LOS ANGELES COUNTY DEPARTMENT OF HEALTH SERVICES
HARBOR-UCLA MEDICAL CENTER

SUBJECT: WARFARIN PER PHARMACY PROTOCOL (ADULT INPATIENT) **POLICY NO.** 325T

CATEGORY: Provision of Care	**EFFECTIVE DATE:** 6/19
POLICY CONTACT: Jennie Ung, PharmD	**UPDATE/REVISION DATE:**
REVIEWED BY COMMITTEE(S):	

PURPOSE:
To provide guidelines for the appropriate dosing of warfarin in adult inpatients to optimize therapy and reduce potential for toxicity.

ABBREVIATIONS:
ACS = Acute coronary syndrome
AF or AFib = Atrial fibrillation
aPTT = Activated partial-thromboplastin time
CBC = Complete blood count
CrCl = Creatinine clearance
DOAC = Direct oral anticoagulant
DTI = Direct thrombin inhibitor
DVT = Deep venous thrombosis
ED = Emergency Department
eHR = Electronic Health Record
HIT = Heparin-induced thrombocytopenia
HITT = Heparin-induced thrombocytopenia and thrombosis
HUMC = Harbor-UCLA Medical Center
INR = International Normalized Ratio
IV = Intravenous
LFT = Liver function test
LMWH = Low molecular weight heparin
NSTEMI = Non-ST-Elevation Myocardial Infarction
PE = Pulmonary embolism
PT = Prothrombin time
RN = Registered Nurse
SQ = Subcutaneous
tPA = Tissue Plasminogen Activator
UFH = Unfractionated heparin
VTE = Venous thromboembolic

NOTE—unless otherwise specified:
Anti-Xa = Anti-Xa, UFH (not the same as Anti-Xa for LMWH)
“Heparin” = unfractionated heparin

POLICY:
Upon authorization of a provider, the pharmacists at Harbor-UCLA Medical Center will monitor and adjust warfarin therapy for adult inpatients on warfarin therapy. The adjustment will be made automatically according to the medical staff-approved warfarin protocol.

REVISED:
REVIEWED: 6/22

APPROVED BY:

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PROCEDURE:

Provider Procedures:

1. Provider orders "Warfarin Per Pharmacy" in eHR.
2. Provider shall document the indication, goal INR, and duration of therapy.
3. Provider contact information shall be documented in the electronic health record for nursing and pharmacy to contact for clarification if needed.
4. Initial warfarin dose will be determined by pharmacist.
5. Provider orders baseline tests (unless tests performed within 24 hours prior to warfarin initiation), including:
   a. CBC
   b. PT/ INR, aPTT, LFT, and BUN/SCr
   c. Baseline tests do not need to be repeated if performed within 24 hours prior to warfarin initiation.
6. Provider and pharmacist are responsible to review the results of baseline labs (e.g., CBC, PT/INR, aPTT, anti-Xa) when available.
7. Provider discontinues all other prophylactic or therapeutic anticoagulants except argatroban, LMWH, or IV UFH bridging therapy.

Pharmacy Procedures:

1. Pharmacist reviews the following for appropriateness:
   a. Warfarin indication, INR goal, and duration of therapy (entered by ordering provider) (see **Appendix A** for guidelines)
   b. Warfarin dosing regimen prior to admission (if on warfarin therapy prior to admission)
   c. Past and current medical history
   d. Potential contraindications (i.e., allergies, pregnancy, etc.) (**Appendix B**)
   e. Potential conditions that can increase INR response or bleeding risk (**Appendix C**)
   f. Current medications for potential drug-drug interactions (**Appendix D**) or drug-herbal/food interactions (**Appendix E**). Pharmacist may contact provider to discontinue as needed (PRN) orders for aspirin, salicylates, non-steroidal anti-inflammatory agents.
   g. Pharmacist will contact ordering provider for clarification with any anticoagulation-related concerns (i.e., potential contraindication, and/or warfarin sensitivity, drug-drug interactions).
2. Pharmacist may order the following blood tests prior to starting warfarin therapy, if not previously ordered by provider:
   a. Baseline CBC, PT/INR, aPTT, BUN, SCr, and LFT
   b. Daily CBC and PT/INR while on warfarin therapy
   c. Twice weekly BUN and SCr while on warfarin therapy
3. Review of laboratory results:
   a. Prior to dispensing initial warfarin, pharmacist will review any *available* results for CBC, PT/INR, aPTT, and anti-Xa. Pharmacist will notify provider if:
      1) INR ≥ 4.0
      2) Platelet count drops by > 50% or platelet count < 100,000 mm^3
      3) PT or aPTT > 1.5 x upper level of normal
      4) Anti-Xa > 0.30 IU/mL (for patient NOT on heparin continuous infusion therapy)
   b. While warfarin therapy is ongoing, pharmacist will review available values for CBC and INR daily. Pharmacist will notify provider if:
      1) INR ≥ 4.0
      2) Platelet count drops by > 50% or platelet count < 100,000 mm^3
      3) Anti-Xa > 0.30 IU/mL (for patient NOT on heparin continuous infusion therapy)

4. Pharmacist will discontinue other parenteral and oral anticoagulants if not discontinued by the provider, with the exception of bridge therapy. The discontinued order will be entered into the electronic health record (eHR) as "Cosign required" to notify provider of change.
5. Pharmacist will initiate, adjust warfarin doses and order PT/INR daily according to protocol (**Appendix F**).
6. Warfarin will be dispensed from the pharmacy ONLY after pharmacist reviews daily PT/INR result.
7. Details of dosage are automatically captured in the order information.
8. Pharmacist will initiate warfarin monitoring form.
9. Pharmacist will document initial warfarin consult note in eHR including indication of therapy, INR goal, and dose prior to admission (if applicable), baseline CBC, PT/INR, aPTT, BUN, SCr, and LFT, initial dose and other factors such as possible drug-drug interactions, patient compliance, and diet.
10. Pharmacist will document subsequent notes in eHR for any changes in warfarin dose, possible drug-drug and drug-food interactions, warfarin therapy withholding, and other factors that may impact warfarin therapy or any communication with provider regarding warfarin therapy.
11. Pharmacist will educate patient and/or patient's family member on warfarin therapy by reviewing:
    a. Indication for and desired therapeutic INR range
    b. Risks and benefits of anticoagulation therapy
    c. How and when to take warfarin and importance of compliance
    d. How to handle missed warfarin doses
    e. Drug-drug interactions (**Appendix D**)
    f. Drug-food interactions (**Appendix E**)
    g. Precautions and adverse drug reactions:
        1) Signs and symptoms of bleeding and thrombosis
        2) Physical activity precautions
    h. How to notify clinic/dentist of health status/medication changes
    i. When to seek emergency medical treatment
    j. Pharmacist will document in eHR that education has been completed.
12. Pharmacist will alert provider when two consecutive therapeutic INRs are achieved if patient also on bridge therapy with LMWH or UFH infusion for minimum of five days.
13. Pharmacist to contact provider if INR falls below 1.7 to see if bridging therapy is needed in patients who have moderate to high thrombotic risk (**HUMC Policy #325-S: Anticoagulation Management Guidelines**) until INR ≥ 2 (or 2.5 if indicated).
14. Pharmacist will contact provider to discuss for any warfarin reversal if needed (**HUMC Policy #325-S: Anticoagulation Management Guidelines**).
15. See **HUMC Policy #325-S (Anticoagulation Management Guidelines)** for general perioperative management of patients receiving warfarin scheduled for surgeries.
16. See **HUMC Policy #325-S (Anticoagulation Management Guidelines)** for thrombotic risk stratification for patients on warfarin.

