MONOGRAPH

WARFARIN

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Perioperative Management	Monitoring

DRUG CLASS

Warfarin is an anticoagulant.[1]

Warfarin is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS

Treatment and prevention of thromboembolism (including prevention of thromboembolism in patients with prosthetic heart valves).[2, 3]

CONTRAINDICATIONS

- Hypersensitivity to warfarin or any component of the formulation.[3]
- Severe active bleeding.[1]
- Disease states with increased risk of severe bleeding (e.g. severe thrombocytopenia, severe uncontrolled hypertension, severe hepatic disease).[1]

PRECAUTIONS

- Marevan® and Coumadin® brands should not be used interchangeably as bioequivalence has not been proven.[1] All PCH inpatients and outpatients should only use the Marevan® brand. If a

brand change is necessary, all tablet strengths given must be of a consistent brand. INR should be closely monitored following brand change until stable.

- Feeds (infant formula vs breast milk) – vitamin K is often added to infant formula while the content of vitamin K in breast milk is very low.[2, 4] Exercise caution when changing feeds.[2, 4]
- Avoid IM injections if possible – increased risk of bleeding, bruising, and haematomas.[2, 3]
- Protein C or S deficiency – increased risk of skin necrosis.[1]
- Heparin-induced thrombocytopenia – risk of skin necrosis and limb gangrene.[2, 3]
- Vasculitis.[3]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

- Marevan® - 1mg (brown), 3mg (blue), 5mg (pink) tablets.[5]

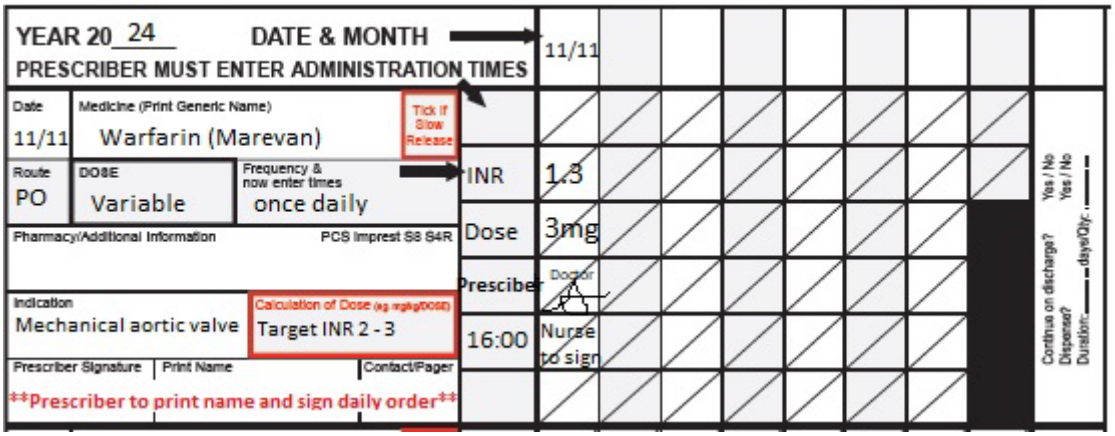
Coumadin® is not available at PCH.

Imprest location: Formulary One

PRESCRIBING

Target INR (International Normalised Ratio) must be specified on the medication order.

Variable daily dose of warfarin for inpatient administration must be prescribed daily in the format below. Each daily order must include prescriber's name and signature.



DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Consult haematologist's advice.

Child ≥ 4 weeks[3, 6, 7]**:**

- Bridging anticoagulant therapy with high/treatment dose IV unfractionated heparin infusion or enoxaparin may be required until target INR is attained.[8] Activated partial thromboplastin time (aPTT) or antifactor-Xa level monitoring as per protocol is required with heparin or enoxaparin use.
- Adjust dose according to target INR (refer to next page)[7, 9]:

- Low target range anticoagulation: 2 to 3 (median 2.5) – includes bioprosthetic mitral valve, mechanical aortic valve, Fontan circulation, Kawasaki's disease with giant coronary aneurysm(s), pulmonary embolus, deep vein thrombosis (DVT) or other venous thromboembolism (VTE).
- High target INR range anticoagulation: 3 to 4 (median 3.5) – mechanical mitral valve.

- Dosing guideline in this monograph is for **initial commencement** of warfarin or **recommencement** of warfarin following prolonged interruption in warfarin therapy (e.g. following treatment cessation pre-operatively).
- For ongoing maintenance therapy dosing guideline, refer to PCH Cardiology Anticoagulation Management for Cardiology Outpatients guideline.
- For more information regarding enoxaparin bridging, refer to the Clinical Nomogram section of the PCH Cardiology Anticoagulation Management for Cardiology Outpatients guideline.

