North East Essex Medicines Management Committee

ORAL ANTICOAGULANT (Vit K antagonist only) MANAGEMENT GUIDELINES

For newer agents please refer to NOAC counselling checklist and NOAC patient information.

1) INITIATION OF ANTICOAGULATION:

The majority of patients will be being anticoagulated for atrial fibrillation. Target INR for this indication is 2.5 [range 2.0-3.0] (for other indications, see later).

In most circumstances, initiation of anticoagulation is best carried out in accordance with the regimen published by Tait & Sellick[(1)]. This results in a lower incidence of over-anticoagulation during induction and generally produces a reliable, predictable maintenance dose by Day 8.

METHOD:

Initial blood tests are taken on days 5 & 8 of treatment, thus the first day of treatment must take this into account;

(i.e. **TREATMENT MUST BE STARTED ON MONDAY, THURSDAY OR FRIDAY. DO NOT COMMENCE TREATMENT ON TUESDAY OR WEDNESDAY OR ON A SATURDAY OR SUNDAY**).

Check baseline **INR**; if this is >1.3 a much lower dose of oral anti-coagulant will be required – discuss with Consultant Haematologist.

For all other patients: **commence warfarin 5mg daily for 4 days**

- Check INR on day 5
- Refer to table for dose of warfarin days 5, 6 & 7 (see Appendix 1)
- Check INR on day 8
- Refer to table for maintenance dose of warfarin
- Check INR again after 1 week (unless a more urgent test is required)

If result is stable within the target range, the interval between tests may be gradually increased – see later.

2) CONTRAINDICATIONS TO ANTICOAGULATION:

There are clearly many reasons why anticoagulation may be inadvisable for individual patients. The following is a list of relative contraindications to consider:

General

- Mental impairment
- Uncooperative patient
- Alcoholism
- Falls
- Malignancy on active treatment (LMWH should be considered in these patients)

Cardiovascular

- Uncontrolled hypertension

Neurological

- Recent non-embolic cerebrovascular accident (CVA)
- Recent surgery/trauma to the Central Nervous System / eye

Gastrointestinal

- Inflammatory bowel disease
- Peptic ulceration
- Oesophageal varices

Liver disease

- Uncomplicated cirrhosis
- Abnormal Liver Function Test's (> x2 upper limit of normal)

Haematological

- Concurrent other haemostatic defect

Clearly the wishes of the informed patient must also be considered.

3) ON-GOING ANTICOAGULATION:

For each patient there should be a record of the:

- Reason for anticoagulation
- Intended duration of the treatment
- Target INR
- Any special precautions

It is recommended that a central practice record of all patients on oral anticoagulants be kept for ease of reference.

Intended duration of treatment and target INR must be based on the British Council for Standards in Haematology (BCSH) guidelines[(2)]. These can be summarised as follows:

Duration of treatment:

- First venous thromboembolic event (DVT/PE) 3-6 months
- All other indications indefinitely

Exceptions may arise, e.g. prophylactic anticoagulation in any setting. In such cases, the intended duration of treatment should be discussed with the Consultant responsible for initiation of the anticoagulant treatment.
In cases where the first event is unprovoked the duration of treatment should be discussed with the consultant and if necessary a referral made to the thrombosis clinic for further assessment.
Unprovoked events in patients over 40 years old would need investigations arranged by primary care as per NICE guidance.

Target INR:

- Treatment of 1st venous thromboembolic event (VTE) 2.5
- Treatment of recurrent VTE "off" Warfarin 2.5
- Treatment of recurrent VTE "on" Warfarin 3.5
- Treatment of recurrent VTE "on" NOAC Warfarin with target range as above or LMWH
- Prophylaxis in atrial fibrillation 2.5 (target range 2-3), if more than 50% of last 20 INR measurements outside 1.8-3.5 consider use of newer anticoagulants
- Prophylaxis for mechanical heart valves 3.5*
- Prophylaxis after stroke/TIA 2.5 (consider use of newer anticoagulants)

*Anticoagulation of patients with prosthetic heart valves may be at a lower target INR, especially if the patient is also given other anti-thrombotic agents. Suggest discuss with Consultant Cardio-thoracic surgeon if necessary.

Frequency of testing:

Patients who are established on oral anticoagulants should be tested no less often than once every 12 weeks. After initiation of anticoagulation, the interval between tests should be gradually increased (by 1 week each time), until the desired interval is reached, provided that the INR remains stable. The majority of stable patients should be tested every 8-12 weeks.

Test should be repeated sooner than the planned date if:

- There is any change in concurrent medication: repeat test 5-7 days after change. **While there are lists of drugs that interact with warfarin, it is wise to assume that all drugs have the potential to do so. Therefore, repeat testing should be considered after any change to the patient's medication**

- There is onset of any significant concurrent illness

NB;For patient on newer anticoagulants hepatic and renal monitoring is required prior to treatment and annually thereafter or more frequently if clinically indicated.

Management of anticoagulation for dental surgery/other minor procedures

Patients who are established on an anticoagulant and whose INR is generally stable within a therapeutic range of 2.0 – 4.0 should be advised that they do not need to stop their anticoagulation for very minor procedures, including most dental surgery. If prophylactic antibiotics are to be given, the patient should have an INR check after 5 – 7 days.[(2)(3)]

Trust bridging guidelines should be used for other procedures including for those patients with mechanical prosthetic heart valves.