Nursing Procedures

1. Review of laboratory results:
    a. Prior to administering warfarin, nurse will review any *available* results for CBC, INR, aPTT, and Anti-Xa. Nurse will notify provider if:
        1) INR ≥ 4.0
        2) Platelet count drops by > 50% or platelet count < 100,000 mm^3
        3) PT or aPTT > 1.5 x upper level of normal
        4) Anti-Xa > 0.30 IU/mL (for patient NOT on heparin continuous infusion therapy)
    b. Nurse will review available values for CBC and INR on a **daily** basis. Nurse will notify provider if:

   1) INR ≥ 4.0
   2) Platelets < 100,000 mm^3
2. Critical INR results:
   a. Critically high INR (≥4) values will be reported according to HUMC's facility policy for notification of critical results **(HUMC Policy #393B: Notification of Critical Diagnostic Results)**.
3. The nurse will draw any "stat" or "timed-stat" orders related to warfarin therapy.
4. Administer daily dose at 18:00, unless ordered otherwise.
5. Required documentation: Nurse will document warfarin administration on Medication Administration Record (MAR).
6. Monitoring: Assess and document signs and symptoms of bleeding, hypersensitivity reactions or exacerbation of thromboembolic disorder. Notify provider and pharmacy if/when abnormal.

Special Situations:

1. Deviation from protocol:
   The pharmacist shall NOT accept any deviation from the approved protocols. If the provider determines, according to clinical judgment, that it would be beneficial to deviate from the approved protocols, the pharmacist must sign off.
   a. Pharmacist must communicate to provider prior to signing off, and document the name of provider along with reason for deviation.
   b. After communicating to provider, pharmacist shall discontinue the "Warfarin Dosing per Pharmacy" entry.
   c. Pharmacist must verbally notify the nurse to obtain further warfarin orders from the provider.
2. Need to hold and/or reverse warfarin for urgent procedure, surgery, or bleeding:
   a. When provider decides to hold warfarin for a planned procedure/surgery, provider will discontinue the warfarin order and communicate with pharmacist to determine if bridging therapy is needed (**HUMC Policy #325-S: Anticoagulation Management Guidelines Appendix F**).
   b. Provider may discontinue warfarin order if patient has signs and symptoms of bleeding. Provider will contact pharmacist to discuss warfarin reversal if needed (**HUMC Policy #325-S: Anticoagulation Management Guidelines Appendix E**).
3. Discontinuation of warfarin:
   a. When provider determines that warfarin therapy is no longer clinically indicated, provider will discontinue warfarin order.
   b. Provider will discontinue "Warfarin Dosing per Pharmacy" orderable.

