Worcestershire Acute Hospitals NHS Trust

Use of Andexanet Alfa for Reversing Anticoagulation from Apixaban or Rivaroxaban

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

This guideline is for use by the following staff groups:
All staff caring for or managing patients taking apixaban or rivaroxaban.

Introduction

Apixaban and rivaroxaban are direct oral anti-coagulants (DOACs) and may require rapid reversal in potentially life-threatening bleeding. Andexanet alfa (Ondexxya) is available for reversal of apixaban and rivaroxaban in adults with life-threatening or uncontrolled bleeding of the gastrointestinal tract.

This guideline outlines how Ondexxya should be prescribed, supplied and administered.

Lead Clinician(s)

Harriet Cook	Lead Pharmacist- Haematology
Keith Hinton	Clinical Team Lead Pharmacist – Surgery and Critical Care
Dr. David Davies	Haematology Consultant
Approved by Trust Thrombosis Committee on:	8th April 2022
Ratified by Medicines Safety Committee on:	14th August 2024
Review Date:	14th August 2026

This is the most current document and should be used until a revised version is in place

Key amendments to this guideline

Date	Amendment	Approved by:
April 2022	New document approved	Trust Thrombosis Committee/ MSC
July 2024	AH EDC location added to 'request for use.' Lead Clinician(s) updated.	Haematology governance / MSC
14th August, 2024	Document re-approved	Haematology Governance/MSC

Use of Andexanet Alfa for Reversing Anti-coagulation from Apixaban or Rivaroxaban

Indication

Andexanet is a specific reversal agent for apixaban or rivaroxaban (a direct factor Xa inhibitor) when reversal of anticoagulation is required for adults with life-threatening or uncontrolled bleeding **IF the bleeding is in the GI tract**. It is a recombinant form of human factor Xa protein which lacks enzyme activity, and binds directly to factor Xa with high affinity to remove anti-coagulant effects of apixaban/rivaroxaban. Maximal reversal is achieved quickly within 2 minutes of completing the bolus administration, followed by a continuous infusion to sustain anti-factor Xa activity. Bleeding from any other parts of the body is not supported unless part of a formal clinical trial [NICE TA697]

The acute major bleeding from the gastrointestinal tract must have one or more of the following features:

- Potentially life-threatening bleeding with signs or symptoms of haemodynamic compromise (e.g. severe hypotension, poor skin perfusion, mental confusion or low cardiac output that could otherwise not be explained.)
- Bleeding associated with a decrease in the haemoglobin level of at least 20g/L (or a haemoglobin of <80g/L if no baseline haemoglobin is available.)
- The last dose of Apixaban or Rivaroxaban must be <48 hours ago

Request for use

Approval for use MUST be obtained by a consultant haematologist and documented in the patients notes.

A Blueteq funding application form must be completed. Paper copies of the Blueteq form will be available with the supply. These must be completed at the time of use and handed to a pharmacist to ensure that the on line authorisation application is completed.

12 vials of Ondexxya are stored in the Emergency Drug Cupboard (EDC) at both the Worcestershire Royal Hospital (WRH) and the Alexandra Hospital (AH) sites. Ondexxya should be stored at 2°C to 8°C and is therefore stored in a fridge.

Within working hours, contact pharmacy for a supply to be made. Outside of working hours, supply can be obtained directly from the EDC. It is essential that the patient's details and ward location are recorded in the pharmacy folder located in the EDC to ensure that pharmacy can book out and replenish stock.

Ondexxya should be used immediately. If any vials are not used, they MUST be returned to the fridge of the EDC or pharmacy dispensary as soon as possible. Ondexxya is a very high cost (>£2000 per vial) and high risk medicine and should not be stored on the ward.

Dosing and administration

- Dosing is recommended based on the dose of apixaban or rivaroxaban that the patient is taking at the time of anticoagulation reversal, as well as on the time since the patient's last dose.

