MIL

Oxford University Hospitals NHS
NHS Foundation Trust

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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.

Reversal of Vitamin K Antagonists (warfarin) in Adult Inpatients

This Medicines Information Leaflet (MIL) is applicable to all inpatients of Oxford University Hospitals NHS Foundation Trust (OUH). For outpatient reversal of anticoagulation, please refer to the Oxford Anticoagulation Service protocol. The text refers to warfarin, but the principles apply to all vitamin K antagonists. This MIL does **not** cover the reversal of other oral anticoagulants such as dabigatran, rivaroxaban, apixaban and/or edoxaban; information on this is provided in a separate MIL..

In all cases of over anticoagulation

1. Identify the precipitating cause
2. Establish whether it is temporary (for example, other medications or permanent (for example liver failure))
3. Review the need for ongoing anticoagulation
4. If the patient is to continue with anticoagulation therapy, decide the degree of reversal required. For example, patients with metallic heart valves will need to continue with warfarin therapy after the event, and complete reversal (except in cases of severe bleeding) may not be clinically indicated.

The risk of bleeding while on warfarin increases significantly with INR levels of 5 and above. Therapeutic decisions regarding management are dependent on the INR and whether there is major or non-major bleeding.

1. Major bleeding requiring immediate complete reversal

Major bleeds are defined as those which are fatal, life-threatening or may cause chronic sequelae. This includes:

1. symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome and/or
2. bleeding causing a fall in haemoglobin level of 20g/L or more, or leading to transfusion of two or more units of whole blood or red cells and/or
3. cardiovascular shock secondary to bleeding.

These patients need urgent clinical assessment of clotting. Patients on warfarin may be haemorrhagic for reasons other than the effect of the anticoagulant, such as Disseminated Intravascular Coagulation (DIC), factor VIII inhibitor.

Request:

- Full blood count (FBC)
- Activated Partial Thromboplastin Time (APTT) and fibrinogen as well as an INR.
- However, **DO NOT WAIT** for these results before reversing warfarin.
- Stop warfarin and reverse anticoagulation with Prothrombin Complex Concentrates (PCC) **and** phytomenadione (vitamin K)
- Anticoagulation can be effectively reversed with PCC **and** phytomenadione 5mg by slow intravenous injection

Table 1: Dose of PCC for reversal of anticoagulation

Weight	Dose of PCC
less than 60kg	1500 units
60-75kg	2000 units
76-90kg	2500 units
greater than 90kg	3000 units

- As soon as PCC has been given perform another clotting screen and assess the degree of correction of the INR. If not corrected discuss with a haematologist.

All patients with bleeding should be evaluated to see if there is a local anatomical reason for bleeding.

2. Non-major bleeding and high INRs in non-bleeding patients

See table below for guidance on how to manage over anticoagulation.

Table 2: Summary of recommendations for the management of over-anticoagulated patients

Presence of bleeding / INR range	Action required
Major bleeding (regardless of INR)	Stop warfarin Give PCC (Table 1) Give 5mg IV phytomenadione
Non-major bleeding (INR 5 or greater)	Omit warfarin Give 1-3 mg IV phytomenadione (or 5-10mg if anticoagulation is to be stopped)
Non-major bleeding (INR less than 5)	Consider if lowering of the INR if required. If so, consider 1-3 mg IV phytomenadione and modification of warfarin dose
No bleeding (INR 12 or greater)	Omit warfarin Give 5mg oral phytomenadione
No Bleeding (INR 8 – 11.9	Omit warfarin Give 2mg oral phytomenadione
No bleeding (INR 5 – 7.9)	Omit warfarin Restart at lower dose when INR less than 5

Repeat INR **8-12 hours after IV phytomenadione** or **24 hours after oral phytomenadione.**

Product details

Vitamin K (phytomenadione)

- Oral phytomenadione will have an effect within 16-24 hours of administration, IV phytomenadione within 6-8 hours.
- For complete IV administration guidelines, please see the Medusa injectables monograph for phytomenadione, available from the pharmacy injectables intranet site .
- IV doses should be prepared and administered immediately to avoid a reduction in clinical effect.
- Oral adult phytomenadione doses should be administered using the paediatric formulation (Konakion MM Paediatric 2mg in 0.2mL oral/IM/IV preparation) and should be administered using the syringe provided in the box.

Prothrombin Complex Concentrate (PCC)

- The main PCC used within the Trust is Octaplex® (if there is a supply problem then Beriplex® will be used instead).
- They are available from Blood Bank, **not** pharmacy. (ED has its own supply of one dose)
- They are derived from human plasma which has been virally inactivated.
- They contain coagulation factors II, VII, IX and X and proteins C and S but no other coagulation factors.
- The dose should be rounded to the nearest complete vial.
- Octaplex® is licensed for administration at initially 1mL per minute, then 2-3mL per minute. However, faster administration is strongly recommended in a patient with major bleeding where the total infusion should be administered over 10 minutes.
- Beriplex® is given by slow intravenous injection up to a maximum rate of 210 units per minute (8.4mL per minute). The total dose should therefore be given over approximately 10 minutes.
- Doses given are based on the **factor IX** content.

Safe medication practice

- Fresh Frozen Plasma (FFP) is not recommended for warfarin reversal. In non-urgent situations phytomenadione is sufficient and in urgent situations PCC is more effective.
- PCC should be prescribed on the prescription chart.
- Oral phytomenadione should be prescribed in multiples of 1mg so that the dose may be accurately measured and administered using the oral syringe provided.
- The effect of PCC will wear off relatively quickly, so IV phytomenadione must be given as well if the effect is to be sustained.
- Please notify a member of the anticoagulation team (JR bleep 1857) if a patient on warfarin is admitted with bleeding.

References

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