Reviewed and approved by:
Medical Executive Committee 06/2022

Beverley A. Petrie

Beverley A. Petrie, M.D.
President, Professional Staff Association

APPENDIX A: Warfarin Indication, INR Goals, and Duration of Treatment GUIDELINES

Indication	INR	Duration	Comment
ATRIAL FIBRILLATION (AF)/ATRIAL FLUTTER (AFL)			
CHA_2DS_2VASc*=0 in male or 1 in female (Low stroke risk)	None		Use aspirin 81 – 325 mg daily alone
CHA_2DS_2VASc*≥1 in male or ≥ 2 in female (Intermediate /High stroke risk)	2-3	Chronic	
Following open heart surgery (in NSR)	2-3	4 weeks	
Pre-cardioversion (AF or AFL > 48 hours or unknown duration)	2-3	3 weeks	Or TEE with abbreviated therapeutic anticoagulation# before cardioversion
Post-cardioversion (in NSR)	2-3	4 weeks	
ISCHEMIC STROKE			
Non-cardioembolic stroke or TIA	None		Use antiplatelet therapy
Cardioembolic stroke or TIA			
• With contraindications to warfarin	None		Use aspirin 81 – 325 mg daily
• Associated with aortic atherosclerotic lesions	None		Use antiplatelet therapy
• Associated with mobile aortic arch thrombi	2-3	Chronic	Or antiplatelet therapy
• Associated with patent foramen ovale	None		Use antiplatelet therapy
MYOCARDIAL INFARCTION (MI)			
Anterior MI and LV thrombus, or at high risk for LV thrombus (EF<40%, anteroapical wall motion abnormality) **who do not undergo stenting**	2-3	At least 3 months	And aspirin 81 mg daily for first 3 months After 3 months, continue DAPT for up to 12months
Anterior MI and LV thrombus, or at high risk for LV thrombus (EF<40%, anteroapical wall motion abnormality) **who undergo bare-metal stent placement**	2-3	At least 3 months	Triple therapy (Warfarin +DAPT) for 1 month then Warfarin + SAPT for 2nd and 3rd month. After 3 months, continue DAPT for up to 12months
Anterior MI and LV thrombus, or at high risk for LV thrombus (EF<40%, anteroapical wall motion abnormality) **who undergo drug-eluting stent placement**	2-3	3-6 months	Triple therapy (Warfarin +DAPT) for 3 to 6 months. Thereafter, continue DAPT for up to 12months
THROMBOEMBOLISM (DVT, PE) (with concurrent UFH/LMWH for at least 5 days and until INR > 2 for ≥ 24 hrs)			
Provoked (Transient risk factors)	2-3	3 months	
Unprovoked: 1st event	2-3	3 months	After 3months, evaluate risk-benefit for extended therapy
Unprovoked: 2nd event	2-3	Chronic	
With malignancy	2-3	Chronic	LMWH preferred over warfarin
Acute extremity DVT associated with central venous catheter that was removed	2-3	3 months	
Acute extremity DVT associated with central venous catheter that was NOT removed	2-3	until catheter removed	
Chronic thromboembolic pulmonary hypertension	2-3	Chronic	
Cerebral venous sinus thrombosis	2-3	Up to 12 months	
Spontaneous superficial vein thrombosis	2-3	4 weeks	Or prophylactic LMWH X 4 weeks

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Indication	INR	Duration	Comment
VALVULAR DISEASE			
Rheumatic mitral valve disease and normal sinus rhythm			
• Left atrial diameter <55mm	None		
• With AF, previous systemic embolism, left atrial thrombus or left atrial diameter > 55mm	2-3	Chronic	
VALVE REPLACEMENT - BIOPROSTHETIC			
Aortic or TAVI	None		Aspirin 81 mg daily alone
Mitral	2-3	3 months	Followed by aspirin 81 mg daily
VALVE REPLACEMENT – MECHANICAL			
Aortic	2-3	Chronic	Add aspirin 81 mg daily if low bleed risk
Mitral	2.5–3.5	Chronic	Add aspirin 81 mg daily if low
Dual Aortic and Mitral valve	2.5–3.5	Chronic	Add aspirin 81 mg daily if low bleed risk
With systemic embolism despite adequate anticoagulation	Increase INR goal	Chronic	Or add aspirin 81 mg daily

* CHA_2DS_2VASc: **C**=Congestive heart failure-1point; **H**=Hypertension-1point; **A_2**≥75-2 points; **D**=Diabete-1point; **S_2**=Stroke/TIA/TE-2 points; **V=**Vascular disease [prior MI, PAD, or aortic plaque]-1 point; A=Age (65-74); **S**=Sex (female-1 point, male-0 point), c=categories
# abbreviated therapeutic AC: LMWH or UFH at full VTE treatment dose started at the time of TEE and cardioversion performed within 24 h of the TEE if no thrombus seen or warfarin with INR 2-3/NOAC started 5 days before cardioversion
TAVI: Transcatheter Aortic bioprosthetic Valve Implantation

