Baxter

PACKAGE LEAFLET: INFORMATION FOR THE USER

Recombinate 1000 IU powder and solvent for solution for injection.
Octocog alfa (recombinat coagulation factor VIII)

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT RECOMBINATE IS AND WHAT IT IS USED FOR

Recombinate belongs to a pharmacotherapeutic group called blood coagulation factor VIII.

Recombinate is used in patients with haemophilia A (congenital factor VIII deficiency) for
- prevention of bleeding
- treatment of bleeding (e.g. muscle bleeding, oral bleeding, bleeding at the site of surgery).

The product does not contain von Willebrand factor and is therefore not to be used in von Willebrand's disease (a special blood coagulation disorder).

2. BEFORE YOU USE RECOMBINATE

Do not use RECOMBINATE
- If you are hypersensitive (allergic) to octocog alfa, to mouse, bovine or hamster proteins or to any of the other ingredients of Recombinate.

If you are unsure about this, ask your doctor.

Take special care with RECOMBINATE

When allergic reactions occur:
- There is a rare chance that you may experience an anaphylactic reaction (a severe, sudden allergic reaction) to Recombinate. You should be aware of the early signs of allergic reactions such as rash, hives, wheals, generalised itching, swelling of lips and tongue, difficulty in breathing, wheezing, tightness in the chest, general feeling of being unwell, and dizziness. These symptoms can constitute an early symptom of an anaphylactic shock, manifestations of which may additionally include extreme dizziness, loss of consciousness, and extreme difficulty in breathing.
- If any of these symptoms occur, the infusion has to be stopped immediately. Severe symptoms, including difficulty in breathing and (near) fainting, require prompt emergency treatment.

When monitoring is required:
- Your doctor may wish to carry out tests to ensure that your current dose is sufficient to reach and maintain adequate factor VIII levels. This is particularly important if you are having major surgery.

When bleeding is still occurring:
- If your bleeding is not controlled with Recombinate, consult your doctor immediately. You may have developed factor VIII inhibitors and your doctor may wish to carry out tests to confirm this. Factor VIII inhibitors are antibodies in the blood that block the factor VIII you are using. This makes factor VIII less effective in controlling bleeding.

If you have previously developed a factor VIII inhibitor and you switch factor VIII products, you may be at risk of your inhibitor coming back.

Taking other medicines

No unfavourable influences with other medicinal products have been observed.

Nevertheless, please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breast-feeding

There is no experience regarding the use of Recombinate during pregnancy and breast-feeding as haemophilia A is rare in women. Therefore, inform your doctor if you are pregnant or breast-feeding. Your doctor will decide if Recombinate may be used during pregnancy and lactation.

Driving and using machines

No effects on the ability to drive or use machines have been seen.

Important information about some of the ingredients of Recombinate

This medicinal product contains 1.5 mmol sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO USE RECOMBINATE

Your therapy should be directed by doctors with experience in the care of patients with haemophilia A.

Recombinate is appropriate for use in adults as well as in children of all ages, including the newborn.

Dosage for prophylaxis of bleeding

If you are using Recombinate to prevent bleeding (prophylaxis), your doctor will calculate the dose for you and tell you. He/she will do this according to your particular needs. The usual dose will be between 20 to 40 IU of octocog alfa per kilogramme of body weight, administered at intervals of 2 to 3 days. However, in some cases, especially in younger patients, shorter intervals or higher doses may be necessary.

If you have the impression that the effect of Recombinate is insufficient, talk to your doctor.

Dosage for treatment of bleeding

If you are receiving Recombinate for treatment of bleeding, your doctor will calculate the dose for you. He/she will do this according to your particular needs using the formula below:

Required IU = body weight (kilogramme) x desired factor VIII rise (% of normal) x 0.5

The following table provides a guidance for factor VIII minimal blood levels. In the case of the haemorrhagic events listed, the factor VIII activity should not fall below the given level (in % of normal) during the corresponding period.

Under certain circumstances, larger amounts than those calculated may be required, especially in the case of a low titre inhibitor.

Degree of haemorrhage/ Type of surgical procedure	***Required peak post-infusion AHF activity in the blood (as % of normal or IU/dL plasma)***	***Frequency of infusions***
Degree of Haemorrhage		
Early haemarthrosis or muscle bleed or oral bleed	20 – 40	Begin infusion every 12 to 24 hours for one to three days until the bleeding episode as indicated by pain is resolved or healing is achieved.
More extensive haemarthrosis, muscle bleed or haematoma	30 – 60	Repeat infusions every 12 to 24 hours for usually three days or more until pain and disability are resolved.
Life threatening bleeds such as intracranial bleed, throat bleed, severe abdominal bleed	60 – 100	Repeat infusions every 8 to 24 hours until threat is resolved.
Surgery		
Type of operation		
Minor surgery, including tooth extraction	30 – 60	A single infusion plus oral antifibrinolytic therapy within one hour is sufficient in approximately 70% of cases. Every 24 hours, at least 1 day, until healing is achieved.
Major surgery	80 – 100 (pre- and postoperative)	Repeat infusions every 8 to 24 hours depending on state of healing.

Monitoring by your doctor

Your doctor will perform appropriate laboratory tests to make sure that you have adequate factor VIII levels. This is particularly important if you are having major surgery.

Patients with factor VIII inhibitors

If the factor VIII level of your plasma fails to reach expected levels, or if bleeding is not adequately controlled following dose increase, the presence of factor VIII inhibitors should be suspected. The presence of factor VIII inhibitors will be checked by your doctor.

If you have developed factor VIII inhibitors, you will possibly need a larger amount of Recombinate to control a bleeding. If this dose does not control your bleeding, your doctor may consider the use of a different product. Do not increase the total dose of Recombinate to control your bleeding without consulting your doctor.

