Disclaimer:
Our recommendations are based on current national guidelines and relevant evidence-base. This guideline helps inform clinicians clinical judgement. However, clinicians will consider the trade-off between the benefits and harms of an intervention before making a clinical decision.

Guideline for the management of direct oral anticoagulant (DOAC) associated bleeding

1.0 Procedure Statement (Purpose / Objectives of the Procedure)

To dictate the management of haemorrhage, from minor to life-threatening, which may be associated with, or worsened by, the use of rivaroxaban, apixaban, dabigatran or edoxaban.

2.0 Accountabilities

The Trust VTE Group will be responsible for the policy content, review, and monitoring of compliance. They will ensure the policy complies with national and international guidelines and reflects best evidence-based practice.

All consultants, clinicians, prescribers, pharmacists and nurses should use this guideline and seek advice from a consultant haematologist if there is any uncertainty regarding how to manage a patient.

All nurses must follow these guidelines and seek advice from a pharmacist should there be any uncertainty regarding how to administer andexanet alfa.

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Management of Rivaroxaban/Apixaban Associated Bleeding

Consider giving activated charcoal orally, if last dose ingested <2 hours ago

Start resuscitation measures as needed

Monitor BP & urine output

Urgent Blood Tests
FBC / clotting screen / fibrinogen / U+E / LFT/ G+S

Mild bleeding

Local haemostatic measures

Consider tranexamic acid 1g orally (excluding GI bleeds)

Delay next dose of rivaroxaban/apixaban

Moderate-to-severe* and life-threatening bleeding &/or uncontrollable bleed

Refer to Massive Haemorrhage Protocol

For life-threatening GI BLEED:
antidote - andexanet alfa
(See table on page 2 for dosing and administration guidance)

Must be discussed with gastroenterology consultant/gastroenterology surgeon and haematology consultant prior to use

Half-life (can be prolonged in severe renal impairment):
- rivaroxaban 5-13 hours
- apixaban 12 hours

N.B. the clotting screen may still be abnormal following reversal. Consult Haematology if concerns.

Tranexamic acid: see master stock list for locations.

Andexanet alfa (ondexxya) is stored in the emergency/out of hours mediwell located on C21.

Key
* Hb drop ≥ 2.0g/L or bleeding in critical site

The **recommended dosage** of andexanet alfa (Ondexxya) is based on:

- The specific FXa inhibitor,
- The dose of the DOAC the pt is taking at the time of anticoagulation reversal,
- Time since the patient's last dose of FXa inhibitor,
- Creatinine clearance – which will influence the half-lives of the FXa inhibitor

Each vial contains 200mg of andexanet alfa

Reconstitution: Each vial must be reconstituted with 20ml water for injection. Use the same number of 20ml syringes (equipped with 20-gauge needle or larger) as vials of andexanet alfa required.

Administration: To administer bolus and continuous infusion via syringe pump, prepare the bolus and continuous infusion in separate large volume syringes (50ml or larger).
For high dose bolus and continuous infusion, the doses will need to be separated into additional syringes (2 syringes each for bolus and continuous infusion).
A 0.2 or 0.22micron in-line polyethersulfone (PES) filter or equivalent low protein binding filter must be used.

Table 1:

Fxa inhibitor	**Dose**	**Time since last dose**		
		<8hours	≥8hours	Unknown
Apixaban	≤5mg	LOW	LOW	LOW
	>5mg	HIGH	LOW	HIGH
	Unknown	HIGH	LOW	HIGH
Rivaroxaban	≤10mg	LOW	LOW	LOW
	>10mg	HIGH	LOW	HIGH
	Unknown	HIGH	LOW	HIGH

Table 2:

	Initial IV bolus	**Continuous IV infusion**	**Total number of 200mg vials needed**
LOW DOSE	400mg over approx. 15minutes at a rate of 30mg/min	4mg/min for 120 minutes (480mg)	5
HIGH DOSE	800mg over approx. 30 minutes at a rate of 30mg/min	8mg/min for 120 minutes (960mg)	9

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Management of Dabigatran Associated Bleeding

Consider giving activated charcoal orally, if last dose ingested <2 hours ago

Start resuscitation measures as needed

Monitor BP & urine output

Urgent Blood Tests
FBC / clotting screen / fibrinogen / U+E / LFT/ G+S/TT

Mild bleeding

Local haemostatic measures

Consider tranexamic acid 1g orally (excluding GI bleeds)

Delay next dose of dabigatran

Moderate-to-severe* and life-threatening bleeding &/or uncontrollable bleed

Refer to Massive Haemorrhage Protocol

Antidote
Idarucizumab administered as 2 consecutive 2.5g IV boluses or infusions. See table on page 2

Must be discussed with consultant haematologist prior to use (and a gastroenterology consultant/surgeon if for GI bleed)

Half-life (can be prolonged in moderate to severe renal impairment) of dabigatran 12-14 hours.

-

N.B. the clotting screen may still be abnormal following reversal. Consult Haematology if concerns.

Tranexamic acid:
see master stock list for locations.

Idarucizumab is stored in the following locations:
Emergency Department &
Emergency Drug Cupboard.

Key
* Hb drop ≥ 2.0g/L or bleeding into critical site

Idarucizumab (Praxbind)

Formulation	2.5g/50mL ready to use solution for injection/infusion
Dose	5g
Administration	IV as two consecutive 2.5g infusions over 5-10mins Or IV as two consecutive 2.5g IV bolus injections
Administration of a second 5g dose may be considered in the following situations after consultation with oncall haematologist: • Recurrence of clinically relevant bleeding together with prolonged clotting times • If potential re-bleeding would be life-threatening and prolonged clotting times are observed	
Restarting anticoagulation after idarucizumab administration	Dabigatran can be re-initiated after 24 hrs if patient is clinically stable and adequate haemostasis achieved Other antithrombotic therapy (e.g., LMWH) can be started at any time if the patient is clinically stable and adequate haemostasis achieved

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Management of Edoxaban Associated Bleeding

Consider giving activated charcoal orally, if last dose ingested <2 hours ago

Start resuscitation measures as needed

Monitor BP & urine output

Urgent Blood Tests
FBC / clotting screen / fibrinogen / U+E / LFT/ G+S

Mild bleeding

Local haemostatic measures

Consider tranexamic acid 1g orally (excluding GI bleeds)

Delay next dose of edoxaban

Moderate-to-severe* and life-threatening bleeding &/or uncontrollable bleed

Refer to Massive Haemorrhage Protocol

- **Half-life** (can be prolonged in severe renal impairment) of edoxaban 10-14 hours

N.B. the clotting screen may still be abnormal following reversal. Consult Haematology if concerns.

Tranexamic acid: see master stock list for locations.

Key
* Hb drop ≥ 2.0g/L or bleeding into critical site

4.0 Equipment Required

None required

5.0 Training

This guideline will be available on the Trust intranet

6.0 Financial Risk Assessment

1	Does the implementation of this document require any additional Capital resources	No
2	Does the implementation of this document require additional revenue resources	No
3	Does the implementation of this document require additional manpower	No
4	Does the implementation of this document release any manpower costs through a change in practice	No
5	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programs or allocated training times for staff.	No
	Other comments	

7.0 Equality Impact Assessment

Not applicable

8.0 Maintenance

The clinical lead for cardiac services and the haematology representative on the VTE Group will ensure the document is reviewed at least every 3 years.

9.0 Communication and Training

This information will be disseminated to all relevant departments

10.0 Audit Process

Criterion	Lead	Monitoring method	Frequency	Evaluation
Monitor anticoagulation related adverse events	VTE Nurse	Datix incident reports	Monthly	VTE Group
Monitor Andexanet alfa usage	VTE Group pharmacist	Via Ascribe log view system	Quarterly	VTE Group

11.0 References –

1. Medicines.org.uk. 2021. *Ondexxya 200 mg powder for solution for infusion - Summary of Product Characteristics (SmPC) - (emc)*
2. Nice.org.uk. 2021. *Overview | Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban | Guidance | NICE*. [online]
3. Hunt B, Allard S, Keeling D, Norfolk D, Stanworth S, Pendry K. A practical guideline for the haematological management of major haemorrhage. British Journal of Haematology. 2015;170(6):788-803.
4. Medicines.org.uk. 2020. *Praxbind 2.5g/50 mL solution for injection/infusion - Summary of Product Characteristics (SmPC) - (emc)*
5. Nice.org.uk. 2016. *Evidence summary | Reversal of the anticoagulant effect of dabigatran: idarucizumab NICE*. [online]
6. Medicines.org.uk. 2020 Lixiana 60mg Film-Coated Tablets - *Summary of Product Characteristics (SmPC) - (emc)*

