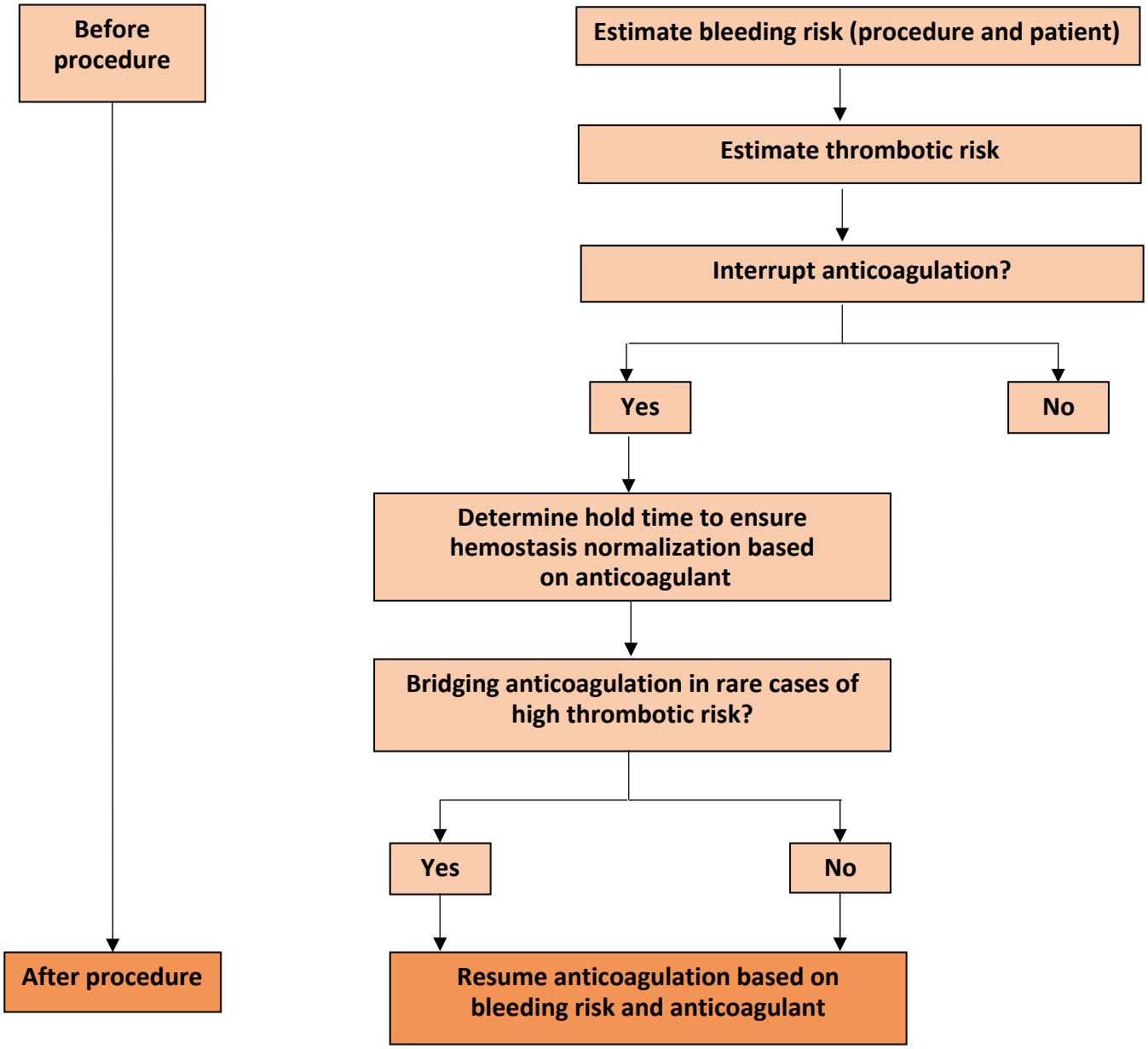
Monitoring anti-factor Xa levels: indicated only when appropriate dosing is difficult to determine – such as in:

- 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 >30kg/m^2)
- 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

Periprocedural Management of Anticoagulation[2,3,34,41,53]

Periprocedural anticoagulation management requires estimation of risk of thrombosis and bleeding, choice of anesthetic, site and length of procedure, multidisciplinary communication and collaboration, and patient engagement and education. First, clinicians should evaluate bleeding risk for the procedure, taking into account patient-specific factors. Next, the patient's risk for thrombosis should be assessed. If interruption of anticoagulation is warranted, ensure normalization of hemostasis prior to procedure. Bridging should be used sparingly and only in select circumstances. Finally, develop a plan to resume therapeutic anticoagulation.



