Use of Andexanet Alfa for reversal of Rivaroxaban and Apixaban in severe/life threatening Gastrointestinal Bleeding in adult patients

Andexanet Alfa is a specific reversal agent for the Factor Xa inhibitors apixaban and rivaroxaban.

NICE TA 697 (May 2021) approved Andexanet for reversal of apixaban or rivaroxaban ONLY in the event of life-threatening or uncontrolled Gastrointestinal bleeding.

- Andexanet Alfa has a rapid onset of action and a short half-life.
- The reversal effect will last 4 hours from the start of the bolus. This can facilitate endoscopic/surgical/ radiological intervention.
- 4 hours after the start of bolus the full anticoagulant effect of rivaroxaban and apixaban will be present and the patient will be fully anticoagulated.
- After discontinuation Rivaroxaban and Apixaban anticoagulant effect will last:
  48hours if GFR >30 mL/min. 72hours if GFR 15-30mL/min.
- Andexanet should not be administered without prior discussion with Haematology.
  Contact Coagulation SpR Bleep 5886 or on call Haematology SpR out of hours.
- Andexanet Alfa is kept in the fridge of the emergency drug cupboard in pharmacy.
  - A "Low dose" (5 vial pack) or "High dose" (9 vial pack) is available, each with 2 *250ml Easyflex plus bags and filters.

Andexanet has **not** been shown to be effective for, and is not indicated for, the treatment of bleeding related to any Factor Xa inhibitor other than rivaroxaban or apixaban. It will not reverse the effects of non-Factor Xa inhibitors.

Dosing of Andexanet Alfa: Either prescribed as high or low dose depending on the strength and timing of last dose of Factor Xa inhibitor.

DOAC	Last dose strength	Timing of last dose before Andexanet Alfa initiation	
		< 8 hours or unknown	≥ 8 hours
Apixaban	≤ 5 mg	Low dose	Low dose
	> 5 mg/ Unknown	High dose	
Rivaroxaban	≤ 10 mg	Low dose	Low dose
	> 10 mg/ Unknown	High dose	

Prescription - Ensure DOAC has been discontinued.

	Initial intravenous bolus	Continuous intravenous infusion	No. of vials
Low dose	400 mg over 15minutes (rate 30mg/min)	480mg over 120 minutes (rate 4mg/min)	5
High dose	800 mg over 30 minutes (rate 30mg/min)	960mg over 120 minutes (rate 8mg/min)	9

Reconstitution

DATE & START TIME	INFUSION FLUID TYPE / STRENGTH	VOLUME	ROUTE	MEDICINE ADDED APPROVED NAME	DOSE	INFUSION RATE OR DURATION	PRESCRIBER'S SIGNATURE	PHARM
21/2/22	High Dose - Bolus Example		IV	ANDEXANET ALFA	800mg	30 mins	Bleep No. 5886	
Batch No.	Device No.			*Prescriber to initial if continuous →				
21/2/22	High Dose - Infusion Example		IV	ANDEXANET ALFA	960mg	120 mins	Bleep No. 5886	
Batch No.	Device No.			*Prescriber to initial if continuous →				
Batch No.	Device No.			*Prescriber to initial if continuous →			Bleep No.	
21/2/22	low Dose - Bolus Example		IV	ANDEXANET ALFA	400mg	15 mins	Bleep No. 5886	
Batch No.	Device No.			*Prescriber to initial if continuous →				
21/2/22	low Dose - Infusion Example		IV	ANDEXANET ALFA	480mg	120mins	Bleep No. 5886	
Batch No.	Device No.			*Prescriber to initial if continuous →				

The following are needed before starting reconstitution:

• Calculated number of vials required

• Same number of 20 mL (or larger) syringes equipped with a 20 gauge (or larger) needle.

• Intravenous 250ml Easyflex Plus bags (2) -provided.

• Water for injections.

• 0.2 micron in-line filters-provided.

Andexanet alfa does not need to be brought to room temperature before reconstitution or administration to the patient. Aseptic technique during the reconstitution procedure should be used

Each vial is reconstituted according to the following instructions:

1. Remove the flip-top from each vial.

2. Wipe the rubber stopper of each vial with an alcohol swab.

3. Using a 20 mL (or larger) syringe and a 20 gauge (or larger) needle, withdraw 20 mL of water for injections.

4. Insert the syringe needle through the centre of the rubber stopper.

5. Push the plunger down to slowly inject the 20 mL of water for injections into the vial, directing the stream toward the inside wall of the vial to minimise foaming.

6. Gently swirl each vial, until all of the powder is completely dissolved. DO NOT SHAKE the vials, as this can lead to foaming. The dissolution time for each vial is approximately three to five minutes.

7. The reconstituted solution (10mg/ml) should be inspected for particulate matter and/or discolouration prior to administration. Do not use if opaque particles or discolouration are present.

8. For the most efficient reconstitution of the needed dose, and to minimise errors, inject each vial needed with 20 mL of water for injections before proceeding to the next step.

9. Use within eight hours after reconstitution when stored at room temperature

Administration using intravenous bags

1. Once all required vials are reconstituted, withdraw the reconstituted solution (10mg/ml) from each vial, using the large volume (50 mL or larger) syringe equipped with a 20 gauge (or larger) needle.

2. Transfer the reconstituted solution from the syringe into the provided Easyflex Plus 250ml bag. There is no need to dilute further.

3. Repeat steps 1 and 2 as necessary to transfer the complete volume of the bolus and the infusion into empty IV bags.

4. It is recommended that the bolus and infusion be split into two separate bags to ensure the correct administration rate.

5. Attach ancillary equipment (i.e. 0.2 micron in-line filter, IV pump) in preparation for administration.

6. Administer the reconstituted solution at the appropriate rate.