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Andexanet Alfa for reversal of Apixaban and Rivaroxaban in adults with acute major gastro-intestinal bleeding

Andexanet Alfa is recommended by NICE (TA 697, May 2021) as an option for reversing anticoagulation from apixaban or rivaroxaban in adults with life-threatening or uncontrolled bleeding only if:

- **the bleed is in the gastrointestinal tract**

Acute major gastrointestinal bleeding in this clinical context is defined by the presence of one or more of the following features:

- **Acute overt bleeding with haemodynamic compromise (e.g severe hypotension, poor skin perfusion, mental confusion, or low cardiac output that could not otherwise be explained)**
- **Acute overt bleeding associated with a decrease in haemoglobin of at least 20 g/L or a haemoglobin level of 80 g/L or less if no baseline haemoglobin level was available**

A joint decision to approve the use of Andexanet Alfa in this clinical context must be made by the attending Medical Registrar and the Consultant Gastroenterologist on call. Andexanet alpha can then be obtained directly from the transfusion labs (please phone ahead) 9am-5.30pm.

RSCH transfusion lab: ext 64577/ 64071	**PRH** transfusion lab: ext 68218/ 68219
WGH transfusion lab: ext 85785	**SRH** transfusion lab: ext 33589

Out of hours BLEEP transfusion on: 8286 (RSCH), 6103 (PRH), 1273 (WGH) or 6070 (SRH)

This drug is <u>NOT</u> NICE approved for bleeding in sites other than the gastrointestinal tract (e.g. Intracranial haemorrhage); or for reversal before emergency surgery; or for any edoxaban related bleeding. <u>Andexanet Alfa will not be given in these circumstances</u>.

<u>Contraindications</u>:
Known allergic reaction to hamster proteins
Hypersensitivity to the active substance or to any other excipients (emc uk andexanet alfa)

Author Clare Proudfoot, Anticoagulation Pharmacist July 2021, approved by Dr B Marson, Cons Haematologist RSCH/PRH and Dr R Cartwright Cons Haematologist WGH/SRH, approved by Medicines Governance Group 10/8/21, Review 10/8/23 or as NICE guidance changes. (Version 2 updated 15/11/22)

Special warnings and precautions for use:

See emc uk Andexanet Alfa precautions and limitations for use for current guidance which includes but is not limited to the following:

- Andexanet Alfa should not be used prior to heparinisation as it has been reported to cause unresponsiveness to heparin.
- Anti-Xa levels should not be used to monitor activity as they can be falsely elevated.

See Safety information from MHRA/CHM regarding Andaxanet Alfa for more information.

Dosing

There are two dosing regimens, Low Dose (Option A) and High Dose (Option B), depending on last dose and time of last dose

Factor Xa inhibitor DOAC	Last Dose	Time since last dose		
		<8 hours	≥8 hours	Unknown
Apixaban	≤ 5mg	Low dose	Low dose	Low dose
	>5mg or unknown	High dose	Low dose	High dose
Rivaroxaban	≤10mg	Low dose	Low dose	Low dose
	>10mg or unknown	High dose	Low dose	High dose

	Initial IV bolus	Continuous IV infusion	Total number of (200mg) vials needed
Low dose (Option A)	400 mg at a target rate of 30 mg/min	4 mg/min for 120 minutes (480 mg)	5
High dose (Option B)	800 mg at a target rate of 30 mg/min	8 mg/min for 120 minutes (960 mg)	9

Administration:

For details on reconstitution and administration, see SPC Andexanet Alfa

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Reversal of apixaban and rivaroxaban in ICH and other major bleeds

NICE have NOT recommended routine use of this agent in ICH (only in research as part of a trial mandated by the regulator) **or in "other major bleeds"** due to the limitations of the clinical evidence and uncertainties in the cost effectiveness estimates of Andexanet Alfa. The average cost of treatment is £15,000 per patient. For more detailed information on the NICE committee's decision making process including evidence relating to ICH and "other major bleeds" please see full guidance NICE TA 697 Andexanet Alfa

Resuming anticoagulation after reversal of apixaban or rivaroxaban

Once the patient is haemo-dynamically stable post endoscopy, consider restarting prophylactic low molecular weight heparin, titrating up to treatment dose only if required.

Dose and duration of LMWH is determined by the indication for anticoagulation & bleeding versus thrombotic risk assessment.

Discussion with Haematology in this regard might help guide decision making.

Avoid returning to a DOAC acutely unless the underlying cause of bleeding has been successfully treated.

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