Specific Clinical Scenarios Cont'd

RISK ASSESSMENT			
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.			
Stratification of Bleeding Risk Associated with Procedures[53]			
Risk Category	**30-Day Risk of Major Bleeding**	**Type of Surgery or Procedure**	**Recommendation**
High	> 2%	• Cardiac surgery (heart valve replacement, CABG) • Vascular surgery (AAA repair, peripheral artery bypass) • Neurosurgery (intracranial or spinal) • Urologic surgery (renal, prostate, or bladder) • Surgery of highly vascularized organs (liver, spleen) • Major cancer surgery • Reconstructive plastic surgery • Colonoscopy with polypectomy* • ERCP with sphincterotomy* • Major orthopedic surgery, (e.g., total hip arthropathy (THA) or total knee arthropathy (TKA)†)	Stop anticoagulation and follow the surgeon's recommendations on preprocedural anticoagulation regimen. For patients with cardiovascular indications for anticoagulation, a multidisciplinary approach with the surgeon and the cardiologist is needed to optimize preoperative interruption of anticoagulation based on patient-specific factors (e.g., thrombotic risk, age, sex, body weight, renal function), surgical bleeding risk, and other drug factors (e.g., pharmacokinetics, dosing, drug interaction). * Full anticoagulation can be continued if no polypectomy or sphincterotomy is anticipated. † If patient has no indication for full anticoagulation, apixaban 2.5 mg BID or rivaroxaban 10 mg daily may be started 12-24 hrs after surgery in patients with CrCl ≥ 15 mL/min for 35 days after total hip and 12 days after total knee for VTE prophylaxis.
Low/moderate	0 – 2%	• Major intraabdominal surgery, (e.g., colectomy, hysterectomy) • Major intrathoracic surgery, (e.g., lobectomy, esophagectomy) • Transfemoral or transradial coronary angiography • Most common cutaneous procedures • Laparoscopic cholecystectomy • Ventral/inguinal hernia repair	Stop anticoagulation For patients with cardiovascular indications for anticoagulation, a multidisciplinary approach with the surgeon and the cardiologist is needed to optimize preoperative interruption of anticoagulation based on patient-specific factors (e.g., thrombotic risk, age, sex, body weight, renal function), surgical bleeding risk, and other drug factors (e.g., pharmacokinetics, dosing, drug interaction).
Minimal	~ 0%	See table below	May not require interruption of anticoagulation

Specific Clinical Scenarios Cont'd

Minimal Bleeding Risk Procedures			
Dental	Restorative Dentistry Periodontics Simple Oral Surgery Endodontics Prosthodontics	Fillings Prophylaxis (cleaning) Scaling and Root Planing Extractions (1-3 teeth) Root Canals Dentures	For most dental procedures no change in anticoagulant dosing is needed and bridging is not recommended. It may be reasonable to allow the patient to "drift" to the low end of their therapeutic INR prior to a dental procedure with a higher risk of bleeding (INR<3.5). Local hemostatic measures by the dental provider to be incorporated. [53,54]
Dermatologic	Mohs surgery Simple excisions	Skin Biopsy Simple excisions	Continue anticoagulant around the time of the procedure and optimize local hemostasis.
Ophthalmologic	Cataract surgery Trabeculectomy		Continue anticoagulant around the time of surgery.
Gastrointestinal	Diagnostic esophagogastroduodenoscopy (EGD) Colonoscopy without biopsy Endoscopic ultrasonography without biopsy Diagnostic endoscopic retrograde Cholangiopancreatography Biliary stent without sphincterotomy		Continue anticoagulant around the time of procedure.

General Guidance for Perioperative Anticoagulation

- For procedures with intermediate- and high-risk of bleeding and for patients with cardiovascular indications for anticoagulation, a multidisciplinary approach with the surgeon and the cardiologist is needed to optimize preoperative interruption of anticoagulation based on patient-specific factors (e.g., thrombotic risk, age, sex, body weight, renal function), surgical bleeding risk, and other drug factors (e.g., pharmacokinetics, dosing, drug interaction).

