STANDING ORDERS FOR THE MANAGEMENT OF WARFARIN Dose adjustment and INR testing frequency	
Applicable to: Pharmacists	Prepared by: Medical Advisor, Community Pharmacy Anticoagulant Management Service
	Contact: Dr Paul Harper, Consultant Haematologist,

Purpose

To improve the safety of Warfarin management by providing anticoagulant control through a pharmacist led service using point of care testing (CoaguChek XS Plus) and online computer decision support (INR Online Ltd).

Scope

Accredited pharmacists participating in the Community Pharmacy Anticoagulant Management Service (CPAMS). The Standing Order is required to enable pharmacists to supervise anticoagulant management.

The Standing Order is an agreement between the general practitioner and the pharmacists providing the service.
The General Practitioner issues the Standing Order which delegates authority to approved pharmacists to provide CPAMS.
Approved pharmacists are pharmacists who have received appropriate training, met the qualification requirements and are accredited by the Pharmaceutical Society to deliver the service.

Issuer

The Standing Order is issued by Dr……..……(GP).

The GP named above act as a representative for all General practitioners (including locum doctors) working within the same Medical Practice.

Medical Practice…….

Address……

Applies to

The Standing Order applies to all appropriately trained pharmacists at

Pharmacy name: ……

Address…….

See appendix 1 for complete list of approved pharmacists working at the above named pharmacy

Clinical Details relating to the Standing Order

Medicine

Name of Medicine
Warfarin

Indications
Anticoagulation therapy initiated or confirmed by a doctor for;

1. Atrial fibrillation
2. Deep vein thrombosis
3. Pulmonary embolus
4. Tissue heart valve
5. Mechanical heart valve
6. Mural thrombus
7. Transient ischaemic attack (TIA)
8. Post myocardial infarction

Method of Administration: Oral
Dosage : see below

Contraindications
High risk of haemorrhage: active ulceration, overt bleeding of gastrointestinal, genitourinary or respiratory tracts, cerebrovascular haemorrhage, cerebral aneurysm.
Pregnancy

Side effects
High incidence of drug interactions
Haemorrhage; GI upset; fever; dermatitis; urticaria; alopecia. hypersensitivity.

Test Procedure

Consent
All patients must be referred to the pharmacist anticoagulant management service by the prescribing doctor.
All patients must give informed consent

Safety
All patients are to be asked about signs and symptoms of bleeding (haematuria, blood in bowel motions, severe bruising, mucosal haemorrhage etc).
If there is minor bleeding the doctor should be informed and the patient reviewed if necessary.
If the patient has significant bleeding the doctor should be informed immediately.

All patients are to be asked about new medication since the previous INR test, including OTC medication and other complementary medicines.
If a significant interaction is identified the doctor should be informed and the patient reviewed if necessary.

All patients are to be asked about warfarin compliance. If a significant number of doses have been omitted the doctor should be informed.

All patients are to be asked if they have been admitted to hospital since their previous INR test. Details of the reason for admission will be recorded.

Dose Adjustment

Dose recommendation

Dose recommendation and interval to next INR test to be determined using INR Online software at the time an INR result is entered from the point of care device (CoaguChek XS Plus with direct data connection).

The recommended dose can be accepted by the supervising pharmacists if the INR is within a specified range

Parameters for warfarin adjustment

- All patients must have a specified target INR and treatment range
- An upper and lower INR value that will trigger a REVIEW must be set for each patient.
- The default values to trigger a REVIEW: lower INR – 1.5 upper INR – 4.0 will be used unless otherwise specified by the doctor.
- The pharmacist can accept the dose recommendation made by INR Online for INR values between the lower and upper limits.
- INR values outside the upper and lower limits will be referred for review by the doctor.
- If the INR is between 4.0 and 5.0 the computer will automatically advise the user to reduce the dose.
- If the INR is >5.0 the computer will advise the patient to miss 1 dose of warfarin and recommend a test the following day.
- The pharmacist can contact the supervising doctor and discuss any dose recommendation if he or she believes that the dose recommendation is inappropriate for the patient.
- The pharmacist must document in the notes box in INR Online the reasons for any deviation in dose recommendation

Test interval

- A maximum test interval must be set for each patient. The default value of 28 days will be used unless otherwise specified by the doctor.
- The test interval varies depending on the patient's anticoagulant control.
- The system defaults to 1 week when the INR is outside the treatment range. The interval increases by 1 week if the INR remains in range up to the maximum (28 days).
- The pharmacist can recommend a shorter test interval at anytime if he or she believes an earlier test is appropriate.
- The pharmacist can recommend test interval up to 42 days if the patient has shown consistent stable control for 2 or more months.
- The pharmacist must document in the notes box in INR Online the reasons for any deviation in the test interval recommendation.

The pharmacist will provide the patient with advice about the warfarin dose and the date of the next INR test and provide a printed dosing calendar.

Starting warfarin

The INR Online software provides a protocol to assist with warfarin loading and initial stabilization.

This stage of treatment can be supervised by the pharmacist but close consultation with the supervising doctor is recommended.

Medical Review

Medical review

If a patient has an INR result outside the specified safe range, the supervising doctor will be informed by e-mail. The contents of the message will include

- The latest INR result
- The recommended dose
- The date of the next test
- A graph showing recent warfarin control
- A list of previous results to enable the doctor to appropriately review the new dose.
- A link to open INR Online on the appropriate page to enable the doctor to edit the dose or date of the next test.

The doctor has two options on reviewing the result

1. Acknowledge result
    - If the doctor agrees with the recommendation made by the INR Online software or the pharmacists, the doctor will need to acknowledge that the result has been seen by clicking on a link in the email. No further action will need to be taken. The patient will have been informed of the dose and the date of the next test.
2. Modify the recommendation
    - If the doctor wishes to modify the dose or date of next test a web-page link is provided in the review message to take the doctor directly to the review page.
    - The doctor can then change the dose or date of the next test and confirm the change.
    - The pharmacist who entered the result will automatically be notified by e-mail that the dose or date has been changed. If the patient has e-mail the patient will also be informed.
    - The doctor does not need to take any further action
    - The responsibility to inform the patient rests with the pharmacist.
    - The review must be completed within 24 hours of the INR test.

Warfarin Reversal

Managing High INR Results

- All INR results >4.0 will trigger a review message to the doctor
- If the INR >4.0, INR Online will recommend a dose reduction.
- If the INR is >5.0,
    - INR Online will provide advice for warfarin reversal in line with the Australasian Guidelines (Appendix 5).
    - All results should be discussed with the supervising doctor
    - If the guidelines recommend treatment with vitamin K, this must be discussed with the supervising doctor. Vitamin K can only be given with authorization from the supervising doctor.

- IF A PATIENT HAS SIGNIFICANT BLEEDING.
    - Refer to the hospital immediately.
    - Inform the supervising doctor.
    - Consider giving 10mg oral vitamin K if there is significant travel time to the nearest hospital. Vitamin K can only be given with authorization from the supervising doctor.

NB: Significant bleeds include: Blood in the urine, Blood in the bowel motions, A prolonged nose bleed, Large bruises (bigger than 4cm in diameter)

Many patients on warfarin have minor bleeds, such as gum bleeding, spotting from the nose, or easy bruising. These do not need urgent attention

Record keeping

Recording results
The INR result, dosage of warfarin and testing interval are to be recorded in the INR-Online software and the same information will be sent automatically to the doctor's patient management system via HealthLink.

INR Online automatically records the date, time and user, when results are entered or any changes made.
Adverse events are recorded during the assessment prior to each test and additional information can be recorded in a notes field with each INR test.

Responsibility of the Issuer

Countersign period

The Doctor initiating anti-coagulation therapy will sign off treatment. Sign off will take place every 3 months at the time a new warfarin prescription is provided.

Annual Review

The Standing Order will be reviewed **once per year**

The review will take place between the GP and a lead pharmacist from the pharmacy. The review is to ensure the correct operation of the Standing Order, and that the GP provides appropriate supervision.

If both parties agree changes should be made that affect the Standing Order, these should be documented on the Standing Order document as an amendment and a new Standing Order should be issued.

The date of each review should be recorded on the Standing Order document (appendix 2).

The review process should ensure that all pharmacists listed on the Standing Order have current accreditation.

