

**D.31 VA WESTERN NEW YORK HEALTHCARE SYSTEM OUTPATIENT ANTICOAGULATION
PROGRAM POLICIES AND PROCEDURES (7.2017)**

**VA Western NY Healthcare System
Outpatient Anticoagulation Program
Policies and Procedures 7.2017**

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Clinic purpose, structure, and policy

CLINIC PURPOSE:

The purpose of the Anticoagulation Clinic (ACC or AC clinic) is to provide continuous outpatient monitoring and management for patients on long-term anticoagulant therapy, with the goal of maximizing benefits of therapy while minimizing any untoward risks. The ACC is structured based on a collaborative agreement with the referring provider. As such, the ACC staff will be responsible for routine and continuous management of fta patient's anticoagulant therapy, in accordance with the most current American College of Chest Physician guidelines and or Anticoagulation Forum or PBM Guidance. ACC staff can make recommendations for initiation or discontinuation of warfarin or injectable anticoagulants, but the referring provider is ultimately responsible for initiation / termination of anticoagulation as well as the patient's overall medical management. The Direct Oral AntiCoaguants (DOACs) will only be initiated by and followed by the Anticoagulation Clinic after review of the referral. In urgent situations, other anticoagulants such as warfarin and low molecular weight (LMWH) heparin are available. Patients enrolled in the ACC must continue to receive medical follow-up by a primary provider or specialty provider at a minimum of every twelve months in order to maintain good standing.

CLINIC PERSONNEL & SCOPE OF PRACTICE:

The ACC staff is comprised of both Clinical Pharmacists, Registered (or Licensed Practical) Nurses, and pharmacy technicians (where assigned) with a designated VAWNYHS Anticoagulant Therapy Program Coordinator and physician support staff for inter-current anticoagulant-related problems.

- ✓ VAWNYHS Anticoagulant Therapy Program Director: Kenneth Kellick, Pharm.D.
- ✓ Anticoagulation Physician Director: Deborah Farolino, MD
- ✓ Clinical Pharmacist- As assigned
- ✓ Nurse- As assigned

The Clinical Pharmacist:

The clinical pharmacist must have a current pharmacy license in a state, must have successfully completed the designated training session within the ACC, and must be able to function as an independent clinician in the ACC.

The Clinical Pharmacist will provide initial and longitudinal patient education, will conduct patient interviews, monitor a patient's INR (International Normalized Ratio) and adjust a patient's warfarin dose with the intent to achieve/maintain therapeutic levels for those patients with INRs that are out of their target range or those patients deemed "unstable", he/she will assess bleeding or thromboembolic complications, will screen for any pertinent changes in medications/diet/health to determine potential interactions, will enter warfarin / enoxaparin prescriptions in CPRS, will establish return visit intervals, will monitor for adverse events, will oversee anticoagulant and non-anticoagulant related problems and refer to alternate medical staff as appropriate, will provide training to new pharmacists, pharmacy residents and students in a structured and approved format.

The Clinical Pharmacist will maintain competency by completing

- 1) PBM TMS Advanced Anticoagulation course, required
- 2) At least: One Hour annually of ACPE accredited anticoagulation education.
- 3) Ongoing OPPE

The Clinical Pharmacist will review the clinic nurse's patient dosing letters for appropriateness using the CPRS Anticoagulation Management Tool flowsheet. This will ensure that an appropriate follow-up lab date and laboratory order has been entered, and will print the completed dosing letter on designated VA letterhead to the printer assigned to the clinic MSA (Buffalo Only). In Batavia the clinical pharmacist will print and mail the letters.

The Pharmacist-in-Training and the Pharmacy Resident:

The pharmacist-in-training and the pharmacy resident will assist trained clinical pharmacist(s) in managing anticoagulation therapy in patients managed by the AC clinic when assigned, and in a structured and supervised fashion. All pharmacy resident care plans must be approved by a licensed and trained clinical pharmacist in the AC clinic. No pharmacist or resident that is undergoing training will be left unsupervised.

The Registered or Licensed Practical Nurse (RN or LPN):

The Registered or Licensed Practical Nurse must have a current nursing license in a state, must have successfully completed the designated training session in the ACC, and must be able to function as an active support staff member in the ACC.

The clinic nurse will conduct patient education regarding warfarin therapy, will provide education and proper administration technique of enoxaparin injections, will obtain vital signs for clinic patients as appropriate, will contact new referral patients to schedule initial appointments, will complete consults, and will assist the MSA in rescheduling patients who cancel or fail to report to their ACC appointment. The clinic nurse will perform patient interviews to those patients already maintained on warfarin for at least 3 months and deemed "stable; for this AC clinic's purposes, a "stable" INR is one within the designated target range and which has been generally therapeutic in the past, with the most recent INR having been within 0.2 (above or below) the target range and drawn at least 14 days prior. The three month assessment of stability may be shortened at the discretion of the clinical pharmacist. Clinical judgment can be used to determine stability, and consultation with a Clinical Pharmacist should occur when possible complications or concerns for instability arise. The clinic nurse may extend the patient's followup interval when there have been 3 within range INR's within 3 months and no complications. Extended INR interval may be up to 42 days.

The Clinic RN or LPN will attend to other pertinent clinical details including faxing,, special travel will be completed by the nurse as appropriate for this specific patient.

The Clinic Nurse will maintain competency by completing

- 1) PBM TMS Advanced Anticoagulation course, required
- 2) Recommended: One Hour bi-annually of ACPE accredited anticoagulation education.
- 3) Ongoing progress note review

The Medical Support Assistant (MSA)-Buffalo Only:

The MSA will perform miscellaneous tasks as assigned, not limited to collecting and tally all patient dosing letters to ensure that all have been printed, then will fold and stuff these letters in VA envelopes; the stuffed envelopes will then be transferred to mailroom staff to be mailed to each patient, rescheduling no show patients. The MSA will alert designated clinic staff of the arrival of a scheduled clinic patient, and will also alert clinic staff in the event of a walk-in

patient. The MSA will answer the main ACC phone and triage calls as appropriate. The MSA will send facsimiles as requested by clinic staff, and perform other clerical duties as warranted.

CLINIC HOURS AND SCHEDULING DETAILS

The Buffalo ACC will be staffed with at least 2.5 Clinical Pharmacists, at least 2 Nurses, and a MSA during normal hours of operation, which are Monday through Friday 8:00am to 4:00pm. All federal holidays are excluded. New patients are scheduled for Friday Group Classes.

All clinic charting will be done utilizing the VA Anticoagulation Management Tool (AMT) via CPRS. This is both for warfarin and DOACs. For warfarin and DOACs the letter sent to the patient will have the day and after hours (emergency only) phone numbers. Per patient instructions for both Buffalo and Batavia, for urgent questions or problems on weekends & evenings call the Emergency Room 862-8774.

Once stabilized, most patients will be telemanaged. Clinic appointments comprise mainly of new patients and initial follow-ups. Exceptions to this include patients with no telephone service, patients that have other complications to telephone follow-up (i.e. extreme hearing impairment), or patients who are very unstable or non-compliant with telephone follow-up. Clinic appointments are generally scheduled between the hours of 8am and 12pm Monday through Friday, however, exceptions can be made at the discretion of the Clinical Pharmacist. Afternoons are typically designated for completion of telemanaged patients.

All patients will have lab or clinic appointment check-in / check-out, the follow-up ACC appointment and laboratory orders entered by the ACC staff member caring for that patient on any given day. All patients are provided with clinic contact information in the event they need to cancel and reschedule an appointment; they are encouraged to do so, as a failure to report will deem them a “no-show” for that appointment date. A patient may contact a Clinical Pharmacist, nurse or MSA within the AC clinic to reschedule an appointment.

Walk-ins will be interviewed and seen if there is an urgent issue that needs addressing. Routine walk-ins are discouraged.

TABLET POLICY

Only warfarin (PBM contracted) brand will be used and dispensed to patients enrolled in the AC clinic at the Buffalo VAMC. A patient must receive warfarin through our facility in order to be enrolled in our ACC. Our ACC uses the following strengths of warfarin in managing our patient population:

- ✓ Warfarin 1mg tablets – pink
- ✓ Warfarin 2.5mg tablets – green

Other strengths of warfarin may be ordered by the clinical pharmacist at his/her discretion, in rare cases and typically to minimize pill burden. In no circumstance will a patient be allowed to split tablets, use more than one strength of warfarin or use a generic equivalent. The ~~lead~~ anticoagulation pharmacist may exempt patients in extreme cases in regards to no tablet splitting. In cases where a patient needs to be transitioned to an alternate tablet strength, he/she will be informed to only use the strength advised by the ACC. Rational for strengths other than the standard strength should be documented anticoagulation progress note.

Once a maintenance dose of warfarin is established, the ACC may dispense 90-day supplies of warfarin to each patient enrolled in the clinic. Exceptions to this include patients whose compliance is questionable or those patients whose safety is a question with large quantities of tablets. In these cases, a smaller supply will be dispensed for safety and compliance purposes.

VISN and National policy does not allow co-management of warfarin. Patients getting warfarin from the VA MUST have their anticoagulation management within the VA.

Direct Oral AntiCoagulants (DOACs)

The Anticoagulation clinic will follow all patients on the DOACS. The director of the anticoagulation clinic (or designee) will be responsible for review and all follow-up of patients on these agents. Providers may request these agents via VISN 2 CPRS approved processes and VA national criteria.

Prior to initiation of any of these agents a face-to-face or telephone visit with the designated patient and the anticoagulation clinic director (or designee) is required to educate patients and explain risk versus benefit of the approved agent. Patients will be followed for hematologic and renal changes according to the below schedule:\

Initial

3 months after initiation and quarterly thereafter

Tablet supplies will not exceed 30 days for the first month may be extended to 90 days (limit one refill) thereafter.

“SNOW BIRDS” AND TRAVELING PATIENTS

Temporary or Permanent Travel out of the WNY area:

For patients leaving WNY for greater than 4 weeks, anticoagulation therapy will be monitored by AC clinic only if the patient seeks care at a local VA and their policy is to only order blood work. Labs will not be ordered or monitored via a Non-VA Laboratory or Facility (i.e. Long-term Care Facility.) Additionally, patients discharged home to contracted nursing services will not be managed by ACC until patient is ambulatory and can come to the clinic for lab work.

Exceptions to these guidelines may be approved by the lead anticoagulation pharmacist, depending on specific patient circumstances, stability of warfarin therapy, ability of the patient to locate alternate means of management while away, etc.

The ACC may discontinue WNY warfarin prescriptions for these patients. Patients will be advised to follow-up at a VA or other healthcare facility while they are away. Upon return to the WNY area, warfarin can be restarted and managed by the Buffalo/Batavia VAMC providing routine follow-up is arranged.

Exceptions to these guidelines may be approved by the Clinical Pharmacist, depending on specific patient circumstances, stability of warfarin therapy, ability of the patient to locate alternate means of management while away, etc.

A traveling (TVC) consult should be initiated to allow for followup blood work as required for warfarin or DOACs.

Traveling Veterans:

At the discretion of the Clinical Pharmacist, and in coordination with a patient's parent VA facility, traveling veterans may be followed by the ACC for up to 3 months if they are visiting from another VA medical center where their anticoagulation is managed, without requiring enrollment in primary care. When feasible, the traveling veteran should make arrangements for care in advance of his/her travels. Where required, traveling veterans with urgent medical

concerns will be referred to the emergency room for medical treatment.

If a patient is planning to relocate to the WNY area, he/she will need to be assigned a Primary Care Provider and will need an ACC consult placed in order for us to continue management of warfarin therapy beyond the 3-month period.

Procedures for laboratory monitoring and follow-up

LABORATORY MONITORING:

Every patient that is warfarin-naïve should have a baseline INR, CMP and CBC obtained prior to initiation of warfarin therapy, in order to evaluate potential sensitivity to therapy and increased bleed risk. In most cases an INR obtained within 30 days of initiation of therapy is appropriate, providing no major health changes have occurred since that time.