DOAC

- **Epidural or spinal hematomas may occur in patients treated with DOACs who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks and follow recommendations from the surgeon.**
- Generally, DOACs are stopped 1-4 days before procedure depending on CrCl (earlier if CrCl <50 mL/min)
  - High bleeding risk: stop DOAC 2 days before procedure (stop 4 days before procedure if taking dabigatran and CrCl <50 mL/min)
  - Low/moderate bleeding risk: stop DOAC 1 day before procedure (stop 2 days before procedure if taking dabigatran and CrCl <50 mL/min)
  - Minimal bleeding risk: interruption of DOAC may not be required
- Generally, DOACs are restarted 1-3 days after procedure
  - High bleeding risk: restart DOAC 2-3 days after procedure
  - Low/moderate bleeding risk: restart DOAC 1 day after procedure
  - Minimal bleeding risk: interruption of DOAC may not have been required

Warfarin

- Check INR 7-10 days before procedure
- Hold warfarin for 5 days before procedure if INR 2.0-3.0
- If bleeding risk is high, check INR day of surgery and consider administering vitamin K if INR > 1.5; comanage with surgeon
- Bridging decision based on Thromboembolic Risk of Underlying Condition – See table below
- Restart warfarin
  - High bleeding risk: restart 24-36 hours after procedure
  - Low/moderate bleeding risk: restart 12 hours after procedure
  - Minimal bleeding risk: interruption of warfarin may not have been required
  - Continue bridging therapy, if warranted until INR 2.0

Specific Clinical Scenarios Cont'd

AHA Perioperative Thromboembolism Risk Stratification[54]		Bridging Considerations
Low Thrombosis Risk	< 5%/year risk of Arterial Thromboembolism (ATE) • Bileaflet mechanical aortic valve without AF/AFL and no other risk factors for stroke (i.e., multiple prior strokes/TIAs, prior perioperative stroke, or prior valve thrombosis) • AF/AFL and CHA_2DS_2-VASc score of 1-4 and no prior stroke or TIA (See Appendix A) • Single VTE more than 12 months ago and no other risk factors	No bridging anticoagulation during preoperative interruption
Moderate Thrombosis Risk	5% -10%/year risk of ATE • Bileaflet mechanical aortic valve and one of the following: AF/AFL, prior (≥3 months) stroke/TIA, prior perioperative stroke, or prior valve thrombosis • AF/AFL and CHA_2DS_2-VASc score of 5 or 6 (See Appendix A) • VTE within past 3-12 months • Recurrent VTE • Non-severe coagulopathy/thrombophilic conditions-such as heterozygous factor V Leiden or prothrombin G20210A gene mutation • Active cancer	Bridging or no bridging decision needs to be individualized based on the surgical risk of bleeding (minimal vs low/moderate vs high) and patient risk factors
High Thrombosis Risk	10%/year risk of ATE • Any mechanical mitral valve • Older aortic valve (i.e., caged ball or tilting-disk valve) • Mechanical heart valve and recent (<3 months) stroke or TIA • AF/AFL and CHA_2DS_2-VASc score of ≥7 (See Appendix A) • AF/AFL and CHA_2DS_2-VASc score of 5 or 6 with recent (<3 months) stroke or TIA (See Appendix A) • AF/AFL with rheumatic valvular heart disease • Recent (<3 months) VTE • Recent (<3 months) cardioembolic stroke • Active cancer associated with high VTE risk • LV thrombus within past 3 months • Antiphospholipid antibodies • Severe thrombophilia such as protein C, protein S or antithrombin deficiency, antiphospholipid syndrome, homozygous factor V Leiden or prothrombin G20210A gene mutation, double heterozygous for factor V Leiden and prothrombin G20210A gene mutation, or multiple thrombophilic abnormalities	Consider bridging anticoagulation with LMWH for patients prescribed VKA

For a detailed timeline of the perioperative management of DOACs and VKS, refer to Appendix C.

Specific Clinical Scenarios Cont'd

Antiplatelet Therapy with Anticoagulation[54,55]

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

- Prior AF/AFL on anticoagulation in need of PCI
- Prior VTE on anticoagulation in need of PCI
- Presence of mechanical heart valve already on anticoagulation
- New-onset AF/AFL requiring anticoagulation in a patient already on antiplatelet therapy for CAD
- New or recurrent VTE requiring anticoagulation in a patient already on antiplatelet therapy for CAD

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. In general, the use of "triple therapy" (dual antiplatelet therapy plus anticoagulation) is not recommended for most patients due to an increased risk of bleeding. If triple therapy is needed, a short duration (e.g., no more than 30 days) is recommended. When combined with an anticoagulant, clopidogrel is the recommended antiplatelet agent for most patients. If aspirin is being used, it should be limited to <100 mg daily dosing. In patients taking oral anticoagulants who require PCI, use of clopidogrel without aspirin was associated with significant reduction in bleeding complications and no increase in thrombotic events.

