MIL

Oxford University Hospitals NHS
NHS Foundation Trust

Volume 5, No. 8 **December 2018**

This Medicines Information Leaflet is produced locally to optimise the use of medicines by encouraging prescribing that is safe, clinically appropriate and cost-effective to the NHS.

Initiating oral anticoagulation with vitamin K antagonists (VKAs) in adult patients

When making the decision to anticoagulate, consideration must be given to the risks of both haemorrhage and thrombosis. Higher INR (International Normalized Ratio) targets and longer durations of anticoagulation increase the risk of haemorrhage. Arrangements **must** be made for the safe monitoring of the patient on discharge from hospital. Warfarin and other vitamin K antagonists (VKAs) act by reducing the levels of vitamin K dependent clotting factors (II, VII, IX, X). Therapeutic depletion of these factors takes several days.

This MIL is designed to aid clinicians in the initiation of vitamin K antagonists, provide guidance on local regimens and information about the Oxfordshire Anticoagulation Service.

Risk assessing the patient

Before starting a patient on a VKA, there are both medical and social factors to consider. If the medication is to be administered by a carer then these factors would apply equally to them:

- Are they capable of safe compliance and understanding of the medication?
- Are they willing and able to have regular INR blood tests for monitoring?
- Do they have any disabilities that may affect the way dose adjustments are communicated to them (e.g. blind, deaf or illiterate)?
- Do they use a medication compliance aid (e.g. a dosette box or nomad tray)? The combination of such compliance aids and VKA treatment is generally not recommended.

The Oxfordshire Anticoagulation Service can be contacted for advice. They manage the majority of local patients on warfarin.

Target INRs and INR ranges

The target INRs used by the service are 2.5 (2 – 3), 3 (2.5 – 3.5) or 3.5 (3 – 4). Tighter target ranges (e.g. 2 – 2.5) are not feasible and they do not improve anticoagulant control.

Before starting a VKA

Before starting a patient on a VKA, a baseline coagulation screen (prothrombin time (PT)/INR and activated partial thromboplastin time (APTT)) must be performed. This will identify any potential underlying clotting abnormalities.

Starting VKA therapy

a) Fast loading regimen with LMWH (e.g. for acute venous thromboembolism (VTE) and new mechanical heart valves)

The LMWH heparin used in the Trust is dalteparin (Fragmin®). For more information on acute VTE, refer to MIL vol. 2, No. 2 *Treatment of DVT and PE with dalteparin (Fragmin®)*. **For acute VTE, LMWH should be continued for 5 days or until the INR has been greater than or equal to 2 for 24 hours (2 consecutive daily readings) – whichever is longer.** For mechanical heart valves continue LMWH until INR within therapeutic range.

Dose recommendations below are given for the most common VKA, warfarin. If your patient requires an alternative VKA, the anticoagulation pharmacist (bleep 4511) or a senior anticoagulation nurse (bleep 5035) can be contacted for advice. The warfarin induction

schedule used in the Trust when fast loading is required is shown in table 1. A starting dose of 5mg is preferred to 10mg as over-anticoagulation is less likely, particularly in the elderly and those with liver disease or heart failure. If the baseline INR is less than or equal to 1.3, give the patient warfarin 5mg once daily for the first 2 days. The INR needs to be checked on the mornings of days 3 and 4 and the dose adjusted according to the regimen in table 1.

Table 1: Standard warfarin induction regimen

Days 1 & 2	Day 3		Day 4	
	INR	**Dose**	**INR**	**Dose**
Give **5mg** each evening if baseline INR less than or equal to 1.3	less than 1.5	**10mg**	less than 1.6	**10mg**
	1.5-2	**5mg**	1.6-1.7	**7mg**
	2.1-2.5	**3mg**	1.8-1.9	**6mg**
	2.6-3	**1mg**	2-2.3	**5mg**
	greater than 3	**0mg**	2.4-2.7	**4mg**
			2.8-3	**3mg**
			3.1-3.5	**2mg**
			3.6-4	**1mg**
			greater than 4	**0mg**

Beyond day 4, clinical judgment should be used to adjust doses. A member of the Thrombosis Team can be contacted for advice.

b) Slow induction of anticoagulation in patients with atrial fibrillation (AF)

It is generally recommended to use a slow loading regimen when starting warfarin for stroke prevention in AF. These patients are more likely to be sensitive to warfarin, risking the potential for raised INRs. If the baseline INR is less than or equal to 1.3 the usual starting dose is 3mg warfarin daily. The INR should be checked in 4 to 7 days. For more information on anticoagulation in patients with AF, please refer to MIL Vol. 8, No. 5 'Atrial fibrillation and Anticoagulation Management'. Inpatients being loaded on warfarin should receive at least prophylactic LMWH, and may be considered for therapeutic LMWH. Patients can be discharged home whilst INR is sub-therapeutic and managed by the anticoagulation service.

