

**GUIDELINES FOR MANAGEMENT OF OVER
ANTICOAGULATION WITH WARFARIN**

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1. INTRODUCTION

1.1. Purpose

Treatment with warfarin is effective anti-thrombotic therapy. It acts by blocking carboxylation of the Vitamin K-dependent clotting factors – II, VII, IX and X. Its therapeutic use is monitored by the INR. The risk of bleeding during warfarin therapy is influenced by;

- Intensity and variability of anticoagulation (aiming for high target INR's or patients with unstable anticoagulation)
- Duration of anticoagulation (Increased bleeding risk when first started on anticoagulation therapy)

For patient related risk factors see [section 3.1](#)

1.2. Scope

Therapeutic decisions on reversal of warfarin therapy depend on the level of the INR and the presence or absence of bleeding. Warfarin is the most common coumarin in general use; however these guidelines also apply for nicoumalone (Sinthrome[®]) and phenindione (Dindevan[®]).

1.3. Definitions

INR = international normalised ratio.

2. THERAPEUTIC INTERVENTIONS

2.1. Withhold Warfarin

Warfarin should be withheld until the situation is controlled but dose omission alone has no significant role in the emergency situation due to slow resolution of the anticoagulant effect.

2.2. Vitamin K

Vitamin K will reverse the action of warfarin partially or wholly depending on the route of administration and the dose used. Intravenous administration results in rapid correction of anticoagulation with significant effects on the INR at 4-6 hours. Rate of reversal with oral vitamin K is slower – satisfactory reversal is achieved by 24 hours. Other factors such as safety, patient preference, availability and ease of administration need to be considered in choosing the preparation.

In the absence of bleeding or with minor bleeding, the aim is to bring the INR back into the therapeutic range. Vitamin K 0.5-1mg intravenously, or 1-2.5mg orally are commonly used doses.

In life-threatening bleeding, intravenous Vitamin K should be used. Anecdotally, a dose of 5mg is the most useful as it provides complete correction in most patients, irrespective of the INR, but does not render the patient resistant to re-anticoagulation.

2.3. Fresh Frozen Plasma (FFP)

In major or life-threatening bleeding, the deficient clotting factors II, VII, IX and X should be replaced as quickly as possible. Previously, FFP has been used for this purpose, at a recommended dose of 15ml/kg. There are a number of reasons why FFP is **not** the optimal form of clotting factor replacement:

- FFP contains insufficient amounts of factors II, VII, IX and X to achieve physiological correction of anticoagulation. After infusion of 15ml/kg of FFP, clotting factor levels typically remain below 20% and there is evidence that 30ml/kg is a more appropriate haemostatic dose.
- The recommended volume for a 70kg patient is 1050ml (approximately 4 units) which may be a problem if there is pre-existing cardiovascular impairment.
- FFP has to be blood group specific so the patient's blood group must be known.
- Thawing may incur a delay in administration
- FFP is a single donor product that has not been subjected to a virus-inactivation procedure and therefore carries a small but definite risk of transmission of blood-borne pathogens.

Therefore, FFP should only be used for reversal of over-anticoagulation when Prothrombin Complex Concentrate is not available or contraindicated.

2.4. Prothrombin Complex Concentrate (PCC) e.g. Beriplex[®], Octaplex[®]

PCC is produced by the fractionation of pooled plasma from non-UK donors. PCC contains factors II, VII IX and X in approximately equal concentrations. It has undergone virucidal treatment during preparation (although some viral risk still remains) and does not need to be blood group specific. PCC is available in lyophilized powder form which is reconstituted in sterile water **immediately** prior to administration. Doses of between 25units/kg and 50units/kg have been used. Reversal of anticoagulation is rapid but due to the short half life of Factor VII (6 hours), it is essential also to give intravenous vitamin K.

Almost all subjects treated with warfarin will, by definition, have a condition predisposing to thrombosis and so risks versus benefits must be assessed on an individual patient basis. Close monitoring should be exercised when administering Beriplex P/N to patients with a history of coronary heart disease or myocardial infarction, liver disease, postoperatively, neonates, disseminated intravascular coagulation. In each of these situations, the potential benefit of treatment with Beriplex P/N should be weighed against the potential risk of such complications.