Heparin-Induced Thrombocytopenia[32]

Heparin-induced thrombocytopenia (HIT) can lead to thromboembolic complications, such as PE, ischemic limb necrosis necessitating limb amputation, MI, and stroke.

- In patients with HIT, use nonheparin anticoagulants such as lepirudin, danaparoid, or argatroban, depending on renal function.
- In patients with strongly suspected or confirmed HIT, avoid starting warfarin until platelets have recovered to ≥ 150,000/mcL. If patient is already on warfarin with platelet count < 150,000/mcL, then administer vitamin K
- Specialty consultation is required.

HIT is typically seen in a hospital setting. However, it can occur in any setting where patient is being treated with heparin products. Thrombocytopenia is the most common manifestation of HIT and typically occurs 5 to 10 days after exposure to heparin. HIT should be considered in a patient with new or worsening thrombocytopenia. A detailed review of all possible exposures to heparin products, such as unfractionated heparin or LMWH, should be done. Venous or arterial thrombosis occurs in up to 50% of patients with HIT, who are not treated with a nonheparin anticoagulant. When HIT is suspected, heparin-PF4 antibody testing is recommended. HIT antibodies can be demonstrated in vitro by functional test and immunoassays. One of the most commonly used tests is an Eliza to detect the HIT antibody that binds to the PF4-heparin complex.

Heparin cessation alone is insufficient since patients with HIT remain at risk for subsequent thromboses. Alternative nonheparin anticoagulants should be used.

Specific Clinical Scenarios Cont'd

Treatment plan should include:

1. Immediate/acute management, which usually occurs in the inpatient setting
   a. Stop all heparin exposure. Individuals with suspected or diagnosed HIT should have immediate discontinuation of all sources of heparin, such as unfractionated heparin or LMWH, heparin flushes, heparin exposure during hemodialysis, heparin bound catheters, and heparin containing medications. Clearly document and relay to all individuals, including providers outside of CCHCS, involved in the care of the patient.
   b. Immediate referral to a specialty provider is required and transfer to HLOC should be considered depending on the severity of thrombocytopenia, presence of thrombus, presence of bleeding, and comorbid conditions.
   c. In patients undergoing PCI with HIT, argatroban and bivalirudin are parenteral direct thrombin inhibitors that may be used as acceptable alternative anticoagulants. Argatroban and bivalirudin may also be used as alternative anticoagulants in the setting of acute limb ischemia.
2. Post-acute and long-term management
   a. Choice and duration of anticoagulant is coordinated with specialty co-management. Take into account all factors one needs to consider for anticoagulation.
3. Clear documentation of the management plan
   a. Document cessation including diagnosis, choice of nonheparin anticoagulant, and duration of anticoagulation after evaluation at HLOC or with specialty provider is required.

During the height of the coronavirus pandemic, some providers may have come across vaccine-induced immune thrombotic thrombocytopenia (VITT), also known as Thrombosis with Thrombocytopenia Syndrome (TTS). There are no current national guidelines to date. This is a rare, but serious syndrome associated with vaccination using an adenoviral vector SARS-CoV-2 vaccine. It is crucial that providers are aware of the syndrome, have a high index of suspicion in patients presenting within 4-30 days of receipt of the Janssen coronavirus vaccine, and rapidly refer these patients to HLOC for expeditious diagnosis and treatment.

Diagnosis meets all four criteria:

- Coronavirus vaccine (Janssen/AstraZeneca) in the past 4-30 days
- Venous or arterial thrombosis, often splanchnic or cerebral
- Thrombocytopenia
  - Patient with thrombosis and a normal platelet count post vaccination may be in early stages of VITT.
- Positive PF4 "HIT" (heparin-induced thrombocytopenia) ELISA test

VITT is an evolving disorder. Fondaparinux has been used for VITT treatment, but the use of heparin products to treat VITT is also evolving. Provider should consult FDA/CDC or other sources for frequent updates. Report any thrombotic, or other, suspected vaccine associated adverse events to the Vaccine Adverse Events Reporting System (VAERS) at https://vaers.hhs.gov.

(See Appendix D for more details)

Appendix A

CHA_2DS_2-VASc Scoring Tool

The CHA_2DS_2-VASc score has been shown to improve stratification of ischemic stroke risk among lower-risk individuals who may not be appropriate for anticoagulation therapy.