INRs are ordered for every patient enrolled in the AC clinic at least monthly (i.e. every 4 weeks). A CBC will be ordered quarterly, unless closer follow-up is warranted, i.e. if a patient is very anemic or at a high risk of bleeding. Significant changes in the CBC (i.e. 1-unit drop in hgb or 2-unit drop in hct from the last CBC, or a general trend downward) will be forwarded to the patient's provider, either electronically or via telephone, as determined by the urgency of notification. In urgent cases a provider must be reached by phone in addition to the electronic alert. Eg. MOD ,PCP. Renal function will be assessed in all patients, particularly those requiring bridge therapy with enoxaparin. Other laboratory tests may be ordered if the Clinical Pharmacist feels they are warranted and may impact anticoagulant therapy, i.e. LFTs, TSH, urinalysis.

INRr results for Warfarin may be venous or POC (Point of Care). POC INR will follow VA Laboratory service procedures.

FAXED OR OUTSIDE LABORATORY RESULTS:

All laboratory analyses are expected to be done on site here at the Buffalo VAMC or one of the approved Community-Based Outpatient Clinics (CBOCs), which include: Lackawanna, Lockport, Niagara Falls, Jamestown, Olean, and Dunkirk. Patients who wish to have laboratory draws done at one of these CBOCs are educated that we receive lab results the day AFTER they have labwork done. Batavia labs are drawn at that facility and processed at Buffalo.

We do not accept outside laboratory results for INRs due to the potential for variability between laboratory analysis, safety implications that may arise from lapses in receipt of outside INR results, patient noncompliance with having blood draws when recommended, the inability of outside laboratories to accept prescriptions/orders from pharmacists, significant time commitment, and inability to reach patients with results. In very rare instances, and based on the discretion of the Clinical Pharmacist, an outside INR may be used to determine appropriate follow-up, although we should not make dosage adjustments based on outside laboratory results. If a patient is physically not capable of presenting to a VA lab, we may explore other options such as community nursing for home draws, or referral to Home Based Primary Care for management.

PROCEDURE FOR RECEIPT OF A CRITICAL LABORATORY VALUE (cascade list):

Under coordination with the automated laboratory service, ACC staff at the Buffalo VAMC are alerted for a critical INR value defined as any INR > 4.5. The automated lab technician first attempts to contact the clinical pharmacist who entered the INR order, by page. If he/she is not available, the lab technician then pages alternate staff sequentially until an alternate clinical

pharmacist is reached. The laboratory value is verified by the automated lab technician stating the patient's name, full social security number, and the INR value; this information then needs to be repeated to the lab technician verbatim. Management of all laboratory values, including critical values, will be discussed in the dosing section of this protocol. For Buffalo and Batavia the Laboratory Service will maintain an updated Cascade list for notification of critical INRs for the OAC patients.

Patient discharge from clinic:

Patients may be discharged from the AC clinic by the clinical pharmacist after completion of treatment duration, cases of patient unreliability, or if therapy complications arise. In these instances, any outstanding warfarin/DOAC prescriptions written by the ACC will be discontinued, and the patient & provider will be advised accordingly.

1) **COMPLETION OF PRESCRIBED TREATMENT DURATION:**

The recommended length of anticoagulant therapy is determined at the time of a new patient's enrollment into the AC clinic. This is determined by review of the original consult, the patient's indication for therapy, past medical history, family history if appropriate, and any risk/benefit analysis.

Once the initially intended duration of anticoagulation is completed, the chart will be reviewed by the clinical pharmacist and consultation with the patient's primary provider is made to determine if it is indeed appropriate to discontinue therapy or if extended therapy is warranted. Although the AC clinic can recommend appropriateness in the initiation or discontinuation of warfarin, this decision falls on the patient's provider. In cases where further expertise is warranted, a consult may be placed to a specialized discipline (i.e. cardiology or hematology) in order to determine the best approach to a patient's care. Patients who are re-admitted to the clinic may not require re-education on warfarin.

2) **PATIENT UNRELIABILITY:**

If a patient is discharged for unreliability, the primary care provider is informed of this discharge and the reasoning behind it. In these cases, the patient will be informed that any warfarin/DOAC prescription within the VA will be canceled, he/she will need to purchase warfarin/DOAC outside the VA, and any further monitoring of warfarin/DOAC therapy will need to be done outside of the Buffalo/Batavia VAMC Anticoagulation Clinic.

Patients who fail to comply with clinic policies may be discharged from the AC clinic for any of the following reasons:

- ✓ the patient continues to drink excessive alcohol and the level of anticoagulation remains unacceptable despite the pharmacist's best efforts and continued patient counseling on the risks of this behavior

- ✓ the patient misses three consecutively scheduled ACC appointments without a valid excuse
- ✓ the patient refuses further medical management by the Buffalo/Batavia VAMC Anticoagulation Clinic, or refuses further warfarin/DOAC therapy despite medical advisement
- ✓ the patient does not follow our dosing recommendations and either self-adjusts his/her own warfarin/DOAC or has another provider who adjusts his/her warfarin/DOAC dose, despite our advisement on the safety implications of doing so and also that we would discharge him/her from clinic for this continued behavior.
- ✓ the patient is noncompliant despite the pharmacists' best efforts of changing this habit. This includes those patients with compliance issues pertaining to memory deficits, where there is no alternate caregiver to take over medication management and where no other safety measures can be implemented to minimize patient's bleed risk (which surely outweigh any benefit to therapy in these situations)
- ✓ non-compliant patients may be subject to a contract which will be signed and scanned into CPRS.

3) COMPLICATION(S) TO THERAPY:

A patient may be discharged from the ACC due to untoward complications to therapy which deem further anticoagulant therapy a contraindication. In the event the decision to discontinue warfarin is made by an outside provider or hospital, the ACC will request written documentation to support this decision. Once this is received, the patient will be discharged from the AC clinic and his/her provider will be notified. Additional supportive documentation would then be needed in the future if anticoagulation is re-recommended to support that the benefit of reintroducing warfarin/DOAC is greater than any risks that may be involved (i.e. a GI bleed that has resolved).

New Patient Referrals

PATIENT INCLUSION

Acceptance of referred patients will be dependent upon the following criteria:

- ✓ Indication for anticoagulation is consistent with those indications depicted in the most current American College of Chest Physician guidelines, Chest supplements, Anticoagulation Forum or PBM guidance.
- ✓ Reliability of patient, family, and/or caregiver
- ✓ Ability and willingness of the patient to follow our recommendations
- ✓ Ability of the patient to travel to a VA clinic
- ✓ Access to a telephone (in cases where the patient does not have a phone, the patient must wait for lab results and dose changes)
- ✓ Lack of absolute and relative contraindications to anticoagulation
- ✓ Routine follow-up on at least a yearly basis with a VA primary care provider or subspecialty clinic which will assume responsibility for inter-current medical problems

Please note that patients may be directly admitted to the clinic as part of transition from inpatient to outpatient care. This function is performed as part of the discharge pharmacist's responsibility.

PATIENT EXCLUSION

Patients who receive only parenteral anticoagulation (i.e. heparin or LMWH) without warfarin/DOAC or those on only prophylactic-dose warfarin are not eligible for enrollment.

Individuals who are non-compliant with scheduled appointments, or who refuse to follow our clinic policy are excluded from clinic enrollment.

PATIENT REFERRAL PROCESS

The patient's provider can make patient referrals by any of the following methods:

- 1) calling or paging a clinical pharmacist within the ACC; an electronic consult must then be completed
- 2) completing an electronic consult (note separate consults exist for DOACs)

The Anticoagulation clinic consult should include the patient's name and last four digits of his/her social security number, indication for warfarin therapy, baseline INR, target INR, and anticipated length of therapy. Any pertinent information regarding past medical history, risk factors for bleeding or thromboembolism, lifestyle limitations to therapy, etc. should be indicated as such on the consult. Patients may be referred to the AC clinic at any stage of warfarin therapy. The DOAC consult must meet PBM criteria and have recent (within ~2months) Hemoglobin, Serum Creatinine and ALT. An ECHO for atrial fibrillation/flutter is essential to evaluate valvular function for inclusion or exclusion.

Scheduling New Clinic Patients:

New patients for warfarin management are scheduled by the ACC clinic nurse or clinical pharmacist once a consult is received. New patients are contacted and an appointment is scheduled within 3 days of receipt of the consult. The initial appointment must occur within 30 days of consult placement, but typically occurs much sooner than this based on how new a patient is to therapy, concurrent health issues, safety concerns and patient availability. All efforts will be made to accommodate a new patient as soon as possible. When a new patient appointment is scheduled, the clinic nurse generates a letter which is then printed to the MSA and mailed to the patient; this letter details to the patient specific instructions for the day of his/her appointment (i.e. "report to the outpatient lab first then proceed to Desk 1 for your appointment"). It also includes contact information in the event this appointment needs to be cancelled by the patient. For Batavia, the pharmacist will send the patient letter or verbally contact the patient.

All efforts will be made to contact a patient once a consult is received. If the patient cannot be reached by phone the patient will receive an "unable to reach" letter requesting a fall back. If the patient does not contact the clinic within 14 days, the consult is discontinued thereby notifying the ordering provider. If a patient does not meet inclusion criteria for anticoagulation therapy and is not a candidate for warfarin therapy based on evaluation by ACC staff, or if a patient refuses warfarin therapy, the provider responsible for the patient's care will be contacted by ACC staff and the reason for refusal will be explained. A note documenting the enrollment denial will be placed in the medical record.

New DOAC patients will be reviewed by the designated clinical pharmacist, educated in person or telephonically and scheduled for follow-up labs by the clinical pharmacist.

NEW Warfarin patient appointments

The initial patient appointment takes 60-90 minutes, depending on the complexity of the case, patient understanding, and whether or not the patient has used warfarin in the past. It comprises of extensive patient education, and so caregivers are encouraged to attend. Patients are seen on a group basis, so that privacy can be upheld and personal attention can be paid to any patient concerns that may arise. The following topics are reviewed and discussed at each initial appointment:

- ✓ Patient-specific indication for warfarin and how warfarin works

- ✓ Review of the patient's past medical history including any previous thromboembolic events; review of the signs/symptoms of a clot
- ✓ Review of any previous bleeding events; review of the signs/symptoms of a minor bleed versus major bleed and when to seek help
- ✓ Review of any previous warfarin dosing history, if applicable and available
- ✓ Evaluation of anticipated duration of treatment with warfarin
- ✓ Review of what an INR is, the patient's goal INR for his/her therapy indication, frequency of INR monitoring, and what it means when an INR is "too high" or "too low"
- ✓ Clinic procedures regarding clinic versus telephone follow-up, and available laboratories within the VA system
- ✓ Effect of vitamin-K on warfarin, what foods to pay attention to, what foods to avoid if possible
- ✓ Review of the patient's current medications, vitamins, alternative medications and dietary supplements. Review of the importance of alerting clinic staff whenever there are changes made; what over-the-counter products and herbal products to avoid while on warfarin
- ✓ Effect of alcohol on warfarin therapy, acceptable limits, increased fall & bleed risk
- ✓ When to take warfarin, and what to do when a dose is missed
- ✓ Know the strength and color of your warfarin tablets
- ✓ Importance of each patient informing all of his/her providers that they are on warfarin
- ✓ Alerting ACC clinic whenever an invasive procedure is planned
- ✓ Importance of female patients informing their provider(s) immediately if they are planning to or become pregnant
- ✓ Verification of all current addresses, telephone number(s) and any alternate phone numbers that the patient feels comfortable allowing us to call for follow-up
- ✓ Review and possible resolution of any potential barriers to adequate follow-up (i.e. transportation, work)
- ✓ New clinic patients also view the patient education video staying active and healthy with blood thinners, provided by the AHRQ.
- ✓ Each patient is provided with a Medic Alert bracelet or necklace (via prosthetics consult), a weekly medication box, and a folder containing: ACC staff telephone numbers, a booklet specific to their therapy indications, "Your Guide to Coumadin®/Warfarin Therapy, provided by the AHRQ and an educational sheet titled "Instructions for Patients on Warfarin".
- ✓ Patient education is documented in CPRS under "Anticoagulation Clinic Comprehensive Note" by the clinic nurse and "Anticoagulation Clinic Provider Note" by the Clinical Pharmacist. Any potential barriers to understanding or compliance are documented, and deficiencies are addressed at subsequent visits. Patient education is consistently reinforced throughout therapy.

