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Please Note: *This policy replaces the following policies:*
Management of Patients with high Prothrombin Time (PTs), International Normalized Ratio (INRs)
Warfarin Management for Invasive Procedures
Warfarin Management in Dental Procedures

ANTI-COAGULANT THERAPY – INITIATION AND MANAGEMENT

OVERVIEW:

ANTICOAGULANT MEDICATION AND ACTIONS

- Anticoagulants, often times called anti-thrombotic drugs are used to decrease the risk of thrombosis by interfering with the clotting mechanism. Physicians and other health care providers must consider the risks and benefits of anticoagulant therapy in regards to the patient’s risk for thrombosis if not treated versus the risk of bleeding, if treated with anticoagulant therapy.
- These guidelines cover the dosing and monitoring of Warfarin and Heparin; managing patients with high Prothrombin Times (PT) and International Normalized Ratios (INR); and Warfarin/Heparin management for patients undergoing invasive procedures.
- The two leading anticoagulants are Warfarin and Heparin.
 - **Warfarin** is a Coumarin derivative that inhibits Vitamin K clotting factors & proteins that is most commonly given orally, but is available for intravenous injection. It is used for long term anticoagulant therapy. Warfarin is most commonly used for prophylaxis and treatment of venous thrombosis, pulmonary embolism, complications of atrial fibrillation and/or cardiac valve replacement, post myocardial infarction and prevention of strokes. Brand names for Warfarin are Coumadin, Jantoven, Warfarin Sodium. Allergic reactions to Warfarin may include acute rash, diarrhea, nausea and hepatitis.
 - **Heparin** is either Unfractionated/UFH or Low Molecular Weight/LMWH. Unfractionated Heparin (UFH) enhances the actions of anti-thrombin III by interfering with several clotting factors. It has a rapid onset of action and is usually the first drug used to treat an acute thrombosis. Low Molecular Weight Heparin (LMWH) is known for its superior absorption and consistent dose effect response. Brand Names are Lovenox (enoxaparin), Fragmin (dalteparin) Heparin is contraindicated for patients with active major bleeding, a thrombolytic given within the past 24 hours for acute stroke, hypersensitivity to heparin or pork products, Heparin induced thrombocytopenia (HIT) and renal failure.

NOTE: Three separate guidelines were historically maintained related to anticoagulant therapy: 1) Management of Patients with high Prothrombin Time (PT), International Normalized ratio (INR); 2) Warfarin Management for Invasive Procedures; and 3) Warfarin Management in Dental Procedures. The three guidelines have been merged under this one guideline and this guideline will be maintained going forward.

INITIATING TREATMENT WITH WARFARIN

Prior to initiation of anti-coagulant therapy, the following tests are recommended:

- Complete Blood Count (CBC)
- Platelet Count, Creatinine
- PT/INR
- Activated Partial Thromboplastin Time (aPTT)

Recommended Dose *(Loading doses for rapid induction of warfarin is not recommended)*

- **5 mg/day (Range = 2.5 through 7.5mg) for the first one to two days.**
- **Further dosing is based on the PT/INR results.**
 - Expect a 15 percent dose adjustment to result in an approximately 1.0 INR change and a 10 percent dose adjustment will result in approximate 0.7-0.8 INR change.
 - Consider a lower dose for patients older than 75 years; patients with co-morbidities; patients with poor nutrition; patients with elevated INR when off warfarin; patients with elevated liver function tests; or with patients who have a changing thyroid status.
 - Consider decreasing the dose by one-half for patients with INR levels of 2.0 or greater after the first three doses.

Monitoring

- **Check PT/INR after 2 or 3 doses.**
 - Understand that a steady state of INR values will not be seen for up to three weeks following a dose adjustment.
 - Check for causes of rapid rise in INR, such as poor nutritional status, infection, or systemic disease process.
- Check daily PT/INR results until stabilized in the therapeutic range.
- Check PT/INR results 2 or 3 times a week for 1 to 2 weeks once stabilized.

MAINTAINING PATIENTS ON WARFARIN

Assess clinical variables that can affect the INR with each dose adjustment. The clinical variables assessed would include:

- Patient compliance
- Other medications being taken
- Food or alcohol consumption
- Activity

Recommended Maintenance Dosing

- Dosing is based on the INR levels.
- Most patients can be maintained on 2 to 10 mg. daily.
 - If large doses are needed to maintain the PT/INR ratio within a normal therapeutic range, consider acquired or inherited Warfarin resistance.
- Changes in anticoagulant dosage should be made in small increments and patient should be closely monitored.

Monitoring of Maintenance Dosing

- Conduct the INR once a month, but no greater than 6 weeks, once stabilized.
- Consider repeating the INR value within seven days and more frequent monitoring if INR values are out of range by 0.5.

Table 1: Recommended Therapeutic Range for Oral Anticoagulation

INDICATION	TARGET INR	RANGE
Mechanical prosthetic valves (high risk)	3.0	2.5 – 3.5
Bileaflet mechanical valve in aortic positions Tissue heart valve Valvular (rheumatic) heart disease Atrial fibrillation Venous thromboembolism – deep vein thrombosis/pulmonary embolism Orthopedic prophylaxis	2.5	2.0 – 3.0

Reference from Antithrombotic Therapy Supplement Health Care Guidelines: Institute for Clinical Systems Improvement – Sixth Edition, August 2007 page 17.

STANDARDIZED HEPARIN DOSING

Unfractionated Heparin (UFH) (Intravenous)	<ul style="list-style-type: none"> • Full dose: (the dose used to treat Deep Vein Thrombosis DVT). <ul style="list-style-type: none"> ○ Use 80 units/kg loading dose followed by 18 mg/kg/hr infusion; and ○ Monitor aPTT or heparin assay and adjust dose according to goal. • Low-dose: <ul style="list-style-type: none"> ○ Prescribe 5,000 units subcutaneously every 8 to 12 hours. • Monitoring: <ul style="list-style-type: none"> ○ Obtain an activated Partial Thromboplastin Time (aPTT) every 6 hours until result falls within the target therapeutic range. Once stable, order once a day until heparin therapy is discontinued. 				
Low Molecular Weight Heparin (LMWH)	Medication	Prophylactic Dose	Full-Dose or Treatment Dose	Renal Adjustment for CrCl <30ml/min (prophylactic dose)	Renal Adjustment for CrCl <30ml/min (treatment dose)
	Dalteparin	2,500-5,000 units once daily	200 IU/kg once daily or 100 IU/kg every 12 hours	2,500-5,000 units once daily or use Enoxaparin	Use Enoxaparin
	Enoxaparin	30mg subcutaneous every 12 hours or 40mg SC once daily	1mg/kg subcutaneous every 12 hours or 1.5mg/kg* once daily	30mg subcutaneous daily	1mg/kg subcutaneous once daily

- 1.5 mg is recommended for inpatient use only

MANAGEMENT OF PATIENTS WITH HIGH PROTHROMBIN TIMES INTERNATIONAL NORMALIZED RATIOS

This table provides guidelines for the management of the patients with high PT/INR (International Normalized Ratios). The table provides recommendations regarding holding and omitting Warfarin doses, as well as Vitamin K dosing. Clinical judgment may be used with clear documentation of rationale.

INR	Recommendations
INR greater than therapeutic range but less than 5.0 No significant bleeding	<ul style="list-style-type: none"> Refer to Treatment Protocol from the Anticoagulant Clinic for dosage adjustment recommendations.
INR greater than or equal to 5.0 but less than 9.0 No significant bleeding	<ul style="list-style-type: none"> <u>Recheck PT/INR to ensure accuracy of results, if INR is greater than 8.0,</u> Omit 1-2 doses. Recheck PT/INR on the 4th day and resume at a 10 to 15 percent weekly dose reduction once PT/INR is back in therapeutic range. Alternate doses if increased risk of bleeding: Omit 1 dose, give Vitamin K (preferably 1 to 2.5 mg orally, but up to 5 mg).
INR greater than or equal to 5.0 but less than 9.0 No significant bleeding Requires urgent surgery	<ul style="list-style-type: none"> <u>Recheck PT/INR to ensure accuracy of results if INR is greater than 8.0.</u> Omit 1 to 2 doses. Vitamin K (preferably 2-4 mg po, but up to 5 mg). Expect reduction in INR in 24 hours. If still high at 24 hours, may give additional Vitamin K (1 to 2 mg po).
INR greater than 9.0 No significant bleeding	<ul style="list-style-type: none"> Refer patient to Urgent Care or, if necessary, the Emergency Room. Hold Warfarin and give higher dose of Vitamin K in 24 to 48 hrs. (3 to 5 mg. orally) Monitor more frequently (i.e., every three to four days) and use additional Vitamin K if necessary. Resume at a 10 to 15 percent weekly dose reduction once PT/INR is back in therapeutic range.
Significant bleeding at any elevation of INR	<ul style="list-style-type: none"> Refer patient to Urgent Care or the Emergency Room. Hold Warfarin and give Vitamin K (10 mg IV). Supplement with fresh frozen plasma (FFP) or prothrombin complex concentrate, depending on the urgency of the situation. Consider recombinant factor VIIa as an alternative to prothrombin complex concentrate. Repeat Vitamin K every 12 hours. Give Vitamin K and Fresh Frozen Plasma (FFP) together.
Life-threatening bleeding	<ul style="list-style-type: none"> Refer patient to the Emergency Room. Hold Warfarin and give prothrombin complex concentrate supplemented with Vitamin K (10 mg IV); recombinant factor VIIa may be considered as an alternative. Repeat if necessary.

