**NHS Grampian Protocol For The Reversal Of Over-Anticoagulation With Warfarin**

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<th>Lead Author/Co-ordinator:</th>
<th>Reviewer:</th>
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<tr>
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<td>Medicines Information</td>
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**Uncontrolled When Printed**

**Version 3**

**Executive Sign-Off**

This document has been endorsed by the Director of Pharmacy and Medicines Management

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Title: NHS Grampian Protocol For The Reversal Of Over-Anticoagulation With Warfarin

Unique Identifier: NHSG/Pro/WAO/MGPG925, Version 3

Replaces: NHSG/Pro/WAO/MGPG778, Version 2

Lead Author/Co-ordinator: Consultant Haematologist

Subject (as per document registration categories): Policy

Key word(s): Reversal over-anticoagulation protocol bleeding warfarin anticoagulants

Policy, Protocol, Procedure or Process Document: Protocol

Document application: NHS Grampian

Purpose/description: To provide best management for patients who are anticoagulated on warfarin in order to reduce the risk of bleeding and to treat active bleeding in those in whom it has occurred.

Responsibility: Responsibility for the effective management of the NHS Grampians policy, protocol, procedure and process documentation ultimately lies with the General Manager for the Acute Sector. Delegation for formulating, disseminating and controlling these documents falls to either a named individual or a working group.

Policy statement: It is the responsibility of supervisory staff at all levels to ensure that their staff are working to the most up to date and relevant policies, protocols and procedures. By doing so, the quality of the services offered will be maintained, and the chances of staff making erroneous decisions which may affect patient, staff or visitor safety and comfort will be reduced.
Responsibilities for ensuring registration of this document on the NHS Grampian Information/ Document Silo:

Lead Author/Co-ordinator: Consultant Haematologist

Physical location of the original of this document: Haematology Department, ARI

Job/group title of those who have control over this document: Consultant Haematologist

Responsibilities for disseminating document as per distribution list:

Lead Author/Co-ordinator: Consultant Haematologist

Responsibilities for implementation:

Organisational: Chief Executive and Management Teams
Hospital/Interface services: Deputy General Managers and Clinical Leads
Operational Management Unit: Unit Operational Managers
Departmental: Clinical Leads
Area: Line Managers

Review: Review 3 yearly. Any significant changes in evidence will result in earlier alteration.

Responsibilities for review of this document:

Lead Author/Co-ordinator: Consultant Haematologist

Revision History:

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<td>‘Fatal haemorrhage complicates warfarin use’ – rephrased.</td>
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<td>‘and by an international expert in the field’ - removed</td>
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<td>List of abbreviations</td>
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<td>Added MI and CVA</td>
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<td>Re-ordered into alphabetical order</td>
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# NHS Grampian Protocol For The Reversal Of Over-Anticoagulation With Warfarin

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NHS Grampian Protocol For The Reversal Of Over-Anticoagulation With Warfarin

Introduction

Around 1 to 1.5% of the population take warfarin to prevent thrombosis. The main complication of warfarin is bleeding. Major or life-threatening bleeding is seen in approximately 2% of patients on warfarin each year. Fatal haemorrhage occurs in approximately 0.25% of warfarin treated patients annually.

Anticoagulation may result in excessive prolongation of clotting times without bleeding or with bleeding.

Protocol Application

This protocol, based on the available evidence, is to be used for all patients on warfarin. The protocol does not deal with the peri-operative management of patients on warfarin - this should be discussed with a consultant haematologist.

Aims

The main aims of this protocol are to prevent bleeding in patients who are over-anticoagulated and to treat bleeding in those in whom it has occurred. While there are randomised controlled studies to inform the use of vitamin K, the recommendations on the use of the prothrombin complex concentrates, which contain coagulation factors II, VII, IX and X (e.g. Beriplex), are based on observational data and expert opinion. The guidance is in keeping with the recommendations of the British Committee for Standards in Haematology (Keeling et al 2011). The recommendations for partial reversal of anticoagulation in asymptomatic patients with International Normalized Ration (INR) values between 5 and 10 have been left in place despite the publication of a randomised controlled study which indicated little benefit in reversal for these patients in terms of the number of bleeding events which were prevented in comparison with a group who received placebo (Crowther et al 2009) – this remains under review.

