Andexanet

CAUTION: High Administration Risk Rating

Form & Storage	Powder for concentrate for solution for infusion. Each vial contains 200mg andexanet alfa	Store in a refrigerator (2°C - 8°C) in the original package to protect from light.

Reconstitution

- Add 20 mL water for injections, using a syringe with a 21-25 gauge needle, directing the liquid down the wall of the vial to avoid excessive foaming.
- Gently swirl the vial for at least 15 seconds. Do not shake vigorously or invert.
- Leave for 3- 5 minutes to allow foam to settle; the vial can be gently swirled occasionally during this time.
- **Low dose**: Reconstitute 5 vials
- **High Dose**: Reconstitute 9 vials
- The reconstituted solution is clear, colourless or slightly yellow.
- Reconstituted solution contains 200mg in 20mL (10mg/mL)

Compatibility & Stability

From a microbiological point of view, once reconstituted, the product should be used immediately.

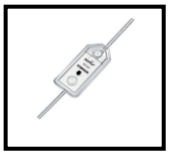
Administration Equipment

1) Syringe Driver

Administer using a Syringe Driver **capable of max rate 160mL/hr.**
All pumps in ED,GITU, CUMH are suitable, other wards/areas including CRC should request the syringe driver pump from the pump library
-Ring **08703523112**

2) 0.2 Micron in-line Filter

Attach a **0.2micron filter** to the end of the administration set, before it is connected to the patient. This filter (pictured) **B Braun Sterifix® 0.2µ Ref 4099303** is kept in Infusion unit, ED & 3A.



Administration

- **IV loading dose** followed by **maintenance dose** using an infusion pump syringe driver
- Withdraw the reconstituted solution from each vial into the large-volume (50mL) syringes (equipped with a 20-gauge or larger needle)
- It is recommended to split the solution intended for loading (bolus) and maintenance (continuous infusion) to ensure the correct administration rate

Low Dose – Reconstitute 5 x 200mg vials

Administration	Dose	Volume	Rate	Time to administer
IV Bolus (Loading)	400mg	40mL	160 mL/hr	15 min
IV Infusion (Maintenance)	480mg	48mL	24 mL/hr	120 min

High Dose – Reconstitute 9 x 200mg vials

Note: for high dose therapy, two syringes will be needed for the loading dose and two for the maintenance dose

Administration	Dose	Volume	Rate	Time to administer
IV Bolus (Loading)	800mg	80mL	160 mL/hr	30 min
IV Infusion (Maintenance)	960mg	96mL	48 mL/hr	120 min

This information has been summarised to act as a guide for those administering IV medication. The monograph should be used in conjunction with the drug data sheet and BNF for information on dose, adverse effects, cautions and contra-indications.
Further information is available from Pharmacy on 22146 or 22542

<table>
<tr><td>Monitoring</td><td>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).</td></tr>
<tr><td>Adverse Drug Reactions</td><td>Common: Back pain; cerebrovascular insufficiency; chest discomfort; cough; dizziness postural; dry mouth; dyspnoea; feeling hot; fever; flushing; gastrointestinal discomfort; headache; hyperhidrosis; muscle spasms; nausea; palpitations; peripheral coldness; skin reactions; taste altered
Uncommon: Cardiac arrest; embolism and thrombosis; iliac artery occlusion; myocardial infarction</td></tr>
<tr><td>Dosing</td><td>

There are dosing regimens, depending on the specific direct factor Xa (FXa) inhibitor, last individual dose of FXa inhibitor and time since last FXa inhibitor dose

<table>
<tr><td colspan="4">Size and timing of last dose of apixaban or rivaroxaban taken determines whether high or low dose regimen is used.</td></tr>
<tr><td rowspan="2">FXa inhibitor</td><td rowspan="2">Last dose</td><td colspan="2">Timing of last dose before andexanet administration</td></tr>
<tr><td>< 8 hours or unknown</td><td>≥ 8 hours*</td></tr>
<tr><td rowspan="2">Apixaban</td><td>≤5mg</td><td>Low dose</td><td rowspan="2">Low dose</td></tr>
<tr><td>>5mg or unknown</td><td>High dose</td></tr>
<tr><td rowspan="2">Rivaroxaban</td><td>≤10 mg</td><td>Low dose</td><td rowspan="2">Low dose</td></tr>
<tr><td>>10 mg or unknown</td><td>High dose</td></tr>
<tr><td colspan="4">*Only patients who had acute major bleeding within 18 hours after administration of an FXa inhibitor were included in studies. Therefore it may NOT be clinically appropriate to administer andexanet alfa in patients where administration of an FXa inhibitor is greater than 18 hours as benefit in this patient cohort has not been demonstrated.</td></tr>
</table>

For patients on edoxaban or patients needing reversal for emergency surgery, please discuss treatment options with CUH haematology team.

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<tr><td>Contraindications and Cautions</td><td>

Andexanet alfa is not suitable for pre-treatment of urgent surgery
Interaction with heparin: Use of andexanet prior to heparinization e.g. during surgery should be avoided as andexanet causes unresponsiveness to heparin
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.
Consider the use of PCC in patients on apixaban or rivaroxaban requiring reversal of anticoagulation where andexanet alfa is contra-indicated or not clinically appropriate. Refer to local guidance for management of acute bleeding in patients on anticoagulation.

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<tr><td>Restarting Anticoagulant</td><td>

Manufacturer advises to consider re-starting anticoagulant therapy as soon as medically appropriate to reduce the risk of thrombosis.

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Information provided relates to Ondexxya® manufactured by or Astra Zeneca.