Condition	Points
Congestive Heart Failure (CHF)	1
Hypertension	1
Age ≥ 75	2
Diabetes Mellitus	1
Stroke or TIA	2
Vascular disease (Coronary Artery Disease, Peripheral Vascular Disease, Aortic plaque)	1
Age 65-74	1
Sex (female)	1
Maximum score = 9	

CHA_2DS_2 VASc Total Score	Adjusted Stroke Rate (At 1 year follow-up)
0	0%
1	1.3%
2	2.2%
3	3.2%
4	4.0%
5	6.7%
6	9.8%
7	9.6%
8	6.7%
9	15.2%

Scoring		
Men	**Women**	**ACC Recommendations**
0	1	No need to treat
1	2	Consider treating
≥ 2	≥ 3	Treat

HAS-BLED Score

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).

	Condition	Points
H	Hypertension	1
A	Abnormal renal/liver function (1 pt each)	1 or 2
S	Stroke	1
B	Bleeding history or Pre-disposition	1
L	Labile INRs	1
E	Elderly	1
D	Current drugs (medication) oralcohol use (1 pt each)	1 or 2
	TOTAL POINTS	

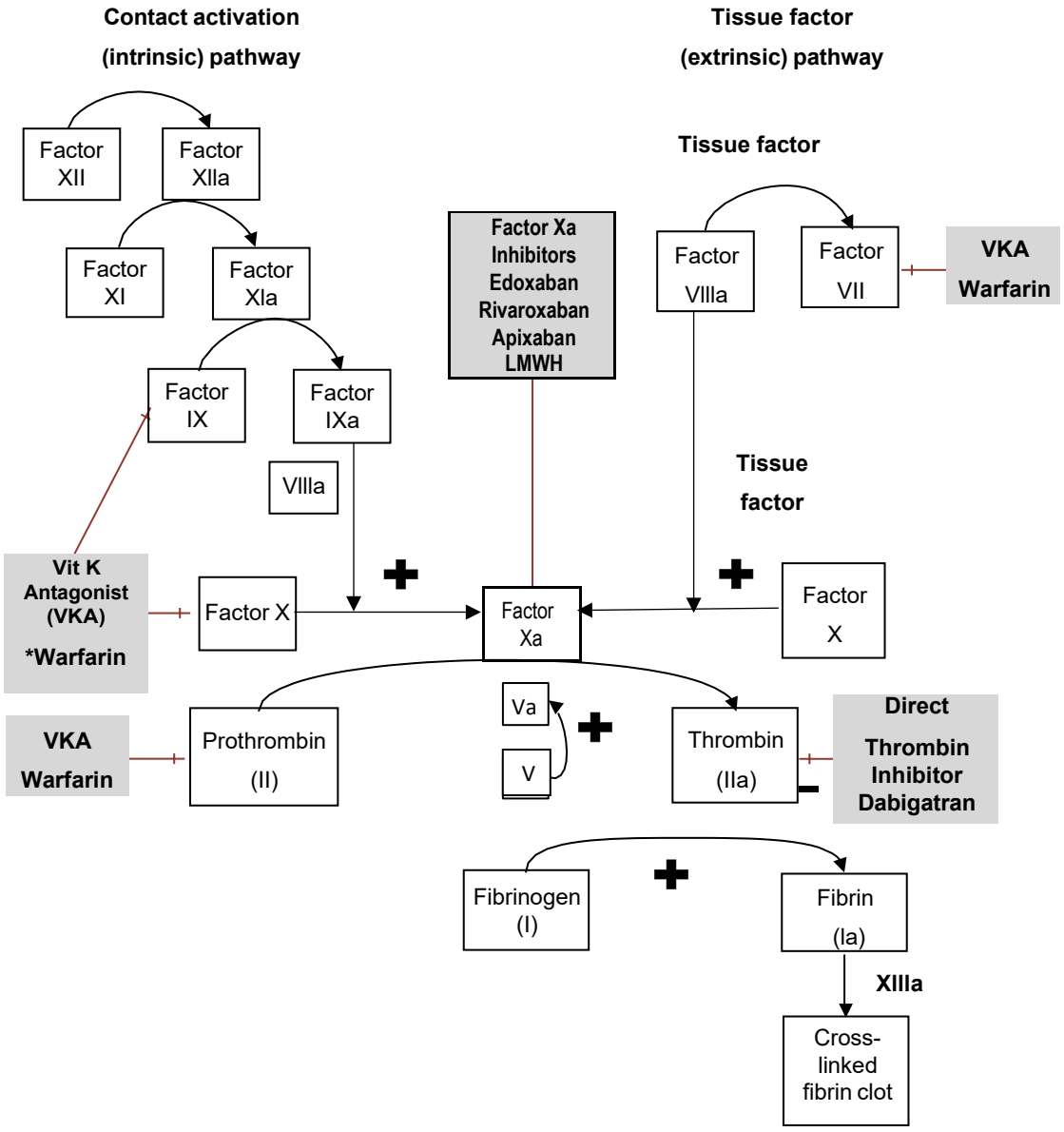
Total Points	Annual Major Bleed Risk %*	Intracranial Bleeds Per 100-pt-yrs	Major Bleed Risk Category
0	1.13		Low
1	1.02		Low
2	1.88	0.6	Moderate
3	3.74	0.7	High
4	8.7	1	High
5	12.5	1.2	High

