

Emergency Reversal of Oral Anticoagulation

Key Point

- In an actively bleeding patient on a DOAC, please seek urgent specialist advice from Consultant Haematologist on call

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Abbreviations

APPT _r	APPT ratio
DOAC	Direct oral anticoagulant
FFP	Fresh frozen plasma
HIT	Heparin-induced thrombocytopenia
LMWH	Low molecular weight heparin
PE	Pulmonary embolism
UFH	Unfractionated heparin
VKA	Vitamin K antagonist

Summary Flowchart: Life-threatening bleeding in patients on DOACs

Patient on a DOAC with life- or limb-threatening bleed,
including intracranial bleed
OR
GI bleed with haemodynamic compromise

Call Consultant Haematologist On Call – give dose and timing of last DOAC ingested.
Reversal agents must be authorised by Consultant Haematologist.
Check FBC / coag screen / renal function / G&S

DABIGATRAN

Give **Praxbind (idarucizumab)** 5g (2x 50ml vials, 2.5G/50ml ready constituted) IV over 5-10 mins.
Order from Blood Bank.
Repeat dose of 5g may be given after discussion with Consultant Haematologist.
See section 5.1

Non drug-specific measures

Stop anticoagulant
Maintain BP and urine output
Mechanical compression to stop bleed if possible
Tranexamic acid

APIXABAN/EDOXABAN/RIVAROXABAN

Stop DOAC.

Give PCC/Beriplex at 30iu/kg. Dose capped at 3000 units. Available from blood bank.

Order Beriplex from blood bank.

Contents

Summary Flowchart: Life-threatening bleeding in patients on DOACs	2
1. Management of a bleeding patient on warfarin or other Vitamin K antagonists - acecoumarin, phenindione (VKA).....	4
2. Summary of treatment for over anticoagulation with coumarins	5
3. Management of a bleeding patient on a DOAC	6
4. General measures in bleeding patient on DOAC	6
5. Specific reversal agents for DOACs.....	7
Reference.....	7
Full version control record.....	8

1. Management of a bleeding patient on warfarin or other Vitamin K antagonists - acecoumarin, phenindione (VKA)

- Vitamin K given IV has effect after just 3 hours of administration and is the recommended product for reversal of warfarin (BCSH guideline 1998, updated 2005, 2011; Level III, grade B evidence).
- FFP is **not** the product of choice for warfarin (or other VKA) reversal in any circumstance
- In cases of blood loss with **life/limb threatening or potential long term neurological consequences**, the use of a concentrated pooled plasma product containing factors II, VII, IX and X (Beriplex, available from blood bank) is the recommended treatment and should be used in preference to FFP (see references below). Use of Beriplex should usually be authorised by on call Haematologist. Immediate issue of Beriplex without authorisation from haematology can occur only if the following criteria are met:

A. Beriplex authorised by ED or stroke **consultant**

AND

B. 1. suspected/known intracranial haemorrhage on warfarin – 50 iu/kg up to 3000iu Beriplex

OR 2. other life-threatening bleeding on warfarin – 30 iu/kg up to 3000iu Beriplex

Higher doses of Beriplex up to 5000iu may be authorised in very rare cases by Consultant Haematologist

- High INRs with minor or no clinical signs of haemorrhage should be managed by discontinuation of warfarin and administration of a small dose of oral or IV vitamin K.
Note: IV preparation of vitamin K may be given orally if for any reason tablets are not available
- It is important to repeat and monitor the INR after reversal

2. Summary of treatment for over anticoagulation with coumarins

Clinical assessment	Treatment
<u>INR 5.0-8.0</u> <u>With no signs of bleeding</u>	- Stop warfarin, restart when INR <5.0 - Consider vitamin K if other risk factors for bleeding
<u>INR >8.0</u> <u>With no bleeding or minor bleeding (not life threatening)</u>	- Stop warfarin, restart when INR <5.0 - Give 2-5mg of vit K orally or 1-2mg IV. If INR still raised after 24 hrs repeat vitamin K dose
<u>Major bleeding</u> <u>i.e. potentially life-threatening</u>	- Stop warfarin - Give 10mg of vitamin K IV (slow IV injection or infusion in 5% dextrose) - Give prothrombin complex (Beriplex) after consultation with a consultant haematologist. Recommended dose (capped at 3000iu unless higher dose specifically requested by Consultant Haematologist): 50units/kg if INR >6 35units/kg if INR 4-5.9 25units/kg if INR 2-3.9

N.B. The target nadir INR is dependent on the clinical scenario *and* the original indication for anticoagulation. Patients with metal heart valves may not tolerate complete reversal of anticoagulation for longer than 24-48hrs.