Maintenance therapy:

All patients maintained on warfarin therapy must have an INR drawn in compliance with the most current American College of Chest Physician guidelines, which currently state a minimum of every 4 weeks. More frequent monitoring will be based upon patient-specific health issues or concerns at the time.

At every routine follow-up, a patient is interviewed by either a clinic nurse (if the INR is stable) or a clinical pharmacist (if unstable). The following list of open-ended questions serves as a guide, with more focused questions being asked where appropriate:

- What is your current dose of warfarin?

- Did you miss any doses, or accidentally take extra? If so, how many and when?
- Any changes in medications, over-the-counter products, or herbal supplements?
- Any changes in diet with regards to vitamin-K? Any changes in dietary supplementation? Any grapefruit or cranberry juices?
- Any recent, excessive alcohol consumption?
- Any bruising/bleeding issues? If so, when and what were the circumstances? Reinforce when to seek medical attention.
- Any recent illness or other changes in health (i.e. CHF exacerbation)?
- Any recent ER visits or hospitalizations?
- Any upcoming invasive procedures or surgeries?

Based on the information gathered from the telephone (or clinic) interview, the nurse will either advise the patient to continue his/her therapy and schedule follow-up in another 4 weeks, or will defer the patient to a clinical pharmacist if a complication to therapy has been noted. Likewise, based on the information gathered from the telephone (or clinic) interview, the clinical pharmacist will adjust the patient's warfarin dosage accordingly and schedule appropriate follow-up for unstable patients. Please see the dosing section for general dosing guidelines.

As noted previously, INR monitoring intervals may be extended up to 42 days for stable patients.

Indications for anticoagulant therapy:

INDICATIONS FOR USE	GOAL INR RANGE	LENGTH OF THERAPY
Atrial Fibrillation, new onset with planned cardioversion	2.0-3.0	At least 3 consecutive weekly INRs within target range before cardioversion, and at least 4 weeks of maintained warfarin therapy after maintenance of NSR. Cardiology consultation should be sought before cessation of warfarin therapy
Atrial fibrillation/Atrial Flutter, with appropriate CHADS ₂ score (see below) [±]	2.0-3.0	Indefinite
CVA/TIA secondary to atrial fibrillation. Otherwise, aspirin is generally more efficacious	2.0-3.0	Indefinite
Treatment of VTE	2.0-3.0	<ul style="list-style-type: none"> - Result of transient risk factor = 3 months - Unprovoked, idiopathic VTE = at least 3 months, with consideration for long-term therapy - Unprovoked, recurrent VTE = indefinite - VTE in active cancer patient = LMWH for the first 3-6 months, then warfarin treatment indefinitely or until the cancer is resolved - First event and hypercoagulable state = at least 3 months, with consideration for long-term therapy
Prevention of Systemic Embolism LV Thrombus AMI	2.0-3.0	Indefinite
Bileaflet Mechanical Valve in aortic position, NSR	2.0-3.0	Indefinite
Mechanical Prosthetic Valves	See below	Indefinite

Bioprosthetic (tissue) Heart Valve	2.0-3.0 – see below	3 Months
AMI (to prevent recurrent AMI)	2.0-3.0	1-3 months to prevent thromboembolism in patients with CHF, severe LV dysfunction, previous emboli, or mural thrombus

±RISK STRATIFICATION:

In patients with the diagnosis of atrial fibrillation (or atrial flutter), the Current American College of Chest Physician guidelines recommend to risk-stratify these patients to determine the optimal course of anticoagulant/antithrombotic treatment.

Definition and Scores for CHA ₂ DS ₂ -VASc		Stroke Risk Stratification With the CHADS ₂ and CHA ₂ DS ₂ -VASc Scores	
	Score		Adjusted stroke rate (% per y)
Congestive HF	1	CHA ₂ DS ₂ -VASc†	
Hypertension	1	0	0
Age ≥75 y	2	1	1.3
Diabetes mellitus	1	2	2.2
Stroke/TIA/TE	2	3	3.2
Vascular disease (prior MI, PAD, or aortic plaque)	1	4	4.0
Age 65–74 y	1	5	6.7
Sex category (i.e., female sex)	1	6	9.8
Maximum score	9	7	9.6
		8	6.7
		9	15.20

Recommendations by AHA-ACC/HRS
For patients with nonvalvular AF with prior stroke, transient ischemic attack, or a CHA ₂ DS ₂ -VASc score of 2 or greater, oral anticoagulants are recommended. Options include:
<ul style="list-style-type: none"> warfarin (INR 2.0 TO 3.0), or dabigatran, or rivaroxaban, or apixaban. (edoxaban not in 2014 guideline but mentioned in 2016 performance measure)
Among patients treated with warfarin, the INR should be determined at least weekly during initiation of antithrombotic therapy and at least monthly when anticoagulation (INR in range) is stable.
For patients with nonvalvular AF unable to maintain a therapeutic INR level with warfarin, use of a direct thrombin or factor Xa inhibitor (dabigatran, rivaroxaban, or apixaban,*edoxaban not noted*) is recommended.
Re-evaluation of the need for and choice of antithrombotic therapy at periodic intervals is recommended to reassess stroke and bleeding risks.
Recommendations by AHA-ACC/HRS
For patients with nonvalvular AF with prior stroke, transient ischemic attack, or a CHA ₂ DS ₂ -VASc

score of 2 or greater, oral anticoagulants are recommended. Options include:
<ul style="list-style-type: none"> warfarin (INR 2.0 TO 3.0), or
<ul style="list-style-type: none"> dabigatran, or
<ul style="list-style-type: none"> rivaroxaban, or
<ul style="list-style-type: none"> apixaban. (edoxaban not in 2014 guideline but mentioned in 2016 performance measure)
Among patients treated with warfarin, the INR should be determined at least weekly during initiation of antithrombotic therapy and at least monthly when anticoagulation (INR in range) is stable.
For patients with nonvalvular AF unable to maintain a therapeutic INR level with warfarin, use of a direct thrombin or factor Xa inhibitor (dabigatran, rivaroxaban, or apixaban,*edoxaban not noted*) is recommended.
Re-evaluation of the need for and choice of antithrombotic therapy at periodic intervals is recommended to reassess stroke and bleeding risks.

Mechanical Prosthetic Heart Valves - All require lifelong anticoagulant therapy

Type	Model	INR therapeutic range	Position
Caged ball	Star-Edward	2.5-3.5	
Single tilting disk	Bjork Shiley - Spherical disk valve - Convexo concave	2.5-3.5 2.0-3.0 for AVR unless with Afib	MVR & AVR
	Medtronic Hall	2.5-3.5 2.0-3.0	MVR AVR
	Omnicarbon	2.5-3.5	MVR & AVR
Bileaflet	St. Jude	2.5-3.5	MVR AVR + Afib
		2-3	AVR*
	Carbomedic	2.5-3.5	MVR
		2-3	AVR*
	Edward-Duromedic	2.5-3.5	MVR
		2-3	AVR*

* Provided Left Atrium is of normal size and normal sinus rhythm

Bioprosthetic (tissue) Heart Valves

Type	Model	INR therapeutic range	Position	Duration*
Heterograft	Hancock	2.0-3.0	MVR & AVR	3 months
	Carpentier-Edwards	2.0-3.0	MVR & AVR	3 months
	Ionescu-Shiley	2.0-3.0	MVR & AVR	3 months

*Bioprosthetic valve + Afib = Long term therapy

*Evidence of left atrial thrombus at time of surgery = long term therapy

*Bioprosthetic valve + Pacemaker = optional therapy; duration uncertain

*Bioprosthetic valve + history of systemic emboli = longer therapy (3-12 months)

Warfarin Dosing guidelines

The following are dosing “guidelines” and, as such, serve as tools for initiating and maintaining anticoagulation therapy. However, clinical judgment needs to be exercised in each patient’s case to determine a most appropriate course of action.

Initiation of Therapy:

- 1) In patients naïve to warfarin, a baseline INR should always be obtained. An INR drawn within the last 30 days of initiation of therapy should suffice, assuming no major health changes have occurred since that time. Patients may be refused for inclusion into the clinic if a baseline INR is not apparent.
- 2) Initiation of warfarin therapy will typically begin at 2.5mg-5mg daily:
 - a. In relatively young, healthy individuals, or those patients who more aggressive treatment is warranted (i.e. new onset VTE), initiation will begin at 5mg daily.
 - b. In elderly patients or those patients who are suspected to be more sensitive to warfarin therapy (i.e. malnourishment, liver dysfunction, CHF, recent major surgery, concomitant drug interactions such as amiodarone), initiation will typically begin at 2.5mg daily. This is dependent on how aggressive treatment needs to be and the severity of concurrent conditions. The Clinical Pharmacist is expected to use good judgment in these cases. For example, the Clinical Pharmacist may choose to initiate therapy in a very frail, debilitated patient at only 1mg or 2mg daily.
- 3) An INR should ideally be drawn on day #4 of dosing, but at least within the first 7 days. If patient availability is a factor in initial follow-up, it is recommended that dosing is not as aggressive in order to minimize potential adverse events and bleeding complications
- 4) Subsequent follow-up should be tailored to initial patient response, but will typically be at increasing increments. It is important to remember that some patients, especially elderly patients, have slower metabolisms and so the INR may spike after it appears to be at steady state!
- 5) An example timeline is as follows:
 - Day #1: baseline INR is obtained and warfarin therapy is initiated
 - Day #4: 1st follow-up INR; dose-adjust accordingly
 - Day #8: 2nd follow-up INR; dose-adjust accordingly
 - Day #15: 3rd follow-up INR; dose-adjust accordingly
 - Day #25: 4th follow-up INR; dose-adjust accordingly

Maintenance Therapy:

Once a patient is on an established dosing regimen and INRs have achieved target range for his/her indication, subsequent INRs can be drawn every 4 weeks. Closer monitoring is warranted in any case where potential instability of anticoagulation may occur. It is important to always screen patients for any pertinent changes, including but not limited to: compliance concerns, changes in medications/vitamins/over-the-counter products, dietary changes, nutritional supplementation, adverse events, alcohol consumption, recent falls, visits to the Emergency Room, recent or upcoming hospitalizations, upcoming procedures, etc.

The following dosing guide should be used as a tool, with good clinical judgment to determine each patient's best approach to care. Always base dosing on any known causative factors, since an acute factor that resolves will be treated differently than one that is a permanent change or factor. Furthermore, it is important to consider a patient's indication for warfarin therapy and their bleeding versus thromboembolic risks. For example, a young healthy patient on warfarin for a recent pulmonary embolism will be treated more aggressively than a 90-year-old frail patient on warfarin for atrial fibrillation.

VHA CPPO Pharmacy Benefits Management (PBM) Strong Practice Recommended Warfarin Management Algorithm (Initiation Phase of Therapy)

Step 1: Begin with 5 mg or 2 mg daily (if patient requires a lower dose).

Lower initial dosing may be appropriate based on the following patient characteristics:

- Age (generally, frail elderly patients are more sensitive to warfarin)
- Weight (generally, low body weight or malnourished patients are more sensitive to warfarin)
- Past medical history (including liver dysfunction, heart failure, end-stage renal disease, hyperthyroidism, or recent major surgery)
- Social history (including alcohol and tobacco use)
- Interacting medications (prescription, herbal, and over-the-counter products)
- Dietary habits and nutritional status (especially dietary vitamin K content)
- Acute illness (including loss of appetite, fever, vomiting, and diarrhea)
- Risk factors for bleeding (including bleeding disorder, history of bleeding, peptic ulcer disease, history of hemorrhagic stroke, high fall risk, and hypertension)

Step 2: Follow warfarin dosing adjustments based on INR results.

