PURPOSE

The Clinical Pharmacists are authorized to prescribe and to manage patients placed on oral anticoagulation (warfarin) therapy, when requested by the physician.

This protocol is applicable to the adult patients, age 18 and older only.

PROCEDURE

Inpatient Consultation

1. The physician may request Clinical Pharmacist assistance in the management of oral anticoagulation therapy by placing a request for "Consult to Pharmacy" through the EHR (electronic health record) system and sending a consultation request to the Department of Medicine. Warfarin therapy must be initiated by the requesting physician. The Clinical Pharmacist will manage the warfarin doses, thereafter.

2. Upon receipt of the referral, the Clinical Pharmacist proceeds to obtain baseline information to include: medical history, including anticoagulation and bleeding/bruising history; pertinent labs, current medications and allergies; diet and social history, including alcohol, and activities/occupations. The requesting physician is responsible for the warfarin management until the patient has been seen by the clinical pharmacist.

3. The Clinical Pharmacist evaluates patient's International Normalized Ratio (INR) lab result and adjusts the oral anticoagulation (warfarin) dose accordingly. Dosage adjustment will follow the "Guidelines for Anticoagulation Therapy" (see attachment).

4 The Clinical Pharmacist will monitor the patient for side-effects, drug-drug interactions, drug-food interactions and provide patient/patient family education to include:

a. Importance of anticoagulation therapy and compliance to therapy
b. Adverse drug reactions
c. Importance of follow-up monitoring
d. Potential drug and food interactions
e. With female patients of childbearing years: complications of warfarin therapy in pregnancy, stress the importance of birth control, pregnancy testing and informing the Clinical Pharmacist if patient becomes or plans to become pregnant
f. Provide supplementary information and/or aids when indicated

5 Clinical Pharmacist will document patient's therapy, lab results, dosage adjustment, and other pertinent information in the patient's EHR.

6 The Clinical Pharmacist enters the respective medication order through EHR system. The order shall include the following:

a. Name of the drug
b. Drug dosage and frequency of administration
c. Laboratory orders
d. Clinical Pharmacist name and title
e. Clinical Pharmacist will sign, date, and time the order

7 The Clinical Pharmacist may sign-off the consultation to the physician once the maintenance dose for warfarin is established. The physician may request another Clinical Pharmacist consult when necessary.

8 The Inpatient Pharmacist reviews INRs daily for patients on warfarin. The Inpatient Pharmacist will contact the physician for patients with INRs greater than or equal to 3.5 on warfarin therapy. The physician may request Clinical Pharmacist assistance in the management of oral anticoagulation therapy by ordering a "Consult to Pharmacy" through the EHR and sending a consultation request to the Department of Medicine.

Outpatient Clinic Anticoagulation Follow-up

1 Refer to the Enrollment and Discharge Criteria from Rancho Los Amigos National Rehabilitation Anticoagulation Clinic (see attachment)

2 Patients being discharged may be referred to the Rancho Los Amigos Oral Anticoagulation Clinic by completing the Anticoagulation New Visit Referral Form in the EHR system. The indication for therapy, target INR, and duration for therapy must be documented in the discharge summary and/or in Anticoagulation New Visit Referral Form.

3 Clinic patients may be referred to the Rancho Los Amigos Oral Anticoagulation Clinic. The indication for therapy, target INR, and duration for therapy must be documented in the medical records and/or in the Anticoagulation New Visit Referral Form in the EHR system for all patients.

4 The referring service is responsible for managing the patient's anticoagulation therapy prior to the patient's first visit to the Oral Anticoagulation Clinic.

5 The Clinical Pharmacist will monitor the patient for side-effects, drug-drug interactions, drug-food interactions and provide patient/patient family education to include:

a. Importance of anticoagulation therapy and compliance to therapy
b. Adverse drug reactions
c. Importance of follow-up monitoring
d. Potential drug and food interactions

f. With female patients of childbearing years: complications of warfarin therapy in pregnancy, stress the importance of birth control, pregnancy testing and informing the Clinical Pharmacist if patient becomes or plans to become pregnant

g. Provide supplementary information and/or aids when indicated

6 Clinical Pharmacist evaluates patient's INR and adjusts the oral anticoagulation (warfarin) dose accordingly. Dosage adjustment will follow the "Guidelines for Anticoagulation Therapy" (see attachment).