Audit

Annually the pharmacist and GP should review the management of a proportion of the cases managed on CPAMS. The number of cases for audit will be determined by the GP.

The audit should be documented (appendix 3). The results of the audit should be recorded along with any required changes or improvements in relation to the Standing Order documentation, processes or training to be undertaken. Prompt action should be taken to address any issues identified.

Responsibility of the Pharmacist

Training and Competency Assessment

Prior to administering Warfarin dose titration under this Standing Order, Accredited pharmacists are required to have:

- Attended a Standing Order education session.
- Meet the required standard for accreditation as assessed by the Pharmaceutical Society
- Completed the INR-Online training session.
- Completed CoaguChek XS Plus Competency Training
- Maintain appropriate training with reaccreditation assessed every 2 years.

Process for audit and review

Participate in annual review and audit with the GP as outlined above.

To report any adverse events to the GP as soon as possible.

Adverse events related to Standing Orders should be reported to the supervising GP. If the adverse event is directly related to medication, it should be reported to CARM by the GP.

Time period for which the Standing Order is valid

This Standing Order is valid until it is replaced by a new Standing Order or cancelled by the issuer.

Limitations

This Standing Order only applies to Pharmacists who are accredited to provide community pharmacy-based anticoagulant management services and who have a current agreement with the district to provide community pharmacy services

Standing Order prepared by
Dr P L Harper. MD, FRCP, FRACP, MRCPath.
Haematologist

Consent

By signing this Standing Order you are consenting to allowing patients at this practice to continue management of their warfarin using a Pharmacy based anticoagulant management service.

I confirm I have read these Standing Orders, and consent to referring selected patients in the practice to _____Pharmacy for Community Pharmacy Anticoagulation Management Services.

NB – this Standing Order may be signed by the practice Clinical Director on behalf of all medical practitioners in the practice, or alternately signed by each GP.

GENERAL PRACTICE: _____

Name of doctor:.....

Signed:.....Date:.....

Name of doctor:.....

Signed:.....Date:.....

Name of doctor:.....

Signed:.....Date:.....

Name of doctor:.....

Signed:.....Date:.....

Name of doctor:.....

Signed:.....Date:.....

Amendments

The above document is a template for the Standing Order for the CPAM Service. It lists the details necessary for the Standing Order as outlined in the Ministry of Health Guidelines for Standing Orders.

However the Standing Order is an agreement between the General Practitioner and pharmacist and additional specific details may be required to ensure the safe delivery of the service. These should be added to the document as amendments agreed by both parties.

For example: Details of how the pharmacists will contact the GP for advice OR the process for managing a high INR out of normal surgery hours etc.

This amendment forms part of the CPAMS Standing Order between ……(GP Practice) and

……..……..pharmacy Dated…….

GP……	Signed……..
Pharmacist……	Signed……..

Appendix 1

Pharmacists Accredited to provide CPAMS at above named Pharmacy

Name	Date Training completed Or Reaccreditation completed	Date next reaccreditation due

Appendix 2

Annual Review[1] of the Standing Order by the Issuer

Date		
Notes		
Attendance General Practitioner: Pharmacist:	 Signed …….. Signed ……..	
Does the Standing Order require amendment?	Yes ☐	No ☐
	Details	
Confirm the list of accredited pharmacists is up to date	Confirm ☐	

Date		
Notes		
Attendance General Practitioner: Pharmacist:	 Signed …….. Signed ……..	
Does the Standing Order require amendment?	Yes ☐	No ☐
	Details	
Confirm the list of accredited pharmacists is up to date	Confirm ☐	

Date		
Notes		
Attendance General Practitioner: Pharmacist:	 Signed …….. Signed ……..	
Does the Standing Order require amendment?	Yes ☐	No ☐
	Details	
Confirm the list of accredited pharmacists is up to date	Confirm ☐	

[1] Annual review of the Standing Order by the Issuer is a requirement in the *Medicines (Standing Order) Regulations 2002*

Appendix 3

Annual Audit

Date	
Number of cases reviewed	
Issues identified	
Action Taken	
General Practitioner: Pharmacist:	Signed ……. Signed …….

