North West Anglia NHS Foundation Trust

Guidelines for the Management of Anticoagulant Reversal in Adults Version 4

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Scope:	Trust-wide		
Standards and Legislation and key related documents:	State any standards, legislation or key related documents that are relevant and current. If you have a SOP, please state the overarching policy name here.		
First-Level Approval: (Specialty)	Hospital Thrombosis Committee	**Date:**	11 May 2022
First-Level Approval: (CBU)	Select	**Date:**	Enter date
First-Level Approval: (Divisional Leadership Board)	Select	**Date:**	Enter date

First-Level Approval: D&TC		**First-Level Approval:** TIPCC		**First-Level Approval:** Safeguarding Committee	
Tick ☑	23 November 22	*Tick* ☐	Enter date	*Tick* ☐	Enter date

Review Date:	12 May 2025		
Second-Level Approval: (if required)	Quality Governance Operational Committee	**Date:**	12 May 22
Target Audience:	Staff across all sites	All clinicians involved in the care of adult patients who need reversal of their anticoagulant therapy	
Trust Joint Consultative Committee Approval:	N/A	**Date:**	Enter date

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Version Control Summary

Version:	Page or section:	Description of change:	Date approved:	Date published:
2007 Version 1		New guideline	February 2007	February 2007
2009 Version 2		Reviewed	April 2009	April 2009
2015 Version 3		Reviewed and reformatted, expanded to include new oral anticoagulants	09/05/2017	10/05/2017
2022 Version 4		Reviewed, criteria to issue PCC by BMS added.	12/05/2022	29/11/2022

Summary of key points in this document

- To provide best management for patients who are anticoagulated on Warfarin, Low Molecular Weight Heparins (Dalteparin), Dabigatran, Rivaroxaban, Apixaban and Edoxaban in order to reduce the risk of bleeding and to treat active bleeding in those in whom it has occurred.

  The guidance is in keeping with the recommendations of the British Committee for Standards in Haematology (Mike Makris et al Nov 2012).

CONTENTS

1. INTRODUCTION

Patients who are taking Warfarin may need, for various reasons, to have the effects of warfarin reversed. Major or life-threatening bleeding is seen in 2% of patients on warfarin each year. Fatal haemorrhage complicates Warfarin use in 0.25% of patients annually. Rata of fatal haemorrhage on DOACs is lower.

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

2. PURPOSE

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

3. SCOPE

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

- Who are on an anticoagulant and have bleeding **or**
- Who require immediate surgery.

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

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

For paediatric guidelines, the advice of a Consultant Haematologist should be sought.

4. PATIENTS WITH BLEEDING

The decisions must be made on an individual basis and should consider:

The presence of major/minor bleeding and risk of bleeding;

Patient factors (including risk of falls).

External factors (need for urgent/semi-urgent invasive procedure and type of procedure).

The current International Normalised Ratio (INR) – the risk of bleeding increases exponentially with an INR >5.

Frequently cessation of anticoagulation and discontinuation of any concomitant medications contributing to risk of bleeding like antiplatelet agents is sufficient to control insignificant bleeding.

Apply endoscopic and radiological techniques where appropriate.

5. VITAMIN K (PHYTOMENADIONE)

Vitamin K is an antidote for Warfarin. Due to near complete absorption, oral vitamin K is as effective as intravenous with the delay in action hardly influenced by the absorption time.

Only 500 microgrammes is required to reduce the INR from > 5.0 to a target level of 2.0 – 3.0.

Vitamin K preparations can be administered 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.

Slow intravenous injection doses should be diluted with 55ml of glucose 5% vitamin K. A sustained response is achieved with intravenous vitamin K. Oral or intravenous administration of vitamin K can be expected to reverse warfarin 4 - 6 hours after administration.

6. PROTHROMBIN COMPLEX CONCENTRATE (PCC) E.G. OCTAPLEX

Please see also Guidelines on the use of OCTAPLEX® (Prothrombin Complex Concentrate/PCC) for rapid reversal of Warfarin in association with life threatening bleeding (C0254).

Octaplex is licensed for Warfarin reversal. It is derived from human plasma (non-UK) and contains clotting factors II, VII, IX and X.

Octaplex is a virally inactivated product which reduces the risk of transmission of viral infections especially enveloped viruses such as HIV. Like other plasma products however, there remains a risk of prion diseases namely variant Creutzfeldt-Jakob Disease (vCJD).

PCCs provide immediate reversal of Warfarin but the effect will begin to wear off after 6-12 hours.

The dose of Octaplex is 25-50 units per kg body weight; (maximum dose 3,000 units).The patient's weight and INR result are required.

Wt(Kg)	INR 2-2.5	INR 2.5-3	INR 3-3.5	INR>3.5
50	1500 iu	2000 iu	2500 iu	2500 iu
60	2000 iu	2000 iu	2500 iu	3000 iu
70	2500 iu	2500 iu	3000 iu	3000 iu
80	2500 iu	3000 iu	3000iu	3000 iu
90	2500 iu	3000 iu	3000 iu	3000 iu
100	3000 iu	3000 iu	3000 iu	3000 iu

Phone the Blood Bank to request the Octaplex, giving full patient details, your name and contact number, patient's weight and their INR result.

Biomedical Scientist on duty will issue Octaplex as per flow chart in *Appendix 2*.

If patient had a thrombotic event within last 4 weeks, Haematologist on call should be contacted for advice.

Octaplex can be collected from the Blood Bank within 10mins of request.

Ensure product is collected immediately and the nurses are aware that Octaplex has been written up and is required immediately.

In the rare event of Octaplex shortage, Fresh Frozen Plasma (FFP) could be used in a case of severe bleeding after authorisation by the Haematologist on call.

7. LOW MOLECULAR WEIGHT HEPARIN (DALTEPARIN) REVERSAL

For LMWH administration within 8h of the time of requirement for correction of anticoagulation: give Protamine sulphate (1 mg per 100 anti-Xa units of LMWH). If ineffective, consider further Protamine sulphate 0.5 mg per 100 anti-Xa units. Protamine sulphate should be given slower than 5 mg/min to minimise the risk of adverse reactions.

For LMWH administration greater than 8h from the time of requirement for correction of anticoagulation: consider smaller doses of protamine.

Consider Recombinant FVIIa if there is continued life-threatening bleeding despite protamine sulphate and the time frame suggests there is residual effect from the LMWH contributing to bleeding.

There is no specific antidote for Fondaparinux. Management of bleeding should be through cessation of treatment and general haemostatic measures. Recombinant FVIIa should be considered for critical bleeding.

8. DABIGATRAN

Management of bleeding should be through cessation of treatment and general haemostatic measures. In bleeding patients who have taken a dose of dabigatran in the last 2 hours, consider oral activated charcoal to prevent further absorption.

In ongoing life-threatening bleeding, a specific antidote Idarucizumab (Praxbind) 5 g can be given as IV bolus. Discussion with the Haematologist on call is necessary.

If patient had a thrombotic event within last 4 weeks, Haematologist on call should be contacted for advice.

9. RIVAROXABAN, APIXABAN, EDOXABAN

Management of bleeding requires cessation of anticoagulation and general haemostatic measures.

Life threatening bleeding on Edoxaban, Apixaban or Rivaroxaban can be managed with Octaplex- a non specific reversal agent used for Warfarin reversal. Maximum single dose is 3000 IU given intravenously.

Coagulation test (PT and APTT) results are not suitable to assess drug level OR monitor response to Octaplex.

Andexanet alfa has been recently approved by NICE and is recommended as option for reversing anticoagulant effect of Apixaban or Rivaroxaban in adults with life-threatening or uncontrolled gastrointestinal bleeding only. For this indication discuss with gastroenterology and haematology.

A blueteq form is required and should be completed by gastroenterology consultant approving treatment

10. GUIDE TO REVERSAL OF ORAL ANTICOAGULATION ON WARFARIN

See *Appendix 1*.

11. APPROVAL

This guideline will be approved by the Hospital Thrombosis Committee, Drugs & Therapeutics Committee, the Surgery Divisional Leadership Board and by the Quality Governance Operational Committee.

12. DISTRIBUTION

This guideline will be available on SharePoint.

13. REFERENCES

Makris M & Watson HG, (2002), Reversal of coumarin-induced over-anticoagulation. British Journal of Haematology 2002;118:926.

Wilson SE, Watson HG, Crowther MA., (2004), The use of low dose oral vitamin K to reverse asymptomatic elevation of the INR: A systematic review. Canadian Med Journal 2004;170(5): 821-824.

David Keeling, Trevor Baglin, Campbell Tait, Henry Watson, David Perry, Caroline Baglin,Steve Kitchen and Michael Makris, (2011), British Committee for Standards in Haematology Guidelines on oral anticoagulation with warfarin – fourth edition British Journal of Haematology 2011;154(3):311-24.

