Taddle Creek

Family Health Team

MEDICAL DIRECTIVE

Title:	Anticoagulation Management	**Number:**	TCFHT-MD08
Activation Date:	10-June-2014	**Review Date:**	10-June-2024
Next Review Date:	01-June-2025		

Sponsoring/Contact Person(s) *(name, position, contact particulars):*

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Order and/or Delegated Procedure:

Appendix Attached: __ No _X_ Yes
Title:
Appendix A – Authorized approval form
Appendix B – Authorized implementer form
Appendix C – Initiation of Warfarin Therapy and Warfarin Initiation Nomograms
Appendix D – Warfarin Dosing Algorithms
Appendix E – Point of Care Anticoagulation Clinic Protocol
Appendix F – Letter to Dentist
Appendix G – Warfarin Drug Interactions

For patients referred by physician for anticoagulation management, the authorized implementers may perform the following:

- *Authorized Pharmacist Implementers Only*: Initiate warfarin therapy for a patient with goal INR as prescribed by physician (Appendix C).
- Obtain INR result using the Coaguchek XS point-of-care (POC) INR testing device using a lancet to obtain a blood sample from the patient's finger.

- Order a lab INR test by generating a laboratory requisition using the supervising PCP/Authorizers initials.
  - On the lab requisition, under "Hematology", check "Prothrombin Time (INR)" and under "Other Tests" may add "Repeat INR as needed." This will be valid for 6 months.
  - The lab requisition must be signed by the implementer as well as state the implementer's name, PCP name, and "as per Medical Directive TCFHT-MD08".
  - Implementer documents that the requisition was provided and the follow up plan.
  - Lab INR may be ordered in circumstances where a patient is unable to attend their POC appointment or for comparison to POC INR.
- Notify patient of INR result.
- If INR is *not* therapeutic:
  - Adjust warfarin regimen as per Warfarin Dosing Algorithms (Appendix D).
  - Notify physician re: out-of-range INR as per Warfarin Dosing Algorithm (Appendix D).
- Inquire about and document any changes to medication regimen (including prescription, non-prescription, vitamins, supplements and herbal medications), or medical conditions.
- Renew warfarin prescriptions as needed, by entering warfarin prescriptions into the EMR for the purpose of recording or printing a prescription with the prescribing physician as a supervising physician.
- If deemed necessary, change the warfarin prescription to an appropriate strength tablet to ensure safe and effective therapy.
  - Ensure patient is counselled regarding this change.
  - Document on the new prescription that a change in tablet strength is requested.
  - Call community pharmacy to clearly communicate change in tablet strength.
- Patients who require management of Rivaroxaban (Xarelto), Apixaban (Eliquis), Dabigatran (Pradaxa), Edoxaban (Lixiana), or Warfarin transitions, may be referred to the Pharmacist.
- Bridging therapy (consult with physician):
  - When necessary, the authorized implementer should determine (and clarify with the physician) whether bridging, adjustment, or cessation of therapy is required.
  - When appropriate, the patient should be referred to a Thrombosis Clinic by their physician if bridging is necessary.
  - In most cases, warfarin does not need to be held for dental procedures; physicians/authorized implementers may use the letter to dentist (Appendix F) when appropriate.

Recipient Patients:

Appendix Attached: __ No _X_ Yes
Title: Appendix A – Authorizer Approval Form

Recipients must:

- Be active patients of a TCFHT primary care provider who has approved this directive by signing the Authorizer Approval Form.
- Be taking warfarin or will be initiating warfarin therapy, pursuant to a physician's order.
- Meet the conditions identified in this directive.

Authorized Implementers:

Appendix Attached: __ No _X_ Yes
Title: Appendix B – Implementer Approval Form

Implementers must be TCFHT employed Regulated Health Care Providers or Physician Assistant (under the supervision of a physician).

Implementers must complete the following preparation and sign the Implementer Approval Form:

- Completed suitable didactic and clinical training.

Examples of suitable training:

- Management of Oral Anticoagulation Therapy CE program through the University of Waterloo, Faculty of Pharmacy. This program consists of a package of readings, practical experience in an anticoagulation clinic, and a written and practical examination.
- TC FHT Anticoagulation Clinic training, under the mentorship of an authorized implementer. This training consists of a package of readings, 3 hours of didactic education, and clinical experience working directly with current TCFHT Anticoagulation Clinic patients under supervision of an authorized implementer (training materials reviewed and approved by Dr. Alissia Valentinis).

Indications:

Appendix Attached: __X_ No __ Yes
Title:

The implementer is authorized to apply this directive pursuant to a physician's order to continue warfarin therapy. Pharmacist implementers may initiate warfarin therapy in consult with the physician.

To monitor INRs in those patients receiving anticoagulation therapy for:

- Atrial fibrillation
- Treatment and prophylaxis of venous thrombosis
- Treatment of pulmonary emboli
- Prevention of systemic embolism
- Tissue heart valves
- Valvular heart disease
- Mechanical prosthetic valves
- Prophylaxis of recurrent MI
- Other conditions (e.g. coagulopathies)

Contraindications:

- Patient/POA refusal
- Active bleeding
- Pregnancy

Precautions:

Antiphospholipid Syndrome: POC INR results should be compared to lab for correlation and be within 15% (INR's must be under 4 for correlation). If there is correlation, POC testing only may be used subsequently. If there is no correlation, patients should go to the lab only for INR testing.

Consent:

Appendix Attached: __X_ No __ Yes
Title:

Consent is implied upon referral from physician to implementer for anticoagulation management. However, at the initial visit, the implementer will explain the purpose and procedures involved with POC INR testing and warfarin dose adjustment to further obtain verbal consent from the patient or POA.

Guidelines for Implementing the Order/Procedure:

Appendix Attached: __ No _X_ Yes
Title: Appendix E – Point of Care Anticoagulation Clinic Protocol

The implementer will perform POC INR testing and make warfarin dose adjustments as outlined in the POC Anticoagulation Clinic Protocol (Appendix E).

Consider referral to the Clinical Pharmacist under the following circumstances:

- Warfarin initiated and patient on concurrent antiplatelet or anticoagulation therapy (.e.g. Aspirin, Dipyridamole/Aspirin (Aggrenox), Clopidogrel (Plavix), Ticlopidine (Ticlid), Ticagrelor (Brilinta), Prasugrel (Effient).
- Patient discharged from hospital on bridging low molecular weight heparins (LMWH) transitioning to warfarin, when Thrombosis Clinic follow-up not yet available.
- Assessment of anticoagulation therapy (e.g., switching to Rivaroxaban (Xarelto), Apixaban (Eliquis), Dabigatran (Pradaxa), or Edoxaban (Lixiana) from Warfarin, or vice versa).
- Assessment of patient who has a scheduled elective operative procedure that requires interruption of anticoagulation.
- Assessment of Warfarin drug interactions (see Appendix G); significant clinical interactions with Warfarin that require close monitoring and dosage adjustment such as Amiodarone.
- Difficulty stabilizing INR for a patient on warfarin.

Documentation and Communication:

Appendix Attached: __ No _X_ Yes
Title: Appendix E – Point of Care Anticoagulation Clinic Protocol; Appendix F – Letter to Dentist; Appendix G – Warfarin Drug Interactions

The implementer will document INR results and any changes to the warfarin regimen in the patient's EMR, specifically on the Custom Form entitled "INR Flow Sheet" flagged as a Special Note. The indication for warfarin treatment, target INR and range, duration of treatment, tablet strengths prescribed to the patient, and community pharmacy phone and fax numbers must be entered on the "INR Flow Sheet".

In addition, the implementer will notify the physician when any of the following situations occur:

- The patient is to have surgery or dental procedures requiring changes to the patient's anticoagulation therapy.
- Actual or suspected signs and symptoms of haemorrhage/bleeding.
- Actual or suspected signs and symptoms of thromboembolism.
- INR values greater than or equal to 5 with or without bleeding.
- INR values less than 1.5 in patients with mechanical heart valves.
- When the duration of therapy has been completed.
- When patients consistently miss appointments or are non-compliant with therapy.
- When clinically significant drug interactions occur, which could place the patient at risk for complications.

Review and Quality Monitoring Guidelines:

Appendix Attached: __ No __ Yes
Title:

- Routine review will occur annually on the anniversary of the activation date. Review will involve a collaboration between the authorizing primary care providers and the authorized implementers.

- If new information becomes available between routine reviews, such as the publishing of new clinical practice guidelines, and particularly if this new information has implications for unexpected outcomes, the directive will be reviewed by an authorizing primary care provider and a mimimum of one implementer.
- At any such time that issues related to the use of this directive are identified, TCFHT must act upon the concerns and immediately undertake a review of the directive by the authorizing primary care providers and the authorized implementers.
- This medical directive can be placed on hold if routine review processes are not completed, or if indicated for an ad hoc review. During the hold, implementers cannot perform the procedures under authority of the directive and must obtain direct, patient-specific orders for the procedure until it is renewed.

References:

Thrombosis Canada Clinical Guidelines [URL: https://thrombosiscanada.ca/hcp/practice/clinical_guides]

CHEST Guidelines [URL: https://journal.chestnet.org/guidelines]

Bungard TJ, Yakiwchuk E, Foisy M. Drug interactions involving warfarin: Practice tool and practical management tips. CJP. Jan/Feb Vol 144. No 1. 2011.

Kovacs MJ, et al. Comparison of 10mg and 5mg warfarin initiation nomograms together with low-molecular-weight heparin for outpatient treatment of acute venous thromboembolism. Ann Intern Med. 2003;138:714-19.

Siguret V, Gouin I, et al. Initiation of warfarin therapy in elderly medical inpatients: A safe and accurate regimen. Am J Med 2005; 118:137-42.

NOTE:
This medical directive is based on TCFHT's previous medical directive CV01 entitled, "Point-of-Care Anticoagulation Clinic: Management of INR and dosage adjustment for patients taking warfarin," which required revision in formatting to reflect the growth of the TCFHT organization. The majority of the content of CV01 has remained the same for the revised TCFHT-MD08 version. Therefore, all approved Implementers and Authorizers for medical directive CV01 "Point-of-Care Anticoagulation Clinic: Management of INR and dosage adjustment for patients taking warfarin," have grandfathered approval for TCFHT-MD08 "Anticoagulation Management."

Appendix A:

Authorizer Approval Form

Name	Signature	Date
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Appendix B:

Implementer Approval Form

To be signed when the implementer has completed the required preparation, and feel they have the knowledge, skill, and judgement to competently carry out the actions outlined in this directive.

Name	Signature	Date
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Appendix C:
Initiation of Warfarin Therapy

****<u>NOTE</u>: Only Pharmacist authorized implementers may *initiate* warfarin under this medical directive.****

For patients who have an indication for warfarin therapy but have not yet started or have not been on warfarin for a long time, the implementer may prescribe the initial dosage of warfarin, monitor INR and adjust therapy accordingly.

Upon initiation of warfarin therapy, authorized implementers may also order blood work for CBC, LFTs (ALT and AST), albumin, and Scr if not done in the past 30 days or if these measurments were previously unstable. Lab results will be input to patient's EMR chart and physician notified of results.

The patient's dosage requirement will be estimated based on factors including:

- Age
- Body weight
- Race
- Nutritional status, diet
- Genetic variation in the enzyme that is the site of warfarin action (VKORC1 phenotype), if available
- Genetic variation in the enzyme system that metabolizes warfarin (CYP450 2C9), if available
- Concomitant drugs
- Alcohol intake
- Comorbidities (e.g. liver disease, heart failure, high risk bleeding, heart valve replacement)
- Activity level
- Indication for warfarin

In most circumstances, the 5 mg warfarin initiation nomogram can be used. Physicians are responsible for determining bleeding/clotting risk and indicate if an initiation nomogram other than 5 mg should be used. It is recommended that physicians complete the "CHA2DS2-VASc Score + HAS-BLED Score for AF" EMR tool for patients with atrial fibrillation to assess risk of clotting and bleeding.

In the elderly, and in patients who are debilitated, malnourished, have congestive heart failure, have liver disease, or have a high risk of bleeding, have had recent major surgery, or are taking medications known to increase sensitivity to warfarin (e.g., amiodarone), a starting dose of 5mg or less will be considered. Use of the 4mg warfarin initiation nomogram may be considered. An initial dose of 2 to 3 mg may be appropriate for patients who have undergone heart valve replacement, given their higher sensitivity to VKAs probably caused by the effects of cardiopulmonary bypass and concomitant therapies.

Additional considerations:

- If patient is on concomitant heparin or low-molecular weight heparin (LMWH) for the purpose of bridging initiation of warfarin, it can be discontinued when the INR has been in therapeutic range for two measurements approximately 24h apart unless otherwise specified. Patients' physician to be notified via EMR message same day.

Appendix C (cont'd): Warfarin Initiation Nomograms

5-mg Warfarin Initiation Nomogram[1]

Day	INR	Warfarin Dose, mg
1		5
2		5
3	< 1.5 1.5–1.9 2.0–3.0 > 3.0	5-10 2.5-5 0-2.5 0
4	< 1.5 1.5–1.9 2.0–3.0 > 3.0	10 5-7.5 0-5 0
5	< 1.5 1.5-1.9 2.0-3.0 > 3.0	10 7.5-10 0-5 0
6	< 1.5 1.5–1.9 2.0–3.0 > 3.0	7.5-12.5 5-10 0-7.5 0

4-mg Warfarin Initiation Nomogram[2]

Day	INR	Warfarin Dose, mg
1		4
2		4
3		4
4	1.0 - 1.2 1.3 - 1.4 1.5 - 1.7 1.7 - 1.9 1.9 - 2.4 > 2.4	5 4 3 2 1 Hold, check INR daily until INR < 2.5, then resume at 1 mg

*This algorithm does not apply to patients who have received warfarin within the preceding week, or who have a pretreatment INR > 1.3.

10-mg Warfarin Initiation Nomogram[1]

Warfarin 10 mg is given on Day 1 and 2.

Day 3 INR	Warfarin Dose on Days 3, 4, *mg*	Day 5 INR	Warfarin Dose on Days 5, 6, 7, *mg*
< 1.3	15, 15	< 2.0	15, 15, 15
		2.0 – 3.0	7.5, 5, 7.5
1.3 – 1.4	10, 10	3.1 – 3.5	0, 5, 5
		> 3.5	0, 0, 2.5
1.5 – 1.6	10, 5	< 2.0	7.5, 7.5, 7.5
		2.0 – 3.0	5, 5, 5
1.7 – 1.9	5, 5	3.1 – 3.5	2.5, 2.5, 2.5
		> 3.5	0, 2.5, 2.5
2.0 – 2.2	2.5, 2.5	< 2.0	5, 5, 5
		2.0 – 3.0	2.5, 5, 2.5
2.3 – 3.0	0, 2.5	3.1 – 3.5	0, 2.5, 0
		> 3.5	0, 0, 2.5
> 3.0	0, 0	< 2.0	2.5, 2.5, 2.5
		2.0 – 3.0	2.5, 0, 2.5
		3.1 – 4.0	0, 2.5, 0
		> 4.0	> 3.5

Note: The American College of Chest Physicians (ACCP) recommends initiation of warfarin 5mg daily or less in elderly patients who: are debilitated, are malnourished, have congestive heart failure, have liver disease, have had recent major surgery, or taking medications known to increase sensitivity to warfarin (e.g. amiodarone). [3] For these patients use the 4 mg warfarin initiation nomogram or lower dose and consult the physician or pharmacist.

References:
1. Kovacs MJ, et al. Comparison of 10mg and 5mg warfarin initiation nomograms together with low-molecular-weight heparin for outpatient treatment of acute venous thromboembolism. *Ann Intern Med*. 2003;138:714-19.
2. Siguret V, Gouin I, et al. Initiation of warfarin therapy in elderly medical inpatients: A safe and accurate regimen. Am J Med 2005; 118:137-42.
3. Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin K antagonists: American college of chest physicians evidence-based clinical practice guidelines (8th edition). Chest 2008;133:160-98.

Appendix D:
Warfarin Dosage Adjustment Algorithms

Potential reasons for non-therapeutic INR:

1. Missed doses of warfarin
2. Extra doses of warfarin
3. Diet change - more or less green leafy vegetables (spinach, broccoli, lettuce etc.); poor appetite
4. Started or stopped any medications in the last 4 weeks
    i. Prescription medications
    ii. Non-prescription medications (e.g. acetaminophen)
    iii. Vitamins
    iv. Dietary supplements
    v. Herbal medications/teas
5. Acute illness (e.g. cold, diarrhea, vomiting, etc.)
6. More or less alcohol in the previous week
7. Changes in level of activity (more or less exercise)

Reasons that the suggested dosage adjustments may not be applied:

1. The INR is within 0.2 of the goal INR
2. The patient missed one or more doses in the last week
3. The patient took one or more extra doses in the last week
4. The patient took an interacting drug that has now been discontinued
5. The patient recently started an interacting drug and the INR is expected to change
6. The patient had a significant change in dietary vitamin K intake
7. The patient had a significant change in alcohol intake
8. The patient has had a significant amount of diarrhea in the last week
9. The INR is being checked prior to a procedure and warfarin is currently being held
10. The warfarin was started or adjusted less than 5 days ago
11. Any other reason based on clinical judgment of the provider. Reasons for not applying the suggested dosage adjustments will be documented in patient's record.

Remember:

1. Always consider trend in INRs when making warfarin management decisions.
2. Consider repeating INR same day or next day if observed value markedly different than expected value.
3. Consider indication for warfarin therapy to help guide dosage adjustments (e.g., mechanical valve in mitral position = higher risk of thromboembolism; atrial fibrillation with no other risk factors = lower risk of thromboembolism).
4. After initiation or dose change, changes in the INR are seen in 1 to 2 days and the full anticoagulant effect is seen in 5 days.
5. The risk of bleeding increases dramatically above an INR of 4.0 to 5.0. The risk of intracranial hemorrhage risk doubles for each increase of 1 of the INR.
6. Risk factors for bleeding: age > 65, history of bleeding (e.g., GI), co-morbid disease states (HTN, CVD, PVD, CAD, renal insufficiency, malignancy and anemia), concomitant drugs (e.g. ASA, NSAIDs, Clopidogrel), and in the first 6 months of therapy.

Management of non-therapeutic INR:

- Enquire about potential reasons.
- Enquire about signs or symptoms of bleeding or thrombembolic events.
    - If patient reports major bleeding or signs/symptoms of major bleeding; send to emergency department.
    - Major bleeding refers to: any non-severe bleeding that does not stop in a reasonable amount of time (e.g., a cut, nose bleed, or bleeding hemmorhoid), suspicion of internal bleeding (e.g., symptoms of GI bleed or hemorrhagic stroke, new severe bruising), or any severe bleeding.
- Adjust dose of warfarin if needed as per protocol.
    - Attempt to adjust dose using strength of tablets patient already has on hand when possible.
    - Attempt to maintain patient on the fewest number of different tablet strengths as possible.
    - Dose adjustments will be based on patient risk for thromboemboli vs. bleed, as well as past individual patient response to anticoagulation therapy adjustment.
    - Work with patient and their pharmacy for the best possible management if warfarin is blister packed. Timing of INR should coincide with dosette filling by pharmacy whenever possible.
- Instruct patient to repeat back dosing instructions to ensure comprehension and consider providing written instructions.
- Schedule patient for next INR measurement:
    - In general, if a new interacting medication is added, recheck INR within 3-6 days (see Appendix H for drug specific recommendations or consult the Clinical Pharmacist).
    - For initiation of warfarin therapy, INR's will be checked on day 3 and 5 (5 mg or 10 mg nomogram) or on day 4 (4 mg nomogram) unless otherwise indicated by the physician.
    - Avoid laboratory testing of INR's on Friday whenever possible.
    - Advise patient's to test at laboratory earlier in the day, before noon, whenever possible.

Managing Single Out-of-Range INR Values:

For patients with previously in-range INR values who present with a single slightly out-of-range INR (e.g. INR 0.5 above or below the target range), there are two management options:

1. Continue current maintenance dose and repeat INR in 1-2 weeks, OR
2. Make a one-time dose change (increase or hold by ½ to 1 single dose) and resume current maintenance dose. Repeat INR in 1-2 week.

The specific approach is influenced by the magnitude of the out-of-range value, previous experience of similar values in the patient and whether the patient has strong risk factors for thrombosis/stroke or bleeding.

INR results between 5.0 and 9.0 will result in a consult with the Physician.

- Authorized implementer to assess whether the patient is currently bleeding, has any signs/symptoms of bleeding, assess adherence, and any other reasons patient's INR is above therapeutic range. Authorized implementer to report to Physician.
- Physician to assess bleeding risk and whether patient should be referred to the emergency department.

INR results greater than 9.0 will result in a consult with the Physician and a referral to the emergency department.

Note: For patients with INRs of >4.5 but <10 and without clinically relevant bleeding, temporary cessation of VKA alone without the addition of vitamin K is suggested. Vitamin K may be given if INR >10, even in the absence of bleeding, depending on individual patient circumstances (e.g. risk factors for bleeding, risk for thrombosis if over-correction of INR, ability to have repeat INR testing).

If the patient has a mechanical heart valve or if they had an acute VTE within the previous 6 weeks, the INR must be greater than 1.5 otherwise consult with the Physician.

- Authorized implementer to assess whether the patient is currently experiencing signs/symptoms of thromboemboli and assess adherence. Authorized implementer to report to Physician.
- Physician or Pharmacist to assess clotting risk and dose adjustment.

Target INR 2.5 (Range 2.0-3.0)

INR Value	Dosing Adjustment	INR Check
Managed by Authorized Implementer		
INR < 1.5	Increase weekly dose by 10 to 20%. Consider extra dose. *Consult clinical pharmacist or MRP if the patient has a mechanical heart valve or if they had an acute VTE within the previous 6 weeks.	Repeat INR in 4-7 days
INR 1.5 to 1.9	Increase weekly dose by 5 to 10%. If INR is below 1.8 consider extra 0-0.5 dose. If INR is 1.8 to 1.9 consider continuing current dose.	Repeat INR in 7-14 days
INR 2.0 to 3.0	Continue current dose.	Monitor INR in: - 5-10 days if 1 INR in range - 2 weeks if 2 INRs in range - 3 weeks if 3 INRs in range - 4 weeks if 4 INRs in range
INR 3.1 to 3.5	Hold 0 to 0.5 dose and decrease weekly dose by 0 to 10%. If INR is 3.1 to 3.2 consider continuing current dose.	Repeat INR in 7-14 days
INR 3.6 to 4.0	Hold 0 to 1 dose and decrease weekly dose by 0 to 15%.	Repeat INR in 4-7 days
INR 4.1 to 4.9	Hold 1 to 2 doses and decrease weekly dose by 5 to 15%.	Repeat INR in 4-7 days
INR ≥ 5.0 – Authorized Implementer to notify Physician		
INR 5.0 to 9.0 (no significant bleeding)	Hold 2 doses and decrease weekly dose by 10 to 20%. **OR** Hold warfarin and send to emergency department if patient is at risk of bleeding. Authorized implementer to follow-up in 24-48 hours for restart. <u>Usual management</u>: Hold 1 dose and administer oral Vitamin K, 1 to 2.5 mg orally* if patient is at risk of bleeding. Resume therapy at a lower dose when INR is therapeutic. * Vitamin K is available in parenteral solution, 10 mg/mL; may be given PO or SC	Repeat INR in 2-4 days Repeat INR in 1-2 days
INR > 9.0 (no significant bleeding)	Hold warfarin and send to emergency department. Authorized implementer to follow-up in 24-48 hours for restart. <u>Usual management</u>: Hold warfarin and administer Vitamin K 2.5 to 5.0 mg orally*. INR will reduce substantially in 24-48 hours. Resume therapy at a lower dose when INR is therapeutic. * Vitamin K is available in parenteral solution, 10 mg/mL; may be given PO or SC	Repeat INR in 1-2 days

<u>Note</u>: TCFHT does not have Vitamin K available on site. If physician consult indicates that Vitamin K is required, patient should be sent to nearest urgent care or emergency department.

