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Guidelines for the management of warfarin reversal in adults

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Guidelines for the management of warfarin reversal in adults

Background and purpose

Patients who are taking warfarin may need, for various reasons, to have the effects of warfarin reversed.

The purpose of these guidelines is to provide best clinical practice when managing warfarin reversal therapy.

They apply to all adult patients identified as at risk of bleeding by their clinician

- who need warfarin reversal to lower their INR or
- who are on warfarin and bleeding or
- who require immediate surgery.

These guidelines are based on scientific evidence and professional consensus, but are not intended to replace clinical judgement

Scope

These guidelines should be used trust wide by all clinicians involved in the care of adult patients who need reversal of their warfarin therapy.

Any deviation from these guidelines should be discussed with a Haematologist.

For paediatric guidelines, the advice of a consultant haematologist should be sought.

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1. Patients who are bleeding

Bleeding while on oral anticoagulants increases significantly with INR levels >5.0. Treatment decisions depend on the INR result and whether there is minor or major bleeding.

The dose of vitamin K used to reverse over- anticoagulation depends on the INR result.

Recommendations for management

INR range/bleeding present?	Action required
INR > 3.0 but < 6.0 (target INR 2.5) INR > 4.0 but < 6.0 (target INR 3.5) No bleeding	1. Reduce warfarin dose or stop 2. Restart when INR < 5.0
INR > 6.0 and < 8.0 No bleeding or minor bleeding	1. Stop warfarin 2. Restart when INR <5.0
INR > 8.0 No bleeding or minor bleeding	1. Stop warfarin 2. Restart when INR < 5.0 3. If other risk factors for bleeding give 1-2mg of vitamin K (oral)
Major bleeding	1. Stop warfarin 2. Give 10mg of vitamin K (oral or I.V) 3. Contact Haematologist

Please note that Fresh Frozen Plasma (FFP) only has a partial effect, is not the optimal treatment, and should never be used for the reversal of warfarin anticoagulation in the absence of severe bleeding. It has been shown that FFP contains insufficient concentration of the vitamin K factors (especially F IX) to reverse the bleeding deficiency (although it will reduce the INR). FFP also carries the risk of transfusion transmitted infection and other transfusion complications. The rationale for prescribing FFP must be recorded in the patient's notes.

1.1 Major life threatening bleeding

- This relates to patients with intracranial or rapid onset neurological signs, intra-ocular (not conjunctival) bleeds, compartment syndrome, pericardial bleeds or those with active bleeding and shock. These patients need urgent clinical assessment of clotting.

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- Patients on warfarin may be haemorrhagic for reasons other than the effect of the anticoagulant such as disseminated intravascular coagulation (DIC). A full blood count, Prothrombin time (PT), Activated partial thromboplastin time (APTT) and fibrinogen should be determined (also Fibrin Degradation Products if DIC is a possibility)
- **Contact a haematologist at this stage**
- Stop warfarin and reverse anticoagulation with vitamin K and Prothrombin Complex Concentrate (Octaplex).
- If Octaplex is contraindicated (in DIC or liver failure) emergency treatment with 15ml/kg of FFP and Vitamin K 5mg (Konakion MM injection) by slow I. V injection will partially reverse anticoagulation, though the levels of the individual factors will typically remain < 20 % and larger doses should be given if possible (recommend 30ml/kg)
- For patients with prosthetic heart valves, full reversal of oral anticoagulants with vitamin K may result in prolonged oral anticoagulant resistance.
- Once Octaplex has been given, wait 20 minutes and perform another clotting screen and assess the degree of correction of INR.
- Seek further advice if no improvement takes place
- The degree of reversal must be decided on an individual basis. All patients with bleeding should be evaluated to identify if there is a local anatomical reason for bleeding.

1.2 Significant bleeding without haemodynamic compromise

- Stop warfarin
- Give vitamin K 2mg (Konakion MM injection) by slow intravenous injection
- Consider using Octaplex (refer to separate policy-Guidelines on the use of OCTAPLEX)
- Recheck clotting screen at 4 hours or sooner if there is clinical deterioration
- Repeat if necessary and seek haematological advice

Bleeding may occur when patients are not over anticoagulated. In these circumstances it may still be necessary to reverse anticoagulation and identify the cause of bleeding.

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1.3 Minor bleeding

Relevant to patients with INR > 8.0, with no bleeding or minor bleeding

- Stop warfarin
- If no other risk factors for haemorrhage stop treatment until INR < 5.0
- If risk factors for haemorrhage or minor bleeding (e.g age > 70 years, previous bleeding complications, epistaxis) consider giving Vitamin K 2mg oral (Konakion MM injection used orally) or 1mg slow intravenous injection (Konakion MM injection)
- Recheck clotting screen at 24 hrs, or sooner if there is a clinical deterioration

2. INR too high but patient not bleeding

2.1 INR > 3.0 and < 6.0 (target INR of 2.5) INR > 4.0 and < 6.0 (target INR of 3.5)

- Reduce warfarin dose or stop altogether, reassess regularly
- Restart warfarin when INR < 5.0

2.2 INR > 6.0 and < 8.0

- Stop warfarin, reassess regularly
- Restart warfarin when INR < 5.0

3. The warfarin patient and surgery

There is evidence that many patients can undergo dental procedures, cataract surgery and diagnostic endoscopy without interruption of anticoagulant ; refer to departmental guidelines.