Warfarin INITIATION dosing guideline for LOW target INR range 2 to 3 (median 2.5)

DAY	INR	DOSE
1 to 3		0.1mg/kg (max 10mg) once daily.
4	**Check INR on DAY 4**	
4 to 6	< 2	Increase dose by 25%.
	2 – 3	Continue with same dose.
	3.1 – 3.4	Reduce dose by 25% of initial dose.
	≥ 3.5	Reduce dose by 50% of initial dose.
7	**Check INR on DAY 7**	
7 to 10	< 2	Increase dose by 25% of previous dose.
	2 – 3	No change.
	3.1 – 3.5	Reduce dose by 25% of previous dose.
	> 3.5	Reduce dose by 50% of previous dose.
11 onwards	Refer to Cardiology outpatient warfarin long term management guideline	

Warfarin INITIATION dosing guideline for HIGH target INR range 3 to 4 (median 3.5)

DAY	INR	HEPARIN or ENOXAPARIN BRIDGING	DOSE
1 and 2		Continue	Loading dose: 0.2mg/kg (max 10mg) once daily. *(0.1mg/kg if patient has significant hepatic dysfunction)*
3	**Check INR on DAY 3**		
3	< 3	Continue	Continue with same dose.
	≥ 3	Stop	Reduce dose by 50%.
4 and 5	**Check INR on DAY 4 and 5**		

4 and 5	< 3	Continue	Repeat initial loading dose; continue heparin.
	3.1 – 4	Stop	Reduce dose by 25% of previous dose; cease heparin.
	4.1 – 5		Reduce dose by 50% of previous dose; cease heparin.
	> 5		Withhold until INR < 4.3; cease heparin. Recommence at 50% of previous dose.
6 onwards	Refer to PCH Cardiology Anticoagulation Management for Cardiology Outpatients guideline.		

Renal impairment:

- eGFR calculator
- Use with caution in patients with mild to moderate impairment.[4] Monitor INR more frequently in patients with severe impairment.[4]

Hepatic impairment:

- Response to warfarin may be significantly increased in obstructive jaundice (reduced vitamin K absorption), hepatitis and cirrhosis – lower doses may be required; monitor INR closely.[3]

ADMINISTRATION

- Warfarin is **teratogenic**, avoid skin contact. Pregnant staff member should avoid handling crushed or dispersed tablet.[10]
- Do not cut or crush tablets. Disperse tablet in an enteral syringe. Marevan® tablet disperses in water within 4 minutes.[10]
- Warfarin may be administered with or without food, around the same time each day.[3] A consistent, balanced diet should be maintained while on warfarin therapy.[1, 3]
- Enteral feed affects warfarin absorption and its clinical effects. Give warfarin one hour apart from enteral feeds. If not possible to administer separately from feeds, always give at the same time in regard to feeds.[10]

MONITORING

- INR, prothrombin time, haematocrit.[3]
- Increase INR monitoring frequency in events of acute illness, dietary changes or concurrent administration of medication that interacts with warfarin.[4]
- Management of excessively prolonged INR (> 8):
  - No significant bleeding – consider administering phytomenadione (vitamin K).[6]
  - Significant bleeding – reverse anticoagulation with fresh frozen plasma, prothrombin complex concentrates or recombinant factor VIIa. Contact haematology for advice.[6]

ADVERSE EFFECTS

Common: Bleeding.[1]

Rare: Allergic reactions, alopecia, skin necrosis, hepatitis, purple discolouration of the toes, tracheobronchial or vascular calcification, gangrene of skin or other tissues.[1, 3]

STORAGE

Store below 30ºC, protected from light.[5]

PERIOPERATIVE MANAGEMENT[7, 11]

Notify the PCH specialty team responsible for managing warfarin therapy. Consider ceasing warfarin therapy prior to invasive procedures with significant risk of perioperative bleeding that is likely to be difficult to control surgically.

Risk of thromboembolism: Moderate – High (on warfarin with target INR 3 – 4)

PRE – operative – where the intention is to achieve normal/near-normal haemostasis (i.e. INR < 2) at time of surgery

- Cease warfarin **5 days** prior to surgery.
- Commence bridging anticoagulant therapy with IV heparin or treatment dose enoxaparin. Monitor therapeutic levels as per protocol.

POST – operative

- Recommence **bridging** anticoagulation therapy with IV heparin or treatment dose enoxaparin **within 6 hours** post-surgery when adequate haemostasis achieved. Monitor therapeutic levels as per protocol.
- Continue bridging therapy until INR > 3.
- Recommence on **warfarin** loading dose (refer to dosing section) **6 hours** post-surgery when adequate haemostasis achieved and oral intake tolerated.

