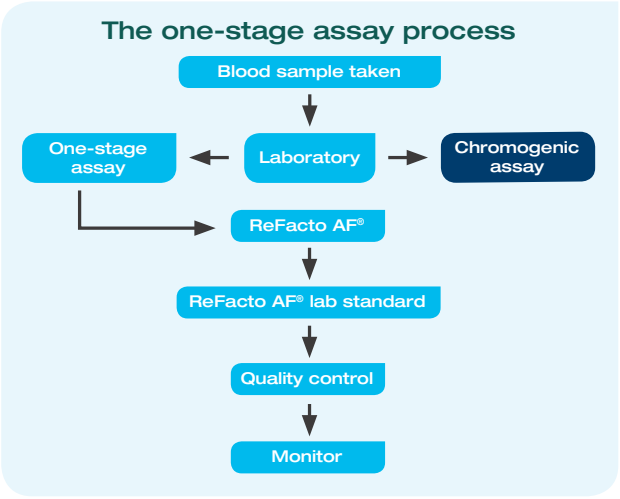
ReFacto AF®
Moroctocog alfa
(Recombinant Coagulation Factor VIII)

ReFacto AF® Laboratory Standard

When to use the ReFacto AF® Laboratory Standard



Considerations when monitoring treatment with ReFacto AF®

- When monitoring patients' factor VIII activity levels during treatment with ReFacto AF®, use of the chromogenic substrate assay is recommended[1]
- The chromogenic assay yields results that are higher than those observed with use of the one-stage clotting assay[1]

Consistent results regardless of assay type

- The use of a product-specific laboratory standard to correct for discrepancies between chromogenic and one-stage assay results has been validated in the literature[2]
- **The ReFacto AF® Laboratory Standard was created for use with the one-stage clotting assay (or the chromogenic assay), when testing plasma samples from patients receiving ReFacto AF®.** It was designed to be used exactly as you would use a normal (plasma-based) laboratory standard. The use of the standard allows for consistent assay results regardless of assay type

Important information

- **This Standard is to be used to measure ReFacto AF® levels and not for performing diagnostic FVIII tests. It should NOT be administered to patients. It is not intended for testing patients with normal levels of FVIII:C or patients receiving other FVIII concentrates other than ReFacto AF®**

References:

1. ReFacto AF® moroctocog alfa (recombinant coagulation factor VIII) Summary of Product Characteristics. https://www.medicines.org.uk/emc/product/7955/smpc
2. Ingerslev J, Jankowski MA, Weston SB, et al. Collaborative field study on the utility of a BDD factor VIII concentrate standard in the estimation of BDDr factor VIII:C activity in hemophilic plasma using one-stage clotting assays. *J Thromb Haemost.* 2004;2:632–8.

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How to prepare the ReFacto AF® Laboratory Standard

Step 1

- Reconstitute the ReFacto AF® Laboratory Standard at room temperature using 1.0 mL of sterile water
- After reconstitution, the vial contents should be transferred to a plastic tube with a stopper
- The reconstituted ReFacto AF® Laboratory Standard solution should be maintained at room temperature and then used within 2 hours*

Step 2

- The ReFacto AF® Laboratory Standard should be prediluted in factor VIII–deficient (haemophilic or artificially depleted) plasma containing normal functional levels of von Willebrand factor to yield a 1.0 IU/mL solution
- The prepared standard should be used once and discarded. DO NOT REFREEZE

Step 3

- The working ReFacto AF® Laboratory Standard solution can now be used to create a standard curve for analysis of plasma samples from patients treated with ReFacto AF®
- Once the standard curve is established, analysis of plasma samples from patients treated with ReFacto AF® may begin
- Discard all unused materials following universal precautions

* The reconstituted ReFacto AF® Laboratory Standard is stable for 2 hours
Unopened vials should be stored at -20°C
Do not use the vial if there is a lack of vacuum when opening

How to order the ReFacto AF® Laboratory Standard

Orders can be placed by e-mail:

AlgeteCustomerservice@pfizer.com

In order to finalise the shipment as soon as possible please include the following information in your request:

1. Contact name†
2. Shipping address
3. Specific delivery time
4. Telephone number†
5. E-mail address
6. Number of ReFacto AF® Laboratory Standard cartons requested (each carton contains 10 vials)
7. The Customs' Import broker name and contact information (If applicable)

†The contact name and telephone number you provide will be included on the shipment's paperwork

Prescribing information and adverse event reporting details are found on reverse

Pfizer Haemophilia

Prescribing Information

PRESCRIBING INFORMATION

Before prescribing ReFacto AF® please refer to full Summary of Product Characteristics.

ReFacto AF® powder and solvent for solution for injection.
ReFacto AF® powder and solvent for solution for injection in pre-filled syringe.
Moroctocog alfa (recombinant human coagulation factor VIII)
Presentations:
1. ReFacto AF 250 IU, 500 IU, 1000 IU and 2000 IU powder and solvent for solution for injection.
Each vial contains nominally 250, 500, 1000 or 2000 IU moroctocog alfa, supplied with a pre-filled syringe containing 4 ml sodium chloride 9 mg/ml (0.9%) solution for injection plus accessories for reconstitution and administration.

2. ReFacto AF 250 IU, 500 IU, 1000 IU, 2000 IU, 3000 IU powder and solvent for solution for injection in pre-filled syringe.
Each syringe contains nominally 250 IU, 500 IU, 1000 IU, 2000 IU or 3000 IU moroctocog alfa and 4 ml sodium chloride 9 mg/ml (0.9%) solution for injection plus accessories for reconstitution and administration.

Indications: Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).
Dosage and Administration: For adults and children of all ages including new-borns. Dose, frequency, and duration of treatment depend on the clinical situation and should be titrated according to the clinical response. Clinical studies did not include subjects aged 65 and over. In general, dose selection for an elderly patient should be individualised. Treatment should be initiated under the supervision of a physician experienced in the treatment of haemophilia A. In the presence of an inhibitor, higher doses or appropriate specific treatment may be required. Administration is by intravenous injection over several minutes. On demand treatment: Required dosage is determined using the following formula: Required units (IU) = body weight (kg) x desired factor VIII rise (% or IU/dl) x 0.5 (IU/kg per IU/dl), where 0.5 IU/kg per IU/dl represents the reciprocal of the recovery generally observed following infusions of factor VIII. For a guide to dosing in bleeding episodes and surgery refer to SPC section 4.2. For long-term prophylaxis against bleeding in patients with severe haemophilia A, the usual doses are 20 to 40 IU of factor VIII per kg body weight at intervals of 2 to 3 days. In some cases, especially in younger patients, shorter dosage intervals or higher doses may be necessary. Dosage adjustment for patients with renal or hepatic impairment has not been studied in clinical trials. The reconstituted product should be used immediately, or within 3 hours after reconstitution. Treatment monitoring: During the course of treatment, appropriate determination of factor VIII levels is advised to guide the dose to be administered and the frequency of repeated infusions. Individual patients may vary in their response to factor VIII, demonstrating different half-lives and recoveries. Dose based on bodyweight may require adjustment in underweight or overweight patients. In the case of major surgical interventions in particular, precise monitoring of the substitution therapy by means of coagulation analysis (plasma factor VIII activity) is indispensable. When monitoring patients' factor VIII activity levels during treatment with ReFacto AF, use of the chromogenic assay is recommended. When using an in vitro thromboplastin time (aPTT)-based one-stage clotting assay for determining factor VIII activity in patients' blood samples, plasma factor VIII activity results can be significantly affected by both the type of aPTT reagent and the reference standard used in the assay. Also there can be significant discrepancies between assay results obtained by aPTT-based one-stage clotting assay and the chromogenic assay. Typically, one-stage clotting assay results are 20-50% lower than the chromogenic substrate assay results. The ReFacto AF laboratory standard can be used to correct for this discrepancy (see section 5.2). This is of importance particularly when changing the laboratory and/or reagents used.
Contra-indications: Hypersensitivity to the active substance or to any of the excipients. Known allergic reaction to hamster proteins.
Precautions: Inform patients of the early signs of hypersensitivity reactions (including hives, generalised urticaria, tightness of the chest, wheezing, hypotension) and anaphylaxis. If symptoms of hypersensitivity occur, patients should be advised to discontinue use of the medicinal product immediately and contact their physician. Patients should be carefully monitored for the development of inhibitors by appropriate clinical observations and laboratory tests. The risk of developing inhibitors is correlated to the severity of the disease as well as the exposure to factor VIII, this risk being highest within the first 50 exposure days but continues throughout life although the risk is uncommon. The clinical relevance of inhibitor development will depend on the titre of the inhibitor, with low titre posing less of a risk of insufficient clinical response than high titre inhibitors. Lack of effect has been reported in clinical trials and in the post-marketing setting. Titrate and monitor individual dosing to ensure adequate therapeutic response. In patients with existing cardiovascular risk factors, substitution therapy with factor VIII may increase the cardiovascular risk. After reconstitution this medicinal product contains 1.27 mmol (29 mg) sodium per vial or pre-filled syringe, equivalent to 1.5% of the WHO recommended maximum daily intake (RDI) of 2 g sodium for an adult. Depending on body weight of the patient and posology of ReFacto AF, patients could receive multiple vials or pre-filled syringes. This should be taken into consideration if the patient is on a low salt diet. If a central venous access device (CVAD) is required, risk of CVAD-related complications including local infections, bacteraemia and catheter site thrombosis should be considered (see SPC section 4.8).
Traceability: In order to improve traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. Patients can affix one of the peel-off labels found on the vial or pre-filled syringe to document the batch number in their diary or for reporting any side effects.
Fertility, pregnancy and Lactation: Use only if clearly indicated.
Side Effects: Adverse reactions are based on experience from clinical trials with ReFacto or ReFacto AF (on a per-patient basis):
Very common (≥1/10): Factor VIII inhibition PUPs, headache, cough, arthralgia, pyrexia.
Common (≥1/100 to < 1/10): Decreased appetite, dizziness, haemorrhage, haematoma, diarrhoea, vomiting, abdominal pain, nausea, urticarial, rash, pruritus, myalgia, chills, catheter site related reaction, antibody test positive, anti-factor VIII antibody test positive.
Uncommon (≥1/1000 to <1/100): Factor VIII inhibition PTPs, anaphylactic reaction, neuropathy peripheral, somnolence, dysgeusia, angina pectoris, tachycardia, palpitations, hypotension, thrombophlebitis, flushing, dyspnoea, hyperhidrosis, asthenia, injection site reaction, injection site pain, injection site inflammation, aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, blood creatinine phosphokinase increased.
Incompatibilities: In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products, including other infusion solutions. Only the provided infusion set is to be used, because treatment failure can occur as a consequence of human-coagulation factor VIII adsorption to the internal surfaces of some infusion equipment.

Legal Category: POM.
Marketing Authorisation Numbers:

Vial and syringe:	Dual chamber pre-filled syringe:
250 IU: EU/1/99/103/001	250 IU: EU/1/99/103/009
500 IU: EU/1/99/103/002	500 IU: EU/1/99/103/006
1000 IU: EU/1/99/103/003	1000 IU: EU/1/99/103/007
2000 IU: EU/1/99/103/004	2000 IU: EU/1/99/103/008
	3000 IU: EU/1/99/103/005

Cost: 250 IU: £125.55; 500 IU: £251.10; 1000 IU: £502.20; 2000 IU: £1004.40; 3000 IU: £1506.60

For further information and details of other side effects see Summary of Product Characteristics.
Further information is available on request from Medical Information Department at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK.

Marketing Authorisation Holder:
Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Pfizer Medical Information on 01304 616161

Ref: RF 12_0

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