Measurement Day	INR	Action
Measure PT/INR on Day 1	Baseline INR	Start patient on 2 to 5 mg depending on risk factors
Measure PT/INR on Day 3-4	<1.5	Increase weekly dose by 5-25%
	1.5-1.9	No dosage change
	2.0-2.5	Decrease weekly dose by 25-50%
	>2.5	Decrease weekly dose by 50% and/or HOLD dose
Measure PT/INR on Day 5-7	<1.5	Increase weekly dose by 10-25%
	1.5-1.9	Increase weekly dose by 0-20%
	2.0-3.0	No dosage change
	>3.0	Decrease weekly dose by 10-25% and/or HOLD dose
Measure PT/INR on Day 8-10	<1.5	Increase weekly dose by 15-35%
	1.5-1.9	Increase weekly dose by 5-20%
	2.0-3.0	No dosage change
	>3.0	Decrease weekly dose by 10-25% and/or HOLD dose
Measure PT/INR on Day 11-14	<1.6	Increase weekly dose by 15-35%
	1.6-1.9	Increase weekly dose by 5-20%
	2.0-3.0	No Dosage Change
	>3.0	Decrease weekly dose by 5-20% and/or HOLD dose

Additional Considerations:

- If patient has not attained an in-range INR result by Day 14, continue Day 11-14 routine until INR is in-range.
- Holding the dose may complicate efforts at dose-finding and is not usually necessary. In our opinion, it should be reserved for INR values above 5.0 in the initiation phase, when bleeding risk is thought to be very high. For less extreme INR elevations, a dose decrease should be sufficient, especially given that follow-up will be quite soon thereafter.
- In some cases, the following may be considered: For patients sufficiently healthy to be treated as outpatients, we suggest initiating VKA therapy with warfarin 10 mg daily for the first two (2) days followed by dosing based on INR measurements (Grade 2C). [CHEST 2012]
- When the patient has achieved three (3) in-range INR results, use the VISA 1 Anticoagulation Management Algorithm (Maintenance Phase of Therapy).

VHA CPPO Pharmacy Benefits Management (PBM) Strong Practice Recommended Warfarin Management Algorithm (Maintenance Phase of Therapy)

Disclaimer: This algorithm is for ongoing management of warfarin. As with any algorithm or guideline, the final decision must always rest with the clinical judgment of the responsible provider.

Goal of INR 2.0-3.0

INR	Action
≤ 1.5	Increase weekly dose by 10-15%; repeat INR within 7 days.
1.51-1.79	If falling or low on two or more occasions, increase weekly dose by 5-10%; repeat INR in 7-14 days.
1.80-1.99	Consider not changing the dose unless a consistent pattern has been observed; ¹ repeat INR in 7-14 days.
2.00-3.00 (in-range)	No change in dose. Follow-up within 28 days. If INR has been in-range 3X consecutively, follow-up within 42 days. ²
3.01-3.20	Consider not changing the dose unless a consistent pattern has been observed; ¹ repeat INR in 7-14 days.
3.21-3.69	Do not hold warfarin. If rising or high on two or more occasions, decrease weekly dose by 5-10%; repeat INR in 7-14 days.
3.70-4.99	Hold for 1 day and decrease weekly dose by 5-10%; repeat INR determination within 7 days.
5.00-9.99	Hold warfarin. Check INR within 5 days. When INR is therapeutic, restart at lower dose (decrease weekly dose by 10-15%). Check INR at least weekly until stable.
≥ 10.0 (without bleeding)	Hold warfarin and give oral vitamin K, 2.5 mg. Check INR at least weekly until stable.
Serious Bleeding Regardless of INR	Hold warfarin and refer patient to emergency department immediately.

Goal of INR 2.5-3.5

INR	Action
≤ 1.5	Increase weekly dose by 10-15%; repeat INR within 7 days.
1.51-1.99	If falling or low on two or more occasions, increase weekly dose by 10-15%; repeat INR in 7-14 days.
2.00-2.29	If falling or low on two or more occasions, increase weekly dose by 5-10%; repeat INR in 7-14 days.

2.30-2.49	Consider not changing the dose unless a consistent pattern has been observed; ¹ repeat INR in 7-14 days.
2.50-3.50 (in-range)	No change in dose. Follow-up within 28 days. If INR has been in-range 3X consecutively, follow-up within 42 days. ²
3.51-3.70	Consider not changing the dose unless a consistent pattern has been observed; ¹ repeat INR in 7-14 days.
3.71-4.19	Do not hold warfarin. If rising or high on two or more occasions, decrease weekly dose by 5-10%; repeat INR in 7-14 days.
4.20-4.99	Hold for 1 day and decrease weekly dose by 5-10%; repeat INR determination within 7 days.
5.00-9.99	Hold warfarin. Check INR within 5 days. When INR is therapeutic, restart at lower dose (decrease weekly dose by 10-15%). Check INR at least weekly until stable.
≥ 10.0 (without bleeding)	Hold warfarin and give oral vitamin K, 2.5 mg. Check INR at least weekly until stable.
Serious Bleeding Regardless of INR	Hold warfarin and refer patient to emergency department immediately.

Disclaimer/Guide to Use: In a well-designed before and after trial, the use of this algorithm improved percent time in range (TTR) by 6%.³ While clinicians will override these recommendations at times, they should keep in mind that when this algorithm was tested, patients whose management conformed most closely to the algorithm had the best TTR.

Additional Recommendation: In addition to this algorithm, ACC clinicians are urged to avoid non-standard target INR ranges such as 2-2.5 or 1.8-2.5. The 2012 CHEST Guidelines state that there should be two target ranges in clinical practice: 2.5-3.5 for patients with mitral prosthetic valves and 2-3 for everyone else.⁴ In some instances, practitioners may choose a goal of 2.5-3.5 for patients with aortic prosthetic valves with additional risk factors. This is the recommendations from the most recent AHA guidelines and may be used at the recommendation of a referring provider.⁵ Other target ranges do not provide additional benefit and place patients at higher risk, and should be avoided.

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BRIDGE THERAPY GUIDELINES

A risk assessment by the clinical pharmacist should be done for all patients requiring bridge therapy; clinic nurses are not authorized to do risk assessments. Patients requiring bridge therapy are those new to warfarin at a high clot risk, or those undergoing invasive procedures that are at a significant clot risk while off warfarin. A patient should be reassessed each time an invasive procedure is scheduled to ensure an appropriate course of therapy is used, and the date of the most recent risk assessment should be indicated as such in the patient's Anticoagulation Clinic Provider Note. It is NOT the policy of the VAWNY Anticoagulation Clinics to provide bridging with a low molecular weight heparin for patients not currently being followed in the respective anticoagulation clinic.

When enoxaparin therapy is required, typically a 10-12 day supply is prescribed unless the Clinical Pharmacist feels more or less is warranted. A CBC should be ordered during enoxaparin therapy, especially in patients new to warfarin/enoxaparin, to screen for any bleeding complications and the rare possibility of HIT (Heparin Induced Thrombocytopenia).

Contraindications to enoxaparin therapy include prior diagnosis of HIT, severe thrombocytopenia (platelets <100,000), those patients receiving hemodialysis, or those patients at a significant bleed risk where risks outweigh any benefit that would be received. Spinal or epidural hematomas may occur in patients who are anticoagulated with enoxaparin and receiving neuraxial anesthesia or spinal anesthesia. These risks must be discussed with the proceduralist prior to using in these situation. The optimal timing between administration of enoxaparin and these procedures is not known.

Warfarin-naïve patients:

Those patients initiating warfarin who are deemed high risk of thromboembolic or ischemic event until a therapeutic INR is achieved will require bridge therapy with enoxaparin. This includes any patient with new onset Venous Thromboembolism (VTE), any new valve replacement, prior history of stroke/TIA, and those patients with atrial fibrillation and a CHADS₂ score of 3 or more (**note:** this will be patient-specific and will weigh risks of ischemic event versus risk of bleeding complications). Please note that bridging is not an exact science and there may be deviations authorized from this protocol. Such deviations should carry an explanation.

In these patients, similar dosing is followed as listed in the "Dosing Guidelines" section. Typically more aggressive dosing is followed, within reason, in an effort to stop enoxaparin therapy as soon as safely possible. A minimum of 5 days is required in order to allow for inhibition of clotting factors. Ideally an INR should be therapeutic for 2 consecutive days before

stopping enoxaparin, however, clinical judgment will be exercised in order to minimize adverse events.

Invasive procedures requiring warfarin interruption:

Patients undergoing invasive procedures requiring interruption of warfarin therapy who are deemed intermediate to high risk will be bridged with enoxaparin, unless contraindicated. Examples of such invasive procedures include: surgeries, colonoscopies, endoscopies, biopsies, some skin excisions, TURP (unless guided-laser). If the invasiveness of a procedure is not known, this should be verified with the specialty clinic or office performing the procedure to determine if warfarin therapy needs to be interrupted. Warfarin should be stopped for 5 full days prior to any invasive procedure with significant bleed risk.

Patients should not hold warfarin for cataract procedure. Patients undergoing minor dental procedures who are not considered to be at high risk for bleeding should NOT stop their warfarin therapy. For patients at high risk for bleeding, or for those patients undergoing more major dental work, warfarin may be held for 1-3 days depending on a patient's indication for warfarin and the good judgment of the Clinical Pharmacist.

Special Considerations for Women of Reproductive age on Warfarin-Refer to PBM Guidance

The following is the risk stratification scheme per 2008 American College of Chest Physician guidelines:

Table 2—Suggested Patient Risk Stratification for Perioperative Arterial or Venous Thromboembolism

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High	Any mitral valve prosthesis Older (caged-ball or tilting disc) aortic valve prosthesis Recent (within 6 mo) stroke or transient ischemic attack	CHADS ₂ score of 5 or 6 Recent (within 3 mo) stroke or transient ischemic attack, Rheumatic valvular heart disease	Recent (within 3 mo) VTE Severe thrombophilia (eg, deficiency of protein C, protein S or antithrombin, antiphospholipid antibodies, or multiple abnormalities)
Moderate	Bileaflet aortic valve prosthesis and one of the following: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 yr	CHADS ₂ score of 3 or 4	VTE within the past 3 to 12 mo Nonsevere thrombophilic conditions (eg, heterozygous factor V Leiden mutation, heterozygous factor II mutation) Recurrent VTE Active cancer (treated within 6 mo or palliative)
Low	Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	CHADS ₂ score of 0 to 2 (and no prior stroke or transient ischemic attack)	Single VTE occurred > 12 mo ago and no other risk factors

*CHADS₂ = Congestive heart failure-Hypertension-Age-Diabetes-Stroke.

Note: As of 7-2017 American College of Chest Physicians is developing other guidance for peri-procedural bridging, the clinician may refer to the IPRO MAPPP application recommendations for other guidance regarding peri-procedural bridging until the Chest guidance is published and the VA develops national policy.

A risk assessment will be performed on all patients potentially requiring bridge therapy for invasive procedures, with pre-procedure enoxaparin dosing as follows:

High-risk patients:

- ✓ patient should stop warfarin 5 days prior to the scheduled invasive procedure
- ✓ enoxaparin administration should begin 3 days prior to the procedure, with the last dose being administered no closer than 24 hours prior to the procedure
- ✓ enoxaparin dosing will be weight-based, either at 1mg/kg every 12 hours OR 1.5mg/kg daily
 - for any new onset VTE, it is generally preferred to use 1mg/kg every 12 hours to ensure adequate anticoagulation coverage throughout the day
 - those with renal impairment, defined as CrCl<30ml/min, should be dosed at 1mg/kg ONCE daily
 - maximum approved dose of enoxaparin is 150mg twice daily

Moderate-risk patients:

- ✓ patient should stop warfarin 5 days prior to the scheduled invasive procedure
- ✓ enoxaparin administration should begin 3 days prior to the procedure, with the last dose being administered no closer than 24 hours prior to the procedure
- ✓ enoxaparin will be dosed prophylactically at 40mg once daily
 - those with renal impairment, defined as CrCl<30ml/min, should be dosed at 30mg ONCE daily

Low-risk patients:

- ✓ patient should stop warfarin 5 days prior to the scheduled invasive procedure
- ✓ enoxaparin bridge therapy is not required in these patients

Enoxaparin doses should always be rounded to the closest available commercial dose.

Post-procedure:

In intermediate-risk to high-risk patients on enoxaparin bridge therapy, both warfarin and enoxaparin should be restarted as soon as safely feasible and enoxaparin should be continued until the INR is again therapeutic. In minor procedures, anticoagulation can typically be resumed 24 hours after the procedure as long as no bleeding is present. Major procedures or surgeries may require delays in resuming anticoagulation, and it may not be appropriate to resume enoxaparin post-surgically at all. In these cases, corroboration should be made with the surgeon or specialist to determine the safest approach to therapy.

Upon resumption of enoxaparin, booster doses of warfarin are typically given in order to aide the warfarin with re-achieving therapeutic levels more promptly. In general 1-3 booster doses of warfarin are given upon initiation of therapy for this purpose, based on the INR at the time of therapy resumption. Repeat INRs are obtained 5-7 days after the procedure, based on clinical judgment. Enoxaparin should be continued until the INR has reached therapeutic goal once again, unless risks of continued bridging outweigh benefits (i.e. patient experiencing significant abdominal hematomas from enoxaparin injections).

Those patients deemed low-risk may resume warfarin as soon as safely feasible, typically 24 hours after the procedure as long as no bleeding is present. No booster doses are required, and the INR can be allowed to trend back into target range on its own in order to minimize any untoward bleeding events.

Bridging During Maintenance Therapy:

If a patient has an INR that becomes subtherapeutic (i.e. <1.5) during maintenance therapy, and the clinical pharmacist feels this patient is at a high clot risk (i.e. patient had a VTE within the past 3 months or has a history of MVR) due to potential inability for the INR to re-achieve target range promptly, he/she may offer enoxaparin bridging. The rationale should be explained to the patient, as well as risks of the patient not using enoxaparin. The clinical pharmacist's offer to bridge, as well as the patient's willingness or refusal, should be documented in CPRS. It is not expected to routinely bridge patients who are not at a high clot risk, or those patients whose INR falls below target range for known, transient causes (i.e. non-compliance) since the INR should rise rapidly with booster doses to minimize thromboembolic risk. Consideration for bridge therapy in patients on maintenance warfarin therapy will be patient-specific, based on the patient's bleed versus clot risk and the clinical pharmacist's best judgment.

BLEEDING RISK INDEX ASSESSMENT

A bleeding risk index is to be assigned to each patient, and may be used as a guide to assign a patient as low, intermediate, or high risk of bleeding. Patients with a change in any of the criteria will have their bleeding risk index updated as needed. Patients classified as "high risk" will be followed no longer than every 4 weeks regardless of therapeutic INR values, will have at least quarterly CBCs done, yearly hemocults or as warranted, and the patient's primary care provider will be alerted of any changes in these parameters. The provider may decide to choose a different anticoagulant/antithrombotic agent in those patients considered high risk for bleeding.

The HAS-BLED SCORE is as follows:

<https://www.mdcalc.com/has-bleed-score-major-bleeding-risk>

MANAGEMENT & DOCUMENTATION OF THERAPY COMPLICATIONS:

Patients reporting a complication to therapy will be referred to either the Emergency Room or their primary care provider as appropriate, based on the severity of the complication. The Clinical Pharmacist will seek medical consultation with any of the following reported complications:

- 1) recent trauma (falls, lacerations, etc.)
- 2) signs/symptoms suggestive of a thromboembolic event
- 3) an acute change in mental status
- 4) an acute change in health status
- 5) uncontrolled bleeding episode (i.e. prolonged or copious hemoptysis, persistent large nosebleeds despite a therapeutic INR, bright red blood without straining, black tarry stools, hematuria)
- 6) large, spontaneous hematomas

Patients reporting with any recent trauma or uncontrollable bleeding episode will be referred to the Emergency Room for immediate evaluation. Minor episodes will be brought to the attention of the Anticoagulation Physician or the patient's primary care provider, who will then determine the necessary course of action. All events identified by nursing staff must be reported to the clinical pharmacist for appropriate referral. All complications will be documented as such in CPRS, and all appropriate providers involved in the patient's care will be alerted to the acute situation. Emergency Room staff will be alerted promptly if a patient is being referred there for care, if they have not already been consulted with.

WARFARIN –HIGH INR

Vitamin-K Administration

The following course of action will be taken by the clinical pharmacist for an elevated INR in patients receiving warfarin therapy:

Condition	Intervention
INR ≥ 5.0 but < 10 , with no significant bleeding evident	Hold 1 to 2 doses, recheck INR more frequently; resume warfarin once INR is back in target range, and adjust dosage accordingly based on causation. For more rapid reversal (i.e. surgery), may administer oral vitamin-K $\leq 5\text{mg}$
INR ≥ 10.0 , with no significant bleeding evident	Hold warfarin; administer oral vitamin-K 2.5mg or 5mg in clinic. Recheck INR 24-48 hours. Administer more vitamin-K if warranted. Resume warfarin once INR is back in target range, and adjust dosage accordingly based on causation
INR > 20 or indeterminable (i.e. pt > 150 seconds) OR major to life-threatening bleeding at any INR elevation	Hold warfarin therapy; administer vitamin-K 10mg by slow IV infusion; may also administer FFP, prothrombin complex concentrate or rVIIa as warranted. Management of these patients occurs by ER staff, and the patient should be referred there ASAP for care

If oral vitamin-K is warranted (i.e. cases where an INR ≥ 10 with no significant bleeding present), this is typically administered in the clinic setting and in the presence of the Clinical Pharmacist. In situations where an INR is indeterminable or in cases of major to life-threatening bleeding, the patient should be taken immediately to the Emergency Room for emergent medical attention.

If warfarin therapy is still indicated after receipt of high doses of vitamin-K, heparin or LMWH (i.e. enoxaparin) may be given if indicated until the effects of vitamin-K have diminished and INRs can be viewed as reliable values.

Urgent Reversal

WARFARIN reversal:

1. Discontinue warfarin
2. STAT PT/INR, CBC
3. IV vitamin K 10mg in NS 0.9% 50 mls over 30 minutes
 - a. IV vitamin K is preferred over PO route based on onset of actions
 - b. Onset of action
 - i. IV vitamin K: 1 – 2 hours
 - ii. PO vitamin K: 6 – 10 hours
 - c. Peak effects:
 - i. IV vitamin K: 12 – 14 hours
 - ii. PO vitamin K: 24 – 48 hours
4. FFP 15-30mls/kg of patient weight, with goal to replace 30% clotting factors.
5. Consider administration of Kcentra (4- factor prothrombin complex concentrate) for **life threatening bleeding** or **intracranial hemorrhage**:

INR	Kcentra Dose	Maximum Dose
1.5 – 3.9	25 units/kg	2500 units
4.0 – 6.0	35 units/kg	3500 units
>6.0	50 units/kg	5000 units

- a. Dose based on actual body weight up to 100kgs. For patients weighing more 100kgs, use max dose.
- b. Maximum dose is 5000 units
- c. Do not infuse Kcentra at a rate faster than 210 units/min
- d. Repeat INR 30 minutes after infusion of Kcentra

UNFRACTIONED HEPARIN (UFH) reversal:

1. Discontinue heparin
2. STAT aPTT, PT/INR, CBC
3. Administer IV protamine according to the chart:

Time since last heparin dose	Protamine dose (IV)
<30 minutes	1mg per 100 units of heparin given
30 – 60 minutes	0.75mg per 100 units of heparin given
61- 120 minutes	0.5mg per 100 units of heparin given
>120 minutes	0.25mg per 100 units of heparin given

Special Considerations:

- To calculate dose of heparin to be neutralized for patients on continuous IV heparin drip
 - Calculate the amount of heparin used in the preceding 3 hours
 - Assume 60 minute half life for heparin
- Maximum single dose of IV protamine to be no greater than 50mg
- Maximum total dose of IV protamine is 100mg
- Do not infuse faster than 5 mg/minute due to increased risk for adverse reactions
- Onset of action: 5 minutes
- **FFP will not reverse heparin. In fact, FFP contains antithrombin and could in theory potentiate heparin.**

LOW MOLECULAR WEIGHT HEPARIN (LMWH) reversal:

1. Discontinue LMWH (i.e. Enoxaparin)
2. STAT aPTT, PT/INR, CBC, fibrinogen, BMP
3. Administer IV protamine according to the chart (assuming normal renal function):

Time since last enoxaparin dose	Protamine dose (IV)
0 – 8 hours	1mg per 1mg of enoxaparin given
8 – 12 hours	0.5mg per 1mg of enoxaparin given
>12 hours	No need for protamine

Special Considerations:

- Protamine will only neutralize 60% of LMWH
 - Reversal is not as complete or as predictable as compared to heparin reversal
- A second dose of protamine can be considered if after 2-4 hours, aPTT remains prolonged
 - Dose to be given 0.5mg per 1mg of enoxaparin given
- Consider FFP or PCC if bleeding persists and is life threatening
- Do not infuse faster than 50 mg per 10 minutes (5mg/min)
- May cause severe hypotension and bradycardia – infuse at 50mg/hr in pts with underlying cardiac history
- Hypersensitivity reactions: may occur in patients allergic to fish, those previously exposed to protamine therapy or protamine containing insulin, or men who have undergone a vasectomy
- Onset of action: 5 minutes

FONDAPARINUX reversal:

1. Discontinue Factor Xa inhibitor (Fondaparinux)
 2. STAT aPTT, PT/INR, CBC, BMP
 3. Page hematology
 4. No specific antidote for reversal
 5. Consider administration recombinant Factor VIIa
 - a. Factor VIIa has been used to reverse fondaparinux with some success
- Recombinant Factor VIIa (NovoSeven):
- Dose: 90 mcg/kg
 - Onset of action: immediate
 - Duration of action: 2 – 6 hours
- Special Considerations:
- May not correct bleeding because it only restores Factor VIIa
 - Risk of thrombosis 5-10%
 - May need repeat dose after 2 hours
6. Hemodialysis reduces fondaparinux levels by approximately by 20%
 7. Consider FFP or Kcentra if persistent bleeding

ARGATROBAN reversal:

1. Discontinue Direct Thrombin Inhibitor (argatroban, bivalirudin)
2. STAT aPTT, PT/INR, CBC
3. Page hematology
4. No specific antidote for reversal
5. Treatment of bleeding is often multifactorial. Consider the following reversal options:
 1. Desmopressin acetate:
 - a. 0.3mcg/kg in NS over 15 – 30 minutes
 2. Cryoprecipitate:
 - a. Initial dose at least 10 units
 3. Anti-fibrinolytic therapy:
 - a. Aminocaproic acid: 0.1 – 0.15g/kg over 30 minutes, then 0.5 – 1 g/hr until bleeding resolves
 - b. Tranexamic acid: 10mg/kg IV Q6h – Q8h until bleeding resolves
 4. FFP:
 - a. 15-30mls/kg of patient weight, with goal to replace 30% clotting factors

Reversal of the direct oral anticoagulants (DOAC/NOAC):

Special considerations for reversal of oral anticoagulants:

1. There are currently NO proven reversal agents or antidotes for the anti-Xa inhibitors
2. The NOAC have relatively short half-lives. Assess last intake of medication, dosing regimen, renal function & hepatic function
3. PT/INR & aPTT do NOT reliably reflect the degree of anticoagulation & may not correlate with anticoagulant effect for NOAC.
4. Thrombin time is sensitive to the presence of dabigatran but is not indicative of drug concentrations
5. FFP and/or cryoprecipitate is NOT recommended as first line therapy due to unclear efficacy and large volume
 - a. Increased risk for transfusion related cardiac overload and cardiogenic shock

Reversal of oral anti-Xa inhibitors (APIXABAN, RIVAROXABAN,

Drug	MOA	Half-life	PT/INR	aPTT
Dabigatran	Direct Thrombin Inhibitor	12 – 17 hours	Potentially useful Elevated levels at therapeutic doses	Elevation indicative of presence but not degree of anticoagulation Plateau occurs at higher doses
Rivaroxaban	Xa inhibitor	5 – 11 hours	Potentially useful Elevated levels consistent with ingestion at higher doses	Typically not significant at standard doses
Apixaban	Xa inhibitor	8 – 14 hours	Potentially useful Elevated levels consistent with ingestion at higher doses	Typically not significant at standard doses
Warfarin	VKA		Potentially useful Elevation in relation to dose	Typically not significant at standard doses