3. DEFINITION OF BLEEDING SEVERITY

3.1. Risk factors for bleeding

The risk of major bleeding with warfarin therapy is influenced by;

- Age (older patients have higher risk of bleeding)
- Co- morbidity (including hypertension, ischaemic stroke, CVS disease, Cardiac failure, diabetes, renal failure, alcohol excess, liver disease and malignancy)
- Concomitant drug therapies (anti-platelet drugs, antibiotic use).
- Previous history of bleeding.(particularly CNS and GI)

3.2. High risk categories

Any patient with the following must be considered as a high risk of bleeding when on warfarin and the reversal of warfarin may be considered at a lower INR. [See appendix 14](#)

- Age >65
- Uncontrolled hypertension
- Diabetes
- Renal failure
- Hepatic failure
- Trauma and recent surgery
- Anti platelet drugs
- Previous major bleeding

3.3. Major/Life-threatening

- Intracranial (confirmed on CT or MRI)
- Retroperitoneal (confirmed on CT or MRI)
- Intraocular (excluding conjunctival)
- Spontaneous muscle haematoma with compartment syndrome
- Urgent invasive procedure required
- Active bleeding leading to hypovolaemic shock
- Any bleeding which does not fit into the above categories but which is clinically felt to be life-threatening should also be discussed with a Consultant Haematologist.

3.4. Minor

- Any other bleeding

4. MANAGEMENT OF OVER ANTICOAGULATION FOR OUT PATIENTS OR OUT REACH

Only for pharmacy and anti coagulation clinics

The target INR must be taken into consideration to determine the level of correction required. Refer to flow chart in appendix for treatment plans

4.1. Hemochron analyser INR 4.5 - 8 in standard risk patient or Hemochron analyser INR 4.5 – 6 in high risk patients

- Withhold warfarin
- Send venous sample to lab to recheck INR

4.2. Hemochron analyser INR 6 – 8 in high risk patient or > 8 in all patients

- Recheck INR on Hemochron analyser to confirm
- Withhold warfarin
- Give 2.5mg of oral vitamin K (one quarter of 10mg Menadiol tablet)
- Send venous sample to lab to recheck INR
- Check INR next day

5. MANAGEMENT OF OVER ANTICOAGULATION FOR IN-PATIENTS

If there is a possibility of urgent surgery in a patient with a deranged INR, consult the haematologist for advice.

The target INR must be taken into consideration to determine the level of correction required. Refer to flow chart in appendix for treatment plans

5.1. Major or life-threatening bleeding

- Send urgent clotting screen (APTT/PT/INR/fibrinogen)
- Obtain relevant history.
- Obtain approximate weight in kg.
- Withhold warfarin and give Vitamin K 5mg by slow intravenous injection over 5 minutes (0.5ml of phytomenadione intravenous preparation (Konakion[®]MM or Konakion[®]MM Paediatric), 10mg/ml, in 100ml bag of 5% dextrose (stocked in resuscitation trolley)).
- Do not give vitamin K subcutaneously as absorption is unpredictable.
- Degree of reversal must be decided on an individual patient basis, especially in patients with prosthetic heart valves for whom prolonged full reversal may increase the risk of valve thrombosis and thromboemboli.
- All patients should be evaluated for a local anatomical reason for bleeding.
- Bleeding may occur when patients are not over-anticoagulated, i.e. within their desired therapeutic range. It may still be necessary to reverse anticoagulation and identify the cause of bleeding.
- PCC is rarely indicated if the INR is less than 2.
- **Contact Consultant Haematologist with clinical details, INR and weight.**
- Obtain agreement for use of PCC (Beriplex[®] is used within this Trust), 25 Units/kg body weight, to nearest 250 Units.)
- Request Beriplex[®] from Blood Bank. They will issue it with instructions for preparation and a flow chart of management of over anticoagulation.
- Prescribe Beriplex[®] on intravenous fluid chart.

