Approved by Quality & Patient Care Committee
15 February 2018

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT

This LOP is developed to guide clinical practice at the Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this LOP.

1. AIM

- To provide safe use and management of warfarin therapy.

2. PATIENT

- All patients prescribed warfarin

3. STAFF

- Medical, midwifery, nursing, pharmacy

4. EQUIPMENT

- National Inpatient Medication Chart (NIMC) or electronic equivalent
- Warfarin education/dosing book

5. CLINICAL PRACTICE

Medical Officers (MO) will:

- Ensure the patient/carer/person responsible has understood the indication for warfarin therapy
- Ensure the patient/carer/person responsible has been provided with education in a way in which they understand, regarding the benefits and risks; and agreed to warfarin therapy (see section 5.5).
- Contact Pharmacy to provide warfarin counselling (available during working hours) where appropriate
- Ensure mandatory baseline bloods are ordered when initiating therapy and the results reviewed as outlined in this document
- Ensure the indication for warfarin is documented in eMEDS as part of the prescription (see educational notes below)
- Ensure warfarin is prescribed as outlined in this document i.e ensure warfarin is prescribed before **the standard administration time of 1600hrs**
- Ensure the prescription of the correct warfarin brand (as warfarin brands are not bioequivalent and so are not interchangeable)
- Ensure the correct actions are taken and documented if **a dose is inadvertently missed** or if a **dose is withheld.**
- Ensure bloods are ordered for INR level and the results reviewed in a timely manner (i.e. aim to have bloods taken before 12 midday)
- Communicate and document the agreed frequency of International normalised ratio (INR) monitoring and the INR target range
- Ensure the correct procedure is followed when withholding or stopping warfarin as outlined in this document
- Seek advice early from **the appropriate specialty consultant MO** (e.g. RHW Physician, Haematologist, Cardiologist) or delegate when there are conflicting concerns related to the risks and benefits of anticoagulation with warfarin and/or other complex management decisions to be made

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

- Prescribe warfarin in eMEDs (when in use) in accordance with the following Quick Reference Guides:
  - eMEDs- Documenting a Medication History
  - eMEDs – Prescribing Warfarin and Warfarin Dose Check
  - eMEDs – Prescribing Warfarin and Warfarin Reminder
  - eMEDs- Admission Reconciliation
  - Administering warfarin
  - eMEDs – Prescribing Warfarin Initiation PowerPlan
  - eMEDs – Adding electronic Discharge Medications to Discharge Referral (eDRS)
  - or
  - in the dedicated warfarin section on the NIMC

Registered Nurses (RN)/ Enrolled Nurses (ENs) will:

- Ensure the patient/carer/person responsible has understood the indication for warfarin therapy
- Ensure the patient/carer/person responsible has been provided with education in a way in which they understand, regarding the benefits and risks; and agreed to warfarin therapy in conjunction with MO.
- Contact Pharmacy to provide warfarin counselling (available during working hours) where appropriate
- Ensure the eMEDs warfarin reminder is appropriately actioned to facilitate warfarin prescription before the **standard administration time of 1600hrs**
- Ensure warfarin is administered as outlined in this document
- Ensure the most recent INR result is within the target range or below (not proceeding with administration if the INR is higher than the upper level of the target range)
- Document the review of the INR by ticking the 'acknowledge' INR section in the administration window in eMEDs
- Ensure the correct procedure is followed when the second person is checking the preparation and administration of the warfarin dose
- Ensure the correct nursing actions are taken (in consultation with the responsible MO) if an INR result is not available when it was expected to be (as per the agreed INR monitoring and target range) and/or if an INR result is outside of (e.g. higher than) the agreed INR target range
- Ensure the correct procedure is followed when preparing and administering the warfarin dose (warfarin brands are not interchangeable, warfarin tablets cannot be crushed or chewed)
- Ensure the correct nursing actions are taken (in consultation with the responsible MO) **if a dose is inadvertently missed**

Pharmacists will:

- Undertake a pharmaceutical review (where possible) as defined in PD2015_029 which includes a review of the warfarin prescription verification, appropriate monitoring and provide appropriate advice to the clinical team as required
- Seek advice early from **the appropriate specialty consultant MO** (e.g. RHW Physician, Haematologist, Cardiologist) or delegate when there are conflicting concerns related to the risks and benefits of anticoagulation with warfarin and/or other complex management decisions to be made
- Provide (or facilitate) appropriate education and counselling for patients prescribed warfarin during this admission
- Ensure written information on warfarin therapy is available in all patient care areas and accompanies any counselling points and is documented appropriately
- Perform audits in relation to the safe use, storage and management of warfarin
- Ensure warfarin prescription, administration and monitoring is undertaken in accordance with the relevant eMEDS Quick Reference Guides (as above)

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

MO procedure for prescribing warfarin
Before prescribing (initiating or continuing) anticoagulation with warfarin:

- Confirm there is an appropriate clinical indication for prescribing warfarin
- Confirm appropriate Target INR
- Confirm appropriate duration of therapy or date/time to review the need to continue warfarin therapy
- Confirm there are no identified contraindications that outweigh the benefit of therapy
- Confirm whether anticoagulation is newly initiated or a continuation of previous therapy so appropriate dosing schedules are followed

Order blood tests-baseline
Baseline blood tests (prior to warfarin initiation) must be ordered and collected. This includes:

- International Normalised Ratio (INR)
- Prothrombin Time (PT)
- Activated Partial Thromboplastin Time (aPTT)
- Full Blood Count (FBC) including haemoglobin and platelet count
- Liver Function Tests (LFTs)
- A pregnancy test (Human chorionic gonadotropin- HCG) is mandatory in women of childbearing age

Prescribing anticoagulation with warfarin

- Follow the appropriate dosing schedule after review of INR.
- Record the prescription in eMEDs (or in the dedicated warfarin section on the NIMC).
- Record as part of the prescription the warfarin brand name, the indication for warfarin, therapeutic INR targets, the warfarin dose and route.
- Ensure warfarin is prescribed before **the standard administration time of 1600hrs**

Initiation of warfarin dosage schedule

Day	**INR result**	**Warfarin Dose (in milligrams)**
Day 1 at 1600 hours	Less than 1.4	10 or 5**
Day 2 at 1600 hours	Less than 1.8 1.8 to 2.0 Greater than 2.0	5 1 WITHOLD
Day 3 at 1600 hours	Less than 2.0 2.0 to 2.5 2.6 to 2.9 3.0 to 3.2 3.3 to 3.5 Greater than 3.5	5 4 3 2 1 WITHOLD
Day 4 at 1600 hours	Less than 1.4 1.4 to 1.5 1.6 to 1.7 1.8 to 1.9 2.0 to 2.3 2.4 to 3.0 3.1 to 3.2 3.3 to 3.5 Greater than 3.5	10 7 6 5 4 3 2 1 WITHOLD
Dose adjustment after Day 4 depends on clinical judgement based on the pattern of the INR and the target INR but daily or every second day is appropriate		
***Use 5mg loading dose in elderly or malnourished patients, low body weight or where serum albumin less than 30g/L, or other bleeding risks e.g. hepatic impairment, severe heart failure or concomitant drugs affecting warfarin metabolism*		

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

When warfarin therapy is initiated for a patient with acute thrombosis, or in patients at high risk of acute thrombosis, heparin or low molecular weight heparin (LMWH) is recommended for at least 5 days and to continue until the INR has reached a therapeutic level for at least two consecutive days.

Administration

- Acknowledge the INR prior to administration of the first warfarin dose and only proceed if the INR is less than 1.4. If INR is 1.4 or higher, discuss with the RHW Physician or Haematologist (or delegate) prior to initial treatment with warfarin.
- Follow correct procedure when preparing and administering the warfarin dose (warfarin brands are not interchangeable, warfarin tablets cannot be crushed or chewed)
- Follow correct procedure when the second person is checking the preparation and administration of the warfarin dose
- Ensure warfarin is administered at **the standard administration time of 1600hrs.**

Documentation of a WITHOLD dose

- If a warfarin dose is to be withheld the responsible MO must record (prescribe) the WITHOLD dose in eMEDs (or in the dedicated warfarin sections on the NIMC).
- Record the reason for the WITHOLD dose in the order comment section in eMEDs and in the patient's health care record (responsible MO).
- Follow correct procedure to 'sign off' the WITHOLD dose (responsible nurse).