4) COMPLETION OF TREATMENT

For patients on short-term anticoagulation who come to the end of treatment there is no need to withdraw anticoagulation gradually. The patient should simply be advised to stop treatment on a given day. Whilst there may be laboratory evidence of a "rebound", this does not cause any clinically significant problems. Further testing of **INR** after stopping treatment is **NOT** required.

In young patients in whom the possibility of an inherited thrombophilic tendency has been considered, "thrombophilia" testing must be deferred until the patient has been "off" treatment for at least four weeks. If it is not deemed possible to stop the anticoagulation, and thrombophilia screening is considered important, please discuss with a Consultant Haematologist.

5) MANAGEMENT OF OVER-ANTICOAGULATION:

INR 4.5 - 8 with no major bleeding

- STOP anticoagulant for 2-4 days and then repeat INR
- Restart warfarin when INR is within 0.5 of target; a lower dose may be indicated.

INR >8, with no bleeding or major bruising

- STOP anticoagulant.
- Consider oral vitamin K (phytomenadione) 0.5 - 5mg in primary care
- Recommended product - Konakion MM® paediatric, 2mg/0.2ml, (Roche).
- 2mg is an average dose; however results this high will normally be phoned through to the GP by the Consultant Haematologist who will discuss management.
- Repeat INR the next day.

NB; The IM route must NOT be used for patients with a risk of bleeding.

Clinically significant bleeding at any INR or those bleeding on newer anticoagulants

- The patient should be referred immediately to hospital for reversal of anticoagulation. IV vitamin K 0.5 – 5mg, +/- FFP or – for severe haemorrhage - Octaplex (Trust guideline no 178) may be required. Idarucizumab is a specific reversal agent for dabigatran and may be used in these patients.
- **A dose of IV vitamin K >5mg is rarely indicated and must be discussed with a Consultant Haematologist.**
  Use of Octaplex must always be discussed with a Consultant Haematologist.

Consideration must be given to the investigation of a possible underlying lesion that may have given rise to the bleeding.

References:

(1) A warfarin induction regimen for outpatient anticoagulation in patients with atrial fibrillation. R.C Tait & A. Sellick;B.J. Haem, 1998, 101: 450-454

(2) Guidelines on Oral Anticoagulation: 3rd Edition. British Committee for Standards in Haematology; B.J. Haem, 1998, 101: 374-387

(3) Surgical Management of the Primary Care Dental Patient on Warfarin. North West Medicines Information Centre, July 2001

(4) A comparison of the efficacy & rate of response to oral & IV vitamin K in reversal of over-anticoagulation with warfarin. Watson, Baglin, Laidlaw, Makris & Preston; B.J. Haem, 2001, 115: 145-149

Appendix 1 - warfarin induction regimen for out-patient or primary care anticoagulation in patients with atrial fibrillation – dosing recommendations from day 5 onwards.[(1)]

INR on Day 5 of warfarin therapy	Warfarin dose for days 5 - 7	INR on Day 8 of warfarin therapy	Warfarin dose from day 8 onwards
1.7 or less	5mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 >3.0	6mg 5mg 4mg 3mg **for 4 days**
1.8 – 2.2	4mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 – 3.5 >3.5	5mg 4mg 3.5mg 3mg **for 4 days** 2.5mg **for 4 days**
2.3 – 2.7	3mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 – 3.5 >3.5	4mg 3.5mg 3mg 2.5mg **for 4 days** 2mg **for 4 days**
2.8 – 3.2	2mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 - 3.5 >3.5	3mg 2.5mg 2mg 1.5mg **for 4 days** 1mg **for 4 days**
3.3 – 3.7	1mg	1.7 or less 1.8 – 2.4 2.5 – 3.0 3.1 – 3.5 >3.5	2mg 1.5mg 1mg 0.5mg **for 4 days** omit **for 4 days**
3.8 or more	0mg	<2.0 2.0 – 2.9 3.0 – 3.5	1.5mg **for 4 days** 1mg **for 4 days** 0.5mg **for 4 days**

Reference

(1) A warfarin induction regimen for out-patient anticoagulation in patients with atrial fibrillation. Tait RC & Sellick A. Br.J.Haem. 1998;101:450-54

Appendix 2 – prescribing and dispensing of warfarin

Warfarin prescribing and dispensing continues to give rise to medicines related incidents. NPSA alert 2007/18 relates to actions that can make anticoagulation therapy safer, and makes the following recommendations:

• use the least number of tablets each day;
• use constant daily dosing and not alternate day dosing;
• do not require the use of half tablets – patients find it difficult to break tablets in half and when necessary would rather use 0.5mg (500mcg) tablets.

In the light of the NPSA alert and previous local concerns prescribers and dispensers are recommended to:

- Where appropriate use 500mcg tablets, ensuring that the prescriptions read "500microgram tablets" and not "0.5mg tablets"
- Cease alternate day dosing by utilising the 500microgram tablet if necessary
- Discontinue the use of 5mg tablets, for all patients except those requiring daily doses of **10mg or greater.** Doses of 5mg – 9.5mg should be made up of 3mg, 1mg and 500microgram tablets as appropriate.