EDOXABAN):

1. Discontinue oral Factor Xa inhibitor
2. STAT aPTT, PT/INR, CBC with differential, BMP
3. Determine last intake & dosing regimen
4. Estimate normalization of hemostasis: 12 – 24 hours
5. Consider contacting hematology
6. If less than 2 hours since administration/ingestion, consider activated charcoal
 - a. Activated charcoal 50 grams orally x 1
 - b. Administer charcoal only if preserved mental status and swallowing ability. Do not place a NG or OG tube to administer due to risks of bleeding and aspiration
7. Consider administration of Kcentra
 - a. NOTE: consider only when other measures fail or in the setting of acute intracranial or life threatening hemorrhage. There is **little evidence** to

support efficacy and clinical application for reversal. Potential benefits need to be weighed against increased risk of thrombosis

- b. Initial Dose: 50 units/kg IV
 - e. Maximum dose: 5,000 units
 - f. Dose based on actual body weight up to 100kgs. For patients weighing more 100kgs, use max dose.
 - g. Round to the nearest vial size
8. May consider FEIBA for reversal in patients with history of HIT
- a. Dose: 50 – 100 units/kg

Reversal of DABIGATRAN:

- 1. Discontinue dabigatran
- 2. STAT aPTT, PT/INR, CBC with differential, BMP
- 3. Determine last intake & dosing regimen
- 4. Estimate normalization of hemostasis:
 - a. Normal renal function: 12 - 24 hours
 - b. CrCl 50 – 80 mls/min: 24 – 36 hours
 - c. CrCl 30 – 50 mls/min: 36 – 48 hours
 - d. CrCl < 30mls/min: > 48 hours
- 5. If less than 2 hours since administration/ingestion, consider activated charcoal
 - a. Activated charcoal 50 grams orally x 1
 - b. Administer charcoal only if preserved mental status and swallowing ability. Do not place a NG or OG tube to administer due to risks of bleeding and aspiration
- 6. If feasible, consider hemodialysis
 - a. Page nephrology
 - b. Can be dialyzed (protein binding is low and water soluble)
 - c. Removes ~ 60% of drug in 2 – 3 hours, data is limited
- 7. Consider administration of Praxbind (Idarucizumab):
 - a. Dose: 5 grams IV x 1 dose
 - b. There is limited data to support doses greater than 5 grams

DRUG INFORMATION:

Prothrombin Concentrate Complex (PCC): Kcentra

Kcentra is a non-activated 4 factor PCC replacement product prepared from human US sourced plasma

FDA indication:

For the urgent reversal of acquired coagulation factor deficiency induced by Vitamin K antagonist in adult patients with **MAJOR** acute bleeding or need for urgent surgery/invasive procedure

Please note that the use of Kcentra for urgent reversal of novel oral anticoagulants is off label indication and potential benefits must be weighed carefully against lack of outcome data and potential risks

Mechanism of action:

Kcentra increases plasma levels of vitamin K dependent Factors II, VII, IX and X & antithrombotic Protein C & S.

Contraindications:

1. Disseminated intravascular coagulation
2. Heparin induced thrombocytopenia (HIT) (Contains heparin)
3. Prior reaction/hypersensitivity to Factors II, VII, X and protein C

Precautions:

1. Increased risk of thromboembolism
2. Caution if major surgery or thromboembolism in the past **6 weeks**
3. MI, CVA, TIA, unstable angina, severe peripheral arterial disease, VTE
4. Has not been studied in patients with thromboembolism within the last **3 months**

Dosing:

1. Use actual body weight when calculating dose up to 100kgs
2. For patients weighing more than 100kgs, use maximum dose as per chart below
3. For reversal of NOAC in the setting of **life threatening bleeding**:
 - a. Kcentra 50 units/kg (maximum dose: 5,000 units IV)
4. For reversal of **warfarin** for **intracranial hemorrhage** or **life threatening bleeding**:

INR	Kcentra Dose	Maximum Dose
1.5 – 3.9	25 units factor IX/kg	2500 factor IX
4.0 – 6.0	35 units factor IX/kg	3500 factor IX
>6.0	50 units factor IX/kg	5000 factor IX

5. Infuse at a rate of 3units/kg/minute. Do not infuse Kcentra faster than 210 units/min

If INR remains elevated after Kcentra administration, repeat dosing of Kcentra is NOT supported by clinical data & NOT recommended

Components:

1. Product potency on vial label is based on the units of Factor IX.
2. Exact components per vial are list on vial. Approximate components in 500 unit vial:

Total protein: 120 – 280mg	Protein C: 420 – 820 units	Sodium Chloride: 60 – 120 mg
Factor II: 380 – 800 units	Protein S: 240 – 680 units	Sodium citrate: 40 – 80 units
Factor IV: 200 – 500 units	Heparin: 8 – 40 units	HCl: Small amounts
Factor IX: 400 – 620 units	Antithrombin III: 4 – 30 units	Sodium hydroxide: Small amounts
Factor X: 500 – 1020 units	Human albumin: 40 – 80 units	

Adverse reactions:

1. Common: headache, nausea/vomiting, hypotension, anemia
2. Serious: thromboembolic events including CVA, VTE

Activated Prothrombin Concentrate Complex (aPCC): FEIBA

FEIBA is an activated prothrombin complex concentrate which contains factors II, IX, X (mainly non-activated) and Factor VII (mainly in the activated form). **FEIBA does not contain heparin.** Factor VIII bypassing activity.

FDA indication:

1. Hemorrhage in patients with hemophilia: For use in hemophilia A and hemophilia B with inhibitors for control and prevention of bleeding episodes
2. Perioperative bleeding management in patients with hemophilia A and hemophilia B
3. Routine prophylaxis of bleeding events in patients with hemophilia A and hemophilia B

Please note that the use of FEIBA for urgent reversal of novel oral anticoagulants is off label indication and potential benefits must be weighed carefully against lack of outcome data and potential risks

Mechanism of action:

FEIBA replenishes factors II, IX, X and VII to reverse bleeding

Contraindications:

1. Disseminated intravascular coagulation
2. Prior reaction/hypersensitivity to Factors II, VII, IX, X
3. Treatment of bleeding episodes from coagulation factor deficiencies in the absence of inhibitors to coagulation factors VIII or IX

Precautions:

1. Increased risk of thromboembolism
2. Caution if major surgery or thromboembolism in the past **6 weeks**
3. MI, CVA, TIA, unstable angina, severe peripheral arterial disease, VTE
4. Has not been studied in patients with thromboembolism within the last **3 months**

Dosing:

1. Range from 50 – 100 units/kg depending on indication, location of bleed and severity of bleeding
 - a. For reversal of NOAC in the setting of **life threatening bleeding**: 80 units/kg
2. Administered as a continuous infusion with rate not to exceed 2 units/kg/min
3. Infusion must be completed within 3 hours from time of reconstitution
4. Maximum single dose should not exceed 100 units/kg

Adverse reactions:

1. Common: headache, nausea/vomiting, hypotension
2. Serious: thromboembolic events including: MI, CVA, VTE
3. Anaphylaxis
4. Hypoaesthesia

Cost considerations:

1. 1 vial of approximately 500 units is \$500 (\$1 dollar per unit)

Idarucizumab: (Praxbind)

Idarucizumab is a monoclonal antibody used for acute reversal of dabigatran in emergency situations.

FDA indication:

1. Dabigatran reversal for emergency situations, urgent surgery or uncontrolled bleeding

Mechanism of action:

Idarucizumab is a monoclonal antibody fragment which binds to dabigatran with higher affinity than dabigatran to thrombin thus neutralizing the anticoagulation effect.

Contraindications/Precautions:

1. Hereditary fructose intolerance
 - a. Due to sorbitol excipient
2. Thrombotic disease
 - a. Reversing dabigatran exposes patients to the thrombotic risk of their underlying disease

Dosing:

1. 5 grams intravenously for 1 dose
2. There is limited data to support the use of doses greater than 5grams

Administration:

1. Administer 5grams (100mls)
 - a. Each vial contains 2.5grams/50mls

Adverse reactions:

1. Thrombosis
2. Hypokalemia (7%)
3. Delirium (7%)
4. Constipation (7%)
5. Fever (6%)
6. Hypersensitivity reactions: rash, pruritis, bronchospasms
7. Headache

Warfarin DOSAGE

WEEKLY DOSE	DAILY ORDER 1MG TABS
5	NONE M,F; 1MG OTHER DAYS
6	NONE SUN, 1MG OTHER DAYS
7	1MG QD
8	2GM M; 1MG OTHER DAYS
9	2MG M,F; 1MG OTHER DAYS
10	2MG M,W,F; 1MG OTHER DAYS
11	1MG M,W,F; 2MG OTHER DAYS
12	1MG M,F; 2MG OTHER DAYS
13	1MG M; 2MG OTHER DAYS
14	2MG QD
15	3MG M; 2MG OTHER DAYS
16	3MG M,F; 2MG OTHER DAYS
17	3MG M,W,F; 2MG OTHER DAYS
18	2MG M,W,F; 3MG OTHER DAYS
19	2MG M,F; 3MG OTHER DAYS
20	2MG M; 3MG OTHER DAYS
21	3MG QD
22	4MG M; 3MG OTHER DAYS
23	4MG M,F; 3MG OTHER DAYS
24	4MG M,W,F; 3MG OTHER DAYS
25	3MG M,W,F; 4MG OTHER DAYS
26	3MG M,F; 4MG OTHER DAYS
27	3MG M; 4MG OTHER DAYS
28	4MG QD
29	5MG M; 4MG OTHER DAYS
30	5MG M,F; 4MG OTHER DAYS
31	5MG M,W,F; 4MG OTHER DAYS
32	4MG M,W,F; 5MG OTHER DAYS
33	4MG M,F; 5MG OTHER DAYS
34	4MG M; 5MG OTHER DAYS
35	5MG QD
36	6MG M; 5MG OTHER DAYS
37	6MG M,F; 5MG OTHER DAYS
38	6MG M,W,F; 5MG OTHER DAYS
39	5MG M,W,F; 6MG OTHER DAYS
40	5MG M,F; 6MG OTHER DAYS
41	5MG M; 6MG OTHER DAYS

Warfarin DOSAGE

WEEKLY DOSE	DAILY ORDER 2.5MG TABS
10	0MG M,W,F; 2.5MG OTHER DAYS
12.5	0MG M,F; 2.5MG OTHER DAYS
15	0MG M; 2.5MG OTHER DAYS
17.5	2.5MG QD
20	5MG M; 2.5MG OTHER DAYS
22.5	5MG M,F; 2.5MG OTHER DAYS
25	5MG M,W,F; 2.5MG OTHER DAYS
27.5	2.5MG M,W,F; 5MG OTHER DAYS
30	2.5MG M, F; 5MG OTHER DAYS
32.5	2.5MG M; 5MG OTHER DAYS
35	5MG QD
37.5	7.5MG M; 5MG OTHER DAYS
40	7.5MG M, F; 5MG OTHER DAYS
42.5	7.5MG M,W,F; 5MG OTHER DAYS
45	5MG M,W,F; 7.5MG OTHER DAYS
47.5	5MG M,F; 7.5MG OTHER DAYS
50	5MG M; 7.5MG OTHER DAYS
52.5	7.5MG QD
55	10MG M; 7.5MG OTHER DAYS
57.5	10MG M,F; 7.5MG OTHER DAYS
60	10MG M,W,F; 7.5MG OTHER DAYS
62.5	7.5MG M,W,F; 10MG OTHER DAYS
65	7.5MG M,F; 10MG OTHER DAYS
67.5	7.5MG M; 10MG OTHER DAYS
70	10MG QD
72.5	12.5MG M; 10MG OTHER DAYS
75	12.5MG M,F; 10MG OTHER DAYS
77.5	12.5MG M,W,F; 10MG OTHER DAYS
80	10MG M,W,F; 12.5MG OTHER DAYS
82.5	10MG M,F; 12.5MG OTHER DAYS
85	10MG M; 12.5MG OTHER DAYS
87.5	12.5MG QD
90	15MG M; 12.5MG OTHER DAYS
92.5	15MG M,F; 12.5MG OTHER DAYS
95	15MG M,W,F; 12.5MG OTHER DAYS
97.5	12.5MG M,W,F; 15MG OTHER DAYS
100	12.5MG M,F; 15MG OTHER DAYS

COMMON DRUG INTERACTIONS

Absorption

- Cholestyramine
- Colestid

Induction of Metabolism

- rifampin
- barbiturates
- carbamazepine
- nafcillin
- primidone
- glutethimide
- griseofulvin
- phenytoin

Protein Binding -

valproic acid
chloral hydrate

CYP450 ENZYME INTERACTIONS

- CYP1A2 - Cimetidine, Ciprofloxacin, Diltiazem, Erythromycin, Gatifloxacin
- CYP2Y9 - Amiodarone, Fluconazole, Fluvastatin, Metronidazole, Miconazole, Propoxyphene, TMP/Sulfa
- CYP3A4 - Clarithromycin, Diltiazem, Erythromycin, Fluconazole, Fluoxetine, Grapefruit Juice, Itraconazole, Ketoconazole, Nefazodone, Omeprazole, Propoxyphene, Quinidine, Ritonavir, Verapamil

HERBAL MEDICATIONS and VITAMINS

See attached sheet – Instruct patients to avoid all herbal/natural products since they are not FDA approved or standardized. Multivitamins are allowed however, the maximum Vitamin E allowance is 30 IU daily unless prescribed by another provider.