Cessation of warfarin therapy

- If warfarin therapy is to be discontinued (e.g. switched to another oral anticoagulant or stopped due to sustained bleeding risk) the responsible MO must record the reason for the cessation of warfarin therapy in the order comment section of the most recent dose and in eMEDs and in the patient's health care record.
- 'Suspend' the reminder prescription (in eMEDs) to minimise the risk a dose being inadvertently prescribed/given (responsible MO).

Re-commencement of warfarin

- Many patients on warfarin require interruption to their warfarin therapy (e.g. surgery) and will require re-commencement of therapy. In this context, the patient's maintenance warfarin dose to achieve their target INR will be already known. While there is no established protocol for recommencement of warfarin, it is recommended to recommence at the patient's usual maintenance dose. If the patient has acute thrombosis or is at high risk of thrombosis concurrent heparin anticoagulation will be required for at least 5 days and/or until 2 consecutive days of therapeutic INR.

6. DOCUMENTATION

- Integrated Clinical Notes
- National Inpatient Medication Chart (NIMC) or electronic equivalent

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

7. EDUCATIONAL NOTES

Warfarin is a Vitamin K antagonist. By inhibiting the Vitamin K cycle warfarin reduces the synthesis of functional vitamin K-dependent clotting factors (II, VII, IX, X) and the antithrombotic factors, protein C and protein S. The suppression of functional prothrombin (Factor II) is principally responsible for the anticoagulant activity of warfarin. After initiation of warfarin, reduction in functional prothrombin to achieve therapeutic anticoagulation takes about 7 days. It is for this reason that patients with acute thrombosis, or at high risk of thrombosis, require anticoagulation with heparin whilst warfarin is initiated. INR reflects the reduction in functional clotting factors and is used to monitor and dose warfarin therapy.

Warfarin is highly susceptible to medication interactions that may affect the absorption and metabolism of warfarin, and the efficacy of warfarin's inhibition of clotting factor synthesis.

The maintenance dose of warfarin to achieve a therapeutic INR varies considerably between individuals, and the dose must be individualised to each patient. The maintenance dose for a given individual may vary considerably over time depending on changes in their health, other medications, changes in diet and lifestyle factors (e.g. alcohol intake). The frequency of INR measurement must take into account these important clinical considerations.

> The two brands of warfarin available in Australia are Coumadin® and Marevan®. Coumadin® and Marevan® are not interchangeable. Swapping brands may affect INR control and therapeutic coagulation. RHW uses the Coumadin® brand. Marevan® is available from pharmacy if required

Indications for anticoagulation with warfarin and recommendations for target INR and range

Warfarin is a highly effective oral anticoagulant used in a wide range of thromboembolic disorders for primary and secondary prevention. Common indications for the use of warfarin include:

- stroke prevention in atrial fibrillation/flutter (AF),
- preventing thrombus formation in mechanical heart valves, and
- the treatment of venous thromboembolism (VTE)

It is important for the responsible MO (usually the admitting team MO) to specify in the health care record:

- the indication for anticoagulation
- the target INR
- timeframe for review and
- whether warfarin therapy is newly initiated or a continuation of previous therapy

The therapeutic targets INR varies depending on the indication for warfarin therapy.

Indication	INR Range
Acute treatment and secondary prevention of vein thrombosis	2.0 to 3.0
Stroke prevention in non-valvular atrial fibrillation	2.0 to 3.0
Bio prosthetic/low risk heart valves	2.0 to 3.0*
Rheumatic heart disease	3.0 to 4.0
High risk/metal heart valves	3.0 to 4.0*

- The duration of warfarin therapy varies according to clinical indication. Most indications require long-term warfarin therapy (e.g. stroke prevention in patients with AF and mechanical heart valves). Patients with vein thrombosis require individualised duration of therapy varying from 4 to 6 weeks to life-long therapy. The intended duration of therapy, or a suitable time to review whether warfarin therapy should continue, should be explained to the patient and documented in the patient's health care record.