Risk of thromboembolism: Low (on warfarin with target INR 2 – 3)

PRE – operative – where the intention is to achieve normal/near-normal haemostasis (i.e. INR < 2) at time of surgery

- Cease warfarin **3 days** prior to surgery.
- Bridging anticoagulant therapy **not** routinely required.
- Proceed with surgery if INR on the day of procedure is < 2.

POST – operative

- Recommence on patient's **usual/pre-operative** warfarin dosing schedule **6 hours** post-surgery when adequate haemostasis achieved and oral intake tolerated.
- Bridging anticoagulation should not be required unless there is a delay in recommencing warfarin. To be discussed with specialty team managing warfarin therapy.

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **warfarin**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures and guidelines

Warfarin Management for Cardiology Outpatients

Heparin Monograph

Enoxaparin Monograph

Useful resources (including related forms)

MR101.12 Cardiology Warfarin Plan

Health Facts – Warfarin and INR

Health Facts – Enoxaparin

Keeping our mob healthy – Warfarin

Keeping our mob healthy – Warfarin and INR

References

1. Australian Medicines Handbook Adelaide SA: Australian Medicines Handbook; 2024. Available from: https://amhonline-amh-net-au.pklibresources.health.wa.gov.au/chapters/blood-electrolytes/anticoagulants/other-anticoagulants/warfarin?menu=hints.
2. Clinical Pharmacology 2024. Available from: https://www-clinicalkey-com.pklibresources.health.wa.gov.au/pharmacology/monograph/650?type=1.
3. Warfarin: drug information: Lexicomp; 2024. Available from: https://www-uptodate-com.pklibresources.health.wa.gov.au/contents/warfarin-drug-information?sectionName=Pediatric&topicId=10050&search=warfarin&usage_type=panel&anchor=F234898&source=panel_search_result&selectedTitle=1%7E150&showDrugLabel=true&kp_tab=drug_general&display_rank=1#F234856.
4. Medicines Complete - BNF for Children: BMJ Group,

Royal Pharmaceutical Society of Great Britain; 2024. Available from: https://www-medicinescomplete-com.pklibresources.health.wa.gov.au/#/content/bnfc/_107604022?hspl=warfarin.
5. MIMS Online 2024. Available from: https://www-mimsonline-com-au.pklibresources.health.wa.gov.au/Search/FullPI.aspx?ModuleName=Product%20Info&searchKeyword=Marevan+Tablets&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=3140001_2.
6. Monagle P, Chan AK, Goldenberg NA, Ichord RN, Journeycake JM, Nowak-Göttl U, Vesely SK. Antithrombotic therapy in neonates and children: antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2):e737S-e801S.
7. PCH Cardiology Department. Warfarin [expert opinion]. 2021.
8. Whitlock RP, Sun JC, Fremes SE, Rubens FD, Teoh KH. Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e576S-e600S. PubMed PMID: 22315272. Pubmed Central PMCID: PMC3278057. Epub 2012/02/15. eng.
9. Whitlock RP, Sun JC, Fremes SE, Rubens FD, Teoh KH. Antithrombotic and thrombolytic therapy for valvular disease: antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2):e576S-e600S.
10. Australian Don't Rush to Crush: Society of Hospital Pharmacists of Australia; 2024. Fourth Edition:[Available from: https://www-mimsonline-com-

au.pklibresources.health.wa.gov.au/Search/DNC.aspx?ModuleName=Product%20Info&searchKeyword=Marevan+Tablets&PreviousPage=~/Search/QuickSearch.aspx&SearchType=&ID=3140001_2.
11. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e326S-e50S. PubMed PMID: 22315266. Pubmed Central PMCID: PMC3278059. Epub 2012/02/15. eng.

This document can be made available in alternative formats on request for a person with a disability.

File Path:	W:\Safety & Quality\CAHS\CLOVERS MEDICAL Pharmacy\Procedures Protocols and Guidelines\Medication Monographs_Word\PCH.MED.Warfarin.DOCX		
Document Owner:	Chief Pharmacist		
Reviewer / Team:	Pharmacist, Cardiology consultant, Haematology consultant, Cardiology CNC		
Date First Issued:	July 2014	**Last Reviewed:**	Oct 2024
Amendment Dates:	Feb 2018, Sep 2021, Jan 2022, Oct 2024	**Next Review Date:**	Oct 2027
Approved by:	Medication Safety Committee	**Date:**	Nov 2024
Endorsed by:	Drugs and Therapeutics Committee	**Date:**	Dec 2024
Standards Applicable:	NSQHS Standards: NSMHS: N/A Child Safe Standards: N/A		

Printed or personally saved electronic copies of this document are considered uncontrolled

Healthy kids, healthy communities

Compassion | Excellence | Collaboration | Accountability | Equity | Respect

Neonatology | Community Health | Mental Health | Perth Children's Hospital