- The regimen is either a **LOW dose** (initial 400mg then 480mg infusion – 5 vials in total) or **HIGH dose** (initial 800mg then 960mg infusion – 9 vials in total). See the table below

Andexanet alfa dosing recommendations				
FXa inhibitor	**Last individual dose**	**Time since last individual dose**		
		< 8 hours	**≥ 8 hours**	**Unknown**
Apixaban	≤ 5 mg	400mg (40ml) over 15mins then 480mg (48ml) over 2hours		
	> 5 mg or unknown	800mg (80ml) over 30mins then 960mg (96ml) over 2 hours	400mg (40ml) over 15mins then 480mg (48ml) over 2hours	800mg (80ml) over 30mins then 960mg (96ml) over 2 hours
Rivaroxaban	≤ 10 mg	400mg (40ml) over 15mins then 480mg (48ml) over 2hours		
	> 10 mg or unknown	800mg (80ml) over 30mins then 960mg (96ml) over 2 hours	400mg (40ml) over 15mins then 480mg (48ml) over 2hours	800mg (80ml) over 30mins then 960mg (96ml) over 2 hours

- Only one dose of andexanet alfa should be given per patient.

- No dose adjustment is required in elderly patients, renal or hepatic impairment. Ondexxya is contra-indicated in patients with known hypersensitivity to the active substance or product excipients or a known allergic reaction to hamster proteins.

- Ondexxya does not need to be brought to room temperature before reconstitution or administration to the patient. Prepare all vials for the complete dose by reconstituting each 200 mg vial with 20ml of water for injection ONLY and allow 3-5 minutes to dissolve. Gently swirl, **do not shake**, the vial.

- Once the reconstituted solution is clear, colourless or slightly yellow, withdraw into a 50ml or 60ml syringe. For the HIGH dose (800mg) use 2 syringes for both the bolus and infusion doses. Large volumes may be transferred to an empty PVC infusion bag (150mL or larger).

- A 0.22 micron in-line filter PES or equivalent low protein-binding filter should be used for IV administration (available with the drug supply).

Resumption of anticoagulant therapy should be considered as soon as medically appropriate, to avoid thromboembolic events, when the patient is clinically stable and adequate haemostasis achieved.

Ondexxya can be used in conjunction with standard haemostatic supportive measures. Safety has not been evaluated in patients who received prothrombin complex concentrates, recombinant factor VIIa, or whole blood within 7 days prior to the bleeding event. Pro-coagulant factor treatments (e.g. 3- or 4- factor prothrombin complex concentrate (PCC) / activated PCC, recombinant factor VIIa, fresh frozen plasma) and whole blood should be avoided unless absolutely required, due to lack of data in combination with these treatments.

Monitoring

Treatment monitoring should be based mainly on clinical parameters indicative of appropriate response (i.e. achievement of haemostasis), lack of efficacy (i.e. re-bleeding), and adverse events (i.e. thromboembolic events.) Treatment monitoring should not be based on anti-FXa-activity. These assays result in erroneously elevated anti-FXa levels, thereby causing a substantial underestimation of the reversal activity of andexanet alfa.

Side effects

Common side effects include back pain, cerebrovascular insufficiency, chest discomfort, cough, postural dizziness, dry mouth, dyspnoea, feeling hot, fever, flushing, gastrointestinal discomfort, headache, hyperhidrosis, muscle spasms, nausea, palpitations, peripheral coldness, skin reactions and altered taste.

Uncommon side effects include cardiac arrest, embolism and thrombosis, iliac artery occlusion and myocardial infarction.

Monitoring Tool
This should include realistic goals, timeframes and measurable outcomes.

How will monitoring be carried out?

Who will monitor compliance with the guideline?

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
	Andexanet alfa shall only be used for the indication outlined in this policy	Completed Blueteq application form	Continuous.	Pharmacy (high cost medicine lead Pharmacist	Trust Thrombosis Committee (via haematologist/pharmacy representative)	As directed by use.

References

- January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation* 2019;**140**(2):e125-151

- NICE. May 2021. TA697: Andexanet alfa for reversing anticoagulation from apixaban or rivaroxaban. Available from: https://www.nice.org.uk/guidance/ta697 (Accessed 7th May 2021)

- Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with atrial fibrillation. *Eur HeartJ.* 2018;**39**(16):1330-1393.

- Tomaselli GF, Mahaffey KW, Cuker A, et al. 2020 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants. *JACC* 2020;**76**(5):594-622.

- WAHT-HAE-002. Warfarin and other oral anticoagulants guidelines and procedures.

