Name of Procedure:	**Ambulatory Anticoagulation Management Service: Consult agreement**	
Policy Number:	3364-133-105	
Department:	Pharmacy	
Approving Officer:	Chief Executive Officer	
Responsible Agent:	Senior Hospital Administrator	
Scope:	University of Toledo Medical Center	**Effective Date**: 7/31/2022 **Initial Date:** 4/1/2015

_____ New policy proposal _____X _____ Minor/technical revision of existing policy
_____ Major revision of existing policy _____ Reaffirmation of existing policy

(A) Policy Statement

The purpose of these guidelines is to assist anticoagulation clinic (ACC) staff with dosing and monitoring of medications when requested by a physician, through a consult agreement. The goal of the ACC is to optimize drug therapy regimens, minimize complications, and optimize patients' quality of life. The anticoagulation clinic staff will receive role appropriate training with the ultimate goal of being credentialed at the University of Toledo Medical Center.

(B) Purpose of policy

The purpose of this policy is to establish uniform procedures within the Pharmacy Department for consult agreements, dosing, and monitoring.

(C) Scope

This policy applies to all outpatient consult agreements in the ACC between University of Toledo Medical Center anticoagulation staff, University of Toledo Medical Center and University of Toledo Physicians, and patients.

This policy applies to all disease states requiring anticoagulation therapy as a primary or comorbid diagnoses; including but not limited to:

a. DVT/PE Prevention
b. DVT/PE Treatment
c. Atrial Fibrillation and stroke prevention
d. Stroke/TIA
e. Heart Valve Replacement
f. Coagulopathy
g. Vascular/Arterial Disease
h. Other indication as deemed necessary by referring provider

This policy applies to "Anticoagulants" as a drug category.

(D) Procedure

If patient is being anticoagulated with warfarin, the ACC staff will obtain a blood sample via blood finger stick and perform a prothrombin time test (PT/INR). Some situations warrant a venipuncture test for PT/INR, ordered by the ACC staff and performed by a phlebotomist. Dose adjustments will be made as outlined in the dosing algorithms, in accordance with the most recent edition of the American College of Chest Physicians (CHEST) guidelines, special population guidelines, recent literature, and/or at the discretion of ACC staff based on patient interview and clinical situation with supporting documentation. Patients treated with an injectable anticoagulant or Direct Oral Anticoagulants (DOAC) require periodic laboratory monitoring and/or other diagnostics for renal function or bleeding as clinically appropriate in the scope of safe anticoagulation management.

Appendices attached to be used for clinical guidance only, clinical staff responsible to check current guidelines

Appendix A: Clinic Visits Procedural Algorithms
Appendix B: Telephone Procedural Algorithms
Appendix C: Indication guidelines and target INR ranges for warfarin therapy
Appendix D: Guidelines for initiating Warfarin therapy
Appendix E: Guidelines for Management of Critical INR Values

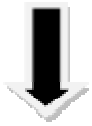
Approved by:		**Review/Revision Date:**
		4/2018 7/2019 6/2022
/s/ Russell Smith, PharmD, MBA, BCPS Senior Hospital Administrator	06/27/2022 Date	
/s/ Rick Swaine Chief Executive Officer	07/11/2022 Date	
/s/ Samer Khouri, MD, MBA Medical Director, Anticoagulation Clinic	08/03/2022 Date	
		Next Review Date: 7/1/2025

Appendix A: Clinic Visits Procedural Algorithm for AC staff (Pharmacists and Nurses)

PATIENT REFERRAL (electronic, verbal)

MEDICAL RECORD REVIEW

PATIENT APPOINTMENT FOR INITIAL EDUCATION SESSION



PATIENT ROUTINE APPOINTMENT (registered, documented in Athena Coumadin Management Flowsheet)
POINT OF CARE INR (entered into Coumadin Management flowsheet)
EVALUATION OF INR
PATIENT INTERVIEW REGARDING:

- Patient specific outcomes assessed
- Discussion of patient specific factors (e.g. diet, drug/food/herbal interactions, medication changes, noncompliance, other symptoms)
- Ongoing risk assessment for hemorrhagic events or thromboembolic events
- Assess dosage and appropriateness of anticoagulant and instruct patient regarding dosage

SET UP FOLLOW UP PLAN

Appendix B: Telephone Procedural Algorithm for AC staff (Pharmacists and Nurses)

PATIENT REFERRAL (electronic, verbal)

MEDICAL RECORD REVIEW

ASSESS WHEN PATIENT ABLE TO MAKE AN APPOINTMENT FOR INITIAL EDUCATION SESSION

PATIENT ROUTINE PHONE MANAGEMENT
(Documented in EMR Coumadin Management Flowsheet)
INR (outpatient lab services, including home health agencies)
Results entered into Coumadin Management flowsheet
EVALUATION OF INR
PATIENT INTERVIEW REGARDING:

- Patient specific outcomes assessed
- Discussion of patient specific factors (e.g. diet, drug/food/herbal interactions, medication changes, noncompliance, other symptoms)
- Ongoing risk assessment for hemorrhagic events or thromboembolic events
- Assess dosage and appropriateness of anticoagulant and instruct patient regarding dosage

SET UP FOLLOW UP PLAN (includes coordination of services with home health agencies, laboratory, or caregivers)

Appendix C: Indication guidelines and target INR ranges for warfarin therapy

Anticoagulation clinic is designed to partner with providers to improve the quality of care provided to patients on oral anticoagulation. The decision to prescribe chronic anticoagulation for a patient is a difficult one, involving balancing the strength of indication(s), the contraindication(s), and the logistical difficulties of monitoring the anticoagulated patients. This information is designed to help anticoagulation clinic staff and providers make the decision for individual patients and can be subject to change based on referring physician clinical decisions

Chest Guidelines 2021 recommend DOAC over warfarin for VTE and stroke prevention in atrial fibrillation patients[2]

Warfarin Therapy Indications and Recommended Goal INR Ranges (subject to clinical situation)[1,2,3,4]

Indication	INR (Range)	Duration	Comments
Thrombophilia with Thromboembolic Event			
VTEs associated with Antiphospholipid Syndrome	2.5 (2-3)	See comments	Repeat testing at 90days, if APL persistently elevated anticoagulation therapy should be chronic
VTEs associated with other non-modifiable genetic disorders (Homozygous Factor V Leiden Deficiency of Protein C, S, or Anti-Thrombin, prothrombin G20210A)	2.5 (2-3)	Chronic	Heterozygous thrombophilia to be assessed on individual basis
Atrial Fibrillation(AF)/Atrial Flutter			
$CHADS_2$, CHA_2DS_2VASc = 0, Low stroke risk	None		May choose aspirin 75-325mg daily
$CHADS_2$ = 1-2, CHA_2DS_2VASc = 1, Intermediate stroke risk	2.5 (2-3)	Chronic	
$CHADS_2 \geq 3$, CHA_2DS_2VASc ≥2, High stroke risk	2.5 (2-3)	Chronic	
With mitral stenosis	2.5 (2-3)	Chronic	
With stable CAD	2.5 (2-3)	Chronic	No aspirin needed
Pre-cardioverson (AF or flutter >48 hr)	2.5 (2-3)	3 Weeks	
Post-cardioverson (in NSR)	2.5 (2-3)	4 Weeks	If $CHADS_2$or CHA_2DS_2VASc 0, may stop warfarin after 4 weeks and choose aspirin
Ischemic Stroke			
Non-cardioembolic stroke or TIA	None	Chronic	Antiplatelet Therapy

Cardioembolic stroke or TIA			
→with warfarin contraindication	None	Chronic	Aspirin 81-325mg daily
→with cerebral venous sinus thrombosis	2.5 (2-3)	3-6 Mos	
→ with other indication for anticoagulation (VTE, AF)	2.5 (2-3)	Chronic	
Thromboembolism (DVT, PE), symptomatic or asymptomatic			
Provoked VTE event	2.5 (2-3)	3 Mos	
Unprovoked: 1st VTE event			
→Proximal or Distal DVT	2.5 (2-3)	3 Mos	After 3 mos, evaluate risk-benefit for extended therapy
→PE (low bleed risk)	2.5 (2-3)	> 3 Mos	After 3 mos, evaluate risk-benefit for extended therapy
→PE (high bleed risk)	2.5 (2-3)	3 Mos	
Unprovoked: 2nd VTE event			
→DVT or PE (low bleed risk)	2.5 (2-3)	> 3 Mos	Consider chronic
→DVT or PE (high bleed risk)	2.5 (2-3)	3 Mos	
With Malignancy	2.5 (2-3)	> 3 Mos	DOAC preferred over LMWH or warfarin, consider chronic until cancer resolved
Acute Upper Extremity DVT			
→Associated w/ central venous catheter that was removed	2.5 (2-3)	3 Mos	
→Associated w/ central venous catheter that was not removed	2.5 (2-3)	Extended	Continue anticoagulation until catheter removed
→Not associated with a central venous catheter	2.5 (2-3)	3 Mos	
Spontaneous superficial vein thrombosis at least 5 cm in length	None	45 Days	Fondaparinux or DOAC
Valve Replacement- Bioprosthetic			
Aortic	2.5 (2-3)	3-6 Mos	Aspirin 81mg daily
Mitral	2.5 (2-3)	3-6 Mos	Aspirin 81mg daily
*If other indication for anticoagulation exists, see specific indication for therapy recommendation			
Valve Replacement- Mechanical			
Aortic	2.5 (2-3)	Chronic	Low bleed risk: add Aspirin 81mg
Mitral	3 (2.5-3.5)	Chronic	Low bleed risk: add Aspirin 81mg
Dual Aortic and Mitral	3 (2.5-3.5)	Chronic	Low bleed risk: add Aspirin 81mg

Orthopedic Surgery			
Total Knee or Hip Arthroplasty	Lovenox (renally adjusted dose)	14-35days	if oral therapy needed, consider rivaroxaban, apixaban, aspirin, or warfarin, assess patient's risk factors for VTEs and bleeding
Hip Fracture Surgery		14-35days	
Trauma Surgery		35 days	

	$CHADS_2$:Stroke Risk Stratification	
	Risk	Score
C	Congestive Heart Failure	1
H	Hypertension	1
A	Age ≥ 75	1
D	Diabetes	1
S	Secondary prevention in patients with prior ischemic stroke, TIA, or systemic thromboembolic event	2
	≥3: High risk for stroke 1-2: Intermediate risk for stroke 0: Low risk for stroke	

	CHA_2DS_2VASc: Stroke Risk Stratification	
	Risk	Score
C	CHF or LVEF ≤ 40%	1
H	Hypertension	1
A	Age ≥ 75	2
D	Diabetes	1
S	Stroke/TIA/Thromboembolism	2
V	Vascular Disease	1
A	Age 65-74	1
S	Female	1
	≥2: Moderate-high risk for stroke 1: Low-moderate risk for stroke 0: Low risk for stroke	

HAS-BLED: Bleed Risk Stratification	
Risk	Score
Hypertension (uncontrolled, >160mmHg systolic)	1
Abnormal renal function (dialysis, transplant, Cr>2.6mg/dL)	1
Abnormal liver function (cirrhosis, bilirubin >2x ULN, AST/ALT/AP >3x ULN)	1
Stroke	1
Bleeding tendency or predisposition	1
Labile INR (unstable/high INRs, TTR <60%)	1

Age (>65)	1
Drugs (antiplatelets, NSAIDs)	1
Alcohol or Drug Usage History (≥8 drinks/week)	
≥3: High risk for major bleeding 2: Moderate risk for major bleeding 0-1: Low risk for major bleeding	

Appendix D: Guidelines for initiating Warfarin therapy

Initial dosing should be based on patient bleeding risk, potential sensitivity to warfarin, indication for anticoagulation, goal INR range, and if potential drug interactions are present.

a. Most newly initiated warfarin therapy patients should be started on a warfarin dose between 5 mg and 10 mg for the first 1 or 2 days. However, if a patient has certain factors (listed below) that increase sensitivity to warfarin, starting at a lower dose may be more appropriate and will be adjusted according to INR:

Increased Warfarin Sensitivity	
Increased INR Response	Increased Bleeding Risk
Baseline INR ≥1.5	Current antiplatelet therapy
Age >65	Thrombocytopenia: platelet <75k/uL
ABW <45kg or ABW<IBW	Significant hepatic disease: cirrhosis or total bilirubin >2.4mg/dL
Malnourished/NPO >3 days	Alcohol abuse history
Hypoalbuminemia <2g/dL	End stage renal disease
Chronic diarrhea	GI bleed within past 30 days
Significant drug interactions	Surgery within past 2 weeks
Decompensated heart failure	Intracranial bleed within past 30 days
*Additionally, ethnicity and genomics should be considered.	

b. An increase of **0.2 - 0.3 INR units/day** from baseline INR is an appropriate response to initial doses of warfarin. If the INR increases too quickly in the first days of therapy, a warfarin dosage reduction is recommended to avoid adverse events.

c. Warfarin dosing algorithms are available but clinical judgment and patient specific conditions must be considered with any algorithm used.

a. Pharmacists should be aware of the many drug-drug and drug-food interactions during the course of the office visit and adjust the dose and monitoring appropriately to reflect this.

b. These practice parameters are designed as guidelines and as such are not substitute for professional judgment and taking into consideration the individual circumstances of the patient

	INR GOAL 2.0-3.0		INR GOAL 2.5-3.5	
Day of Therapy	**INR Value**	**Dose Adjustment**	**INR Value**	**Dose Adjustment**
Day 1		5mg daily (2.5mg daily if high sensitivity to warfarin and at risk for increase response to INR)		5mg daily (2.5mg daily if high sensitivity to warfarin and at risk for increase response to INR)
2-3 Days after	<1.5	5-7.5mg daily	<1.5	5-10mg daily
	1.5-1.9	2.5-5 mg daily	1.5-1.9	5-7.5mg daily

Initiation	2.0-2.5	2.5mg daily	2.0-2.5	2.5-5mg daily
	2.6-3.0	0-2.5mg daily	2.6-3.0	2.5mg daily
	>3.0	Hold & recheck INR next day	>3.0	0-2.5mg daily
In additional 2-3 days after last INR check	<1.5	7.5-10mg daily	<2.0	7.5-10mg daily
	1.5-1.9	5-10mg daily	2.1-2.4	5-7.5mg daily
	2.0-3.0	2.5-5mg daily	2.5-3.5	5mg daily
	>3.0	Hold & recheck INR in 1 day	>3.5	Hold & recheck INR in 1 day

INR Check Frequency	
Every 3-5 days	Until INR within therapeutic range on 2 consecutive INR checks
Then, every 1-2 weeks	Until INR within therapeutic range on 2 consecutive INR checks
Then, every 2-3 weeks	Until INR within therapeutic range on 2 consecutive INR checks
Then, every 4-6 weeks	When dose is stable, may consider 2-3 months for stable, adherent patients without complications

2. Established Warfarin Patients Dosing and Follow Up
Providers should consider other clinical factors before determining dose changes, including but not limited to:

- recent trend in INR values
- dietary changes
- changes in health status
- changes in concomitant medications
- alcohol intake
- missed doses
- other possible explanations for out of range INRs

Additional considerations:

- INR goals may be individualized using clinical judgment with discussion with referring provider
- In some cases, a dose change may not be necessary if a probable cause for out of range INR is identified. Algorithms can be used to help guide dosing changes but, clinical judgment should be used in implementation of algorithms and plan should be individualized to specific patient cases.
- Special consideration for cancer patients; Chest guidelines recommendation on cancer associated thrombosis[2]
    - In patients with DVT of the leg or PE and cancer ("cancer-associated thrombosis"), as long-term (first 3 months) anticoagulant therapy, suggest oral Xa inhibitor over LMWH while apixaban or LMWH may be preferred in luminal GI malignancies.
    - In patients with DVT of the leg or PE and active cancer ("cancer-associated thrombosis") and who (i) do not have a high bleeding risk, we recommend extended anticoagulant therapy (no scheduled stop date) over 3 months of

therapy, or (ii) have a high bleeding risk, we suggest extended anticoagulant therapy (no scheduled stop date) over 3 months of therapy

- NCCN guideline on cancer-associated venous thromboembolism disease, updated version 2. 2018[18]:
    - DOACs are reasonable alternative oral therapy to enoxaparin. Contraindications and patient's specific criteria should be considered for agent choice according to NCCN recommendation data.
    - Relative contraindications, use with caution:
        - DOACs have been associated with urinary and intestinal tract bleeding, and should be used with caution in patients with urinary or gastrointestinal tract lesions, pathology, or instrumentation.
        - Use with caution in patients with compromised renal or liver function.
        - For patients receiving nephrotoxic or hepatotoxic chemotherapy consider monitoring patients more closely with laboratory testing.
        - Consider drug-drug interactions
    - Duration of anticoagulation as recommended by guideline:
        - Minimum time of 3 months, with triggered events >6 months
        - For non-catheter-associated DVT or PE recommend indefinite anticoagulation while cancer is active, under treatment, or if risk factors for recurrence persist.
        - For catheter-associated thrombosis, anticoagulant as long as catheter is in place.

- Providers should continue to discuss with patients the risks/benefits of anticoagulation to determine the appropriate duration of therapy
- Injectable Anticoagulation with a Low Molecular Weight Heparin may be warranted in some situations as indicated for treatment and prevention of thromboembolic events during the course of ambulatory anticoagulation management.
- Dosing recommendations of DOACs and initiations will be based on individual drug package inserts and Chest Guidelines recommendations[1,5,6,7]

Appendix E: Guidelines for Management of Critical INR Values[1]

Clinical Scenario*	Treatment of Elevated INR	Time to Recheck INR
No clinically significant bleeding, no urgent/emergent surgery/procedure		
INR 5.0-9.9	Omit 1-2 doses of warfarin. Resume at lower dose when INR therapeutic.	24-48 Hours
INR >9.9	Omit 1-2 doses of warfarin, Consider Vitamin K 2.5mg PO x 1 Resume at lower dose when INR therapeutic. May refer patient to nearest emergency department for evaluation under the clinic discretion	24-48 Hours
Clinically significant bleeding		
Any INR	Refer patient to nearest emergency department for evaluation.	

*American College of Chest Physicians Clinical Practice Guidelines.[1]

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