3.1 Planning for minor surgery (partial reversal)

- For minor surgical procedures the oral anticoagulant dose should be stopped or adjusted to achieve a target INR of approximately 2.0 on the day of surgery.
- The INR should be checked pre-operatively and if < 2.5 the patient can proceed to surgery
- If the INR is > 2.5 the surgeon, anaesthetist and haematologist together must decide if the level of anticoagulation is safe for surgery to take place.

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3.2 Planning for Major surgery

- For major surgery, oral anticoagulants should be stopped at least 4 days prior to surgery as once warfarin is stopped it typically takes about 4 days for the INR to reach 1.5. In some cases low molecular weight heparin may need to be introduced at this time, e.g. for patients with prosthetic heart valves.

3.3 Full warfarin reversal

- Request that the patient stops their warfarin 4 days before the operation
- Check INR on admission or on the morning of the procedure
- If INR is still raised, clinicians must discuss the most appropriate action and follow rapid reversal directions as below if necessary

3.4 Rapid reversal necessary (urgent surgical procedure)

Urgent means clinically essential, not administratively convenient, to do immediate surgery. Always consult a haematologist.

For reversal in **4 to 24 hours**:

- Vitamin K 5mg oral (Konakion MM injection used orally) or 3mg slow intravenous injection (Konakion MM injection)

For reversal within **1 hour**:

- Contact Haematologist for advice

4. Reintroduction of oral anticoagulants

- Timing of reintroduction of oral anticoagulants will depend on the risk of post operative haemorrhage
- The 48-72 hour delay for achievement of anticoagulation with oral vitamin K antagonists will also influence this decision
- In many instances oral anticoagulants can be started again as soon as the patients has an oral intake

5. Vitamin K (phytomenadione)

- Due to near incomplete absorption, oral vitamin K is as effective as intravenous with the delay in action hardly influenced by the absorption time

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- Only 500 microgrammes is required to reduce the INR from > 5.0 to a target level of 2.0 – 3.0
- Vitamin K tablets contain 10mg phytomenadione which will completely reverse anticoagulation. Therefore, when partial correction is required it may be necessary to give intravenous vitamin K or alternatively give the intravenous preparation orally
- Allergic reactions following intravenous administration are rare with newer preparations of vitamin K. If the INR is still too high at 24hours the dose of vitamin K can be repeated
- Subcutaneous absorption of vitamin K is erratic and not recommended
- Slow intravenous injection doses should be diluted with 55ml of glucose 5%

6. Description of a target INR

The international normalised ration (INR) is a recommended method for reporting prothrombin time results for control of oral anticoagulation. Since adoption of the INR system it has been usual practice to adjust the dose of warfarin, or other oral vitamin K antagonists, to maintain the INR within therapeutic range.

The INR should not be used as a routine measure of coagulation in areas other than warfarin therapy; e.g. the prothrombin time is the primary measurement in assessing the severity of paracetamol overdose.

References

British Committee for Standards in Haematology (1998) Guidelines on Oral Anticoagulation: Third Edition *British Journal of Haematology* 101: 374-387

British Committee For Standards in Haematology (2005) Guidelines on oral anticoagulation (warfarin): Third Edition -2005 update *British Journal of Haematology* 132 : 277 - 285

British Committee for Standards in Haematology (2004) Guidelines for use of Fresh Frozen Plasma, cryoprecipitate and cryosupernatant *British Journal of Haematology* 126 : 11-28

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Patient Bleeding

Major/life threatening bleeding

- Intracranial
- Intraocular
- Compartment syndrome
- Pericardial
- Active bleeding and shock

Urgent clinical assessment

Check clotting screen

Contact haematologist

- Stop warfarin
- Vitamin K 10mg (Konakion MM injection) by slow IV injection
- PCC (Octaplex) - see separate policy for Guidelines for use of Octaplex

Check clotting screen 20 minutes post administration

- Adequate correction- recheck in 4 hours
- Inadequate correction – consider other causes, seek Haematological advice

Significant bleeding without Haemodynamic compromise

- Stop warfarin
- Vitamin K 2mg (Konakion MM injection) by slow IV injection
- PCC (Octaplex) - see separate policy for Guidelines for use of Octaplex
- Contact Haematologist
- Check clotting screen at 4 hours or sooner if clinical deterioration

Minor Bleeding

- Stop warfarin
- Consider Vitamin K 2mg Oral (Konakion MM injection used orally) or 1mg slow IV injection (Konakion MM injection)
- Check clotting screen at 24 hours or sooner if clinical deterioration

INR too high, but not bleeding

INR > 3.0 and < 6.0 (target INR of 2.5)
INR > 4.0 and < 6.0 (target INR of 3.5)

- Reduce warfarin dose or stop
- Restart warfarin when INR < 5.0

INR > 6.0 and < 8.0

- Stop Warfarin
- Restart warfarin when INR , 5.0

The Warfarin patient and surgery

- Elective surgery – always plan in advance
- Decide on a 'safe' INR (usually <2) for the procedure
- If surgery is postponed, reassess coagulation

Full warfarin reversal

- Stop warfarin 4 days pre-op
- Check INR on admission or morning of operation

Rapid reversal necessary (urgent surgical procedure)

Reversal in 4 to 24 hours

- Vitamin K 2mg oral (Konakion MM injection used orally) or 1mg slow IV injection (Konakion MM injection)

Note:-

- In serious but non life threatening bleeding (eg GI bleeding or epistaxis without haemodynamic compromise) prompt reversal with IV Vitamin K is indicated.
- Vitamin K (phytomenadione) may rarely cause anaphylaxis. Give by slow IV bolus.
- For more information please refer to the BCSH *Guidelines on oral anticoagulation 3rd edition 1998* or contact the transfusion laboratory on 8451 or bleep 1151 out of hours