APPENDIX B: Potential Contraindication to Warfarin Therapy

- Hypersensitivity to warfarin
- Blood dyscrasias (prone to bleeding)
- Recent or planned neuro, ocular, or traumatic surgery resulting in large open surfaces
- Overt bleeding or active ulcerations
- Current or recent cerebrovascular hemorrhage
- Threaten abortion, eclampsia, or preeclamsia
- Spinal puncture
- 1st Trimester of Pregnancy (esp. week 6-12)
- 2nd and 3rd Trimester of Pregnancy (relative)
- Senility (relative)
- Alcoholism (relative)
- Poor patient reliability/compliance (relative)

APPENDIX C: Conditions that may increase INR response or increase risk of bleeding

Increased INR Response	Increased Bleeding Risk
Baseline INR ≥ 1.5 Age > 65 Actual BW < 45 kg or Actual BW<IBW Malnourished/NPO > 3 days Hypoalbuminemia <3.5 g/dL Chronic diarrhea Significant drug interactions Decompensated heart failure Asian race (Filipino) Malignancy	Concurrent antiplatelet therapy Thrombocytopenia: Platelet < 75K/uL Significant hepatic disease: cirrhosis or total bilirubin >2.4 mg/dL Alcohol abuse history ESRD GI bleed within past 30 days Surgery within past 2 weeks Intracranial bleed within past 30 days

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APPENDIX D: Clinical Significant Drug Interactions with Warfarin

1. Most drug interactions with warfarin will start to have an effect within 3-5 days of concomitant therapy. A total weekly warfarin dose adjustment of either an increase or decrease by 30% may be needed.
2. There are some notable exceptions, including **amiodarone**, **carbamazepine**, and **rifampin** that will start to have an effect within 7-14 days of dual therapy.
   - A total weekly warfarin dose **decrease** of 50% may be needed if patient is on **amiodarone** concomitantly
   - A total weekly warfarin dose **increase** of 50% may be needed if patient is on **rifampin** concomitantly
3. This list is not all inclusive. Reliable references such as Micromedex, Lexi-Comp must be consulted for complete drug interaction information.

Clinical Significant Drug-Drug Interactions			
Increase Bleeding Risk	**Enhance Warfarin Effect**		**Decrease Warfarin Effect**
Adrenal corticosteroids	Alcohol (acute)	**Fenofibrate**	Aluminum hydroxide
Antimetabolites	Allopurinol	**Fluorouracil**	Barbiturates
Antiplatelets	**Amiodarone**	**Fluoxetine**	Bonsetan
Aspirin containing products	**Anabolic steroids**	**Fluvoxamine**	Carbamazepine
Cephalosporin	**Anti-infectives (especially, fluoroquinolones, metronidazole, sulfamethoxazole/Trimethoprim)**	Gemfibrozil	Cholestyramine
Gemcitabine		Isoniazid	Dicloxacillin
NSAIDS		Levothyroxine	Estrogens
Penicillin, parenteral		**Methotrexate**	Griseofulvin
Quinidine	**Azole Antifungals**	**Paroxetine**	Mesalamine
Quinine	**Capecitabine**	**Procarbazine**	Nafcillin
Tamoxifen	**Carboplatin**	Propafenone	Oral contraceptives
	Celecoxib	Proton pump inhibitors	Phenobarbital
	Chloral hydrate		**Phenytoin**
	Citalopram	Protease inhibitors	Ribavirin
	Clofibrate	**Ropinirole**	Rifabutin
	Cyclophosphamide	**Sertraline**	**Rifampin**
	Diazoxide	**Statins**	Ritonavir
	Diltiazem	**Sulfisoxazole**	Sucralfate
	Disulfiram	Sulfonamide	Vitamin K
	Doxorubicin	Sulfonylurea	
	Escitalopram	**Tamoxifen**	
	Ethacrynic acid	**Venlafaxine**	
	Etoposide	**Vincristine**	

