STANDING ORDERS FOR THE MANAGEMENT OF WARFARIN

Dose adjustment and INR testing frequency

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<th>Applicable to: Pharmacists</th>
<th>Issued by: Pharmacy warfarin management project medical advisor</th>
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<td>Standing Order used for the Pharmacy based anticoagulant management Project.</td>
<td>Contact: Dr Paul Harper, Consultant Haematologist, Palmerston North Hospital</td>
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26 October 2012

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 who are participating in the Community Pharmacy Anticoagulation Management (CPAM) Service. The standing order is required to enable pharmacists to supervise anticoagulant management.

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
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 including OTC medications and/or other complementary medicines since the previous INR test.
- 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.

Criteria for referral of new patients

Referral criteria for new patients
In general, patients who have recently started on warfarin require stable control before referral to the community pharmacy service.

Stable control is defined as:
- Patients must have at least two INR measurements within the therapeutic range appropriate for their condition at least 1 week apart. This level of control would normally be achieved after 4 to 6 weeks of treatment.
- For patients transitioning from heparin to warfarin stable control is defined as patients achieving two consecutive INRs between 2.0 and 3.0 (or 2.5 and 3.5 for mechanical heart valves) at least 24 hours apart.¹

Referral to the service is at the discretion of the General Practitioner. If the doctor believes a specific patient requires close supervision, the doctor should indicate this to the pharmacist and arrange a process of individualised “shared care”. This could involve more frequent consultation with the doctor during the period of instability.

Criteria for discontinuing services and referral back to general practice

Criteria for discontinuing services

Once a patient is referred to the CPAM service it is best practice that they remain with pharmacist management unless the doctor or pharmacist elects to remove them, or the patient chooses an alternative service, or the medication is discontinued or replaced.

The patient should only be referred back to the GP after consultation between the GP and pharmacist. The reasons for referral back to the GP care are most likely to relate to poor control or poor compliance. Where possible, a shared care arrangement with close supervision should be considered.

Dose Adjustment

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: 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.
- An INR >4.5 will automatically 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. For stable patients the maximum interval can be increased to 42 days after consultation with the doctor.
- The test interval varies depending on the patient’s anticoagulant control.
- The system automatically reduces the test interval when the INR is outside the treatment range. The test interval increases in a step wise manner if the INR remains in range up to the maximum (42 days).
- The pharmacist can recommend a shorter test interval at anytime if he or she
believes an earlier test is appropriate.

- 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**

**Review process**

Where the INR is outside the specified range, the INR-Online software will automatically set the result for review

- The pharmacist can accept the recommended dose from INR Online and advise the patient that the result has been sent for review by their doctor.
- The patient is advised to continue on the recommended dose unless they are informed otherwise. If their doctor wishes to modify the dose they will be informed of the change either by e-mail or by telephone by the pharmacist.

**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 is >4.5 INR Online will recommend missing a dose and repeating a test the following day
- If the INR is >5.0
  - INR Online will provide advice for warfarin reversal in line with the Australasian Guidelines (Appendix 2).
  - 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 and the Laboratory Test Repository, if available, 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.

### 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.
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.
- Completed the INR-Online training session.
- Completed CoaguChek XS Plus Competency Training

Process for audit and review

The correct operation of this Standing Order will be reviewed once per year.
The individual pharmacists competency in applying the order accurately will be assessed.
Adverse events related to Standing Orders will be monitored by Dr Paul Harper and reported to CARM or other relevant body.

Responsibility for Review

Dr Paul Harper is responsible for the review of this Standing Order.

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 DHB to provide community pharmacy services.

Standing order

Issued by: Dr Paul Harper

Date: 19/11/12

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Ian McMichael, Pharmacist
Amanda Kiss, Clinical facilitator.
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.

(Use another page if necessary)

GENERAL PRACTICE: __________________________

Name of doctor:…………………………………………

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

Name of doctor:…………………………………………

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Appendix 1

Summary of the testing process
The patient will attend their allocated pharmacy.

The patient will be interviewed by the pharmacist.
The patient will be identified on INR Online (search by NHI or name)

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 pharmacists and accepted if appropriate.
- Calendar printed

INR outside safe range
- Recommendation reviewed by pharmacists and accepted if appropriate
- Calendar printed
- Patient informed that result has been sent to their doctor for review and 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 an email stating the INR result is outside the safe range.
- The email 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 2

#### 3 Guidelines for the management of an elevated international normalised ratio (INR) in adult patients with or without bleeding

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Action</th>
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| INR higher than the therapeutic range but <5.0, bleeding absent | • Lower the dose or omit the next dose of warfarin. Resume therapy at a lower dose when the INR approaches therapeutic range.  
• If the INR is only minimally above therapeutic range (up to 10%), dose reduction may not be necessary. |
| INR 5.0–9.0, bleeding absent | • Cease warfarin therapy; consider reasons for elevated INR and patient-specific factors.  
• If bleeding risk is high, give vitamin K₁ (1.0–2.0 mg orally or 0.5–1.0 mg intravenously).  
• Measure INR within 24 hours, then resume warfarin at a reduced dose once INR is in therapeutic range. |
| INR > 9.0, bleeding absent | • Where there is a low risk of bleeding, cease warfarin therapy, give 2.5–5.0 mg vitamin K₁ orally or 10 mg intravenously. Measure INR in 6–12 hours, then resume warfarin therapy at a reduced dose once INR < 5.0.  
• Where there is high risk of bleeding, cease warfarin therapy, give 10 mg vitamin K₁ intravenously. Consider Prothrombinex-HIT (25–50 IU/kg) and fresh frozen plasma (150–300 mL), measure INR in 6–12 hours, then resume warfarin therapy at a reduced dose once INR < 5.0. |
| Any clinically significant bleeding where warfarin-induced coagulopathy is considered a contributing factor | • Cease warfarin therapy, give 5.0–10.0 mg vitamin K₁ intravenously, as well as Prothrombinex-HIT (25–50 IU/kg) and fresh frozen plasma (150–300 mL), assess patient continuously until INR < 5.0, and bleeding stops.  
• If Prothrombinex-HIT is unavailable, cease warfarin therapy, give 5.0–10.0 mg vitamin K₁ intravenously, and fresh frozen plasma (150–300 mL), assess patient continuously until INR < 5.0, and bleeding stops.  
• If fresh frozen plasma is unavailable, cease warfarin therapy, give 5.0–10.0 mg vitamin K₁ intravenously, and Prothrombinex-HIT (25–50 IU/kg), assess patient continuously until INR < 5.0, and bleeding stops.  
• If fresh frozen plasma is unavailable, cease warfarin therapy, give 5.0–10.0 mg vitamin K₁ intravenously, and 10–15 mL/kg of fresh frozen plasma, assess patient continuously until INR < 5.0, and bleeding stops. |

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Appendix 3

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 >4.5, 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 4

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 over due 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.