- Summary of Product Characteristics. Ondexxya 200mg powder for solution for infusion. Apr 2021. Accessed at www.medicines.org.uk 3/2/22

Contribution List

This key document has been circulated to the following individuals for consultation;

Designation

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Trust Thrombosis Committee
Haematology and Palliative Care Governance

Supporting Document 1 - Equality Impact Assessment Tool

Appendix- 1 Equality Impact Assessment Tool

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

Herefordshire & Worcestershire STP - Equality Impact Assessment (EIA) Form
Please read EIA guidelines when completing this form

Section 1 - Name of Organisation (please tick)

Herefordshire & Worcestershire STP		Herefordshire Council		Herefordshire CCG	
Worcestershire Acute Hospitals NHS Trust	x	Worcestershire County Council		Worcestershire CCGs	
Worcestershire Health and Care NHS Trust		Wye Valley NHS Trust		Other (please state)	

Name of Lead for Activity	

Details of individuals completing this assessment	**Name**	**Job title**	**e-mail contact**
	Harriet Cook	Lead Pharmacist - Haematology	Harriet.cook4@nhs.net
Date assessment completed	**25/07/2024**		

Section 2

Activity being assessed (e.g. policy/procedure, document, service redesign, policy, strategy etc.)	**Title:** Use of Andexanet Alfa for Reversing Anticoagulation from Apixaban or Rivaroxaban			
What is the aim, purpose and/or intended outcomes of this Activity?	See body of document			
Who will be affected by the development & implementation of this activity?	❑ x ❑ ❑	Service User Patient Carers Visitors	❑ ❑ ❑ ❑	Staff Communities Other _____
Is this:	x Review of an existing activity ❑ New activity ❑ Planning to withdraw or reduce a service, activity or presence?			
What information and evidence have you reviewed to help inform this assessment? (Please name sources,	See body of document			

eg demographic information for patients / services / staff groups affected, complaints etc.	
Summary of engagement or consultation undertaken (e.g. who and how have you engaged with, or why do you believe this is not required)	See body of document
Summary of relevant findings	See body of document

Section 3

Please consider the potential impact of this activity (during development & implementation) on each of the equality groups outlined below. **Please tick one or more impact box below for each Equality Group and explain your rationale**. Please note it is possible for the potential impact to be both positive and negative within the same equality group and this should be recorded. Remember to consider the impact on e.g. staff, public, patients, carers etc. in these equality groups.

Equality Group	Potential positive impact	Potential neutral impact	Potential negative impact	Please explain your reasons for any potential positive, neutral or negative impact identified
Age		x		
Disability		x		
Gender Reassignment		x		
Marriage & Civil Partnerships		x		
Pregnancy & Maternity		x		
Race including Traveling Communities		x		
Religion & Belief		x		
Sex		x		
Sexual Orientation		x		
Other Vulnerable and Disadvantaged Groups (e.g. carers; care leavers; homeless; Social/Economic deprivation, travelling communities etc.)		x		
Health Inequalities (any preventable, unfair & unjust differences in health status between groups, populations or individuals that arise from the unequal distribution of social, environmental & economic conditions within societies)		x		

Section 4

What actions will you take to mitigate any potential negative impacts?	Risk identified	Actions required to reduce / eliminate negative impact	Who will lead on the action?	Timeframe
	N/A	.		
How will you monitor these actions?	See body of document			
When will you review this EIA? (e.g in a service redesign, this EIA should be revisited regularly throughout the design & implementation)	See body of document			

Section 5 - Please read and agree to the following Equality Statement

1. Equality Statement

1.1. All public bodies have a statutory duty under the Equality Act 2010 to set out arrangements to assess and consult on how their policies and functions impact on the 9 protected characteristics: Age; Disability; Gender Reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual Orientation

1.2. Our Organisations will challenge discrimination, promote equality, respect human rights, and aims to design and implement services, policies and measures that meet the diverse needs of our service, and population, ensuring that none are placed at a disadvantage over others.

1.3. All staff are expected to deliver services and provide services and care in a manner which respects the individuality of service users, patients, carer's etc, and as such treat them and members of the workforce respectfully, paying due regard to the 9 protected characteristics.

Signature of person completing EIA	
Date signed	25/07/2024
Comments:	
Signature of person the Leader Person for this activity	
Date signed	
Comments:	

Supporting Document 2 – Financial Impact Assessment

To be completed by the key document author and attached to key document when submitted to the appropriate committee for consideration and approval.

	Title of document:	Yes/No
1.	Does the implementation of this document require any additional Capital resources	No
2.	Does the implementation of this document require additional revenue	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 programmes or allocated training times for staff	No
	Other comments:	

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval.