Policy category	BC - Best Care		
Best care goals	☒ Safe ☐ Personal ☐ Connected ☐ Effective		
Applies to	National		
Version	**Approval authority**	**Effective from**	**'Review by' date**
2	National Medical Director, WA	15/04/2024	15/04/2027

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1. Rationale

The purpose of this Clinical Protocol is to provide a guiding framework for Warfarin management in the Hospital at the Home service and is relevant for Medical Practitioners and all clinical staff.

2. Scope

The Clinical Protocol applies Nationally for clients where there is new commencement of Warfarin, recommencement of warfarin after a break, and Warfarin management in the context of supra- or sub- therapeutic INRs, labile INRs.

It includes information on bridging with Low Molecular Weight Heparin (LMWH) where this is required.

The advice and guidance in this document is specific to Enoxaparin as it is the most commonly used LMWH for bridging. Please reference local guidelines for other types of LMWH

3. Acceptance to HATH criteria and pathway

RED Unacceptable for community admission to HATH Note: May become suitable for HATH after ED or inpatient stabilisation	• Co-existing medical conditions requiring hospital admission. • Known or suspected hypersensitivity to Warfarin or heparins • Pregnant - Warfarin is teratogenic and is a Pregnancy category D If for Enoxaparin bridging: • Severe Thrombocytopenia i.e Platelets ≤50x10⁹/L • Known or suspected hypersensitivity to Heparins e.g. LMWH or Unfractionated Heparin (unless under the governance of Haematology Consultant or thrombosis clinic)
ORANGE Requires discussion with Medical Governor prior to acceptance.	• Over 13 years, suitable for adult dosing and under the care of a specialist team • Supratherapeutic INR > 4.5 • If Enoxaparin bridging needed: ○ Obesity, weight >150kg (Enoxaparin dose needs confirming with Haematology) ○ Underweight, weight <50kg (Enoxaparin dose needs confirming with Haematology) ○ Renal impairment, eGFR (CG) < 30 ml/min (Enoxaparin dose may need adjusting) ○ Thrombocytopenia where platelets >50x10⁹/L
GREEN Accepted for HATH	• Clients requiring warfarinisation: ○ for sub-therapeutic INR ○ post procedure (re-commencement of Warfarin) ○ where other medical conditions/treatments require close monitoring of INR and Warfarin dosing • Client's medical condition has been assessed as stable, and client has a clear diagnosis, management plan, prognosis and is at low risk of deterioration.

4. Pathology work up

Verify and review the required pathology (via referral documentation or referral source):

- Full Blood Count (FBC) for baseline platelet counts
- Urea & electrolytes (U&E) to assess renal function
- Coagulation profile (INR, APTT, fibrinogen)
- Liver function tests

5. Anticoagulation therapy principles

5.1 Warfarin

- Warfarin can be used in patients with severe kidney disease. Its use is limited by its narrow therapeutic index, interactions with other drugs and food, and the necessity to perform regular blood tests to monitor anticoagulation.
- The effect of warfarin is measured by a blood test referred to as INR (International Normalised Ratio). The safety and efficacy of warfarin depends on maintaining the INR within the target range. Please see Appendix A for INR target ranges according to indication.
- When commencing Warfarin, measure the baseline INR. If baseline INR is 1.4 or above without Warfarin, then further patient assessment and specialist advice should be sought regarding the patient's suitability for Warfarin as may indicate liver impairment.
- When starting or restarting Warfarin, there can be a delay in achieving therapeutic anticoagulation because it takes several days for circulating coagulation factors to decrease. When first initiated, movement in the INR result may only be seen after 5-7 days
- Once the INR has started to respond, changes in INR are often seen approximately 2-3 days after dose adjustment. This should be kept in mind when adjusting Warfarin dosages.
- A patient's response to Warfarin is driven mainly through genetic variance in the hepatic clearance, and vitamin K handling. Diet, age, weight changes, dosing and medication interactions also influence the anticoagulant effect.
- The list of medications that interact with Warfarin (both prescription and non- prescription) is extensive. Tables detailing these medications may be found on Australian Therapeutic Guidelines, and this should be kept in mind when troubleshooting unexpected changes in INR.
- Warfarin takes a number of days to achieve therapeutic anticoagulation and causes an initial increase in prothrombotic potential. Consequently, when immediate anticoagulation is required (eg treatment of acute venous thromboembolism) Warfarin must be started with concurrent parenteral anticoagulant therapy e.g Enoxaparin bridging.
- When immediate anticoagulation is not required (e.g low thromboembolism risk), Warfarin can be started without concurrent parenteral therapy. See Appendix D.
- Advise client regarding warfarin use, including its potential complications and interactions with diet and alcohol as per *Living with Warfarin* booklet.
- Several nomograms exist to guide Warfarin dosing (e.g. age adjusted, day of therapy based etc). These can be used as a guide as deemed necessary, but do not replace clinical acumen to account for the various patient and situational factors that determine Warfarin dosing.
- When a patient is new to Warfarin, suggest initial dosing of 5mg daily for the first 2 days. **Consider lower starting doses** when the patient is elderly, has low body weight, abnormal liver function tests, severe renal impairment or high bleeding risk.

- When a patient is recommencing Warfarin, a patient's regular dose should be prescribed, unless bleeding risk is high.
- Warfarin is contraindicated in pregnancy

5.2 Bridging anticoagulation

- Bridging involves the practice of prescribing Heparin (usually Enoxaparin) concurrently with Warfarin to cover the pro-coagulant phase of Warfarin therapy and high thrombosis risk until the INR is within the target therapeutic range.
- Bridging with Enoxaparin is not always needed when Warfarin is initiated in patients. This decision will depend on the risk of thromboembolism, and other clinical factors.
- If acute venous thromboembolism is present (e.g. DVT/PE), enoxaparin bridging is required for a minimum of 5 days and 2 consecutive days of target INR range - whichever is later. This is due to the pro-thrombotic effect in the early stages of starting Warfarin and high thrombosis risk in the acute phase.
- In patients post procedure, the decision to bridge is based on the estimated thromboembolic risk balanced with the procedural bleeding risk. This should also be discussed with the referrer as needed. Appendix D provides a guide to peri-operative thromboembolic risk and who may need bridging therapy.
- If bridging with Enoxaparin is recommended at the time of Warfarin initiation or recommencement:-
    - In severe thrombosis risk, the enoxaparin is usually continued until 2 consecutive days of target INR readings are achieved.
    - In the moderate thrombosis risk, the enoxaparin bridging is continued for at least 1 day after target INR reading is achieved, and sometimes 2 depending on clinical assessment.
    - There may be certain clinical scenarios (e.g. High bleeding risk, large jump in INR) where it may be decided to cease Enoxaparin after 24hours of therapeutic INR.
- Twice daily dosing of Enoxaparin is generally preferred for patients at high risk of bleeding, high risk of thrombosis, acute coronary syndrome plus patients who are older, obese or have a malignancy.
- If the Enoxaparin dose required is greater than 150mg, dose must be given as a twice daily dose.
- The minimum time interval between twice daily Enoxaparin dosing is 10 hours. The maximum time interval between twice daily Enoxaparin dosing is 14 hours.
- Enoxaparin dosing is dependent on renal function which is calculated using the Cockroft- Gault calculation (CG):-
    - Measure/obtain client's height and measure the weight.
    - Ascertain the Ideal Body Weight (IBW) for the gender and height of the client using the table in Appendix B. CG calculation is based on ideal or actual body weight, whichever is less.
    - If the client's weight is at or below the estimated IBW, then use the actual measured body weight in the CG formula to calculate Creatinine clearance.
    - If the measured body weight is above the IBW for the height, use the ideal body weight for the CG formula to calculate Creatinine clearance.

