Package leaflet: Information for the user

ReFacto AF 250 IU powder and solvent for solution for injection
ReFacto AF 500 IU powder and solvent for solution for injection
ReFacto AF 1000 IU powder and solvent for solution for injection
ReFacto AF 2000 IU powder and solvent for solution for injection

moroctocog alfa (recombinant human coagulation factor VIII)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What ReFacto AF is and what it is used for

ReFacto AF contains the active substance moroctocog alfa, human coagulation factor VIII. Factor VIII is necessary for the blood to form clots and stop bleedings. In patients with haemophilia A (inborn factor VIII deficiency), it is missing or not working properly.

ReFacto AF is used for the treatment and prevention of bleeding (prophylaxis) in adults and children of all ages (including newborns) with haemophilia A.

2. What you need to know before you use ReFacto AF

Do not use ReFacto AF

- if you are allergic to moroctocog alfa or any of the other ingredients of this medicine (listed in section 6).

- if you are allergic to hamster proteins.

If you are unsure about this, ask your doctor.

Warnings and precautions

Talk to your doctor or pharmacist before using ReFacto AF
- if you experience allergic reactions. Some of the signs of allergic reactions are difficulty in breathing, shortness of breath, swelling, hives, itching, tightness of the chest, wheezing, and low blood pressure. Anaphylaxis is a severe allergic reaction that can cause difficulty in swallowing and/or breathing, red or swollen face and/or hands. If any of these signs occur, stop the infusion

immediately and contact a doctor or seek immediate emergency care. In case of severe allergic reactions, alternative therapy must be considered.

- the formation of inhibitors (antibodies) is a known complication that can occur during treatment with all factor VIII medicines. These inhibitors, especially at high levels, stop the treatment working properly and you or your child will be monitored carefully for the development of these inhibitors. If your or your child's bleeding is not being controlled with ReFacto AF, tell your doctor immediately.

- if your bleeding does not stop as expected and contact your doctor or seek immediate emergency care.

Other medicines and ReFacto AF

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Driving and using machines

ReFacto AF has no influence on the ability to drive or use machines.

ReFacto AF contains sodium

After reconstitution, ReFacto AF contains 1.27 mmol (or 29 mg) sodium (main component of cooking/table salt) per vial. This is equivalent to 1.5% of the recommended maximum daily dietary intake of sodium for an adult. Depending on your body weight and your dose of ReFacto AF, you could receive multiple vials. This should be taken into consideration if you are on a low salt diet.

3. How to use ReFacto AF

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Treatment with ReFacto AF should be started by a doctor who is experienced in the care of patients with haemophilia A. Your doctor will decide the dose of ReFacto AF you will receive. This dose and duration will depend upon your individual needs for replacement factor VIII therapy. ReFacto AF is given by injection into a vein lasting several minutes. Patients or their carers can give injections of ReFacto AF, provided that they have been trained appropriately.

During your treatment, your doctor may decide to change the dose of ReFacto AF you receive. Consult with your health care provider before you travel. You should bring enough of your factor VIII product for anticipated treatment when travelling.

It is recommended that every time you use ReFacto AF, you record the name on the carton and batch number of the product. You can use one of the peel-off labels found on the vial to document the batch number in your diary or for reporting any side effects.

Reconstitution and administration

The procedures below are provided as guidelines for the reconstitution and administration of ReFacto AF. Patients should follow the specific reconstitution and administration procedures provided by their doctors.

Use only the pre-filled syringe provided in the box for reconstitution. Other sterile disposable syringes may be used for administration.

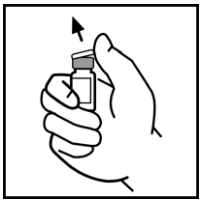
ReFacto AF is administered by intravenous (IV) infusion after reconstitution of the lyophilised powder for injection with the supplied solvent [sodium chloride 9 mg/ml (0.9%) solution] syringe. ReFacto AF should not be mixed with other infusion solutions.

Always wash your hands before performing the following reconstitution and administration procedures. Aseptic technique (meaning clean and germ-free) should be used during the reconstitution procedure.

Reconstitution:

1. Allow the vial of lyophilised ReFacto AF and the pre-filled solvent syringe to reach room temperature.

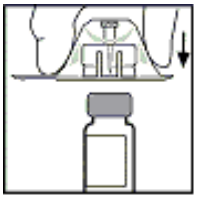
2. Remove the plastic flip-top cap from the ReFacto AF vial to expose the central portion of the rubber stopper.



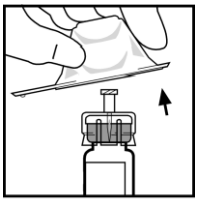
3. Wipe the top of the vial with the alcohol swab provided, or use another antiseptic solution and allow to dry. After cleaning, do not touch the rubber stopper with your hand or allow it to touch any surface.

4. Peel back the lid from the clear plastic vial adapter package. Do not remove the adapter from the package.

5. Place the vial on a flat surface. While holding the adapter package, place the vial adapter over the vial. Press down firmly on the package until the adapter snaps into place on top of the vial, with the adapter spike penetrating the vial stopper.

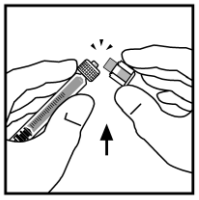


6. Lift the package away from the adapter and discard the package.

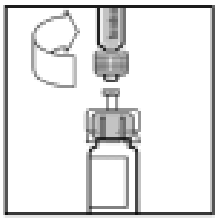


7. Attach the plunger rod to the solvent syringe by inserting the rod into the opening in the syringe stopper and pushing and turning the rod firmly until it is securely seated in the stopper.

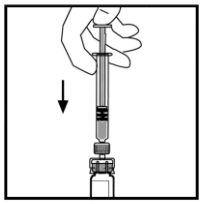
8. Break off the tamper-resistant plastic tip cap from the solvent syringe by snapping the perforation of the cap. This is done by bending the cap up and down until the perforation is broken. Do not touch the inside of the cap or the syringe tip. The cap may need to be replaced (if not administering reconstituted ReFacto AF immediately), so set it aside by placing it on its top.



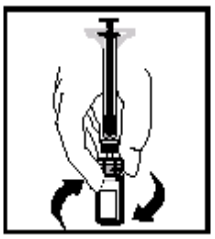
9. Place the vial on a flat surface. Connect the solvent syringe to the vial adapter by inserting the tip of the syringe into the adapter opening while firmly pushing and turning the syringe clockwise until the connection is secured.



10. Slowly depress the plunger rod to inject all the solvent into the ReFacto AF vial.



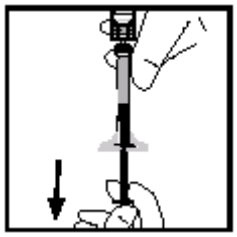
11. With the syringe still connected to the adapter, **gently** rotate the vial until the powder is dissolved.



12. The final solution must be inspected visually for particulate matter before administration. The solution will appear clear to slightly opalescent and colourless.

    Note: If you use more than one vial of ReFacto AF per infusion, each vial should be reconstituted as per the previous instructions. The solvent syringe should be removed, leaving the vial adapter in place, and a single large luer lock syringe may be used to draw back the reconstituted contents of each of the individual vials.

13. Ensuring that the syringe plunger rod is still fully depressed, invert the vial. Slowly draw back all the solution through the vial adapter into the syringe.



14. Detach the syringe from the vial adapter by gently pulling and turning the syringe counter-clockwise. Discard the vial with the adapter attached.

    Note: If the solution is not to be used immediately, the syringe cap is to be carefully replaced. Do not touch the syringe tip or the inside of the cap.

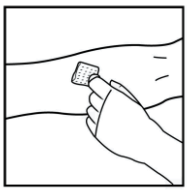
ReFacto AF must be used within 3 hours of reconstitution. The reconstituted solution may be stored at room temperature prior to administration.

Administration (Intravenous Infusion):

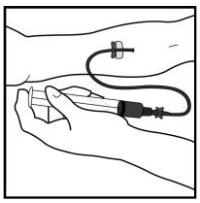
ReFacto AF should be administered using the infusion set provided in this kit and the pre-filled solvent syringe provided or a single sterile disposable plastic luer lock syringe.

1. Attach the syringe to the luer end of the infusion set tubing.

2. Apply a tourniquet and prepare the injection site by wiping the skin well with an alcohol swab provided in the kit.



3. Insert the needle on the infusion set tubing into the vein as instructed by your doctor, and remove the tourniquet. Remove any air in the infusion set tubing by drawing back on the syringe. The reconstituted product is to be injected intravenously over several minutes. Your doctor may change your recommended infusion rate to make the infusion more comfortable.