Vitamin E - interacts with warfarin

MAJOR DRUG INTERACTIONS

Must reduce dose by 1/2 before start of these antibiotics-follow-up in 1 week and sooner if possible with TMP/SMX.

- TMP/SMX
- Erythromycin
- Clarithromycin
- Azithromycin
- Azoles

Try to avoid:

Aspirin or Aspirin Containing Products

IBU/ Naproxen

NSAIDS

***** However, if patient needs these meds- may check CBC more frequently for bleeding and give home guaic tests - Alternative may be 1st - Salsalate up to 750 mg TID or COX2 Inhibitors for chronic pain;. Also must be seen at 4-5 week intervals maximum. *****

Alcohol

Chronic - increases warfarin metabolism

Acute/Binge - decreases warfarin metabolism

Attachments:

Warfarin/Herbal Interaction Sheet

Potential Interaction Between Herbal Products and Crystalline warfarin sodium

Common Name(s)	Scientific Name(s)	Therapeutic Uses	Precautions	Mechanism of Interaction with warfarin	Applicable References
Cranberry	<i>Vaccinium macrocarpon</i>	UTI prophylaxis	Increased risk of hemorrhage	Unknown No studies to correlate any interaction	43-50
Garlic, allium, stinking rose, rustic reacle, nectar of the gods, camphor of the poor, poor man's reacle Perennial bulb with tall erect flowering stem, 2-3ft Composition: Alliin, Ajoenes, proteins, minerals and vitamins, riboflavin, thiamine, niacin. Component of the constituents of garlic & pharmacological activity depends on dosage form.	Allium sativum L. Family: Liliaceae or Amaryllidaceae Allicin is made by crushing the bulb, alliin which has no odor & no activity is converted to allicin by allicinase. Allicin responsible for odor and most pharmacological activity. Very high in sulfur. Causes hypoglycemia, hypocholesterolemia. Contains methyl allyl tri-sulfide-inhibits platelet aggreg. Found mostly in cloves a powder form. Ajoene-are in products	<ul style="list-style-type: none"> • Leprosy • Slow Atherosclerosis Process • ↓ Total cholesterol, LDL and ↑ HDL • Inhibit Platelet Aggregation • ↓ Blood Pressure • ↓ Blood Glucose • Antibacterial and antiseptic <p>Doses of garlic- Adult 4-12 mg of allicin or 0.4-12 grams of dried powder, or 2-5 gms of fresh bulb.</p>	<ul style="list-style-type: none"> • Burning of the mouth, esophagus & stomach • Nausea • Sweating • Light-headedness • Increase bleeding events 	<ul style="list-style-type: none"> • Allicin contains methyl allyl trisulfide inhibits platelet aggregation • Ajoene (4,5,9 trithiadodeca-1,6,11-triene 9-Oxide) has anti-thrombotic activity by inhibiting exposure of fibrinogen receptor on platelet membranes. <p>Interactions reported: Two cases have been published of increase INR assoc with ingestion of garlic pearls or tablets, dose unknown, in pts previously stabilized on warfarin. Two case reports have described bleeding events in pts not receiving anticoagulants who were consuming large amounts of garlic. In one of the cases pt consumed an average of 4 cloves of garlic per day, approx. 2000mg. It is recommended that therapeutic doses of garlic should be avoided in all pts with prolonged coagulation times & used with caution in those pts receiving ac therapy.</p>	14-20

	containing garlic macerated in oils, more potent platelet inhibitor but less abundant.				
Ginger	Zingiber officinale Roscoe Z. capitatum Z. zerumbet Smith. Family Zingiberaceae	<ul style="list-style-type: none"> • Prevention of motion sickness • Anti-emetic • Relief of Skin Burns • Anti-inflammatory for arthritis 	<ul style="list-style-type: none"> • Can result in prolonged bleeding time 	<ul style="list-style-type: none"> • Ginger oleoresin containing gingerol inhibits the enzyme prostaglandin synthetase 	20-22

Ginkgo, maidenhair tree, kew tree	Ginkgo biloba L. Family: Ginkgoaceae	<ul style="list-style-type: none"> • Heart disease • Tinnitus • Cerebral and peripheral vascular insufficiency • Cognitive disorders • Vertigo • Anti-asthmatic • Inhibitor of platelet aggregation • Raynauds Disease • Various inflammatory, cardiovascular and respiratory disorders 	<ul style="list-style-type: none"> • Gastrointestinal upset • Headache • Severe allergic reactions, pulp and seed are toxic if ingested 	<ul style="list-style-type: none"> • Leaves and root contain terpenoids - Ginkgolides, A,B, C, and M. Ginkgolide A inhibits platelet activating factor (PAF), preventing PAF-induced clot formation and promoting clot breakdown. 	20,23,24
Fever Few, featherfew, altamisa, bachelor's button,	Tanacetum parthenium Schulz-Bip.(syn. Chrysanthemum	<ul style="list-style-type: none"> • Prophylactic for migraine headaches • Asthma • Dermatitis • Arthritis 	<ul style="list-style-type: none"> • Mouth Ulceration • Lip Swelling • Loss of taste • Dermatitis 	<ul style="list-style-type: none"> • Parthenolide is the Inhibitor of prostaglandin synthesis, by preventing the release of 	20,25-27

featherfoil , febrifuge plant, midsumm er daisy, nosebleed, Santa Maria, wild chamomil e, wild quinine	parthenium L. Bernh., Leucanthemu m parthenium L. Gren and Godron, and Pyrethrum parthenium L.) Family: Asteraceae Compositae	<ul style="list-style-type: none"> • Anti-pyretic • Antidote for opium overdose • Inhibit platelet aggregation 		arachidonic acid and inhibit in vitro aggregation of platelets stimulated by adenosine diphosphate or thrombin.	
Indian tobacco,w ild tobacco, asthma weed, gagroot, emetic herb and vomit wort	Lobelia inflata L. Family Campanulaceae	<ul style="list-style-type: none"> • Smoking cessation • Diuretic • Expectorant • Emetic • Cancers • Respiratory stimulant 	<ul style="list-style-type: none"> • Convulsions or collapse 	<ul style="list-style-type: none"> • Metabolized by the Cytochrome P-450 hepatic enzyme system 	28,29
White Willow	Salix purpurea, Salix fragilis, Salix daphnoides, Salix alba	<ul style="list-style-type: none"> • Anti-pyretic • Anti-inflammatory • Analgesic 	<ul style="list-style-type: none"> • Gastric Ulcers • Tinnitus • ↓ platelet aggregation 	<ul style="list-style-type: none"> • Active constituent, salicylic acid, shares the same precautions as aspirin 	20
Pau D' Arco, Taheebo, Trumpet bush, lapacho	Tabebuia impetiginosa Lapacho colorado Tabebuia avellanedae Tabebuia altissima	<ul style="list-style-type: none"> • Fungal Infections • Cancer • ↓ Blood Glucose 	<ul style="list-style-type: none"> • Nausea • Vomiting • Dizziness • Anti-coagulation Effect 	<ul style="list-style-type: none"> • Contains natural coumarins and could potentially cause anti-coagulation 	20,29-31
Asafetida, asafoetida, gum asfetida, devil's dung, and	Ferula assafoetida L. or other Ferula spp. Family: Umbellifera	<ul style="list-style-type: none"> • ↓ blood pressure • Inhibit platelet aggregation • Expectorant • Chronic 	<ul style="list-style-type: none"> • Nausea • Abdominal upset 	<ul style="list-style-type: none"> • Ferulic Acid and its sodium salt (sodium ferulate) inhibit platelet aggregation 	32

food of the gods	e or Apiaceae	Bronchitis			
Woodruff, sweet woodruff, master of the wood, woodward	Galium odoratum L. Scop. also known As Asperula odorata L. Family: Rubiaceae	<ul style="list-style-type: none"> • Anti-inflammatory • Sedative/hypnotic • Diuretic • Wound healing • Expectorants 	<ul style="list-style-type: none"> • Impaired blood clotting 	<ul style="list-style-type: none"> • Coumarin content of the plant cause synergy with warfarin 	33
Tonka Bean, tonga bean, tonco seed, tonquin bean, cumaru, tonco bean	Dipteryx odorata (Aubl.) Willd. D. oppositifolia Family: Fabaceae (Leguminosae)	<ul style="list-style-type: none"> • Cramps • Nausea • Aphrodisiac 	<ul style="list-style-type: none"> • Hepatic damage 	<ul style="list-style-type: none"> • Coumarin content of the plant cause synergy with warfarin 	34
Ganoderma, Ling-zhi, reishi	Ganoderma lucidum, Ganoderma japonicum	<ul style="list-style-type: none"> • HIV/AIDS 	<ul style="list-style-type: none"> • Inhibition of platelet aggregation, anticoagulation 	<ul style="list-style-type: none"> • Coumarin content of the plant cause synergy with warfarin 	35,36,37
Isatis, Pan-lan-ken, dyers' wood root	Isatis tinctoria	<ul style="list-style-type: none"> • HIV/AIDS 	<ul style="list-style-type: none"> • Inhibition of platelet aggregation, anticoagulation 	<ul style="list-style-type: none"> • Contains salicylic acid 	37,38
Red Clover	Trifolium pratense	<ul style="list-style-type: none"> • HIV/AIDS 	<ul style="list-style-type: none"> • Anti-coagulation 	<ul style="list-style-type: none"> • Causes excessive prolongation of INR and PT when used with warfarin 	37,39
Salvia, Tan-shen	Salvia miltiorrhiza	<ul style="list-style-type: none"> • HIV/AIDS • Blood Pressure 	<ul style="list-style-type: none"> • Sedation • Hypotension • Diuretic 	<ul style="list-style-type: none"> • Inhibition of platelet aggregation causes excessive prolongation of INR and PT 	37

				when used with warfarin	
Shiitake	Lentinus edodes	<ul style="list-style-type: none"> HIV/AIDS 	<ul style="list-style-type: none"> hypotension Inhibition of platelet aggregation Dermatitis 	<ul style="list-style-type: none"> Inhibition of platelet aggregation causes excessive prolongation of INR and PT when used with warfarin 	37, 40,41
St. John's Wort	Hypericum perforatum	Antidepressant Mood Stabilizer	<ul style="list-style-type: none"> 	Induces CYP1A2 and 2C9 causing warfarin levels and INR to drop	
Tang-kuei, Du-huo, bai-zhi	Angelica sinensis, Angelica pubescens, Angelica polymorpha, Angelica dahurica	<ul style="list-style-type: none"> HIV/AIDS Expectorant Diuretic Anti-flatulant 	<ul style="list-style-type: none"> Inhibition of platelet aggregation Photosensitivity 	<ul style="list-style-type: none"> Coumarin content of the plant cause synergy with warfarin, also contain psoralens 	35,37
Yarrow, Mifoi	Acillea millefolium	<ul style="list-style-type: none"> HIV/AIDS 	<ul style="list-style-type: none"> Anti-coagulation Dermatitis Anaphylaxis Photosensitivity 	<ul style="list-style-type: none"> Coumarin content of the plant cause synergy with warfarin, also contain psoralens 	37
Yohimbe Bark Extract	Pausinystalia yohimbe	<ul style="list-style-type: none"> Erectile dysfunction Hypertension Angina Age-related cognitive disorders 	<ul style="list-style-type: none"> FDA considers it unsafe for OTC sale 	<ul style="list-style-type: none"> Inhibits platelet aggregation, therefore increased risk of bleeding 	43-50
Other Herbal Products that Have the Potential to Interact with Warfarin: Asian Ginseng (Panax ginseng, Lycium barbarum, Green tea (Camellia sinensis), Dong quai, Devil's claw (Harpagophytum procumbens), SAME, Licorice, Grape seed, Bladderwrack					