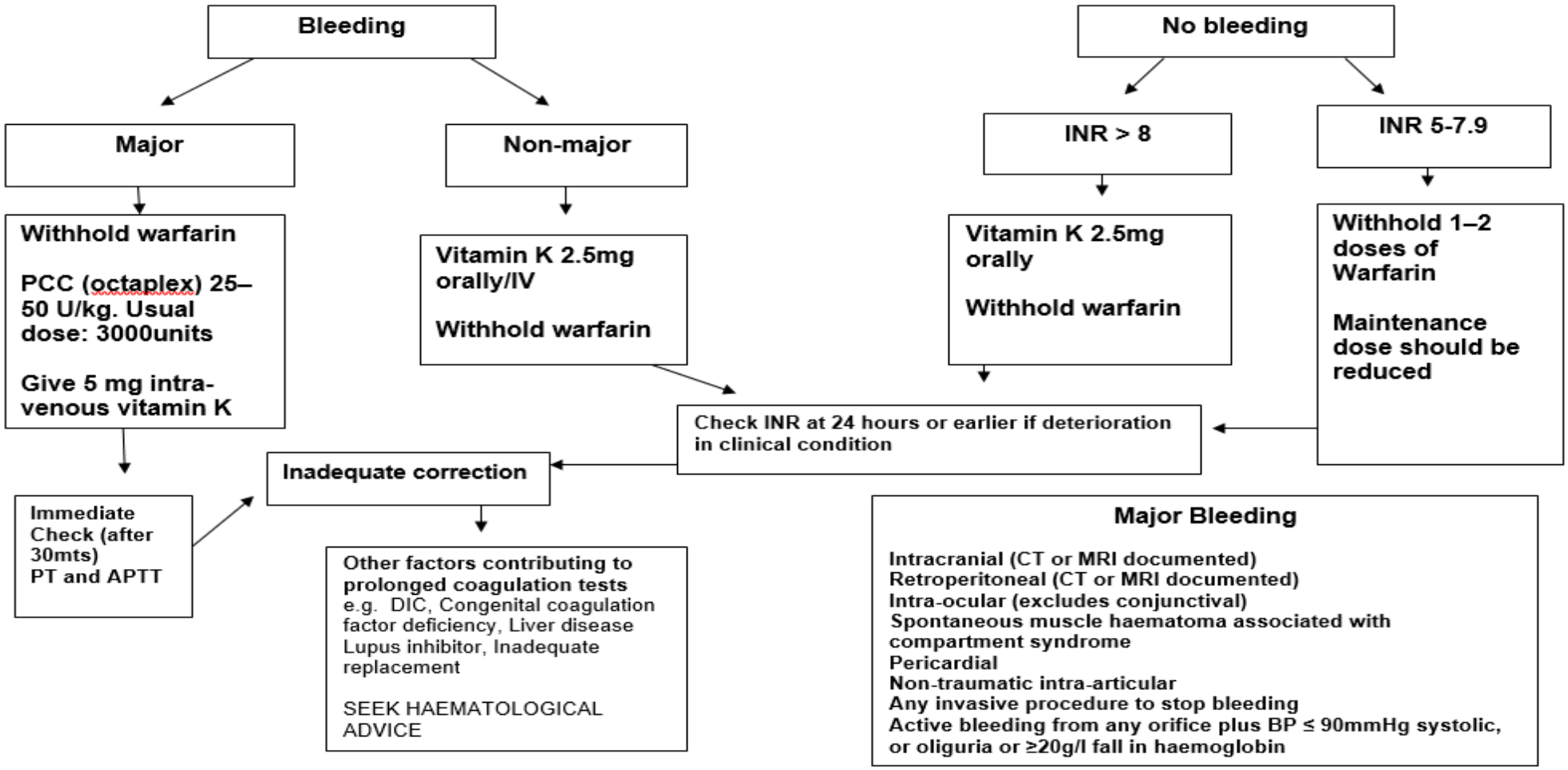
Mike Makris, Joost J. Van Veen,Campbell R. Tait, Andrew D. Mumford and Mike Laffan on behalf of the British Committee for Standards in Haematology, (2012), Guideline on the management of bleeding in patients on antithrombotic agents, British Journal of Haematology, 2012, 160,35–46

Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban, Technology Appraisal Guidance TA697, May 2021

14. ASSOCIATED DOCUMENTS

Guidelines on the use of OCTAPLEX rapid reversal of warfarin in association with life threatening bleeding (C0254).