7 When interruption of a Vitamin K antagonist (VKA) and subsequent bridging with subcutaneous Low Molecular Weight Heparin (LMWH) are required for perioperative management of patients who are receiving VKAs, the Clinical Pharmacist will follow guidelines from the *Antithrombotic and Thrombolytic Therapy: ACCP Evidence Based Clinical Practice Guidelines, 9th ed, 2012* and *Antithrombotic Therapy for VTE Disease: Chest Guideline and Expert Panel Report. Chest 2016*

8 For medical complications that arise, the Clinical Pharmacist will seek consultation with the supervising physician and/or refer the patient to, the emergency room, or urgent care centers.

9 Clinic patients are advised to carry information identifying their anticoagulation therapy, given contact information of Clinical Pharmacist and advised to have treating clinicians contact the Clinical Pharmacist; when medical complications arise from anticoagulation therapy.

10 The ancillary clinic staff will identify patients who have missed appointments after every clinic session and notify them to reschedule.

11 The ancillary clinic staff will notify the referring service (i.e. clinician and/or case manager) of patients who are discharged from the Anticoagulation Clinic as a result of failing 2 or more appointments OR have not been seen for 3 or more months by the clinic.

12 The ancillary clinic staff will reschedule established clinic patients with missed appointments. Case management staff and the ambulatory appointment staff will contact and notify the patient of the appointment.

Guidelines for Anticoagulation Therapy

From Antithrombotic Therapy and Prevention of Thrombosis, 9th Edition, American College of Chest Physicians Evidence Based Clinical Practice Guidelines; Chest 2012 141(suppl 2);1-801.
and Antithrombotic Therapy for VTE Disease: Chest Guideline and Expert Panel Report. Chest 2016; 149:315-352