Other Herbal Products that Have Potential to Interact with warfarin: alfalfa, aniseed, arnica, bogbean, celery, seed or extract, Chamomile, Clove,

fenugreek, [Akyoh (Glutinum), Gaiyoh (Artemisiae folium), Sanshishi (Gardeniae fructus), Kizutsu)Surantii fructus), Taisoh (Zizyphi fructus)].⁴²

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APPENDIX A

ABSOLUTE CONTRAINDICATIONS TO ANTICOAGUATION

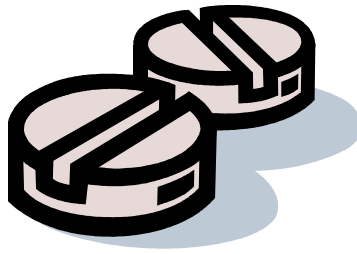
1. history of recent major bleeding episode: GI, GU, CNS, etc
2. acute, chronic alcoholism
3. history of non-compliance and unreliability in the absence of a responsible caregiver
4. active bleeding
5. unexplained anemia
6. severe hypertension
7. pregnancy (warfarin)
8. uncontrolled psychiatric disturbance
9. need for high dose salicylate therapy (rheumatoid arthritis & warfarin)

RELATIVE CONTRAINDICATIONS TO ANTICOAGULATION

1. remote history of major bleeding episode
2. peptic ulcer disease, hepatic cirrhosis or other liver disease
3. recent surgery or trauma
4. diabetic retinopathy
5. cancer
6. steroid therapy

inadequately confirmed indication for anticoagulation

ANTICOAGULATION CLINIC VA WNY HEALTHCARE SYSTEM BUFFALO, NY



INSTRUCTIONS for Patients on WARFARIN

WHAT IS WARFARIN?

WARFARIN, COUMADIN, is an anticoagulant medication or “blood thinner”. It helps to prevent formation of blood clots by slowing down the body's clotting process.

WHAT IS THE ANTICOAGULATION CLINIC?

Our Anticoagulation Clinic includes pharmacists and nurses. Our goal is to make certain that the dose of warfarin you are taking is the correct dose for you and that you are not experiencing the major side effect which is bleeding. We determine the best warfarin dose for you on a blood test called the INR, which tests us how long it takes your blood to clot. At each clinic visit an INR will be drawn in the outpatient lab. For each lab draw we will also review your medications, diet and health status, as all of these things factor into your warfarin dose.

WHAT DOES WARFARIN LOOK LIKE?

Warfarin is a round tablet that comes in several different colors. MOST patients in our clinic are on either GREEN 2.5mg warfarin tablets –or- PINK 1mg warfarin tablets. The strength of the warfarin is imprinted directly on the tablet. Your warfarin tablet color is _____ and the milligram strength is _____ mg. You will be advised on what dose you should take (how many warfarin tablets each day) every time you have your INR drawn. All warfarin tablets prescribed for a given day should be taken at the same time, preferably after 4:00 PM. If you find it difficult to take your warfarin in the evening, and find that you miss doses because of this, please let us know and we will then try to find a better time of day for you to take you warfarin.

WHAT IS THE PROCEDURE AT EACH CLINIC VISIT



New Patients

All patients that are new to our clinic are required to meet with the clinic nurse and pharmacist at least once. We may need to see you more than this depending on your situation.

Please go to the outpatient lab **BEFORE** your clinic appointment time, so that we can give you dosing instructions without having you wait long. After your blood is drawn, please report to Desk 1 Anticoagulation Clinic at the scheduled time of your appointment.

During your first appointment with us, you will receive a pill box, med-alert necklace or bracelet, and a folder containing important education information and Anticoagulation Clinic contact information. We will supply you with warfarin tablets and the dosing schedule we want you to take.

For each clinic appointment, you will speak with a nurse and/or clinical pharmacist about the dose of warfarin you have been taking, changes in any other medicines, variations in your diet, and any other issues you may wish to mention.

Lab-Only Patients

Once we have educated you in clinic and your INR (warfarin lab) is stable, you will then become a “LAB ONLY” patient. You will still need to present to the VA outpatient lab for regular blood draws so that we can monitor your INR (this is usually about every 4 weeks, but may be more often if your INR is not

stable). When you are a “Lab Only” patient, you can go home after your lab draw.

Once we receive your INR, we will call you to give you your dosing instructions.

- ❖ **Therefore, you must be available by phone on the day of your lab draw. Please make sure we have your current contact information.**
- ❖ **If you go to a CBOC (ie. Lackawanna, Lockport, Olean, etc) for lab work, we will not have your INR result until the NEXT day, so please be available the DAY AFTER for dosing instructions in this case.**

**If your INR is “good” a nurse will call you to check up on you and verify your warfarin dosing

**If your INR is “not good” (too “thick” or too “thin”) a pharmacist will call you to ask about any changes, and to give you new dosing instructions



TIPS TO MINIMIZE YOUR BLEEDING RISK WHILE TAKING WARFARIN

1. *Protect your body from injury:*

- use a SOFT toothbrush with gentle motion
- use an electric razor rather than a safety/disposable razor
- do not walk barefoot
- use caution when handling sharp objects (knives, scissors, tools)
- avoid icy pavement; wear sturdy, good quality boots in snowy weather to avoid falling
- use Vaseline or saline nasal spray, or a humidifier in your home to reduce the chance of occasional nosebleeds especially during winter weather

2. *Know the signs of possible bleeding:*

- Inspect your skin daily for black and blue marks. Sudden and excessive bruising may indicate bleeding
- Get into the habit of looking into the toilet bowl before you flush, to look for possible blood in your urine (may be pink, red or brown) or stool (may be bright red or black-tarry consistency)
- If you injure yourself and cannot control the bleeding, or have a nosebleed that bleeds heavily for more than 20 minutes, go immediately to the Emergency Room

OTHER IMPORTANT NOTES ON YOUR WARFARIN

1. *Take your warfarin at the same time each day.*

- Late afternoon (after 5pm) or early evening is best
- Use your pill box provided by the clinic
- It is important to remember to take your dose each day
- Do not double your dose if you forget a dose. Simply make a note of the date on which you missed the dose and report that missed dose and date in clinic.

2. *At the beginning of any office visit, let your health care provider know you are taking warfarin.*

3. *Limit your intake of ALCOHOL to NO MORE THAN 2 servings in a given day.*

More than this will increase your bleeding risk, and will also increase your risk of falling

- Examples of serving sizes:
 - 12 oz of beer
 - 5 oz of wine
 - 1.5 oz of distilled spirits (8- proof)

3. *Eat a balanced, regular diet consisting of a variety of foods*

- Eat usual portions of fruits and vegetables
- Avoid excessive amounts of green leafy vegetables, but DO NOT STOP eating these. A consistent diet is the key
- Try to eat the same amount of vitamin k in your diet from week to week



- Avoid large doses of vitamins that exceed the Recommended Daily Allowance (RDA). This is very important especially for Vitamin E. Do not exceed 30IU of vitamin E per day unless prescribed by your physician. Instead, choose a preparation from our list of vitamins or one similar to it (list will be provided upon request). Always let our clinic staff know what you are taking. It is best to bring the bottle to clinic.
 - Avoid herbal (complementary) preparations since many contain products that may interact with warfarin and cause harmful effects such as bleeding.
7. Do not take any medicines not prescribed by your doctor. This includes over-the-counter medicines (pain pills, antacids, laxative, and cold & flu remedies). Call the clinic before taking any of these medicines.
- Never take aspirin or aspirin-containing medicines unless directed by your doctor who is aware that you are also taking warfarin.
 - Do not take ibuprofen (Motrin, Advil) or ketoprofen (Actron, Orudis KT) or naproxen (Aleve) since these may cause stomach irritation & bleeding.
 - If you need medicine for an occasional headache or minor aches, use acetaminophen (Tylenol) rather than aspirin, ibuprofen, naproxen or ketoprofen. Do not use more than 2000mg of acetaminophen per day without calling the clinic:
 - No more than 6 Regular-strength 325mg acetaminophen tablets
 - No more than 4 Extra-strength 500mg acetaminophen tablets
 - No more than 3 Arthritis-strength 650mg acetaminophen tablets
 - Let us know when new medicines are added or old medicines are stopped. This is important because many medicines interfere with warfarin and the clinical pharmacist may need to change your warfarin dose.
8. Always carry your ***Emergency Medical Identification Card*** and wear your med-alert necklace or bracelet. This way, if you are ever in an emergency situation, healthcare personnel will know you are on warfarin and care for you with this in mind



WHEN TO CALL YOUR PHYSICIAN OR GO TO AN EMERGENCY ROOM

1. Bleeding from cuts which does not stop after 20 minutes of direct pressure
2. Major blows, injuries such as severe falls or large cuts
3. Spontaneous bleeding from mouth, nose or rectum
4. Appearance of dark brown, pink or red urine
5. Black, tarry stools or the presence of blood with a bowel movement
6. Appearance of blood when you cough
7. Appearance of blood or "coffee ground" material when you vomit
8. Large bruised areas that are growing bigger
9. Episodes of fainting, passing out, or persistent abdominal pain.

WHEN TO CALL THE ANTICOAGULATION CLINIC

1. Recent illness or hospitalization
2. Major change in diet
3. Change in your medications
4. If you become pregnant or are planning pregnancy. Also call your physician immediately. Warfarin is harmful to the fetus.
5. If it is necessary to miss an appointment- we will gladly reschedule
6. If another doctor changes your warfarin dose
7. If you have ANY questions about your warfarin

IMPORTANT PHONE NUMMERS

- Call the Anticoagulation Clinic Weekdays from 8am to 4:30pm:

Clinic nurses:

- Patients with last name A-L : Call 862-8764
- Patients with last name M-Z: Call 862-8763
- Desk 1 (Coumadin Clinic)- 862-8934

Clinic Pharmacist : Call 862-7212

- Call PCG when you cannot reach Coumadin Clinic
- Your provider is:

Primary Care Call Center 862-8567

For urgent questions or problems on weekends & evenings call the Emergency Room 862-8774

For emergencies call 911

ADDITIONAL EDUCATIONAL PACKET MATERIAL:



NonVA_Emergency_
Care_FactSheet_GFR



Warfarin Blood
Thinner Pills - Patient



Drug Interaction w.
Warfarin.pdf



Apixaban v2.pptx



PatientEducation
PVD.pdf



Dabigatran v2.pptx



blood-clots-fact-shee
t patient education C



Rivaroxaban v2.pptx



Deep Vein
Thrombosis.EBSCO.pr



Warfarin v2.pptx



Peripheral Vascular
Stenting.pdf



edoxaban
FINAL.pptx



PatientEducation (1)
PE.pdf



Lovenox.pptx



Peripheral Vascular
Stenting.pdf