Please dispose of all unused solution, the empty vial(s) and the used needles and syringes in an appropriate container for throwing away of medical waste as these materials may hurt others if not disposed of properly.

If you use more ReFacto AF than you should

Check with your doctor or pharmacist.

If you stop using ReFacto AF

Do not stop using ReFacto AF without consulting your doctor.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Allergic reactions

If **severe, sudden allergic reactions** (anaphylactic) occur, the infusion **must be stopped immediately**. You must **contact your doctor immediately** if you have any of the following early symptoms of allergic reactions:

- rash, hives, wheals, generalised itching
- swelling of lips and tongue
- difficulty in breathing, wheezing, tightness in the chest
- general feeling of being unwell
- dizziness and loss of consciousness

Severe symptoms, including difficulty in breathing and (nearly) fainting, require prompt emergency treatment. Severe, sudden allergic (anaphylactic) reactions are uncommon (may affect up to 1 in 100 people).

Inhibitor development

For children not previously treated with factor VIII medicines, inhibitor antibodies (see section 2) may form very commonly (more than 1 in 10 patients); however patients who have received previous treatment with factor VIII (more than 150 days of treatment) the risk is uncommon (less than 1 in 100 patients). If this happens, your or your child's medicines may stop working properly and you or your child may experience persistent bleeding. If this happens, you should contact your doctor immediately.

Very common side effects (may affect more than 1 in 10 people)

- inhibitor development for patients who have never been previously treated with factor VIII products
- headache
- cough
- joint pain
- fever

Common side effects (may affect up to 1 in 10 people)

- bleeding
- dizziness
- decreased appetite, diarrhoea, vomiting, stomach pain, nausea
- hives, rash, itching
- muscular pain
- chills, catheter site reaction
- certain blood tests may show an increase in antibodies to factor VIII

Uncommon side effects (may affect up to 1 in 100 people)

- inhibitor development for patients who have been previously treated with factor VIII products (less than 1 in 100 patients)
- severe allergic reaction

- numbness, sleepiness, altered taste
- chest pain, rapid heart beat, palpitations
- low blood pressure, pain and redness of veins associated with a blood clot, flushing
- shortness of breath
- excessive sweating
- weakness, injection site reactions including pain
- slight increase in heart enzymes
- increased liver enzymes, increased bilirubin

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store ReFacto AF

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer carton and vial label after EXP. The expiry date refers to the last day of that month.

Store and transport refrigerated (2°C – 8°C). Do not freeze, in order to prevent damage to the pre-filled solvent syringe.

For your convenience, the medicine can be removed from such storage for one single period of maximum 3 months at room temperature (up to 25°C). At the end of this room temperature storage period, the product must not be put back in the refrigerator, but must be used or discarded. Record on the outer carton the date ReFacto AF is removed from the refrigerator and set at room temperature (up to 25°C).

Keep the vial in the outer carton in order to protect from light.

Use the reconstituted solution within 3 hours of reconstitution.

The solution will be clear to slightly opalescent and colourless. Do not use this medicine if you notice that it is cloudy or contains visible particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What ReFacto AF contains

- The active substance is moroctocog alfa (recombinant coagulation factor VIII). Each vial of ReFacto AF contains nominally 250, 500, 1000, or 2000 IU of moroctocog alfa.

- The other ingredients are sucrose, calcium chloride dihydrate, L-histidine, polysorbate 80 and sodium chloride (see section 2 “ReFacto AF contains sodium”). A solvent [sodium chloride 9 mg/ml (0.9%) solution for injection] is also supplied for reconstitution.

- After reconstitution with the supplied solvent [sodium chloride 9 mg/ml (0.9%) solution], each vial contains 62.5, 125, 250, or 500 IU, respectively (based on the strength of moroctocog alfa,

i.e., 250, 500, 1000, or 2000 IU), of moroctocog alfa per 1 ml of the prepared solution for injection.

What ReFacto AF looks like and contents of the pack

ReFacto AF is provided as a powder for injection in a glass vial and a solvent is provided in a pre-filled syringe.

The contents of the pack are:
- one vial of moroctocog alfa 250, 500, 1000, or 2000 IU powder
- one pre-filled syringe of solvent, 4 ml sterile sodium chloride 9 mg/ml (0.9 %) solution for injection for reconstitution, with one plunger rod
- one sterile vial adapter reconstitution device
- one sterile infusion set
- two alcohol swabs
- one plaster
- one gauze pad

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This leaflet was last revised in 01/2021

Ref: RF 14_0