INDICATION	RECOMMENDATION	DURATION	COMMENT
ATRIAL FIBRILLATION			
CHADS2 = 0	No antithrombotic therapy	n/a	See AF Stroke Prevention Guidelines Summary below
CHADS2 = 1	DOAC or Warfarin (INR 2-3)	chronic	
CHADS2 ≥ 2	DOAC or Warfarin (INR 2-3)	chronic	
With mitral stenosis or prosthetic heart valve	Warfarin (INR 2-3 or higher valve-specific goal)	chronic	
Pre-cardioversion (AF>48 hrs)	DOAC or Warfarin (INR 2-3)	3 weeks	
Post-cardioversion (in NSR)	DOAC or Warfarin (INR 2-3)	4 weeks	
CORONARY ARTERY DISEASE			
Primary prevention/age ≥ 50	ASA 81mg daily	chronic	In pts without symptomatic cardiovascular disease
CAD > 12 mo after PCI/stent/ACS	ASA 81mg daily or clopidogrel	chronic	
Elective PCI			
No stent	ASA 81-235mg + clopidogrel	1 month	then single antiplatelet therapy (SAP)
BMS	ASA 81-325mg + clopidogrel	1monthy	then ASA 81mg + clopidogrel x 11 months, then chronic SAP
DES-sirolimus	ASA 81-325mg + clopidogrel	3 months	then ASA 81mg + clopidogrel x 9 months, then SAP
DES - paclitaxel	ASA 81-325mg + clopidogrel	6 months	then ASA 81mg + clopidogrel x 6 months, then SAP
Anterior MI with LV thrombus or EF<40% or antero-apical wall motion abnormality			
No stent	Warfarin (INR 2-3) + ASA 81mg	3months	then dual antiplatelet therapy (DAP) x 9 months, then SAP
BMS	Warfarin (INR 2-3) + DAP	1 month	then warfarin + SAP x 2 mo, then DAP x 9 mo, then SAP
DES sirolimus	Warfarin (INR 2-3) + DAP	3 months	then DAP x 9 months, then SAP
DES - paclitaxel	Warfarin (INR 2-3) + DAP	6 months	then DAP x 6 months, then SAP
Acute Coronary syndrome			
Without PCI	Ticagrelor 90mg bid + ASA 81mg	12 months	or ASA + clopidogrel, then SAP
With PCI	DAP	12 months	See stent-specific recommendations for Elective PCI
LEFT VENTRICULAR DYSFUNCTION			
No CAD/no LV thrombus	No antithrombotic therapy		Warfarin (INR 2-3) considered by some patients
No CAD/+ LV thrombus	Warfarin (INR 2-3)	≥ 3 months	
PERIPHERAL ATERIAL DISEASE			
asymptomatic disease	ASA 81mg daily	Chronic	
symptomatic disease	ASA 81mg or clopidogrel	chronic	Do not use DAPT (or APT if on warfarin for another reason)
s/p angioplasty +/- stenting	ASA 81mg or clopidogrel	Chronic	Do not use DAPT
asymptomatic carotid stenosis	ASA 81mg daily	chronic	
symptomatic carotid stenosis	Antiplatelet therapy	Chronic	Clopidogrel 75mg or Aggrenox over ASA 81mg daily
THROMBOEMBOLISM (UE DVT/LE DVT/PE)	**Warfarin with concurrent UFH/LMWH/fondaparinux for at least 5 days and until INR>2 With compression stockings as needed for symptomatic management**		
Provoked	DOAC or Warfarin (INR 2-3)	3 months	DOAC recommended over VKA
Unprovoked/first event			
Low/moderate bleed risk	DOAC or Warfarin (INR 2-3)	≥ 3months	DOAC recommended over VKA; see UWMedicine *Recommendations for Duration of Anticoagulant Therapy for VTE*
High bleed risk	DOAC or Warfarin (INR 2-3)	3 months	
Unprovoked/recurrent event			
Low/moderate bleeding risk	DOAC or Warfarin (INR 2-3)	≥ 3 months	DOAC recommended over VKA; see UWMedicine *Recommendations for Duration of Anticoagulant Therapy for VTE*
High bleeding risk	DOAC or Warfarin (INR 2-3)	3 months	
Cancer-associated	Anticoagulation	chronic	3 months LMWH, followed by chronic anticoagulation [warfarin (INR 2-3) or DOAC or LMWH]
Central line associated UE DVT			**Do not remove line if it is functional and necessary Same duration of therapy regardless of use of thrombolysis**
Line removed	Anticoagulation	3 months	Same duration for cancer and non-cancer patients
Line not removed	Anticoagulation	≥ 3 months	Minimum 3 months and continue until line removed
Portal/mesenteric/splenic/hepatic vein thrombosis			
Transient risk factors	Anticoagulation	3 months	LMWH preferred over warfarin (INR 2-3) for cancer-associated events or if hepatic insufficiency is present
Persistent risk factors	Anticoagulation	≥ 3 months	
Cerebral Venous Sinus Thrombosis			
Transient risk factors	Warfarin (INR 2-3)	3-6 months	
Persistent Risk Factors	Warfarin (INR 2-3)	chronic	

From Nishimura RA, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2017; 70:252-89.