Date	
Number of cases reviewed	
Issues identified	
Action Taken	
General Practitioner: Pharmacist:	Signed ……. Signed …….

Appendix 4

CPAMS – Overview of the Test Process

Safety questions

- Bleeding complications
- Compliance
- New medication – Drugs recorded – Potential interactions identified
- Adverse events – Hospital admission: Date of admission

INR Test

- Performed on CoaguChek XS Plus. NHI number recorded on the device
- Result automatically transferred to INR Online
- Automatically calculate recommended dose and date of next test

INR within safe range

- Recommendation reviewed by the pharmacist and accepted if appropriate
- Calendar printed
- Patient informed of the result and dose

INR outside safe range

- Recommendation reviewed by the pharmacist and accepted if appropriate
- Calendar printed
- Patient informed that the result has been sent to their doctor for review, and the dose may be altered
- The patient should continue with the recommended dose unless told otherwise

Data storage

INR Result. Test date. Dose and date of next test sent to GP PMS

Review by doctor

- The GP will receive a notification stating the INR result is outside the safe range
- The notification will display the latest result and recommended dose and a list of recent results
- There will be a link taking the doctor directly to the review page
- The doctor will have the option to alter the result, or make no change

If result changed

- If the patient has requested email notification – the patient will receive an email
- Otherwise an email will be sent to the allocated pharmacy

Data Storage

Amended result sent to GP PMS

Appendix 5

Guidelines for the management of an elevated international normalized (INR) in adult patients with or without bleeding

Clinical Setting	Action
INR higher than the therapeutic range, but <4.5; bleeding absent	- Lower the dose or omit the next dose of warfarin. Resume therapy at a lower dose when the INR approaches the therapeutic range. - If the INR is only minimally above the therapeutic range (up to 10%), dose reduction may not be necessary.
INR 4.5-8.0[1]; bleeding absent	- Cease warfarin therapy; consider reasons for elevated INR and patient-specific factors. - If bleeding risk is high, give vitamin K[2] (1.0-2.0mg orally or 0.5-1.0mg intravenously). - Measure INR within 24 hours, resume warfarin at a reduced dose once INR is in therapeutic range.
INR >8.0; bleeding absent	- Where there is a low risk of bleeding, cease warfarin therapy. - Give 2.5- 5.0mg vitamin K[2] orally or 1.0mg intravenously. - Measure INR in 6-12 hours, resume warfarin therapy at a reduced dose once INR approaches the therapeutic range. - Where there is a high risk of bleeding[3], cease warfarin therapy, - Give 1.0mg vitamin K[2] intravenously. - Consider Beriplex (25-50IU/kg). Measure INR in 6-12 hours, resume warfarin therapy at a reduced dose once INR approaches the therapeutic range.
Any clinically significant bleeding where warfarin-induced coagulopathy is considered a contributing factor	- Cease warfarin therapy, give 5.0-10.0mg vitamin K[2] intravenously, as well as Beriplex (25-50IU/kg) assess patient continuously until INR approaches the therapeutic range, and bleeding stops[4]. OR - If Beriplex is unavailable, cease warfarin therapy, give 5.0- 10.0mg vitamin K[2] intravenously, and 10-15ML/kg of fresh frozen plasma, assess patient continuously until INR approaches the therapeutic range, and bleeding stops[4].

1. Bleeding risk increases exponentially from INR 5 to 8. INR greater or equal to 6 should be monitored closely.
2. Vitamin K effect on INR can be expected within 6-12 hours.
3. Examples of patients in whom the bleeding risk would be expected to be high include those with active gastrointestinal disorders (such as peptic ulcer or inflammatory bowel disease), those receiving concomitant antiplatelet therapy, those who underwent a major surgical procedure within the preceding two weeks, and those with a low platelet count.
4. In all situations carefully reassess the need for ongoing warfarin therapy.

Note: This guideline is modified to align with the CoaguChek (Maximum INR on the device is 8.0).

Ref: D Robinson, J McFayden, E Merriman, T Chee Wee, R Baker, H Tran . Updated recommendations for warfarin Reversal in the setting of four-factor prothrombin complex concentrate. MJA 2024.

How INR Online Automated dosing differs from the Australasian Guidelines.