- Reconstitute Beriplex[®] on the ward according to instructions delivered with product.
- Administer Beriplex[®] as a slow intravenous bolus over at least 5 minutes. Rapid infusion may lead to thrombosis or allergic reaction.
- Recheck coagulation screen (APTT/PT/INR/fibrinogen) at the end of the infusion and 6 hours later.
- Repeat doses are rarely required.
- If Beriplex[®] is not available or is contraindicated; 15ml/kg FFP with 5mg intravenous vitamin K will partially reverse anticoagulation. 30ml/kg FFP should be given if possible. [See section 2.3](#)
- The rationale for use of Beriplex[®] or FFP should be documented in the notes.
- TED stockings should be used and thromboprophylaxis with LMWH considered when the bleeding risk has passed.
- The need for reintroduction of oral anticoagulants should be considered on an individual patient basis in consultation with a pharmacist.

5.2. Minor bleeding or no bleeding

5.3. INR 4.5 – 10 in standard risk patient or 4.5 – 6 in high risk patient

- Withhold warfarin.
- repeat INR at 24 hours
- The need for reintroduction of oral anticoagulants should be considered on an individual patient basis in consultation with the pharmacist.

5.4. INR 6 – 10 in high risk patient or > 10 in all patients

- Withhold warfarin
- Give 2.5mg of oral vitamin K (one quarter of 10mg Menadiol tablet) **or** 2mg of intravenous vitamin K preparation given orally (0.2ml of phytomenadione, (Konakion[®]MM or Konakion[®]MM Paediatric) 10mg/ml) diluted in water or juice **or** 1mg of intravenous vitamin K (0.1ml of phytomenadione, 10mg/ml) if unable to use oral route.
- Recheck INR at 24 hours
- If INR becomes sub therapeutic consider LMWH and/or TEDS depending on clinical situation
- The need for reintroduction of oral anticoagulants should be considered on an individual patient basis in consultation with a pharmacist.

6. ROLES AND RESPONSIBILITIES

Beriplex[®] should be given only after discussion between the Medical staff involved in the situation and the Consultant Haematologist.

The Consultant Haematologist is responsible for advice re the transfusion requirements of the patient.

All Clinicians will be responsible for ensuring the guidance is adhered to and accountable for the decision making process.

The information chart should be available for use by all clinicians. Any deviation from the guideline should be thoroughly discussed with a Haematologist.

The clinical staff must reconstitute Beriplex® immediately prior to administration as described on the user instructions contained with the drug information.

The use of Beriplex® and Vitamin K must be prescribed and thoroughly documented in the patient's medical notes which must include details of the indication for use. The dosage, date(s) and timing (s) of injections must be documented on the drug chart along with the signature of the prescriber.

Any reaction to the product should be noted and reported to the Hospital Transfusion Team and an IR1 completed.

Response to the treatment and patient outcome should also be documented in the medical notes.

7. POLICY DEVELOPMENT

7.1. Equality Impact Assessment

This policy does not require a stage 2 equality impact assessment.

8. APPROVAL AND RATIFICATION PROCESS

The authors of this document are the Blood Transfusion Practitioner and Consultant Haematologist in consultation with the Hospital Transfusion Committee, the pharmacy department and the Transfusion department Staff. The methodology used has been through open consultation and discussion with the parties involved.

9. REVIEW AND REVISION ARRANGEMENTS

The guideline will be reviewed every 2 years or before if new procedures highlight a review

10. DOCUMENT CONTROL

10.1. Publication

This guideline will be published in the Trust electronic document library.

10.2. Archiving Arrangements

Any earlier versions of the guideline will be archived on the document library by Rose Gill.

10.3. Access

Copies of policy documents should not be printed unless it is absolutely necessary, to reduce the risk that out of date copies may be in circulation. Requests for this policy in an alternative language or format (such as Braille, audiotape, large print etc) will be considered and obtained whenever possible.

10.4. Protective Marking

This guideline will be electronically accessible in the document library.

11. DISSEMINATION AND IMPLEMENTATION

11.1. Dissemination and Communication

Dissemination of the guideline will be delivered to the relevant staff members by targeted email

12. MONITORING COMPLIANCE AND EFFECTIVENESS

The arrangement will be monitored by annual audit and reviewing effectiveness of treatment. This will be fed back to the Hospital Transfusion committee.

13. REFERENCE DOCUMENTS

British Committee for Standards in Haematology. Guidelines on oral anticoagulation: Third edition (including 2005 update)
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14. APPENDICES

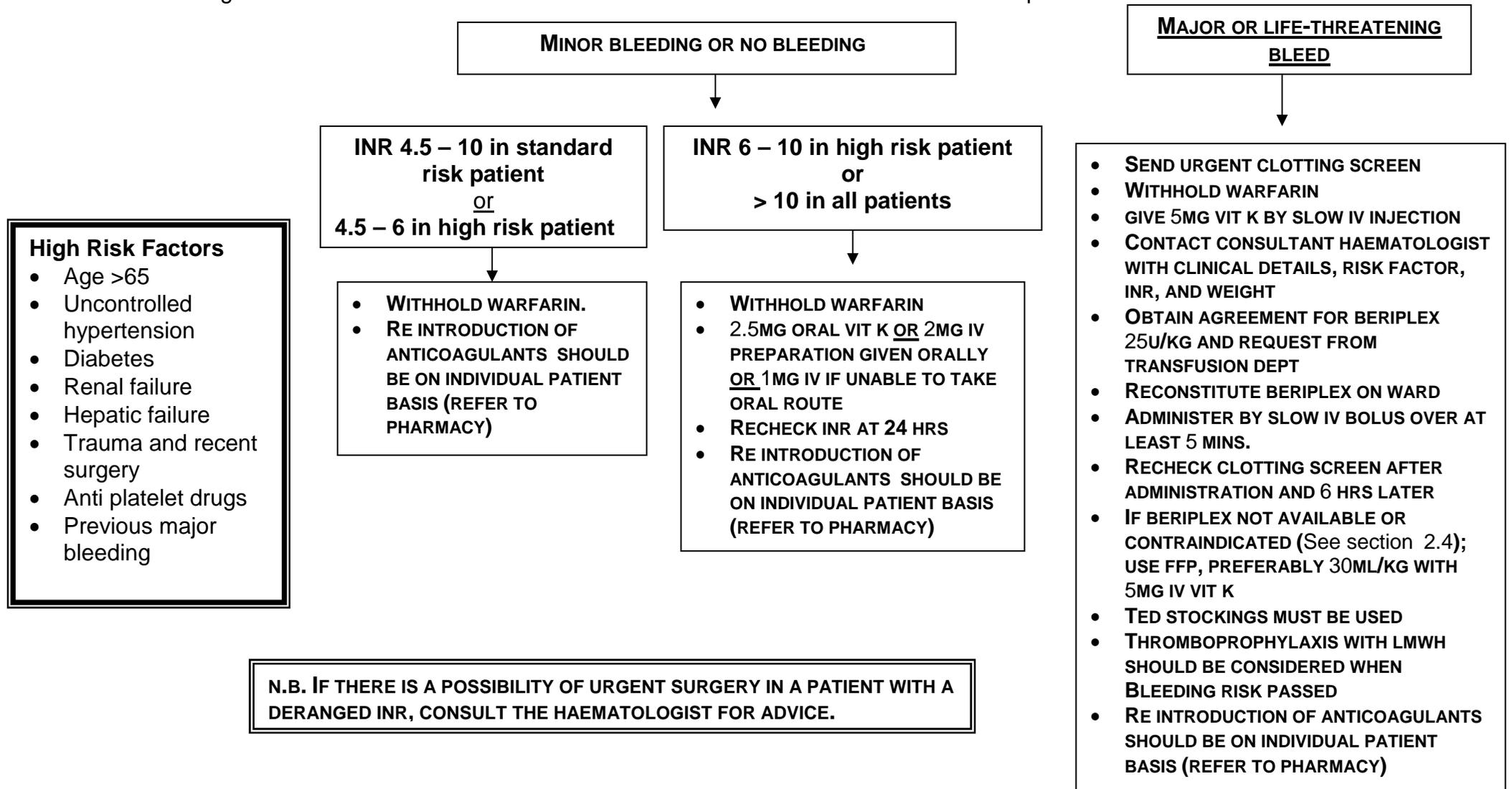
[Flowchart for the management of over anticoagulation with warfarin for in-patients](#)

[Flowchart for the management of over anticoagulation with warfarin for out patients/outreach](#)

[Approximate Dose/weight calculations and administration information for Beriplex®](#)

14.1. Flowchart for the management of over anticoagulation with warfarin for in-patients

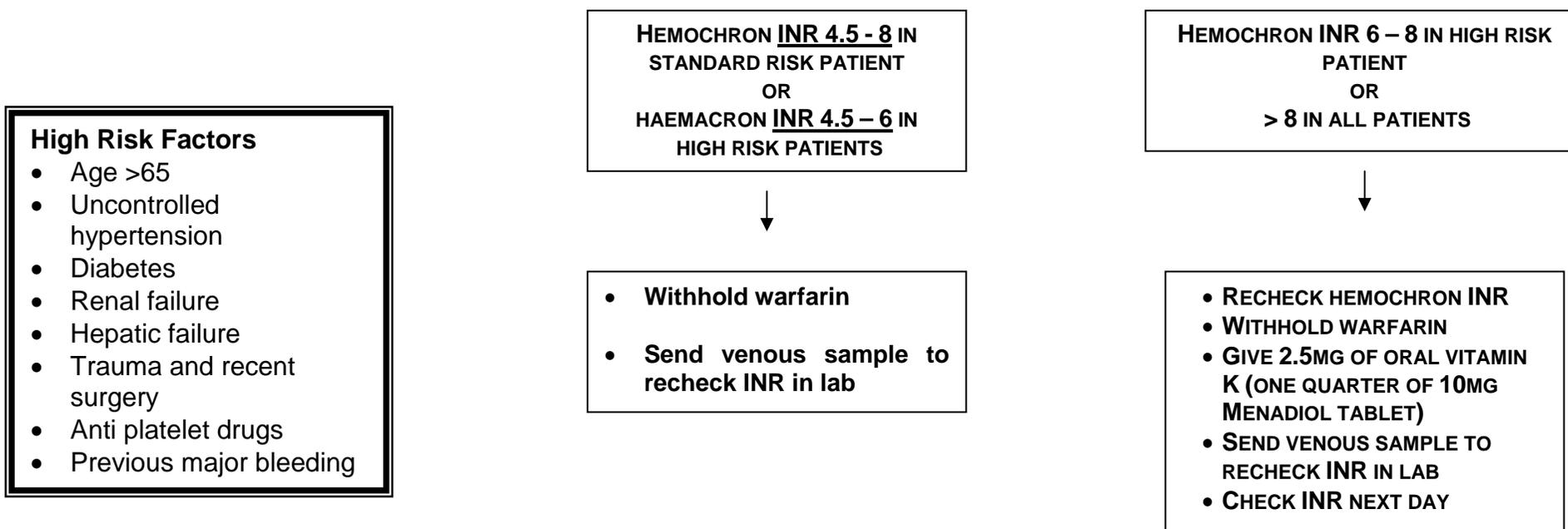
Always refer to the Guidelines for inpatient management of over anticoagulation with Warfarin
The target INR must be taken into consideration to determine the level of correction required



14.2. Flowchart for the management of over anticoagulation with warfarin for out patients/outreach

Always refer to the Guidelines for the management of over anticoagulation with Warfarin

The target INR must be taken into consideration to determine the level of correction required.



14.3. Approximate Dose/weight calculations and administration information for Beriplex®

Dose/weight calculations

To the nearest 250u

50kg – 59kg = 1250u
60kg – 69kg = 1500u
70kg – 79kg = 1750u
80kg – 89kg = 2000u
90kg – 99kg = 2250u
100kg - 109kg = 2500u

Administration information

Reconstitution

Reconstitute as directed overleaf on the product information sheet **immediately** prior to administration.

Administration

Slow Bolus IV injection over at least 5 mins through any available vein.
Do not give as an infusion.

**Beriplex is obtained through Transfusion Laboratory
Ext 3069. (Bleep 3066 out of hours)
Medical staff must always consult the Consultant
Haematologist before use**