VALVULAR HEART DISEASE GUIDELINES			
INDICATION	**RECOMMENDATION**	**DURATION**	**COMMENT**
VALVULAR ATRIAL FIBRILLATION			
with rheumatic mitral stenosis	Warfarin (INR 2-3)	chronic	
with aortic valve disease and $CHAD_2S_2$-Vasc Score ≥ 2	Warfarin (INR 2-3) or DOAC	chronic	
with tricuspid valve disease and $CHAD_2S_2$-Vasc Score ≥ 2	Warfarin (INR 2-3) or DOAC	chronic	
with mitral regurgitation and $CHAD_2S_2$-Vasc Score ≥ 2	Warfarin (INR 2-3) or DOAC	chronic	
VALVE REPLACEMENT - BIOPROSTHETIC			
Mitral			
first 3-6 months/NSR	Warfarin (INR 2-3)	3 - 6 months	Plus ASA 81mg daily
after 3-6 months/NSR	Antiplatelet therapy	chronic	ASA 81mg daily
Aortic			
first 3-6 months/NSR	Warfarin (INR 2-3)	3 - 6 months	Plus ASA 81mg daily
After first 3-6 months/NSR	Antiplatelet therapy	chronic	ASA 81mg daily
Transcatheter Aortic (TAVR)			
First 3 months	Warfarin (INR 2-3)	3 months	Plus ASA 81mg daily + clopidogrel 75mg daily x 6 months
After first 3 months/NSR	Antiplatelet therapy	chronic	ASA 81mg daily + clopidogrel 75mg daily x 6 months
VALVE REPLACEMENT - MECHANICAL			
Mitral	Warfarin (INR 2.5-3.5)	chronic	Plus ASA 81mg daily
Aortic			
On-X valve	Warfarin (INR 2.0-3.0)	chronic	Plus ASA 81mg daily
On-X valve, after 3 months and with no risk factors for thromboembolism	Warfarin (INR 1.5-2.0)	chronic	Plus ASA 81mg daily
Bileaflet or current generation tilting disk with no risk factors for thromboembolism	Warfarin (INR 2-3)	chronic	Plus ASA 81mg daily
With risk factors for thromboembolism (AF, previous thromboembolism, LV dysfunction, hypercoagulable condition)	Warfarin (INR 2.5-3.5)	chronic	Plus ASA 81mg daily
Older generation (eg: ball-in-cage)	Warfarin (INR 2.5-3.5)	chronic	Plus ASA 81mg daily
Aortic + mitral	Warfarin (INR 2.5-3.5)	chronic	Plus ASA 81mg daily

II. Dosing adjustment guidelines: These are guidelines only. The final decision for any dosage adjustment will be based on the Clinical Pharmacist's clinical judgment after considering the overall situation including patient compliance, diet changes, concurrent medications, bleeding /bruising events, thromboembolic events, non-steady state conditions, and other criteria that may affect anticoagulation therapy.

A. No dosage adjustment is required for patients (at steady state) whose INR is within the therapeutic range.

B. Dosage/INR recommendations (for steady-state conditions):
(*adapted from Wilson Norton, J; Gibson D. AJHP 1996;53(10):1151-1157)*

INR	**Target INR: 2.0 – 3.0**
Less than 2.0	Increase weekly warfarin dose by 5 – 20%
3.0 – 3.5	Decrease weekly warfarin dose by 5 – 15%
3.6 – 4.0	Hold 0 – 1 dose; decrease weekly warfarin dose by 10 – 15%
Greater than 4.0	Hold 0 – 2 doses; decrease weekly warfarin dose by 10 – 20%

INR	**Target INR: 2.5 – 3.5**
Less than 2.0	Reload X 1; Increase weekly warfarin dose by 10 -20%
2.4 – 2.4	Increase weekly warfarin dose by 5 – 15%
3.6 – 4.6	Decrease weekly warfarin dose by 5 – 15%
4.7 – 5.2	Hold 0 – 1 doses; decrease weekly warfarin dose by 10 – 20%
Greater than 5.2	Hold 0 – 2 doses; decrease weekly warfarin dose by 10 – 20%

C. Patient at either extreme, but still within the accepted therapeutic range may receive a 5 to 10% dosage adjustment to approach the middle of the therapeutic range.

D. In patients with risk factors for bleeding the INR will be maintained towards the lower end of the therapeutic range as appropriate.

III. INR follow-up

INR tests will be drawn as often as reasonably needed during the initiation period of therapy. Follow-up INR test intervals will gradually be lengthened as the patient stabilizes on anticoagulation therapy.