The reason there are difference is that it is hard to give precise advice under all circumstances.

If you have concerns always err on the side of caution.

You can override the INR Online advice at any time.

	INR Online advice	**Note for pharmacists**
INR above therapeutic range		
If INR between 4.0 and 5.0	INR Online advises to reduce the dose.	How this INR range is managed varies depending on the patient's circumstances. If the patient has been stable for several months • A dose adjustment may not be necessary if they have a one off INR between 4.0 and 4.5. • The dose should be reduced for an INR is between 4.5 and 4.9 If the patient is less stable • The dose should be reduced if the INR is between 4.0 and 4.5. • The patient should be advised to miss a dose if the INR >4.5
INR >5.0	INR Online advises to miss a dose	In all cases at least one dose of warfarin should be withheld if the INR is >5.0
Test Interval		
INR >4.5		The time to the next test is at the discretion of the pharmacist. It is recommended that you repeat the INR within 24 hours if the INR is >4.5

Appendix 6

Procedure to manage patients when unable to communicate with INR Online

The following procedure should be followed if access to INR Online is interrupted due to local computer problems, lost internet connection, problems with the INR Online server, or the INR Online program stops running.

1. Interview patient and record as a hard copy any missed medication, history of bleeding since the last visit, new medication since the last visit and any hospital admissions.

2. Perform the INR test as usual on the CoaguChek XS Plus. Enter the NHI number if known.If the patient does not know their NHI Number perform the INR test without a reference number.
3. Record the following information as a hard copy
   - Patient's name,
   - NHI number (if known) or date of birth
   - Present warfarin dose
   - INR result
   - Patient's GP details

INR within the therapeutic range

If the INR is within the therapeutic range, advise the patient to continue on the same dose and recommend a dose interval the same as the previous interval.
Record the dose recommended and the date of the next test

If the INR Is outside the therapeutic range

Warfarin dosing is the responsibility of the patient's general practitioner. You should therefore contact the GP practice, advise them that you are unable to contact INR Online and require dosing advice.
The dose recommendation from the doctor and the date of the next test should be recorded and the patient should be contacted with this information.

If the INR is >4.0, advise the patient to miss a warfarin dose and repeat the INR the next day.

When access is resumed

The missing results should be entered into INR online.

Enter the results by using the *add result* tab on the top of the left-hand column on the overview page.
This will ensure that the results are sent to the doctor's PMS and an e-mail will be sent to the patient.

When you enter a result the computer will recommend a new dose. Edit this to the dose you gave and edit the recommended date of the next test to the date you recommended. Then confirm the result.

DO NOT ENTER THE MISSING RESULT USING THE *EDIT RESULT* TAB. If you do, the result will not be sent to the doctor's PMS and the patient will not receive an e-mail.

Appendix 7

Procedure for the management of non-compliant patients

Note: The responsibility for the patient's warfarin management rests with the supervising doctor.

It is important that the supervising doctor is informed if a patient is a regular poor complier. It may be appropriate for the doctor to reassess the risks and benefits of warfarin in such cases and may recommend discontinuing warfarin if the risk of poor compliance is assessed to be potentially dangerous.

The following is a recommended procedure for managing non-attenders. Where possible we suggest this is followed but individual patient circumstances must be considered with these recommendations. It is important to document all deviations from the procedure and to maintain good communication with the supervising doctor.

Procedure if patient fails to attend for INR testing on the specified date

- As a general rule the patient should go no more than 6 weeks between tests.
- If the patient fails to attend within 3 days of the specified test date, the patient should be contacted by phone to remind the patient that the test is due.
- If the patient fails to attend within 4 to 6 days of the first reminder, a second call should be made to the patient.
- If the patient fails to attend within 1 week of the second reminder, the patient should be contacted a third time and the patient's doctor should be informed that the test is 2 weeks overdue and a maximum of 6 weeks since the last test and you will only send further reminders at the doctor's request. Further follow up of the patient is the responsibility of the doctor.
- Each contact with the patient and the doctor should be documented in INR Online.
- If a patient presents for a test more than 2 weeks after the expected date of the test, the test should be performed and the doctor should be informed.
- If a patient regularly fails to attend on time, discuss management with the supervising doctor.