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

Appendix B

Site of Action for Oral Anticoagulants[1]

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.

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

Appendix C

AHA Perioperative Management of DOACs and VKAs[54]

Perioperative DOAC Schedule												
	Procedure Bleeding Risk	Preoperative Anticoagulation Interruption						Surgery	Postoperative DOAC Resumption			
		Day -6	Day -5	Day -4	Day -3	Day -2	Day -1	Day 0	Day +1	Day +2	Day +3	Day +4
Apixaban, **rivaroxaban**, and edoxaban	High	*	*	*	*	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	*	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Apixaban, **rivaroxaban**, and edoxaban with renal impairment (CrCl <30 mL/min)	High	*	*	*	†	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	†	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Dabigatran CrCl ≥50 mL/min	High	*	*	*	*	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	*	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Dabigatran CrCl <50 mL/min	High	*	*	†	†	†	†	†	†	†	*	*
	Low/Moderate	*	*	*	*	†	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Perioperative VKA Schedule												
	Procedure Bleeding Risk	Preoperative Anticoagulation Interruption						Surgery	Postoperative VKA Resumption			
		Day -6	Day -5	Day -4	Day -3	Day -2	Day -1	Day 0	Day +1	Day +2	Day +3	Day +4
Warfarin in low/moderate thrombotic risk	High	*	†	†	†	†	†	†	*	*	*	*
	Low/Moderate	*	†	†	†	†	†	†	*	*	*	*
	Minimal	*	*	*	*	*	*	*	*	*	*	*
Warfarin in high thrombotic risk	High	*	†	†	‡	‡	‡	†	*	*	* #	* #
	Low/Moderate	*	†	†	‡	‡	‡	†	*	* #	* #	* #
	Minimal	*	*	*	*	*	*	*	*	*	*	*

For optimal management for perioperative bleeding risk and DOAC or VKA schedule, incorporate team-based decision-making, especially in high thrombotic risk patients or when undergoing procedures with higher risks of adverse outcomes, should bleeding occur (e.g., neuraxial anesthesia). Minimal bleeding risk = 30-day risk of major bleeding 0% (e.g., cataract surgery, minor dental/dermatologic procedures). Low/Moderate bleeding risk = 30-day risk of major bleeding <2% (e.g., complex dental, gastrointestinal, breast surgery, procedures using large-bore needles). High bleeding risk = 30-day risk of major bleeding ≥2%.

* *Administer DOAC or VKA*

† *Withhold DOAC or VKA*

‡ *While withholding VKA in select very high thrombotic risk patients, preoperative bridging with parenteral heparin once INR less than desired therapeutic range.*

\# *Resuming postoperative LMWH bridge at either full- or prophylaxis dose until INR within therapeutic range is team-based decision weighting risks and benefits*

Appendix D

Thrombosis with Thrombocytopenia Syndrome (TTS)[25]

Also called Vaccine-induced Thrombotic Thrombocytopenia VITT. This is a rare, but serious syndrome associated with vaccination using an adenoviral vector SarsCoV2 vaccine. It is crucial that providers are aware of this syndrome, have a high index of suspicion in patients presenting within 4-30 days of receipt of the Janssen COVID vaccine, and rapidly refer these patients to higher level of care for expeditious diagnosis and treatment.