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Part A - Document Control

Procedure/ Guidelines number and version 1.0	Title of Procedure/Guidelines **Management of direct oral anticoagulant (DOAC) associated bleeding**	**Status:** Final		**Author: Cardiac Services Pharmacist** **For Trust-wide Procedures and Guidelines Chief Officer Sponsor:** **Chief Medical Officer**
Version / Amendment History	Version	Date	Author	Reason
	1.0	November 2022	Cardiac Services Pharmacist	Introduction of Guideline
Intended Recipients: All medical, nursing, and pharmacy staff				
Consultation Group / Role Titles and Date: VTE Group, Blood transfusion team, Consultant clinical haematologist blood products lead, Division 1 clinical director, Surgical nurse practitioners, Gastroenterology clinical director, Acute medicine consultant, Haematology principle clinical scientist				
Name and date of group where reviewed	Venous Thromboembolism Group 19/7/2022 Trust Policy Group – November 2022			
Name and date of final approval committee (if trust-wide document)/ Directorate or other locally approved committee (if local document)	Medicines Management Group 6/9/2022 Trust Management Committee – November 2022			
Date of Procedure/Guidelines issue	December 2022			
Review Date and Frequency (standard review frequency is 3 yearly unless otherwise indicated – see section 3.8.1 of Attachment 1)	November 2025			

Training and Dissemination: No training required. Details of new guideline to disseminated via Trust Brief, e-mail information of guideline to key stake holders i.e. clinical directors, matrons, stakeholders contacted during	
Publishing Requirements: Can this document be published on the Trust's public page: **Yes**	
To be read in conjunction with: Guideline for the Management of Massive Blood Loss in Adults	
Initial Equality Impact Assessment: N/A	
Contact for Review	Cardiac Services Lead Pharmacist
Monitoring arrangements	Annual andexanet alfa and idarucizumab usage. VTE Group to receive data
Document summary/key issues covered. This document provides guidance for the management of minor, moderate-to-severe, and life-threatening bleeds in patients receiving rivaroxaban or apixaban; and directs staff towards the location of the reversal agent, providing clear instructions on how to reconstitute and administer it.	
Key words for intranet searching purposes	Rivaroxaban Apixaban Edoxaban Dabigatran Direct Oral Anticoagulant Reversal Haemorrhage Bleed Andexanet alfa Ondexxya Idarucizumab

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(Part B) **Ratification Assurance Statement**

Name of document: Management of Edoxaban associated bleeding

Name of author: Liam Cullen **Job Title: Cardiac services pharmacist**

I, the above named author confirm that:

- The Strategy/Policy/Procedure/Guidelines (please delete) presented for ratification meet all legislative, best practice and other guidance issued and known to me at the time of development of the said document.
- I am not aware of any omissions to the said document, and I will bring to the attention of the Executive Director any information which may affect the validity of the document presented as soon as this becomes known.
- The document meets the requirements as outlined in the document entitled Governance of Trust-wide Strategy/Policy/Procedure/Guidelines and Local Procedure and Guidelines(OP01).
- The document meets the requirements of the NHSLA Risk Management Standards to achieve as a minimum level 2 compliance, where applicable.
- I have undertaken appropriate and thorough consultation on this document and I have detailed the names of those individuals who responded as part of the consultation within the document. I have also fed back to responders to the consultation on the changes made to the document following consultation.
- I will send the document and signed ratification checklist to the Policy Management Officer for publication at my earliest opportunity following ratification.
- I will keep this document under review and ensure that it is reviewed prior to the review date.

Signature of Author:

Date: 19/8/2022

Name of Person Ratifying this document (Chief Officer or Nominee):
Job Title: CMO
Signature:

Dr. B. C. McKaig
Consultant
GMC: 3275948

- I, the named Chief Officer (or their nominee) am responsible for the overall good governance and management of this document including its timely review and updates and confirming a new author should the current post-holder/author change.

To the person approving this document:

Please ensure this page has been completed correctly, then print, sign and email this page only to: The Policy Management Officer

Written by Liam Cullen
Approved by VTE committee: 19/07/2022

Review date: 19/07/2024

IMPLEMENTATION PLAN

Procedure/Guidelines number and version Version 1.0	**Title of Procedure/Guidelines** Management of direct oral anticoagulant (DOAC) associated bleeding	
Reviewing Group	VTE Group	**Date reviewed: 19.7.22**
Implementation lead: Mr Hart		

Implementation Issue to be considered (add additional issues where necessary)	**Action Summary**	**Action lead / s (Timescale for completion)**
Strategy; **Consider** (if appropriate) 1. Development of a pocket guide of strategy aims for staff 2. Include responsibilities of staff in relation to strategy in pocket guide.	N/A	
Training; Consider 1. Mandatory training approval process 2. Completion of mandatory training form	N/A	
Development of Forms, leaflets etc.; Consider 1. Any forms developed for use and retention within the clinical record **MUST** be approved by Health Records Group prior to roll out. 2. Type, quantity required, where they will be kept / accessed/stored when completed	N/A	
Procedure/Guidelines communication; Consider 1. Key communication messages from the policy / procedure, who to and how?	N/A	
Financial cost implementation Consider Business case development	Nil	
Other specific issues / actions as required e.g. Risks of failure to implement, gaps or barriers to implementation	Nil	