Method and route of administration

Recombinate is administered into a vein (intravenously) after preparing the solution with the solvent provided, either
- by injecting by your doctor or nurse
- by infusion by your doctor or nurse

The rate of administration should be determined by the patient's comfort level. The preparation can be administered at a rate of up to 10 ml per minute.

Frequency of administration

Your doctor will tell you how often and at what intervals Recombinate is to be administered. He will do this according to the effectiveness in your individual case.

Duration of treatment

Usually, the replacement therapy with Recombinate is life-long treatment.

If you use more RECOMBINATE than you should

- No symptoms of overdose with recombinant coagulation factor VIII have been reported. If you have any doubts, please consult your doctor.

If you forget to use RECOMBINATE

- Do not take a double dose to make up for forgotten individual doses.
- Proceed with the next regular administration immediately and continue at regular intervals as advised by your doctor.

If you stop using RECOMBINATE

Do not stop using Recombinate without consulting your doctor because life-threatening bleeding might occur.

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

4. POSSIBLE SIDE EFFECTS

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

The following side effects occurring during the use of this product have been reported :

nausea, flushing, mild fatigue, transient skin rash (rash), haematoma, sweating, chills, shaking, fever, leg pain, cold hands and feet, sore throat, ear infection, failed hearing test, nose bleed and paleness.

Sporadically, adverse events resembling hypersensitivity have also been reported, including :

generalised urticaria and hives (skin rash with severe itching and formation of wheals), rash, shortness of breath, cough, tightness in the chest, wheezing, a too low blood pressure (hypotension);

severe hypersensitivity reaction that may cause difficulty in swallowing and/or breathing, a red swollen face and/or hands (anaphylaxis).

If allergic or anaphylactic reactions occur, stop the injection/infusion immediately and contact your doctor.

The formation of neutralising antibodies (inhibitors) to blood coagulation factor VIII is a known complication in the management of individuals with haemophilia A.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE RECOMBINATE

- Keep out of the reach and sight of children.
- Store in a refrigerator (2°C – 8°C).
- Do not freeze.
- Do not use after the expiry date stated on the labels and carton.

The expiry date is stated on the carton after the abbreviation “Exp.”.

The expiry date refers to the last day of that month.

Within its shelf life you may store the product at 15°C – 25°C prior to use for up to six months. Do not return to refrigeration following storage at 15°C – 25°C. Recombinate should be administered within three hours after Reconstitution.

Storing after preparation:

- This product is for single use only. Use the product within three hours after preparation.
- Do not refrigerate the solution after preparation.

Do not use Recombinate if you notice deposits or the solution is cloudy.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Any unused product or waste material should be disposed of in accordance with local requirements.

6. FURTHER INFORMATION

What RECOMBINATE contains

- The active substance is octocog alfa, recombinant coagulation factor VIII 25 IU/ml, 50 IU/ml or 100 IU/ml.
  The product is presented in three strengths: 250 IU, 500 IU or 1000 IU (International Units) per vial of the active substance.
- The other ingredients are
  - **for the powder:** human albumin, sodium chloride, histidine, macrogol 3350 and calcium chloride dihydrate
  - **for the solvent:** water for injections.

What RECOMBINATE looks like and contents of the pack

Recombinate is provided as a powder and solvent for solution for injection and is a white to off-white friable powder. After reconstitution, the solution is clear, colorless and free from foreign particles. The solvent (sterilised water for injections) is a clear and colorless liquid.

The package contains either 250 IU or 500 IU or 1000 IU of powder in a vial, 10 ml of solvent in a vial, a device for reconstitution (BAXJECT II), a sterile single-use plastic syringe, a sterile mini-infusion set, 2 alcohol swabs and 2 plasters.

Alternatively to BAXJECT II a needle device for reconstitution comprising one sterile double-ended needle (to transfer the solvent into the Recombinate vial), one sterile filter needle (to transfer the reconstituted solution into the syringe) can be provided.

Pack size of 1.

Manufacturer

Baxter S.A., Bd. René Branquart 80, B-7860 Lessines, Belgium

This medicinal product is authorised in the member states of the EEA under the following names:

Belgium:	Recombinate 250 (500, 1000) UI
Czech Republic:	Recombinate 250 (500, 1000) IU
Cyprus:	Recombinate 250 (500, 1000) IU
Denmark	Recombinate 250 (500, 1000) IE
Germany:	Recombinate Antihämophilie Factor (recombinant) 250 (500, 1000)
Greece:	Recombinate 250 (500, 1000) IU
Espana:	Recombinate 250 (500, 1000) UI
Lithuania:	Recombinate 250 (500, 1000) IU
Luxembourg:	Recombinate 250 (500, 1000) UI
Hungary:	Recombinate 250 (500, 1000) NE
Netherlands:	Recombinate 250 (500, 1000) IE
Norway:	Recombinate 250 (500, 1000) IU
Austria:	Recombinate Antihämophilie Factor 250 (500, 1000) I.E.
Poland:	Recombinate 250 (500, 1000) IU
Estonia:	Recombinate 250 (500, 1000) IU
France:	Recombinate 250 (500, 1000) UI
Ireland:	Recombinate 250 (500, 1000) IU
Iceland:	Recombinate 250 (500, 1000) IU
Italy:	Recombinate 250 (500, 1000) UI
Latvia:	Recombinate 250 (500, 1000) IU
Portugal:	Recombinate 250 (500, 1000) UI
Slovenia:	Recombinate 250 (500, 1000) IU
Slovak Republic:	Recombinate 250 (500, 1000) IU
Finland:	Recombinate 250 (500, 1000) IU
Sweden:	Recombinate 250 (500, 1000) IU
United Kingdom:	Recombinate 250 (500, 1000) IU