Diagnosis (meet all four criteria):

1. COVID vaccine (Janssen/AstraZeneca only to date) 4 to 30 days previously
2. Venous or arterial thrombosis (often cerebral or abdominal)
3. Thrombocytopenia*
4. Positive PF4 "HIT" (heparin-induced thrombocytopenia) ELISA test

Urgent referral to HLOC for medical evaluation for TTS is indicated if any of the following develop 4 to 30 days after vaccination:

- Severe headache (may be Cerebral Venous Sinus Thrombosis)
- Visual changes
- Abdominal pain (splanchnic vein thrombosis has been seen)
- Nausea and vomiting
- Back pain
- Shortness of breath (Can see pulmonary emboli)
- Leg pain or swelling (Can be associated with deep venous thrombosis)
- Petechiae, easy bruising, or bleeding

If TTS is suspected:

Immediately refer to higher level of care for emergent CBC, imaging and other labs.

Initial work-up (a normal platelet count is less concerning for TTS, but does NOT exclude early TTS, maintain suspicion if patient recently vaccinated with Janssen)

- CBC with platelet count and peripheral smear
- Imaging for thrombosis based on signs/symptoms
- PF4-ELISA (HIT assay); draw blood prior to any therapies
- Fibrinogen and D-dimers

Treatment:

- Patient should be managed by a hematologist experienced with coagulation disorders
- High-dose intravenous immune globulin
- Nonheparin anticoagulation
- Avoidance of platelet transfusions unless other treatments have been initiated AND life-threatening bleeding or imminent surgery

NOTE:

TTS is an evolving disorder and provider should consult FDA/CDC or other sources for frequent updates. Report any thrombotic, or other, suspected vaccine associated adverse events to the Vaccine Adverse Events Reporting System (VAERS) at https://vaers.hhs.gov

*A patient who presents with thrombosis and a normal platelet count post-vaccination might be in an early stage of TTS. If clinical S/S are consistent these patients also need to be sent to a higher level of care and be followed closely, and treatment with heparin should be avoided until diagnosis ruled out.

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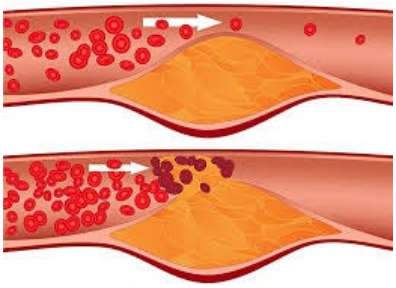
PATIENT EDUCATION/SELF MANAGEMENT

BLOOD CLOTS



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.

Risk for blood clots

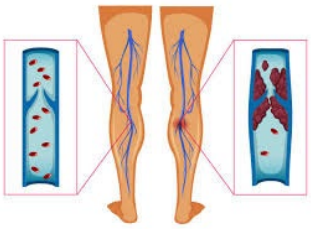
The following factors increase your risk for developing a blood clot:

- 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

Signs of blood clots

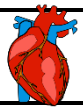
People who may have a blood clot in a vein might feel or see:

- 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



Symptoms of blood clots

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

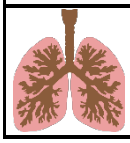
Chest heaviness or pain, shortness of breath, sweating, nausea, lightheadedness

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

PATIENT EDUCATION/SELF MANAGEMENT

TREATING BLOOD CLOTS WITH BLOOD THINNERS

What are blood thinners?

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 on your period; you bleed more than normal.
- Your gums bleed.
- You have a bad headache or stomach pain that does not go away.
- You get sick or feel weak, faint or dizzy.
- You think you are pregnant.
- You often find bruises or blood blisters.
- You have an accident of any kind.
- Please make sure your dentist/medical providers know you are taking blood thinners.
- Please make sure your dentist/medical providers know if your primary doctor has changed your blood thinner medication recently.
- Please make sure your dentist/medical providers know if you have had any excessive bleeding since you began taking blood thinner medication.

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

PATIENT EDUCATION/SELF MANAGEMENT

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, submit a CDCR 7362.

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

PATIENT EDUCATION/SELF MANAGEMENT

BLOODTHINNERS: 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:

1mg	*2mg*	*2.5mg*	*3mg*	*4mg*	*5mg*	*6mg*	*7.5mg*	*10mg*
pink	*light purple*	*green*	*tan*	*blue*	*orange*	*blue-green*	*yellow*	*white*

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.