Duration of therapy

Patients with proximal DVT or PE should be treated for at least 3 months. Long term treatment should be considered for recurrent thrombosis, patients with an on-going risk factor or unprovoked proximal DVT or PE. The duration of treatment or review date should be stated on the discharge summary. Lifelong anticoagulation is indicated for patients with mechanical heart valves and AF.

Patient (or carer) counselling

It is imperative that all patients new to VKA treatment are offered verbal counselling and provided with written information. It is vital every patient (and/or carer) fully understands this information to support safe management of anticoagulation. The responsibility for providing this counselling rests with prescribers, doctors and pharmacists. Counselling guides to assist with this are available on the anticoagulation website. In addition, patients under Oxfordshire Anticoagulation service should be offered an appointment at the new patient clinic at the Churchill or Horton where they can receive further counselling by a specialist anticoagulation nurse.

Referring patients to the Anticoagulation Clinic

As soon as possible after starting VKA therapy, all new patients must be referred to the Anticoagulation Clinic at the Churchill to initiate remote postal dosing. This is a telephone referral via bleep **1857 or extension 23729**. Full details of the referral procedure are available via the website. For patients who are not covered by the Oxfordshire Anticoagulation Service, a referral must be made to the patient's GP or local anticoagulation service. Contact details for out of area anticoagulation services are available on the website.

Monitoring VKA therapy

Clinical judgment is required when deciding the interval between INR measurements. When adjusting doses it should be borne in mind that it takes up to a week for the full effect of any dose

change to be seen. The INR should be monitored more frequently when interacting medication is co-prescribed and should be measured 3 - 5 days after any changes in medication.

Interactions

Many medications, supplements and foods interact with VKA therapy. Additional INR monitoring is recommended when any changes are made to a patient's medication regimen. Some of the more significant interacting medicines are co-trimoxazole, carbamazepine, rifampicin, ciprofloxacin, erythromycin, amiodarone and fluconazole. *For a full list of interacting medicines, please see the latest edition of the BNF and/or discuss with pharmacy.*

Discharging a patient on VKA therapy

Before discharging a patient on VKA therapy, follow up arrangements for INR monitoring **must** be confirmed. For **all** patients ensure each of the following steps are done:

1. The anticoagulation section of the TTO is fully completed
2. The TTO is fully published
3. A verbal referral is made

All patients must be given the supporting printed information about their VKA therapy ('*Important information about anticoagulation with vitamin K antagonists'*). These booklets are available in clinical areas and from pharmacy. The first appointment for an INR check should usually be within the first 48 hours after discharge. **Please do not request routine post-discharge INR tests for a Friday, Saturday, Sunday or Bank Holiday. If there is a clinical need for the INR to be measured on one of these days, please contact the Anticoagulation Service (bleep (JR) 1857) for advice**.

Patients new to VKA and still on LMWH

Please call the DVT clinic to discuss these patients on bleep 5165 or extension 25629.

Out of hours: dvt.service@nhs.net

Patients reloading on VKA and still on LMWH

Please call the Anticoagulation Clinic to discuss on bleep 1857 or extension 23729.

Out of hours: ac.service@nhs.net

Management of overdose

Separate guidance has been produced for the management of elevated INRs. Please refer to MIL Vol. 5 No. 9 *Reversal of oral anticoagulation in adult inpatients.*

The Oxfordshire Anticoagulation Service

The Oxfordshire Anticoagulation Service operates a 'dose & post' service for most GP surgeries in Oxfordshire. The Service operates 9am – 5pm, Monday to Friday (excluding Bank Holidays). For more information refer to the website.

References

1. British National Formulary (BNF) 74th Edition British Medical Association and the Royal Pharmaceutical Society of Great Britain London, UK. September 2017- March 2018

2. Kearon, C *et al*. (2016) Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. *Chest*, **149** (2), 315-352

3. Keeling, D. (2017) Oxford Haemophilia & Thrombosis Centre Protocols for Anticoagulation with Vitamin K Antagonists

4. Keeling, D *et al*. (2011) Guidelines on oral anticoagulation warfarin 4th Edition. Br J Haematol, **154**, 311-324

5. NICE (2015) CG144 Venous thromboembolic diseases: diagnosis, management and thrombophilia testing

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Review date: *December 2021*