…./6

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

Contraindications for anticoagulation with warfarin
As with all anticoagulant therapy before initiating or re-commencing warfarin, there is a need to consider contraindications as listed below. The lists below are not exhaustive. Absolute contraindications to warfarin therapy include:

- active bleeding
- recent (within 1 month) bleeding affecting eye, spine or brain
- recent (within 1 month) surgery of eye, spine or brain
- recent (within 72 hours) major surgery or trauma with risk of bleeding
- disease states with an increased risk of bleeding including:
- uncontrolled hypertension
- significant thrombocytopenia (platelet count less than 50 x 109 /L)
- known bleeding disorder (e.g. haemophilia)
- decompensated liver disease or deranged baseline clotting screen (initial INR greater than 1.5)
- known oesophageal varices
- previously documented hypersensitivity to warfarin (e.g. priapism or ischaemic necrosis)
- concomitant use with another oral anticoagulant unless in process of switching (e.g. apixaban, dabigatran, rivaroxaban)
- early pregnancy
- inadequate laboratory facilities for monitoring
- lack of patient co-operation with dosing or INR monitoring

Precautions for anticoagulation with warfarin

- concomitant use of antiplatelets or Non-Steroidal Ant-inflammatory Drugs (NSAIDs) (i.e. patient at risk of arterial thrombosis)
- elderly patients at risk of falls
- infectious diseases or disturbances of intestinal flora (e.g. Coeliac disease)
- known or suspected deficiency in protein C mediated anticoagulant response
- Invasive procedures and surgery
- medication interactions (refer to CIAP)

Warfarin and interactions with other prescribed medicines
Many medicines interact with warfarin. An alternative non-interacting medicine should always be considered and chosen over an interacting medicine in a patient taking warfarin. The INR should be tested more frequently (within 48 to 72 hours) after starting, stopping or changing the dose of a medicine that potentially interacts with warfarin. More frequent monitoring is at the discretion of the MO. The following concomitant treatments should be avoided:-

- Medicines that affect platelet function (e.g. aspirin, clopidogrel) except in situations where benefit is known or is highly likely to be greater than harm from bleeding, such as patients with acute coronary syndrome, recent coronary stents or bypass surgery.
- Non-steroidal anti-inflammatory medicines (NSAIDs) (e.g. diclofenac, ibuprofen) and cyclooxygenase (COX)-2-inhibitors (e.g. celecoxib) may increase the risk of bleeding.
- Medicines that can affect the clotting process may result in a great risk of bleeding and are contra-indicated unless transitioning between anti-coagulants.
- Direct oral anticoagulants (e.g. apixaban, dabigatran, rivaroxaban) are contra-indicated with concomitant

…./7

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

Monitoring the patient for bleeding

- Monitor patients for bleeding or new or extending thrombosis. Vigilance and monitoring should be ongoing during warfarin therapy and continue after therapy cessation.
- If warfarin therapy is discontinued, patients, carers and clinical staff should be cautioned that the anticoagulant effects of warfarin may persist for up to 5 days.
- Potential adverse reactions to warfarin may include fatal or nonfatal haemorrhage from any tissue or organ. The signs, symptoms and severity will vary according to the location and degree or extent of the bleeding .
- The possibility of haemorrhage should be considered in evaluating the condition of any anticoagulated patient with complaints that do not indicate an obvious diagnosis.
- Bleeding during anticoagulant therapy does not always correlate with Prothrombin Time (PT) and/or INR.
- Instructions for monitoring patients for bleeding must be recorded in the patient health care record. For example, laboratory tests, clinical observation requirements and actions to be taken
- Any signs or symptoms of bleeding (including vital signs) must be recorded in the patient's health care record as well as the subsequent clinical management

Management of Bleeding

If major bleeding is suspected in a patient anticoagulated with warfarin then:

1) Immediate response must assess the need for Basic Life Support. Immediately activate PACE and/or code blue as clinically appropriate and clinically respond to the patient's signs and symptoms of clinical deterioration
2) If the patient has clinically significant bleeding requiring reversal of warfarin (any level of INR) manage as per table below.
3) Actively pursue signs and symptoms of bleeding/haemorrhage by taking a history and physical examination, a rectal examination and urinalysis for macroscopic haematuria.
4) Collect bloods for Full Blood Count (FBC), repeat INR, Liver Function Tests (LFTs), Electrolytes, Urea and Creatinine (EUCs) and Blood Group and Antibody Screen ("Group & Hold").
5) Seek advice from the RHW Physician or POW Haematologist (or delegate)

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

Clinical Setting	Action
If the patient has clinically significant bleeding requiring reversal of warfarin (any level of INR)	Cease warfarin Administer phytomenadione (Vitamin K) 5 to 10mg as slow **IV** injection over at least 30 seconds 28 Urgent consultation with the RHW Physcian or POW Haematologist (or delegate) is required to approve Prothrombinex-HT dosing. Dosing is according to body weight, usually 25 to 50 units per kg for major or life threatening bleeding. Patient will require clotting factor replacement either fresh frozen plasma (FFP) alone, or with Prothrombinex-HT Patients with major or life-threatening haemorrhage should preferentially receive Prothrombinex-HT and FFP
If the patient has minor bleeding with elevated INR	Withhold warfarin Consider phytomenadione (Vitamin K) 1mg **oral (**Note: use Konakion MM® orally) Measure INR the following day and adjust warfarin dose
INR 4.0 to 6.0 (no bleeding)	Withhold 1 to 2 doses of warfarin Measure INR daily and recommence at lower dose when INR less than 4.0 Search for the reason(s) for supratherapeutic INR
INR greater than 6.0 but Less than 10.0 (no bleeding)	Cease warfarin Administer phytomenadione (Vitamin K) 1 mg **oral** (Note: use Konakion MM® orally) Measure INR the following day anticipating that the INR will be in the therapeutic range of 2.0 to 3.0 within 24 hours If INR in therapeutic range recommence warfarin at reduced dose.
INR greater than or equal to 10.0 (no bleeding)	Cease warfarin Administer phytomenadione (Vitamin K) 2mg as a slow **IV injection.** Measure INR after 12 hours to ensure INR less than 10.0. Repeat INR the following day Recommence warfarin at reduced dose once INR is less than 5.0. If INR less than 2.0 give enoxaparin (Clexane®) 1.5mg/kg/day subcutaneous or heparin IV infusion until INR is greater than 2.0 If high risk of bleeding (recent bleeding, thrombocytopenia, liver disease, concurrent anti-platelet therapy) then in addition to the above also consider Prothrombinex. Note: Consultation with the POW Haematologist is required to approve Prothrombinex dosing.

LOCAL OPERATING PROCEDURE

CLINICAL POLICIES, PROCEDURES & GUIDELINES

Approved by Quality & Patient Care Committee
15 February 2018

WARFARIN – ADMINISTRATION AND DOSAGE ADJUSTMENT cont'd

8. RELATED POLICIES / PROCEDURES / CLINICAL PRACTICE LOP

- Bridging anticoagulation
- Heparin

9. RISK RATING

- Medium- review in 3 years

10. NATIONAL STANDARD

- Medication safety

11. REFERENCES

- Prince of Wales Clinical Business Rule. Warfarin guidelines for prescribing, administration, monitoring and dosage adjustment. July 2017
- Therapeutic Goods Administration -TGA Guidelines Product Information Warfarin: Coumadin. Accessed 15/07/16.

REVISION & APPROVAL HISTORY

Reviewed and endorsed Therapeutic & Drug Utilisation Committee 12/12/17
Approved Quality & Patient Safety Committee 18/8/11
Therapeutic & Drug Utilisation Committee 14/6/11
Approved Patient Care Committee March 2008

FOR REVIEW : DECEMBER 2020