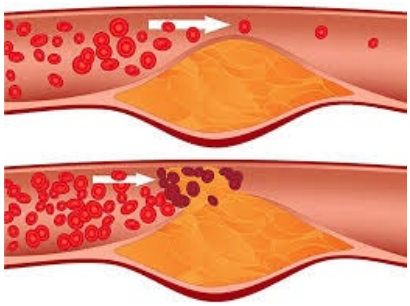
The medicines below can change your INR and increase your risk for bleeding or blood clots:

Aspirin	• Be aware that Alka-Seltzer and Pepto-Bismol contain aspirin. • Avoid using ointments or gels that have aspirin.
Anti-inflammatories	• Includes Ibuprofen (Motrin, Advil), naproxen (Aleve), also known as NSAIDs
Cold medicines and over-the-counter medications	• 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 oranti-inflammatories.
Herbs/Supplements	• 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.

EDUCACIÓN PARA EL PACIENTE/CONTROL PERSONAL DEL CASO

COÁGULOS SANGUÍNEOS

La coagulación de la sangre o coagulación es un proceso importante que evita el sangrado excesivo cuando se lesiona un vaso sanguíneo.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 despuésde 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

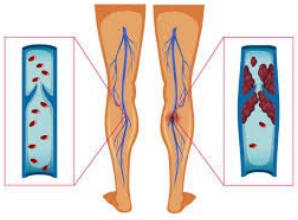
Los siguientes factores aumentan el riesgo de desarrollar un coágulo sanguíneo:

- Obesidad
- Embarazo
- Sentarse en una posición durante largos períodos
- Fumar
- Píldoras anticonceptivas
- Algunos cánceres
- Trauma
- Algunas cirugías
- Edad (especialmente si es mayor de 60 años)
- Historial familiar de coágulos sanguíneos
- Diabetes
- Presión arterial alta
- Colesterol alto

Indicios 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 conocersus 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 cabezarepentino 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 queproduce sangre

EDUCACIÓN PARA EL PACIENTE/CONTROL PERSONALDEL CASO

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 puedeninteractuar con ciertos alimentos, medicamentos, vitaminas y alcohol.

Asegúrese de que su proveedor de atención médica conozca todos los medicamentos y suplementosque 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 hemorragiaintestinal.
- 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.
- Asegúrese de que su dentista y proveedores médicos sepan que está tomando anticoagulantes.
- Asegúrese de que su dentista / proveedores médicos sepan si su médico de cabecera cambió recientemente su medicamento anticoagulante.
- Asegúrese de que su dentista / proveedor médico sepa si ha sangrado excesivamente desde quecomenzó a tomar medicamentos anticoagulantes.

¿Cuándo se usan los anticoagulantes?

Los anticoagulantes se utilizan con una serie de enfermedades cuando hay un mayor riesgo de coágulossanguíneos. 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

EDUCACIÓN PARA EL PACIENTE/CONTROL PERSONAL DEL CASO

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 restode su vida.

¿Cómo debo tomar el medicamento?

Siga siempre las instrucciones del médico o enfermera y tome las píldoras exactamente como selo 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 paratomar o para resurtirlos, envíe una solicitud CDCR 7362.

¿Qué pruebas necesitaré si tomo anticoagulantes?

Depende del tipo de anticoagulante. Un simple análisis de sangre llamado “índice internacionalnormalizado” (internacional normalized ratio, INR) debe hacerse regularmente cuando se toma warfarina. Su médico ajustará su dosis para llegar a un cierto “INR.”

Cuando 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 cuandoestoy 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 deventa 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 cuandose 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 alquitrán
- 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

EDUCACIÓN PARA EL PACIENTE/CONTROL PERSONALDEL CASO

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 deCorreccionales y Rehabilitación de California (CDCR) utiliza:

1 mg	*2 mg*	*2.5 mg*	*3 mg*	*4 mg*	*5 mg*	*6 mg*	*7.5 mg*	*10 mg*
rosa	*lila*	*verde*	*tan*	*azul*	*naranja*	*verde*	*Amarillo*	*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 seanecesario reducir su dosis de warfarina
- ***Si su número de INR es demasiado bajo***: podrían formarse coágulos, por lo que podría sernecesario 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 verdurasde hoja verde oscura).
- El té verde, la margarina, la mayonesa y muchos aceites (canola, soya, oliva) también pueden afectar sus nivelesde INR.
- No beba alcohol manufacturado en la prisión (Pruno), que puede causar graves efectos secundarios con lawarfarina.
- Hágale saber a su proveedor si está en ayunas o en huelga de hambre, esto puede afectar su nivel demedicamento.
- 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 for-men 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 esteroideos (AINEs)
Medicamentos parael 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 conteneraspirina 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, hierbade San Juan, cúrcuma.