<p>FACTORS AFFECTING INR/PTs</p>	<p>Check for the following factors that may affect INRs/PTs:</p> <ul style="list-style-type: none"> • Prescription medication interactions: <ul style="list-style-type: none"> ○ Drugs that affect absorption of warfarin; and ○ Drugs that increase or decrease the effect of warfarin • Over the Counter medications (Aspirin, Tylenol, Acetaminophen, laxatives, antacids, non-steroidal anti-inflammatory drugs (NSAIDs), etc.) • Herbal & Dietary Supplements. (Many of these contain coumarins and salicylates. Others have fibrinolytic, coagulant and antiplatelet properties)
<p>PATIENT EDUCATION</p>	<ul style="list-style-type: none"> • Advise patient to take anticoagulant once a day at the same time each day. • Educate on the importance of regular lab monitoring of the INR. • Educate on the side effects of the anticoagulants and the signs of bleeding. • Teach patient about the effects/interactions of diet, herbal supplements, and other prescribed and over the counter medications. • Advise patient on when to seek medical care and what to do if they forget to take their medications. • Encourage patients to wear a “medication alert bracelet” and/or carry an “alert card” with the anticoagulant medication listed.

MANAGING WARFARIN and HEPARIN FOR PATIENTS UNDERGOING INVASIVE PROCEDURES

This document provides guidelines for the management of anticoagulation therapy in patients undergoing invasive procedures. It provides recommendations regarding Warfarin holding and dosings, risk-stratification based on diagnosis, and bridge-therapy.

<p>RISK STRATIFICATION DEFINITIONS:</p>	<p><u>Low risk for thromboembolism:</u></p> <ul style="list-style-type: none"> • No recent (less than 3 months) venous thromboembolism • Atrial fibrillation without history of stroke or other risk factors • Bileaflet mechanical cardiac aortic valve • Dilated cardiomyopathy with normal sinus rhythm and no history of intra cardiac clot or cardio embolism. <p><u>Intermediate risk for thromboembolism:</u></p> <ul style="list-style-type: none"> • Atrial fibrillation with history of other risk factors including: prior ischemic stroke, transient ischemic attack, systemic embolism, age greater than 75 years, moderately or severely impaired left ventricular systolic function and/or congestive heart failure, history of hypertension, diabetes mellitus • Mitral Stenosis requiring warfarin therapy. <p><u>High risk for thromboembolism:</u></p> <ul style="list-style-type: none"> • Recent (less than 3 months) venous thromboembolism. • Mechanical mitral valve. • Old model of cardiac valve (ball/cage). <p><u>High risk procedures (for thromboembolism):</u></p> <ul style="list-style-type: none"> • Major open abdominal or urological procedure. • Cranial and spinal neurosurgical procedure. • Open gynecological procedures. • Lower extremity joint replacement or hip fracture repair.
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Table 2: Annualized Risk of Thrombotic Complication in the absence of anticoagulant Therapy for Selected Conditions

Managing patients receiving long term anticoagulation therapy who require invasive procedures is based on the risks of continuing or stopping therapy	
CONDITION	ANNUALIZED THROMBOSIS RISK PERCENT (%)
Lone atrial fibrillation	1
Average risk atrial fibrillation	5
High risk atrial fibrillation	12
Dual-leaflet (St. Jude)aortic valve prosthesis	10 – 12
Single-leaflet (Bjork-Shiley) aortic valve prosthesis	23
Dual-leaflet (St. Jude) mitral valve prosthesis	22
Multiple St. Jude prosthesis	91

MANAGING WARFARIN and HEPARIN for PATIENTS REQUIRING PROCEDURES.