Recommended Enoxaparin dose (weight range 50-150kg, not pregnant)

Renal function	Treatment Dose	VTE Prophylaxis dose
CG CrCl > 30mL/min	1.5mg/kg SC daily* or 1mg/kg SC BD**	40mg once daily
CG CrCl ≤ 30mL/min	1mg/kg SC daily	20mg once daily
* If dose required is greater than 150mg, dose must be given as twice daily dose which is the preferred choice in obese patients. **Twice-daily dosing of Enoxaparin is preferred for patients at high risk of bleeding, high risk of thrombosis, acute coronary syndrome plus patients who are older, obese or have a malignancy.		

- Patients with a weight of 12-150kg may be referred with a different lower starting dose to the above calculation based on emerging guidelines around this weight range. Clarify the dose with the referrer if needed. They should have anti- Xa testing to check if the dose needs adjusting.
- If the patient is pregnant, weight >150kg, weight <50kg, impaired renal function (CrCl < 30ml/min), active bleeding/significant unexplained bruising; use of anti-Xa level monitoring is recommended for reviewing Enoxaparin treatment dose (not for prophylactic doses).
    - consult with haematology, obstetric or renal team for starting dose.
    - Blood test for Anti-Xa should be performed 4 hours post dosing and may be performed after 3rd or 4th dose post commencement of Enoxaparin.
    - Review results with haematologist for advice re dosage adjustment and recheck anti- Xa and above process until dose stabilised.

5.2.1 Commencement of Enoxaparin in combination or post treatment with Nirmatrelvir/Ritonavir (Paxlovid®) for the treatment of COVID-190

- Some patients may be required to withhold anticoagulation when on COVID 19 treatments such as Paxlovid and may require bridging with Enoxaparin.
- Enoxaparin sodium may be co-administered with Nirmatrelvir/Ritonavir without dose adjustment or increased monitoring requirements.
- Clinicians must be aware of the various drug interactions with Nirmatrelvir/Ritonavir.
- Consider expert consultation for clients receiving highly specialised therapies or medicines prone to concentration dependant toxicities

See Appendix E (below) for guidance on the use of Nirmatrelvir/Ritonavir and anticoagulant/antiplatelet medications.

6. General Management

- Nursing assessment as per warfarinisation Clinical Pathway. Collaborate with medical governance doctor if any deterioration in client's condition.
- Access blood results from referral source. Collaborate with Medical Governance doctor regarding any abnormal test results.

- In conjunction with Medical Governance, collect the following information to allow admission on to service:
  - Reason for anticoagulation
  - Target INR range (Appendix A has a guide to target INR ranges based on conditions). Clarify with medical governance if discrepancy.
  - Usual dose of Warfarin (if been on warfarin previously)
  - If Warfarin has already been commenced, obtain last 2-3 days of INR results and Warfarin doses from referral source.
  - Note the brand of Warfarin (Marevan/Coumadin) and document this in the notes. If client has been on Warfarin before, continue the usual brand the client is familiar with and has been stable on prior. Please note that brands are NOT interchangeable as there is a lack of data on bioequivalence.
  - If Enoxaparin bridging treatment required, determine if: prophylactic vs therapeutic bridging, dosing, frequency, when to start, when to cease.
  - Contact person and contact details if queries regarding anticoagulation plan (eg treating specialist or GP).
- Check renal function, calculate creatinine clearance with Cockcroft Gault (CG) equation for all clients as below:-
  - Measure/obtain client's height and measure the weight
  - Ascertain the Ideal Body Weight (IBW) for the gender and height of the client using the table in Appendix B. CG calculation is based on ideal or actual body weight, whichever is less.
  - If the client's weight is at or below the estimated IBW, then use the actual measured body weight in the CG formula to calculate Creatinine clearance.
  - If the measured body weight is above the IBW for the height, use the ideal body weight for the CG formula to calculate Creatinine clearance.