*Major drug interaction with warfarin in **bold** letters

APPENDIX E: Clinical Significant Herbal and Food Interactions

Dietary Interactions

- Patients on long term warfarin therapy can be sensitive to the fluctuating levels of vitamin K from both external dietary sources and internal gastrointestinal sources. Increased dietary intake of vitamin K from either food sources or nutritional supplement sources can reduce the effectiveness of warfarin and decreased the INR.
- Since warfarin is a high protein bound drug with up to 99% of the drug bound to plasma proteins, patients who are malnourished with low albumin levels will have higher concentrations of unbound drug and may experience faster INR response.
  Conversely, patients receiving enteral nutrition will have more bound drug due to the high protein concentration in these products.
- Promote consistent intake of dietary vitamin K and not avoidance.
- For enteral nutrition, hold the tube feed 1 hour before and 1 hour after warfarin administration.
  - If unable to hold enteral nutrition, increase warfarin dose until a therapeutic INR is achieved.
  - If on cycled tube feeding, administer warfarin at a time when tube feeds are off.

Clinical Significant Herbal and Food Interactions	
Increased Effect of Warfarin	**Decreased Effect of Warfarin**
Alcohol (acute ingestion) Cranberry juice Dong Quai Danshen Evening primrose oil Fenugreek Ginko Glucosamine Grapefruit Licorice Omega-3 fatty Acids Willow bark	Alcohol (chronic daily alcohol consumption) Co-Enzyme Q10 Ginseng Goldenseal Green tea St. John's Wort Yarrow **Foods**- avocado, asparagus, canola oil, soybean oil, mayonnaise, green leafy vegetables (spinach, kale, chard, cabbage, romaine lettuce, mustard greens, bok choy, broccoli, brussel sprouts, green beans, green onions, green peppers)

APPENDIX F: Adult Warfarin Dosing Protocol

Initial Dose Determination in Warfarin Naïve

1. Initial dosing should be tailored upon patient bleed risk, potential sensitivity to warfarin, indication with goal INR range, and potential drug interactions.
2. Initial dose is 5mg for all patients, however, dosage less than 5mg must be consider for the following:
   - Age over 60 years
   - Weight less than 45kg
   - Asian ethnicity (Filipino)
   - Suspected or documented AKI, ESRD, CHF or liver disease
   - Recent major surgery or high risk of bleeding
   - Malnourished or NPO for more than 3 days
   - Significant drug interaction that will increase warfarin effect

Note: pharmacist to document rationale for not reducing initial dose to < 5mg if patient met 1 or more criteria above.

3. During Heparin/LMWH and warfarin overlap, start warfarin therapy on day 1 or 2 of bridging for improved outcomes in patients with acute VTE.
4. **These are dosage guidelines and the pharmacist should always incorporate clinical judgment into the guidelines to determine appropriate dose for patient.**
5. There is no maximum dose which can be ordered. If patient apparently fail to respond to conventional dosing, the case should be discussed with providers/consultants and more aggressive plan decided upon and documented.

Initial Dose in Warfarin Naïve (Loading dose of warfarin is NOT recommended)

Day	INR	Dose (mg)
1	≤ 1.5 1.6 to 2 > 2	2.5-5 1-2.5 Recommend no dosage
2	< 1.5	2.5-5
	1.5-1.9	2.5
	2-2.5	1-2.5
	> 2.5	0
3	< 1.5	5-10
	1.5-1.9	2.5-5
	2-3	0-2.5
	> 3	0
4	< 1.5	10
	1.5-1.9	5-7.5
	2-3	0-5
	> 3	0
5	< 1.5	10
	1.5-1.9	7.5-10
	2-3	0-5
	> 3	0

6	< 1.5	7.5-12.5
	1.5-1.9	5-10
	2-3	0-7.5
	> 3	0

Maintenance: Beyond 6 days of therapy initiation or Continuation of therapy

1. If patient was maintained on warfarin prior to admission and INR is within therapeutic range, evaluate patient for any changes in co-morbidity (i.e., CHF, liver disease), warfarin sensitivity, warfarin clearance or potential drug interactions.
   - If there are no changes, continue same dose and monitor patient daily
   - If there are changes, evaluate patient for a dosage change and try to identify reason for current INR value
2. Warfarin should be adjusted based on current INR measurements. Prior to making dose adjustment, address for any missed doses, drug interactions, diet changes, documentation of bleeding, or other changes that may affect INR.
3. Previously stabilized warfarin patients often have elevated INRs when admitted with decompensated heart failure. This often requires holding or reducing warfarin dose by ~50% for 1-2 days after admission, but as they get diuresis and improve, they often require their previous warfarin dose
4. **These are just dosage guidelines and the pharmacist should always incorporate their clinical judgment into the guideline to determine appropriate dose for the patient.**

INR 2-3	**Dose Adjustment**	**INR 2.5-3.5**
< 1.5	• Consider booster dose (1.5-2 times daily maintenance dose) • Consider resumption of prior maintenance dose if factor causing decreased INR is transient, (i.e., missed warfarin doses) • If dosage adjustment is needed, increase maintenance dose by 10%-20% weekly dose	< 2
1.5-1.7	• Consider booster dose (1.5-2 times daily maintenance dose) • Consider resumption of prior maintenance dose if factor causing decreased INR is transient, (i.e., missed warfarin doses) • If dosage adjustment is needed, increase maintenance dose by 5%-15% weekly dose	2-3
1.8-1.9	• No dosage adjustment may be necessary if the last two INR values are in range • Consider booster dose (1.5 times daily maintenance dose) • Consider resumption of prior maintenance dose if factor causing decreased INR is transient, (i.e., missed warfarin doses) • If dosage adjustment is needed, increase maintenance dose by 5%-10% weekly dose	2.3-2.4
2-3	**Desired range—no dosing adjustment needed**	**2.5-3.5**
3.1-3.2	• No dosage adjustment may be necessary if the last two INR values are in range • Consider resumption of prior maintenance dose if factor causing increased INR is transient, (i.e., acute alcohol ingestion) • If dosage adjustment is needed, decrease maintenance dose by 5%-10% weekly dose	3.6-3.7

3.3-3.4	• Consider holding ½-1 dose • Consider resumption of prior maintenance dose if factor causing increased INR is transient, (i.e., acute alcohol ingestion) • If dosage adjustment is needed, decrease maintenance dose by 5%-10% weekly dose	3.8-3.9
3.5-3.9	• Consider holding 1 dose • Consider resumption of prior maintenance dose if factor causing increased INR is transient, (i.e., acute alcohol ingestion) • If dosage adjustment is needed, decrease maintenance dose by 5%-15% weekly dose	4-4.4
≥ 4	• Hold warfarin until INR is below upper limit of therapeutic range • Consult provider if warfarin reversal may be indicated	≥ 4.5

Estimated maintenance dose of warfarin:

When the INR is in range for 2 consecutive days, calculate the average dose given, including all doses given (up to 2 weeks), to estimate the maintenance dose:

$$\text{Estimated Maintenance Dose} = \frac{\text{(Sum of All Doses Given in Past 2 weeks)}}{\text{(Total Number of Days since 1st dose)}}$$

Guide to warfarin overlap therapy

- When patients require urgent therapeutic anticoagulation, warfarin should be initiated in combination with a parenteral anticoagulant (such as LMWH or heparin). This is referred to as “overlap” therapy.
- During overlap therapy, coverage with a parenteral anticoagulant should be continued at least 5 days and until the INR is at goal for 24 hours.
  - Overlap therapy recommended for acute DVT/PE, acute cardiac thrombus, protein C or S deficiency.
  - Overlap therapy usually not indicated for non-valvular AF.
- Overlap therapy differs from perioperative bridging therapy (which refers to the use of parenteral anticoagulants during a temporary interruption of warfarin). Refer to **HUMC Policy #325-S: Anticoagulation Management Guidelines** for additional guidance.
- Overlap therapy does not apply to initiation of other non-VKA oral anticoagulants.