CONDITION	DESCRIPTION
Low Risk of Thromboembolism	<ul style="list-style-type: none"> • Stop Warfarin <u>4 days prior to surgery</u> to allow INR to return to near normal. • Restart warfarin <u>post-op</u> and if procedure increases the risk of thromboembolism, may start low-dose UFH or prophylactic dose LMW until INR is therapeutic, if needed.
Intermediate Risk of Thromboembolism	<ul style="list-style-type: none"> • Stop Warfarin <u>4 days prior to surgery</u>, to allow INR to fall. • Begin low-dose unfractionated heparin (UFH) or prophylactic dose of low molecular weight heparin (LMWH) <u>2 days prior to surgery</u> • Restart Warfarin <u>post-op</u> and continue low-dose UFH or prophylactic dose LMWH until INR is therapeutic.
High Risk of Thromboembolism	<ul style="list-style-type: none"> • Stop Warfarin <u>4 days prior to surgery</u>, to allow INR to return to normal. • Begin full dose UFH or LMW <u>2 days prior to surgery</u>. (discontinue 12-24 hours prior to surgery). • Restart warfarin <u>post-op</u> and add low-dose UFH or LMWH until INR is therapeutic.
Low Risk of Bleeding	<ul style="list-style-type: none"> • Lower dose <u>4 to 5 days prior to surgery</u>, to reach INR 1.3-1.5. • Restart Warfarin therapy post-op. <u>Add</u> low dose UFH or LWMH, in conjunction, if necessary
An Alternate Approach	<ul style="list-style-type: none"> • Stop Warfarin <u>two days prior to surgery</u>, • Give low-dose oral Vitamin K along with LMW or UFH <u>24 hours prior to surgery</u>. • Continue LMWH or UFH if risk stratification indicates until INR is therapeutic, <u>post-op</u>.

MANAGING WARFARIN IN DENTAL PROCEDURES

This document provides guidelines for the management of anticoagulation therapy in patients undergoing dental procedures. It provides recommendations regarding the necessity of holding Warfarin dosing.

OVERVIEW:	<p>In the case of dental procedures, case reports and studies have indicated the risk of serious bleeding problems is minimal in patients receiving Warfarin. However, serious embolic complications have been reported in patients in whom Warfarin therapy has been stopped for a dental procedure.</p> <ul style="list-style-type: none"> • INRs should be in the therapeutic range within 24 hours to dental procedures or up to 72 hours for stable anticoagulated patients. • Patient's primary care physician should be consulted prior to procedures. 	
	Procedure	INR (International Normalized Ratio) Range
	Exams, x-rays, models, simple restorations, and supragingival prophylaxis	Safe throughout the range of less than 1.5 - 3.5
	Complex restorations, scaling and root planning, and endodontics	Safe if less than 1.5 - 3.0, probably safe to 3.5
	Simple extractions, and curettage, gingivoplasty	Safe if less than 1.5 - 2.5, probably safe through 3.5 but use local measures to limit bleeding when greater than 2.5*
	Multiple extractions, and removal of bony impaction	Safe if less than 1.5 - 2.0, probably safe through 3.5 but use local measures to limit bleeding when greater than 2.0 *
	Gingivectomy, apicoectomy, minor periodontal flap surgery, and placement of single implant	Probably safe if less than 1.5 - 2.5, not advised when greater than 2.5.
	Full mouth/full arch extractions	Probably safe if less than 1.5 - 2.0, but use local measures to limit bleeding when greater than 2.0.* Not advised when greater than 2.0
	Extensive flap surgery, extraction of multiple bony impactions, and multiple implant placements	Probably safe if less than 1.5, not advised when greater than 1.5.
	Open-fracture reduction, orthognathic surgery	Not advised when anticoagulated.
PATIENT EDUCATION	<ul style="list-style-type: none"> • Rest after procedure until anesthetic wears off and clotting begins. • Avoid rinsing the mouth for 24 hours. • Avoid sucking. • Avoid hot liquids or hard food. • Do not chew on affected side until your are sure bleeding has stopped and clotting is stable. 	

* Local hemostatic measures include use of tranexamic acid or e-aminocaproic acid mouthwash, gelatin sponges with silk sutures, vasoconstrictors in local anesthetic and atraumatic surgical techniques, electrocautery, topical thrombin powder, cold water rinses, and local pressure (biting on gauze or tea bags)

REFERENCE PERSON(S):

Steven Evans, MD, Director, Pharmacy Services

Bennett E. Mitchell, MD, Medical Director, Anticoagulation Clinic

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