7. Monitoring

- Regular INR to guide Warfarin dosing.
- When treating with Enoxaparin, measure the patient's FBC (specifically platelet count) at baseline.
  - If the patient has not previously been treated with any type of Heparin, measure the platelet count on Day 5 post commencement, and re-check the platelet count every 2-3 days/twice weekly during therapy until Day 14.
  - If the patient has previously been treated with Heparin, measure the platelet count on Day 2 after starting Enoxaparin and re-check the platelet count every 2-3 days/twice weekly during therapy, until at least Day 14.
  - If platelets drop by more than 30% from baseline or <100x10^9/L, the 4T's score for HIT can help with assessment and then subsequent decision with a Haematology consultant for a plan re: enoxaparin and any investigations needed.
- Renal function up to twice weekly until stable especially if moderate to severe renal impairment. Less frequent if stable.
- If the patient is pregnant, weight>150kg, weight <50kg, impaired renal function (CG CrCl < 30ml/min), active bleeding/significant unexplained bruising on treatment; use of anti- Xa level

monitoring is recommended for reviewing enoxaparin treatment dose (not for prophylactic doses).

- consult with haematology, obstetric (if pregnant) or renal team for starting dose.
- Blood test for Anti-Xa should be performed 4 hours post dosing, and ideally done after 3rd or 4th dose post commencement of Enoxaparin.
- Review results with haematologist for advice re dosage adjustment and recheck ant-Xa and above process until dose stabilised.

8. Medical Governance

- The client must have access to medical governance support for 24 hours per day, 7 days per week.
- Primary medical governance can be by referring medical specialists, credentialed referring GPs or by Silver Chain medical staff.
- When governance is retained by a Silver Chain medical officer the client will have a medical review within 48 hours of admission and the medical officer will determine when the scheduled follow up and discharge will occur.
- Where the primary medical governor is unavailable the Silver Chain medical officer can provide the medical governance.
- Care delivery is planned and provided in consultation with the client, medical officer/specialist holding medical governance and nursing staff.
- In the instance when a client's condition deteriorates the Silver Chain medical officer or nursing staff will confer with an emergency department medical officer.
- A summary of the episode of care is sent to the referrer or the client's GP at discharge and must clearly state the plan for when next INR or other monitoring needs to occur (if required).

9. Discharge Planning

- Ensure the client has an appointment arranged with own General Practitioner (GP) or Warfarin care program service prior to discharge to ensure continuity of care. This needs to be in a timely fashion to ensure INR monitoring.
- Fax client discharge summary to GP/warfarin care service provider and other relevant specialists involved in client's care.
- Fax client discharge summary to GP/warfarin care program service including Anti-Xa results if done (+/- subsequent haematology advice), other pertinent results, INR and warfarin doses for last 2-3 days to assist GP with ongoing management.
- In addition, nursing team to provide patient with a copy of POC and warfarin dosing chart to take to their GP appointment.
- If patient has pathology laboratory led anticoagulation care, contact the lab to find out process for transfer of anti-coagulation care.

10. Supporting documents

Silverchain policy and related documents that directly relate to and inform this procedure are available with this document in the Policy Document Management System (PDMS).

Other documents that directly relate to and inform this procedure are as follows:

- Therapeutic Guidelines. eTG complete: Cardiovascular Anticoagulant Therapy https://tgldcdp-tg-org-au.silverchain.idm.oclc.org/viewTopic?topicfile=anticoagulant-therapy
- https://www.nps.org.au/australian-prescriber/articles/anti-xa-assays
- Australian Commission on Safety and Quality in Health Care National Safety and Quality Health Service Standards (2nd), Sydney. Australia
- eTG complete. 2023.. Therapeutic Guidelines. CCG and Ideal body weight tables. https://tgldcdp-tg-org-au.silverchain.idm.oclc.org/viewTopic?etgAccess=true&guidelinePage=Antibiotic&topicfile=antimicrobial-dosing-renal-impairment&guidelinename=Antibiotic&sectionId=toc_d1e65#toc_d1e65
- Government of Western Australia Department of Health. 2020. Guidelines for Anticoagulation using Warfarin.

  https://ww2.health.wa.gov.au/-/media/Files/Corporate/general-documents/WATAG/Warfarin-guidelines-for-anticoagulation.pdf
- Clinical Excellence Commission. Guidelines on Perioperative Management of Anticoagulant and Antiplatelet Agents. 2018; https://www.cec.health.nsw.gov.au/__data/assets/pdf_file/0006/458988/Guidelines-on-perioperative-management-of-anticoagulant-and-antiplatelet-agents.pdf
- Queensland Health. Guidelines for warfarin management in the community. 2016.

  https://www.health.qld.gov.au/__data/assets/pdf_file/0025/443806/warfarin-guidelines.pdf
- Government of Western Australia Department of Health. 2022. Guidelines for the WA Anticoagulation Medication chart (WA AMC).

  https://www.health.wa.gov.au/~/media/Corp/Documents/Health-for/MTU/User-guidelines-WA-AMC.pdf

11. Document details

Document owner	Executive Medical Director, East Coast
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Functional area	Acute
Risk rating	Moderate
Periodic review	36 months

Silverchain Group policies align with relevant legislation and standards and are based on providing a fair, inclusive, and safe working environment free from bullying and discrimination and one that enables equal opportunity for all Silverchain Group staff.

Our policies embody our values of integrity, respect, trust, and compassion.

Appendix A Guide to INR target ranges based on conditions (noting that Medical Governance will usually specify a target range)

Target Range	Condition
2-3	DVT/PE Atrial Fibrillation with high stroke risk factors/previous stroke. Hypercoagulable conditions e.g. thrombophilias. Preventing systemic Embolism: AF, Valvular heart disease, post MI and bioprosthetic heart valves (3 months) Aortic bileaflet mechanical valves with no other risk factors Cardiac thrombus Preventing DVT in high-risk patients e.g. post knee/hip surgery
2.5- 3.5	Starr-Edwards mechanical heart valves/other high risk mechanical valves Mitral mechanical valves Aortic heart valve with risk factors (AF, previous thromboembolism, hypercoagulable condition, left ventricular dysfunction, older generation AVR)
Other	Under instructions from haematologist or other treating specialist

Appendix B Ideal Body Weight for Height and Sex

Height		Ideal body weight in kg	
cm	Feet (‘) & Inches (“)	Female	Male
155	5’	48	53
160	5’ 2”	53	57
165	5’ 4”	57	62
170	5’ 6”	62	66
175	5’ 7”	66	71
180	5’ 9”	71	75
185	6’	75	80
190	6’ 2”	80	84
195	6’ 4”	84	89
200	6’ 6”	89	93
205	6’ 7”	93	98
210	6’ 9”	98	102
215	7’	102	107
220	7’ 2”	107	111

Modified from eTG complete. 2023.. Therapeutic Guidelines. CCG and Ideal body weight tables

Appendix C Ideal Body Weight for Height and Sex

- INR ≥ 3.5 on Point of Care (POC) machine e.g. Coaguchek mandates laboratory specimen to be taken.

Laboratory specimen is considered as 'gold standard' and should be utilised in preference to POC machine.

Management of patients on anticoagulants with bleeding*

Inform and discuss plan with medical governance in all clinical settings

Clinical setting	Recommendation
Life threatening bleeding	Basic life support protocol, ring 000 for immediate hospital transfer. Withhold all anticoagulation.
Clinically significant bleeding	Cease anticoagulation and transfer immediately to hospital (BLS and 000 if clinically indicated)
Minor bleeding whilst on anticoagulation therapy	Discuss with Medical Governance for tailored plan. Recommendations may include actively managing/monitoring bleeding based on clinical judgement, omit/reduced anticoagulant therapy, close monitoring of INR if applicable, anti-Xa tests and transfer to hospital if worsening bleeding/concerns.