Reference: BCSH (2011): 'Guidelines on oral anticoagulation with warfarin'

3. Management of a bleeding patient on a DOAC

Not all of the DOACs (dabigatran, apixaban, rivaroxaban, edoxaban) are readily reversible and a bleeding patient may need supportive measures until the drug is eliminated – the relative short half-life of these agents means that specific measures may not be necessary if patient's condition is stable.

Standard coagulation assays will not predict the degree of anticoagulation in a given patient but abnormalities of APTT (dabigatran) and PT (rivaroxaban, apixaban, edoxaban) are consistent with ongoing presence of the anticoagulant and hence increased bleeding risk. Please note that standard tests of coagulation may be normal despite the presence of clinically relevant levels of DOACs.

In an actively bleeding patient on a DOAC, please seek urgent specialist advice from Consultant Haematologist on call.

Please note that these guidelines relate to **emergency** anticoagulation reversal in a bleeding patient; they do not apply to elective or semi-elective procedures where DOACs should be stopped in accordance with Trust guidelines (Management of anticoagulated patients undergoing elective surgery or invasive procedures).

4. General measures in bleeding patient on DOAC

1. Stop the anticoagulant drug
2. Document the timing and amount of the last drug dose
3. Check renal function, FBC, Group and save, PT, APTT
4. Maintain BP and urine output as DOACs are renally excreted.
5. Apply mechanical pressure to the bleed, if possible
6. Use endoscopic, radiological, surgical measures as appropriate
7. Consider tranexamic acid 1g qds (first dose IV).
8. Discuss use of Beriplex 30iu/kg iv with Consultant Haematologist on call. Available from blood bank. Dose capped at 3000 units.
9. **In the event of an intracranial bleed and the time of last dose of DOAC taken is unknown or within the last 48 hours, proceed with Beriplex 30iu/kg urgently. AE and Stroke Consultant can authorise this without Haematology discussion. If unsure/borderline indication, please discuss with oncall Haematologist urgently.**
10. Ensure all other drugs that potentiate bleeding (e.g., antiplatelet agents) are stopped
11. If ingestion was in the last 2 hours, then consider oral liquid charcoal 50g (consult Toxbase).

5. Specific reversal agents for DOACs

5.1 Dabigatran

Dabigatran has a specific and immediate reversal agent available – Praxbind® (Idarucizumab). This agent cannot be administered without authorisation by the on-call Consultant Haematologist.

Praxbind® at a dose of 5g (2 x 50ml vials, 2.5g/50ml ready constituted) is administered intravenously as two consecutive infusions over 5 to 10 minutes each or as a bolus injection. This product is kept in blood bank, although it is not a blood product.

Administration of a second 5 g dose of Praxbind® (idarucizumab) may be considered in the following situations:

- recurrence of clinically relevant bleeding together with prolonged clotting times, or
- if potential re-bleeding would be life-threatening and prolonged clotting times are observed, or
- patients require a second emergency surgery/urgent procedure and have prolonged clotting times.

5.2 Rivaroxaban and Apixaban

We no longer recommend the use of Andexanet Alfa for reversal of Apixaban & Rivaroxaban in patients with life threatening GI bleed. This decision was made following reports of increased thrombotic events associated with the use of Andexanet Alfa. Any patient on Apixaban & Rivaroxaban experiencing bleeding symptoms should be managed as per Section 4 of this guideline.

Reference

British Committee for Standards in Haematology [BCSH] (2011) 'Guidelines on oral anticoagulation with warfarin – fourth edition', *British Journal of Haematology*, 154(3), pp. 311-324. Available at: <https://doi.org/10.1111/j.1365-2141.2011.08753.x>

Full version control record

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This guideline has been registered with the Trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Caution is advised when using guidelines after the review date.

This guideline is for use in Frimley Health NHS Foundation Trust hospitals only. Any use outside this location will not be supported by the Trust and will be at the risk of the individual using it.

Version History

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1.2	Jan 2023	Dr C Rees, Dr N Philpott	Interim	Update to allow immediate issue of Beriplex without haematology approval in specific life-threatening scenarios
1.3	Feb 2025	Dr C Rees, Dr N Philpott	Draft	Scheduled review
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Related Documents

Document Type	Document Name
Guideline	Management of anticoagulated patients undergoing elective surgery or invasive procedures