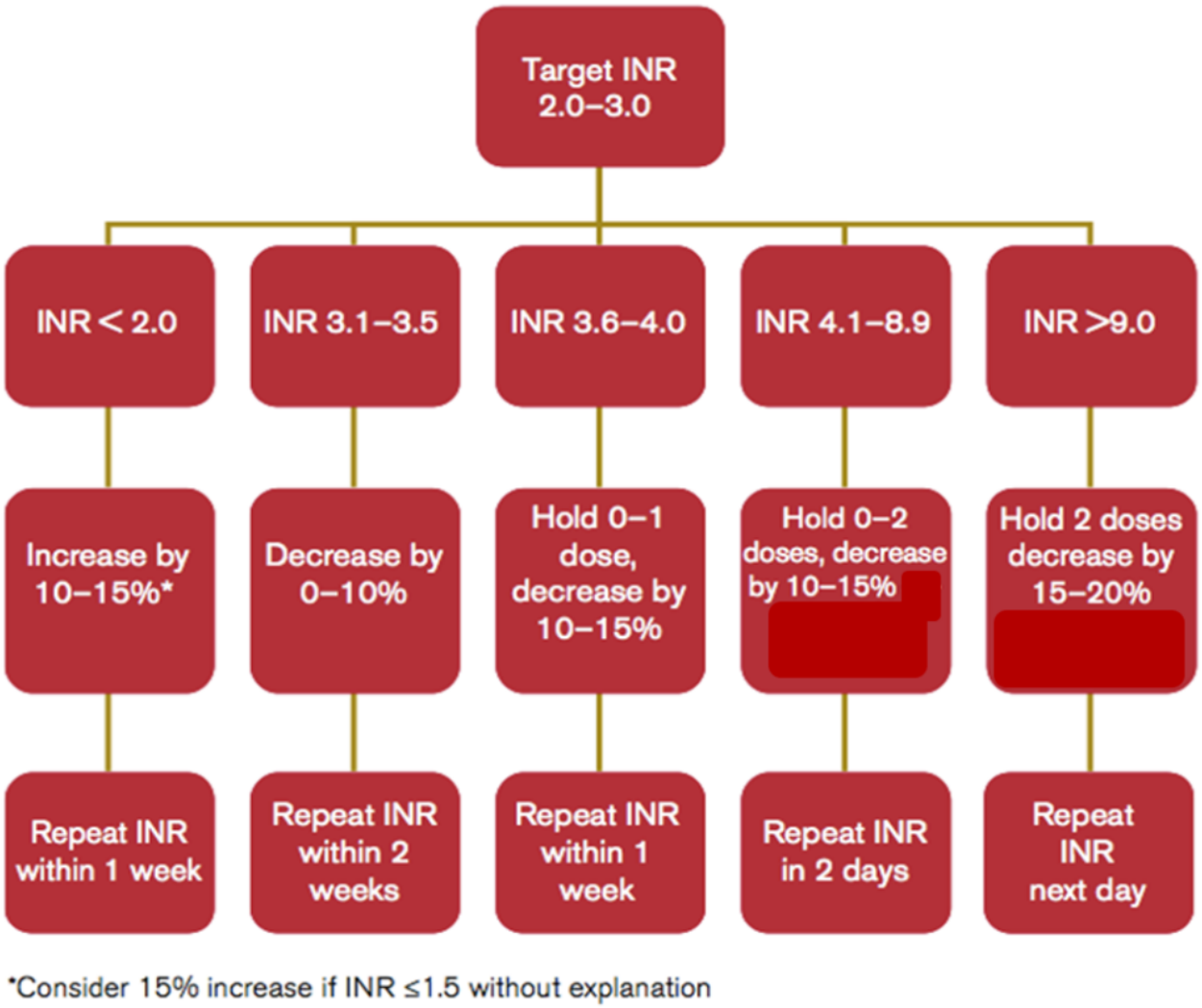
Target INR 3.0 (Range 2.5-3.5)

INR Value	Dosing Adjustment	INR Check
Managed by Authorized Implementer		
INR < 1.5	Increase weekly dose by 10 to 20%. Consider extra dose. *Consult clinical pharmacist or MRP if the patient has a mechanical heart valve or if they had an acute VTE within the previous 6 weeks.	Repeat INR in 4-7 days
INR 1.5 to 2.4	Increase weekly dose by 0 to 15%. If INR is below 2.3 consider extra 0-1 dose. If INR is 2.3 to 2.4 consider continuing current dose.	Repeat INR in 7-14 days
INR 2.5 to 3.5	Continue current dose.	Monitor INR in: - 5-10 days if 1 INR in range - 2 weeks if 2 INRs in range - 3 weeks if 3 INRs in range - 4 weeks if 4 INRs in range
INR 3.6 to 4.0	Hold 0 to 0.5 dose and decrease weekly dose by 0 to 10%. If INR is 3.6 to 3.7 consider continuing current dose.	Repeat INR in 7-14 days
INR 4.1 to 4.5	Hold 0 to 1 dose and decrease weekly dose by 0 to 15%.	Repeat INR in 4-7 days
INR 4.5 to 4.9	Hold 1 to 2 doses and decrease weekly dose by 5 to 15%.	Repeat INR in 4-7 days
INR ≥ 5.0 – Authorized Implementer to notify Physician		
INR 5.0 to 9.0 (no significant bleeding)	Hold 2 doses and decrease weekly dose by 10 to 20%. **OR** Hold warfarin and send to emergency department if patient is at risk of bleeding. Authorized implementer to follow-up in 24-48 hours for restart. <u>Usual management</u>: Hold 1 dose and administer oral Vitamin K, 1 to 2.5 mg orally* if patient is at risk of bleeding. Resume therapy at a lower dose when INR is therapeutic. * Vitamin K is available in parenteral solution, 10 mg/mL; may be given PO or SC	Repeat INR in 2-4 days Repeat INR in 1-2 days
INR > 9.0 (no significant bleeding)	Hold warfarin and send to emergency department. Authorized implementer to follow-up in 24-48 hours for restart. <u>Usual management</u>: Hold warfarin and administer Vitamin K 2.5 to 5.0 mg orally*. INR will reduce substantially in 24-48 hours. Resume therapy at a lower dose when INR is therapeutic. * Vitamin K is available in parenteral solution, 10 mg/mL; may be given PO or SC	Repeat INR in 1-2 days

<u>Note</u>: TCFHT does not have Vitamin K available on site. If physician consult indicates that Vitamin K is required, patient should be sent to nearest urgent care or emergency department.

Alternative Maintenance Dosing Algorithm

Figure: Warfarin Dose Adjustment in Non-bleeding Patients by % Dose Change of Total Weekly Dose (adapted from Cushman et al, 2014).



*Consider 15% increase if INR ≤1.5 without explanation

This algorithm is based on making a dose change as a percentage of the total weekly dose.

For patients with INRs of > 4.5 but < 10 and without clinically relevant bleeding, temporary cessation of VKA alone without the addition of vitamin K is suggested. Vitamin K may be given if INR > 10, even in the absence of bleeding, depending on individual patient circumstances (e.g. risk factors for bleeding, risk for thrombosis if over-correction of INR, ability to have repeat INR testing).

Appendix E:
Point-of-Care Anticoagulation Clinic Protocol

CLINIC DESCRIPTION

The Point-of-Care Anticoagulation Clinic will be run by an implementer (a pharmacist, registered nurse and/or physician assistant) with training in anticoagulation. Patients on oral anticoagulation drugs will visit the Point-of-Care Anticoagulation Clinic as prescribed by their physician. They will have a blood sample taken, international normalized ratio (INR) measured, results communicated and medication adjusted in a 15-minute appointment. If patients are capable and have a desire to learn more about their chronic condition, then they will have an opportunity to discuss their condition and medications with the implementer. The implementer will conduct the Anticoagulation Clinic through authority conferred by a medical directive (TCFHT-MD08) signed by the physicians of Taddle Creek Family Health Team.

OBJECTIVES

1. To improve the quality of anticoagulation management in primary care
2. To improve patient satisfaction with anticoagulation management
3. To improve provider satisfaction with anticoagulation management
4. To reduce costs

LOCATION

The TC FHT Point-of-Care Anticoagulation Clinic will be located at:

TC FHT		
790 Bay Street, Suite 306	AND	726 Bloor Street West, Suit 207/B102
Toronto, ON		Toronto, ON
M5G 1N8		M6G 4A1

OR at the patient's home, with patient consent, MD notification and at discretion of INR clinician.

HOURS OF OPERATION

The clinic will be available at the discretion of the INR clinician operating the clinic. This can be on an appointment basis or a "first-come, first-serve" basis.

After Hours/Home Visits:

Patients that need to be seen outside of normal clinic hours should make an appointment with the INR clinician. This includes newly referred patients and patients for whom more frequent INR testing is required.

If the obtained INR is outside of therapeutic range requiring consult with a physician (as per Appendix D), the implementer will contact the on-call physician at the after hours clinic to assess whether the patient should go to the emergency department. The implementer will then notify the patient's physician of the INR result by the next business day with appropriate documentation in patient chart.

PERSONNEL

Pharmacists – Suite 522

Registered Nurses – from Suites 300/302 and 522 at 790 Bay Street and from Bloor site Suites 207/B102

Physician Assistant – from Suites 300/302 at 790 Bay Street and through Primary Care@Home team

RESPONSIBILITIES OF PERSONNEL

- Maintain adequate inventory of supplies required for the clinic (e.g., test strips, lancets).
- Operation and maintenance of the Point-of-Care Coaguchek XS Machine once weekly using 99% isopropyl alcohol on meter cover and test strip guide/cover.
- Quarterly quality control testing through OneWorld Accuracy.
- Provide patient with education regarding warfarin therapy at the initial visit and reinforce this education at each visit.
- Review INR result and adjust warfarin dose as needed.
- Maintain documentation of INR results and warfarin doses.
- Arrange date for patient's next visit to Anticoagulation Clinic.
- Provide patient with prescription and/or communicate prescription to patient's pharmacy.
- Keep the physician updated on INR results.
- Notify physician when INR levels are sub- or supratherapeutic, as per Appendix D.
- Notify physician when patient is experiencing actual/suspected signs and symptoms of hemorrhage or thromboembolism.
- Participation in research and teaching.

Clerical Staff

- Assist with booking patient appointments.
- Assist with obtaining supplies for the clinic.

PROCEDURES

REFERRALS TO THE CLINIC

Patients will be referred to the Anticoagulation Clinic by their primary care physician or nurse practitioner. Ideally, the patient should be referred to the implementer assigned to his/her respective physician's office or according to the patient's preference.

The physician/NP should communicate the following information to the authorized implementer:

- Name of patient and contact information.
- Indication for anticoagulation therapy, target INR range, and anticipated duration of therapy.
- Patient's medical history and diagnoses.
- Most current medication list.
- Most recent warfarin dosages and INR results (if available).

The above should be sent via the EMR system to the authorized implementer.

Clerical staff will contact the patient and book an initial appointment with the implementer.

INITIAL APPOINTMENTS

The initial appointment for a newly referred patient can be conducted by the implementer. The implementer will provide education, and determine the most appropriate dose of warfarin and a monitoring schedule.

Patient Education:

Education of the patient is vital for ensuring safe and effective use of warfarin therapy. The education provided during the session and comprehension will be documented in the patient's EMR.

Compliance aids (e.g., a calendar) and written education material will be provided to the patient as necessary at the initial and follow-up visits.
Upon initial visit to the clinic, the implementer will provide education including, but not limited to:

- Purpose of the medication and how it works
- Drug names, strength and description of tablets
- Importance of maintaining anticoagulation
- Recognition of signs of bleeding and appropriate procedures to follow
- Importance of compliance with drug regimen and follow-up monitoring – advise patients to take Warfarin dose in evening to allow same-day dosage adjustment if required by INR result
- How to handle missed doses
- Dietary considerations and medication interactions
- Importance of informing other health care providers of warfarin use
- Importance of avoiding pregnancy, if appropriate

MAINTENANCE VISITS

The implementer will schedule regular clinic visits, during which the patient will have his/her INR tested and warfarin dosage adjusted as needed. Patient response to warfarin therapy will be evaluated on the basis of the INR results and information gathered through patient interview. Criteria as outlined in Appendix D will be used to assess patient response to warfarin therapy and detect any potential problems prior to dosage adjustments.

Frequency of Maintenance Visits

Stable patients: INR monitored every 4-6 weeks, up to 3 months for appropriate patients
Unstable patients: INR monitored weekly or as needed until INR is stable

OBTAINING INR RESULTS

The implementer will operate and maintain the point-of-care INR machine, as described in the machine's user manual. Implementers operating the point-of-care INR machine should follow appropriate infection control strategies including: use of gloves, use of separate lancet for each patient and disposal of lancets and test strips into a biohazard container with a secure lid.

CONDITIONS UNDER WHICH LABORATORY INR TESTING IS RECOMMENDED

As per Roche Diagnostics, manufacturer of Coaguchek XS, the INR result obtained via point-of-care testing may be inaccurate under the following conditions, thus laboratory INR testing is recommended:

- Abnormally high or low hematocrit (HCT <25% or >55%)
- Systemic lupus erythematosus (SLE)
- Antiphospholipid antibody syndrome

DOCUMENTATION

All INR results and details of INR appointments will be documented into the patient's chart within the EMR using the custom form entitled "INR flow sheet" flagged as a Special Note.

EVALUATION OF THE SERVICE / QUALITY ASSURANCE

The designated pharmacist is responsible for performing periodic evaluation of the anticoagulation service – at least annually. This should include, but is not limited to, evaluation of: amount or % of time patients are within therapeutic range, time spent per visit, incidence of bleeding, incidence of thromboembolism, cost of providing service, patient satisfaction and provider satisfaction. The pharmacist will assess competency on an ongoing basis through clinical discussions with the anticoagulation team.

A designated authorized implementer at each site is responsible for quarterly Coaguchek XS quality assurance testing using control samples provided by OneWorldAccuracy. Quarterly QA testing will be documented on the "Coagucheck XS INR Test Strips Log" kept in the Pharmacists' office (Bay Suite 522) [Also accessed on shared network folder under: Public —> Program Folders —> Cardio —> INR Clinic —> INR Clinic Admin —> Coaguchek XS INR test strips log.]

Example of Coagucheck XS INR Test Strip Log:

Coaguchek XS INR Test Strips Log

**Explanation of Process: Inventory of INR test strips will be maintained in the Pharmacy office (S522). One vial of test strips may be signed out at one time. The chip code in the machine must match the test strip codes - please indicate who is obtaining a new vial of strips and have another implementer of the medical directive (#TCFHT-MD08) double-sign that the chip code matches the test strip code.

Date	Asset # of Coaguchek XS	# vials dispensed	# vials remaining	Expiry Date of Test Strips	Chip Code	Strip Code	Name of person signing out	Name of person double-checking	Date of Quarterly QA Testing

VARIATIONS BETWEEN INR RESULT FROM LABORATORY VS. POC TESTING

Although there may be numeric differences in INR results between POC- and laboratory-based INR measurements, the INR values should be within 0.5 of each other. When comparisons are made between laboratory-based and POC-based INR measurements, the differences between values are generally within 15%. Such differences are similar to the variability in INR results obtained in different laboratories using anticoagulant-spiked plasmas. In addition, such differences have been shown to not result in different dosing instructions when assessed by experienced anticoagulation clinicians.

INR TESTING SUPPLIES

The designated Pharmacist is responsible for ensuring adequate supply of Coaguchek test strips and lancets for the clinic. All test strips will be dispensed out of a central location at the Pharmacist's office at the Bay Site Suite 522. The Bloor site RN may distribute a limited supply to other site implementers. All implementers must use the test strip inventory sign-out sheet ("Coagucheck XS INR Test Strips Log") which requires double-signing by 2 authorized implementers to ensure that the Coaguchek XS code chip matches the test strip code prior to use.

Appendix F (Warfarin):

Letter to Dentist (INRDDS)

Dear Dentist:

Regarding our mutual patient, patName, s/he is currently receiving warfarin for <<INDICATION FOR WARFARIN>>, and the INR is being titrated for a value between <<TARGET INR RANGE>>. I have enclosed the current medication list (as per our records) and patient history.

Allergies:
patALLR

Medications:
patRX

Medical History:
patHPH
patPROB

Based on best practice literature (references below), stopping warfarin for even 2 days, may cause an increase in thromboembolic events by up to up to 1% (range 0.02% – 1%). We understand the risk of post-operative bleeding not controlled by local measures can be up to 3.8%, dependent on the procedure and local measures taken, however post-operative bleeds can usually be managed quickly. Based on the best evidence available, continuing the patient's regular dose of warfarin does not seem to confer an increased risk of bleeding (if INR <4) when compared with discontinuing or modifying warfarin dose in patients undergoing dental procedures. We advise patients receiving warfarin to **not** discontinue warfarin for routine dental procedures.

To help ensure appropriate care of our patient, please feel free to advise the patient to book an appointment to have his/her INR measured before your procedure, and we will supply documentation of that INR for your appointment.

If based on your clinical judgment, patName **MUST** be off warfarin to safely be treated, please contact patMdName as soon as possible (at least 7 days before the procedure) so the patient can be appropriately anticoagulated for the duration of care.

Thank you for the care you provide.

patMdName
patMdPhysNum

References:

1. Dental Surgery for Patients on Anticoagulant Therapy with Warfarin: A Systematic Review and Meta-analysis. JCDA. 2009;75:41-50.
2. Al-Mubarak S, Rass MA, Alsuwyed A, Alabdulaaly A, Ciancio S. Thromboembolic risk and bleeding in patients maintaining or stopping oral anticoagulant therapy during dental extraction. *J Thromb Haemost*. 2006;4:689-91.

3. Point of Care. Do patients taking oral anticoagulants need to discontinue their medication before surgical procedures? JCDA. 2004;70:482-3.
4. Lack of a scientific basis for routine discontinuation of oral anticoagulation therapy before dental Treatment. JADA. 2003; 134:1492-7.
5. Myths of dental surgery in patients receiving anticoagulant therapy. JADA. 2000;131: 77-82.
6. Wahl MJ. Dental surgery in anticoagulated patients. *Arch Intern Med*. 1998;158:1610-6.
7. Cosgriff SW. Chronic anticoagulant therapy in recurrent embolism of cardiac origin. Ann Intern Med. 1953;38:278-87.
8. North West Medicines surgical management of the primary care dental patient on warfarin. Information Centre. Available at: http://www.dundee.ac.uk/tuith/Static/info/warfarin.pdf [Accessed 17Mar09]

Appendix F (DOAC):

Letter to Dentist (DOACDDS)

Dear Dentist:

Regarding our mutual patient, patName, s/he is currently receiving <<apixaban>> <<dabigatran>> <<edoxaban>> <<rivaroxaban>>, a direct oral anticoagulant (DOAC) for <<INDICATION>>. I have enclosed the current medication list (as per our records) and patient history.

Allergies:
patALLR

Medications:
patRX

Medical History:
patHPH
patPROB

Current evidence (references below), suggests that dental extractions and less-invasive procedures with minimal bleed risk may be safely performed using local hemostatic measures, if necessary, without modifying or interrupting ongoing oral anticoagulant therapy. Holding or modifying DOAC therapy may cause an increase in thromboembolic events such as venous thromboembolism and stroke. We advise patients receiving DOAC therapy **not** to discontinue or modify therapy for routine dental procedures.

If based on your clinical judgment, patName **MUST** be off their DOAC to safely be treated, please contact patMdName as soon as possible (at least 7 days before the procedure) so the patient can be appropriately anticoagulated for the duration of care.

Thank you for the care you provide.

patMdName
patMdPhysNum

References:
1. Dental Management of Patients Undergoing Antithrombotic Therapy. JCDA. 2020;86;k17.
2. NOACS/DOACS: Perioperative Management. Thrombosis Canada. 2021-Aug-07.

Appendix G:
Warfarin Drug Interactions

Important Interactions with Warfarin (Medications, Foods, Herbs and Supplements)

- Starting, changing or stopping any drug, herbal product, or supplement can potentially affect the activity of warfarin. Monitoring frequency should be increased.
- The following list includes only commonly used agents and only those with more than two case reports of clinically significant interaction and/or serious adverse effect. For a complete listing refer to the drug monograph.
- Also refer to *WARFARIN and Food: A Guide For Patients at bcguidelines.ca*

Medications

Increased bleeding risk due to increased effect of warfarin: ↑ INR

Analgesics
- acetaminophen[1]
- aspirin (high dose)
- salicylates, topical
- tramadol

Antiarrhythmics
- amiodarone
- propafenone

Antibiotics e.g.
- amoxicillin
- cephalosporins (some)
- isoniazid
- fluoroquinolones[2]
- macrolides[3]
- metronidazole
- sulfonamides
- telithromycin
- tetracyclines[4]

Anticonvulsants e.g.
- phenytoin (early on)
- sodium valproate

Antidepressants e.g.
- duloxetine
- venlafaxine
- SSRI
  - fluoxetine
  - fluvoxamine
  - paroxetine
  - sertraline
  - citalopram

Antifungals e.g.
- fluconazole
- itraconazole
- ketoconazole
- miconazole (oral,vaginal)
- voriconazole

Antihyperlipidemics
- ezetimibe
- fenofibrate
- fluvastatin
- gemfibrozil
- rosuvastatin

Other
- allopurinol
- cimetidine
- corticosteroids (oral)
- proton pump inhibitors (PPI)
  - isolated case reports with all PPIs
- thyroid supplements

Decreased effect warfarin: ↓ INR

Antibiotics e.g.
- rifampin

Antidepressants
- trazodone

Antiepileptics e.g.
- carbamazepine
- phenobarbitone
- primodone
- phenytoin (later on)

Other
- antithyroid agents
- cholestyramine

Increased bleeding risk due to non-warfarin mechanisms

Analgesics
- aspirin
- cox II inhibitors
- nonsteroidal anti-inflammatory drugs

Anticoagulants/Antiplatelet agents
Antidepressants
- selective serotonin reuptake inhibitors

Foods, Herbs and Supplements

Increased bleeding risk due to increased effect of warfarin: ↑ INR

Alcohol (binges)[5]
Birch
Chitosan
Cranberry Juice/extract (dose dependent)
Danshen
Dong Quai
Fish oil
Garlic supplements[6]
Glucosamine±chondroitin
Grapefruit
Mango
Papaya extract

Increased bleeding risk due to non-warfarin mechanisms

Alcohol (heavy drinkers)
Garlic supplements[6]

Decreased effect warfarin: ↓ INR

Alcohol (chronic)[5]
Coenzyme Q10
Ginseng (American,Asian)
Smoking
St. John's Wort
Vitamin C (high dose)
Vitamin K

1. Randomized controlled trials suggest 2-4 g acetaminophen daily has a clinically significant effect on INR [Parra, 2007; Mahe, 2006].
2. Fluoroquinolones e.g. ciprofloxacin, Levofloxacin, moxifloxacin.
3. Macrolides include azithromycin, erythromycin, clarithromycin.
4. Tetracyclines including tetracycline and doxycycline.
5. Consuming small or moderate amounts of alcohol in patients with normal liver function is unlikely to have an effect.
6. Consuming foods with small amounts of garlic is unlikely to have an effect.

Reference: Warfarin Therapy Management. British Columbia Guidelines & Protocols Advisory Committee, 2010.

For management of specific medications see: Bungard TJ, Yakiwchuk E, Foisy M. Drug interactions involving warfarin: Practice tool and practical management tips. CJP. Jan/Feb Vol 144. No 1. 2011.