REVERSING WARFARIN OVER-TREATMENT (bleeding risk increases exponentially from INR 5 to 9. Monitor closely INR ≥ 6)				
Clinical Setting		Management		
INR	**Bleeding**	**Warfarin**	**Vitamin K *(seek advice if cardiac valve replacement)***	**Comments**
Greater than therapeutic range but less than <4.5	Absent	Reduce dose or omit next dose		Resume warfarin at reduce dose when INR approaches therapeutic range. If INR <10% above therapeutic level, dose reduction may not be necessary.
4.5-10	Absent (Low risk)	Stop		Measure INR within 24 hours. Resume warfarin at reduced dose when INR approaches the therapeutic range.
	Absent (*High risk)	Stop	Consider 1-2mg (oral) or 0.5-1mg IV	Measure INR within 24 hours. Resume warfarin at reduced dose when INR approaches the therapeutic range.
>10	Absent (Low risk)	Stop	Consider 3-5mg (oral) or transfer to hospital for IV	Measure INR in 12-24 hours. Resume warfarin at reduced dose when INR approaches the therapeutic range.
	Absent (*High risk)	Stop	Transfer to hospital for IV vitamin K and possible prothrombinex VF.	

*High bleeding risk = one of more of →	Recent surgery/trauma/bleed	Renail failure	Alcohol abuse	Antiplatelet therapy
	Advanced age	Hypertension	Active GI bleed	Other relevant co-morbidity eg severe liver disease

Modified from Government of Western Australia Department of Health. 2020. Guidelines for Anticoagulation using Warfarin

Appendix D Perioperative Thromboembolic risk Stratification

Thrombosis Risk	Mechanical Heart valves	Atrial fibrillation (AF)	Venous Thromboembolism (VTE)
Low (Bridging not recommended)	• Bi-leaflet aortic valve prosthesis without AF and no other risk factors for stroke	• $CHAD_2DS_2$-VA score of 3 or less and no prior history of stroke or TIA.	• A single VTE episode that was not life-threatening more than 12 months ago with no other risk factors
Moderate (asses on case by case basis)	• Bileaflet aortic valve prosthesis and one or more of the following risk factors: • AF • Prior stroke or TIA • Hypertension • Diabetes • Congestive cardiac failure • Age >75 years	• $CHAD_2DS_2$-VA score of 4 or 5 • $CHAD_2DS_2$-VA score less than 4 with prior history of stroke/TIA or peripheral arterial embolism >3 months	• VTE within the past 3-12 months • Non- severe thrombophilia (e.g. heterozygous Factor V Leiden or prothrombin gene mutation) • Recurrent VTE or a single non-provoked life threatening VTE • Active cancer (treated within last 6 months or palliative)
High (Bridging recommended)	• Any Mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent stroke or TIA (within 6 months)	• Recent stroke or TIA (within last 3 months) • AF with Rheumatic valvular disease (mitral valve disease i.e. stenosis/regurgitation) • CHA_2DS_2-VA score of 6 or more	• Recent VTE (within last 3 months) • High risk thrombophilia (e.g. deficiency of protein C, protein S or antithrombin III; antiphospholipid antibodies, multiple abnormalities)

Appendix E Drug interactions between Nirmatrelvir/Ritonavir (Paxlovid®) and anticoagulant/Antiplatelet medications

Note: Co-administration of medications with Nirmatrelvir/Ritonavir has not been studied. Advice is based on metabolism and clearance.

Use of Nirmatrelvir and Ritonavir (Paxlovid®) tablets and oral anticoagulants

- Warfarin

Co-administration may increase or decrease Warfarin concentrations. Closely monitor INR if co-administration is necessary. Educate clients on potential adverse effects.

- Apixaban / Rivaroxaban / Dabigatran

DO NOT co-administer. Consider switching to Enoxaparin. Potentially increased concentrations of Apixaban / Rivaroxaban / Dabigatran which may lead to an increased bleeding risk.

The usual Apixaban / Rivaroxaban / Dabigatran treatment should be resumed 3 days after the last dose of Nirmatrelvir/Ritonavir (Paxlovid®).

A.

Use of Nirmatrelvir and Ritonavir (Paxlovid®) tablets and oral antiplatelets

- Ticagrelor

DO NOT co-administer. Use is contraindicated and may lead to a substantial increase in exposure to Ticagrelor.

- Clopidogrel

Co-administration should be avoided. May decrease the concentration of Clopidogrel and reduce its effect.

- Aspirin / Prasugrel

No interaction expected. Clinically significant interactions are unlikely.