APPENDIX 1: GUIDE TO REVERSAL OF ORAL ANTICOAGULATION ON WARFIN INVESTIGATE CAUSE OF RAISED INR



APPENDIX 2: OCTAPLEX ISSUE BY BIOMEDICAL SCIENTIST PROFORMA

PATIENT DETAILS	**SURNAME**	**FORENAME**	
HOSPITAL NUMBER		**DOB**	

DATE requested		**TIME requested**	
NAME of requesting Clinician		**Contact/Bleep**	

Call received in lab due to patient having confirmed, life-threatening bleeding/requires surgery within 2 hours AND a raised INR due to warfarin -	Confirmed (tick) ☐ Latest INR result …… (Sample Number……) Proceed to clinical questions below:
1 a) Why is the patient on warfarin? Stroke ☐ DVT ☐ PE ☐ MechHeartValve ☐ Other ☐ ……	b) Did this event occur in the last 4 weeks? Yes ☐ STOP – Refer to haematology consultant No ☐ Proceed to question 2 below
2. Does the patient have: *(tick if yes)* ☐ Known or previous Heparin-Induced Thrombocytopaenia (HIT)	Yes : STOP – Refer to haematology consultant Unknown: Request clinician to check, if still unknown, advise that product will be issued and that they are accepting any associated risk. Document this in the patient notes. Proceed to question 3 below. No to all : Proceed to question 3 below
3. Is the Weight of the patient known? Weight ……Kg	**Yes:** Advise clinician to request appropriate dosage as per the table within the Trust policy, print the ICE request form and pod directly to the laboratory. **No:** Advise clinician to obtain weight (in Kg) (and/or INR if this is not yet available) in order to proceed.
Referral to Haematology Consultant required? Yes ☐ No ☐	
Octaplex issued? Yes ☐ Dose ……iu Date …… Time …… No ☐ Reason ……	

YOUR DETAILS	NAME		
DATE		TIME	

APPENDIX 3: QUALITY ASSURANCE CHECKLIST

		Y/N/ n/a	COMMENTS (to author for amendments)
1	**Title of document** Guidelines for the Management of Anticoagulant Reversal in Adults(C0161)		
	Is the title clear and unambiguous	Y	
2	**Type of document (e.g. procedure, guidance)**	**Guideline**	
	Is it clear whether the document is a procedure, guideline, standard operating procedure?	Y	
3	**Introduction**		
	Are reasons for the development of the document clearly stated?	Y	
4	**Content**		
	Is the standard model template used?	Y	
	Is the document in the correct format?	Y	
	• Paragraphs numbered consecutively	Y	
	• Headers: only on front page to contain logo	Y	
	• Footers: on every page except front page	Y	
	Are the Version Control numbers correct in the panel and the footer	Y	
	Are the objectives/aims clearly stated?	Y	
	Does this document concern the handling, moving or storage of personal identifiable or commercially sensitive information? If yes, has a Summary Privacy Impact Assessment been completed?	NA	
5	**Evidence Base**		
	Is the type of evidence to support the document explicitly identified?	Y	
	Are associated documents referenced?	Y	
6	**Approval Route**		
	Does the document identify which committee/group will approve it?	Y	
7	**Review Date**		
	Is the review date identified?		

If answers to any of the above questions is 'no', then this document is not ready for approval, it needs further review.

COMPLIANCE TEAM:		
1.	Date Comments returned to author by Compliance Lead	21/2/2022
2.	Date of Compliance Team approval	23/11/2022
3.	Name of Compliance Lead	Louisa Scoggins

Please do not delete any of the below approval sections.
If certain sections are not applicable to the document's journey please enter 'N/A'

SPECIALTY APPROVAL MEETING: Hospital Thrombosis Committee			
If the committee/group is happy to approve this document would the chair please sign below and send the document and the minutes from the approval committee to the Corporate Governance Team. **To aid distribution all documentation should use electronic signatures and be sent electronically wherever possible.**			
Name	Subash Kandikattu	**Date**	11/05/2022
Signature	SUBASH KANDIKATTU		

CBU APPROVAL MEETING: N/A			
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*Name of relevant Care Quality Committee		Drugs & Therapeutics Committee	
Name		**Name**	**SUZANNE HAMILTON**
Date	Enter date	**Date**	23/11/2022
Signature		**Signature**	
Trust Infection and Prevention Control Committee N/A		**Safeguarding Committee N/A**	
Name		**Name**	
Date	Enter date	**Date**	Enter date
Signature		**Signature**	

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SECOND-LEVEL APPROVAL COMMITTEE: Quality Governance & Operational Committee			
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Name	**Kanchan Rege**	**Date**	12/05/2022
Signature			