Development

This protocol was devised by the author, reviewed by the Medicines Guidelines and Policies Group and approved by the Chair of the Medicines Guidelines and Policies Group.
Guide to Reversal of Oral Anticoagulation on Warfarin Classification of Bleeding Complications

**BLEEDING**

♥MAJOR

†Vitamin K 5 mg IV and ♦Beriplex P/N IV
Withhold warfarin

- Initial INR
  - 1.4-3.9: 1 mL/kg (approx 25 iu/kg)
  - 4.0-6.0: 1.4 mL/kg (approx 35 iu/kg)
  - >6.0: 2 mL/kg (approx 50 iu/kg)
- Maximum single dose of 2500iu for an INR of 2.0-3.9, 3500iu for an INR of 4.0-6.0 and 5000iu for an INR of >6

- Immediate check PT and APTT
- Adequate correction (INR ≤1.3)
- Repeat PT and APTT in 4-6 hours

NO BLEEDING

INR ≥ 8

♦High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

INR 5 – 7.9

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

MINOR

Vitamin K
2mg IV †
Withhold warfarin

Check INR at 24 hours or earlier if deterioration in clinical condition

INR 5 – 7.9

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

INR 3 – 4.9

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

INR 1.5 – 3.9

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

INR ≤ 1.4

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

INR 0.5 – 1.4

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

INR 0 – 0.5

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

INR 0

- High Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

♦Low Risk

✈Vitamin K 1mg orally
Withhold warfarin

Check INR at 24 hours

Reduce warfarin dose or withhold one dose
Recheck INR at 24 hours

Inadequate Correction

Consider other factors contributing to prolonged coagulation tests
- Disseminated Intravascular Coagulation
- Congenital coagulation factor deficiency
- Liver disease
- Lupus inhibitor
- Inadequate replacement

SEEK HAEMATOLOGICAL ADVICE
Classification of Haemorrhage

Fatal

Death due to haemorrhage
(Demonstrated at autopsy, radiologically or clinically obvious)

Major

Intracranial (CT or MRI documented)
Retroperitoneal (CT or MRI documented)
Intra-ocular (excludes conjunctival)
Spontaneous muscle haematoma associated with compartment syndrome
Pericardial
Non-traumatic intra-articular
If any invasive procedure is required to stop bleeding
Active bleeding from any orifice plus BP≤90mmHg systolic, or oliguria or ≥20g/l fall in haemoglobin

Minor

Any other bleeding that would not influence your decision to anticoagulate a patient

Cautions

† Intravenous vitamin K may rarely cause anaphylaxis. Administration should be:
   ❖ By slow IV bolus
   ❖ Withheld in patients with a history of previous severe allergic reaction to vitamin K

♦ Beriplex P/N contains heparin and is contraindicated in patients with heparin induced thrombocytopenia (present or previous)
   Beriplex P/N is also relatively contraindicated in patients with:
   1. An increased risk of thrombosis.
   2. Angina pectoris and after recent myocardial infarction.

Maximum single dose of Beriplex is 5000iu
Adhere to the product SPC for administration. In all clinical situations an assessment of the likely risks and benefits of administration needs to be made.

In disseminated intravascular coagulation, prothrombin complex-preparations (e.g. Beriplex) may only be administered after termination of the consumptive state.

♣ Oral Vitamin K – preparation used is the preparation for injection (10mg/ml) Konakion MM (Roche). The dose can be diluted in small amount of water after drawing up in an oral syringe. This is an off-label use of the product.

♠ Low risk patients do not require INR reversal at INR 5 – 7.9 but correction should be considered in "high risk" patients whose risk of bleeding is approximately 15 fold higher.

Patients at high risk of warfarin associated bleeding:

Elderly
Previous GI bleed
Previous CVA (haemorrhagic or ischaemic)
Anaemia
Renal failure
Diabetes mellitus
Previous MI
Bibliography


Distribution List

Director of Pharmacy and Medicines Management
Professor Mark Vickers, Blood Transfusion Service
All Physicians
All Receiving Surgeons
All Accident and Emergency Consultants
All Haematologists
Blood Transfusion Service Consultants and Associate Specialists
Policy will be contained in Induction brief for Doctors
Primary Care/GMED/Community Hospitals
Grampian Medicines Information Centre

Appendix 1

List of abbreviations

APTT  - activated partial thromboplastin time
CT    - computerised tomography
CVA   - cerebrovascular accident
DIC   - Disseminated Intravascular Coagulation
INR   - international normalised ratio
iu    - international units
IV    - intravenous
MI    - myocardial infarction
MRI   - Magnetic resonance imaging
PT    - prothrombin time