The suggested INR follow-up draw schedule is as follows:

<u>Maintenance Therapy</u>	
Dose held today in patient with significant over anticoagulation	In 1 – 2 days
Dose change today	Within 1 – 2 weeks
Dose change < 2 weeks ago	Within 2 – 4 weeks
Routine follow-up of medically stable & reliable patients	Every 4 – 8 weeks
Routine follow-up of medically unstable or unreliable patients	Every 1 – 2 weeks
<u>After Hospital Discharge</u>	
If patient or therapy is unstable	In 1 – 3 days
If patient or therapy is stable	In 3 – 7 days

RANCHO LOS AMIGOS NATIONAL REHABILITATION CENTER
ANTICOAGULATION CLINIC

WARFARIN (brand name: Coumadin®)

Warfarin (Coumadin®) is a medication used to prevent blood clots in the legs, the lung, in patients with artificial heart valve, atrial fibrillation and other potential clotting medical conditions.

You are currently taking Warfarin (Coumadin®) to prevent blood clot due to:

_____Deep Vein Thrombosis (blood clot in the leg)
_____Pulmonary Embolism (blood clot in the lung)
_____Heart Valve replacement
_____Atrial Fibrillation (Irregular heart rhythm)
_____Other _____

It is important that you come to your scheduled clinic appointment to have your blood test (PT-INR) done. INR is the blood test we use to check if the Warfarin (Coumadin®) dose you are taking is right for you.

Your PT-INR range is:_____

If your PT-INR test number is below your range, there is not enough Warfarin (Coumadin®) in your body.

If your PT-INR test number is higher than your range, you have too much Warfarin (Coumadin®) in your body needed to prevent blood clot and may increase risk of bleeding.

Excessive bleeding is a major concern while you are taking Warfarin (Coumadin®)
It will take longer for bleeding to stop if you have too much Warfarin (Coumadin®) in your body. You need to go to the nearest Emergency Room (ER) for any excessive bleeding and tell the ER staff that you are taking Warfarin (Coumadin®)

Many medications, herbal supplements, vitamins, nutritional drinks such as Ensure or Boost, green leafy vegetables and alcohol are known to interfere and may change the level of Warfarin (Coumadin®) in the body.

It is important that you tell your Provider of any change in your medical condition, any scheduled dental or surgical procedures, any change in all your medications or vitamins, change in your daily diet or if you missed taking a Warfarin (Coumadin®) dose. Your Provider will review your PT-INR test result and adjust your Warfarin (Coumadin®) accordingly.

Always discuss any concern about your Warfarin (Coumadin®) therapy with your Provider.

Enrollment and Discharge Criteria from Rancho Los Amigos National Rehabilitation Anticoagulation Clinic

Inclusion Criteria

- Patients discharged to be followed at or referred from:
  - Rancho's Medical Homes
  - Cardiology Service
  - Arthritis Surgery Service

NOTE: Referral will include indication for Warfarin therapy, target INR and duration of Warfarin therapy. Patient's referral will be denied if these information are not specified.

Exclusion Criteria

- Patients who do not fall into the Inclusion Criteria
- Patients who are transferred to Skill Nursing Care or other Long-term Care Facilities
- Patients who have Outside Primary Care following Anticoagulation therapy
- Patients who are on Heparin or Low Molecular Weight Heparin, only.

Discharge Criteria

- Warfarin therapy completed
- Patient has failed 2 or more appointments (These patients will require referral by one of the Services in the Inclusion Criteria to be enrolled back to the Anticoagulation Clinic)
- Patient who has not been seen for 3 or more months (These patients will require referral by one of the Services in the Inclusion Criteria to be enrolled back to the Anticoagulation Clinic)

Referral Questions

Winston Wong, Pharm.D. (562) 385 -7207
Case Management Department (562) 385 -7164

References

1. OPTIMAL THERAPEUTIC RANGE AND DURATION OF ANTICOAGULATION (see attached Recommendations for Chronic Antithrombotic Therapy) *(adapted from Antithrombotic and Thrombolytic Therapy: ACCP Evidence Based Clinical Practice Guidelines,9h ed, 2012*

2. The UWMedicine *Recommendations for Chronic Antithrombotic Therapy*. March 2017

3. Antithrombotic Therapy for VTE Disease: Chest Guideline and Expert Panel Report. Chest 2016; 149:315-352

4. Nishimura RA, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol