ADVATE®

Octocog alfa (rch) [Recombinant Antihaemophilic FVIII, Plasma / Albumin Free Method (rAHF-PFM)] injection

Consumer Medicine Information

What is in this leaflet?

This leaflet answers some common questions about ADVATE.

It does not contain all of the available information.

It does not take the place of talking to your doctor or pharmacist.

All medicines have risks and benefits. Your doctor has weighed the risks of you using ADVATE against the benefits they expect it will have for you.

If you have any concerns about having this medicine ask your doctor or pharmacist.

Please read this leaflet carefully and keep it for future reference.

Please also note that this leaflet is subjected to change, therefore, ask your doctor whether this is the latest information regarding this medicine.

What is ADVATE

ADVATE belongs to the group of medicines called blood coagulation factor VIII.

What ADVATE is used for

It is used for the treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency).

This preparation does not contain von Willebrand factor and is therefore not suitable for use in von Willebrand's disease.

ADVATE is a recombinant factor VIII, which has been shown successfully to correct factor VIII deficiency.

How does ADVATE work

Under normal physiological condition, factor VIII is essential for blood clotting and maintenance of a bleeding episode.

Individuals with haemophilia A disease, which is a hereditary disorder of blood coagulation have a low level of factor VIII in their blood circulation. As a result of factor VIII deficiency, the individual with this disease may have a heavy bleeding into joints, muscles or internal organs either spontaneously or as a result of accidental or surgical trauma.

ADVATE is similar to plasma-derived factor VIII. As it works in the same way, it can be used as a replacement therapy in patients with haemophilia A.

Before you are given the ADVATE

ADVATE should not be given to you if:

- you are allergic (hypersensitive) to mouse, hamster proteins or any other ingredients in this product.
- you have tendency of allergic reaction or hypersensitivity to any human derived injection. Some of the symptoms of allergic reaction may include skin rash, swelling of the face, lips or tongue, which may cause difficulty swallowing or shortness of breath, tightness of the chest.
- it has expired.

You must tell your doctor if you:

- have any other illness
- are taking any prescription medicine or any other medicines purchased from a pharmacy, health food store or supermarket. Some medicines and ADVATE may interfere with each other.

You must tell your doctor if you are pregnant, planning to become pregnant or breast-feeding.

How ADVATE is given

How much is given

Your doctor will decide how much ADVATE will be given to you, which depends on your need and condition. Each individual will receive a different dosage, which in itself may vary between doctor visits. The dose you receive will be based on:

- body weight;
- the amount of antihaemophilic factor (AHF) your body is able to make;
- how much and how often and which sites (knees, muscles etc) of your body are bleeding;
- whether your body may build up antibodies to this medicine. After a while your body may build up these antibodies, leading to a less effective treatment than the usual.

Method of Administration (use aseptic technique):

ADVATE is usually administered in a hospital. However, some individuals may be trained to use this product at home. It is administered by intravenous injection.

If you have been trained to inject at home, take the dry medicine vial and the small vial of water out of the refrigerator and let them come to room temperature (15°C to 30°C). Visually examine the dry medicine vial and contents, and do not use if there is any sign of damage or discolouration. The dry medicine should appear clear, colourless.

After preparation, the medicine should be used immediately or at least within 3 hours after it is reconstituted. Do not refrigerate after reconstitution. Please refer to the directions on the package or talk to your doctor.

Do not reuse syringes and needles. Place them in a puncture resistant disposable container, or otherwise dispose of them as directed by your doctor. Likewise, discard any unused solution as directed by your doctor.

How often is it given

Your doctor will tell you how often and what intervals ADVATE is to be administered. Usually, a substitution therapy, such as ADVATE is a lifetime treatment. Although no overdose adverse effect has been reported with ADVATE, if you have used this product more often than you should you must tell your doctor.

If you miss/forget your injection

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

How it is given

ADVATE is intended for intravenous injection only and must be administered within 3 hours after reconstitution. Aseptic conditions (meaning clean and germ free) are required during the reconstitution and administration. Use only the medical devices for reconstitution and administration provided with each package of 250 International Units (IU), 500 IU, 1000 IU, 1500 IU, 2000IU, 3000 IU and 4000 IU (see, INSTRUCTION FOR USE). ADVATE must not be mixed with other infusion solutions. It is to be used in one patient on one occasion only.

Overdose

No symptoms of overdose with ADVATE have been reported.

While you are being treated with ADVATE

Discuss with your doctor the progress you have experienced after the treatment, especially during the first few days. As ADVATE is given in a hospital, your healthcare professional will take records of the progress and unexpected reactions.

Side Effects

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are under ADVATE treatment.

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

A rare adverse reaction known as "anaphylactic shock", which was not experienced during clinical studies with ADVATE, may nevertheless occur as the active ingredient is a protein. If any of the following symptoms happen, for example, rash, swelling of the face, lips, mouth or difficulty in breathing, tell your health professional on duty immediately. These symptoms can constitute an early warning for a serious allergic reaction. Then your healthcare professional will take an appropriate action promptly to reverse the symptoms.

Due to the decrease in injection volume for ADVATE reconstituted in 2 mL, the time to react to hypersensitivity reactions during an injection is further reduced. Therefore, caution is advised during injection of ADVATE reconstituted in 2 mL.

You must contact your doctor immediately if you have any of the following early symptoms of allergic (hypersensitivity) 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.

Side effects may occur with certain frequencies, which are defined as follows:

- very common: affects more than 1 user in 10
- common: affects 1 to 10 users in 100
- uncommon: affects 1 to 10 users in 1,000
- rare: affects 1 to 10 users in 10,000
- very rare: affects less than 1 user in 10,000
- not known: frequency cannot be estimated from the available data.

Common side effects

Factor VIII inhibitors development, headache and fever.

Uncommon side effects

itching, increased sweating, unusual taste in the mouth, hot flushes, migraines, dizziness, memory impairment, fainting, tremors, palpitations, chills, diarrhoea,

stomach pain, nausea, vomiting, shortness of breath, sore throat, infection of the lymphatic vessels, whitening of skin, eye inflammation, rashes, excessive sweating, foot and leg swelling, increase in enzymes that track liver function, reduced percentage of red blood cells and pain in the upper abdomen or lower chest.

Related to surgery

catheter-related infection, decreased red cell blood count, swelling of limbs and joints, prolonged bleeding after drain removal, decreased Factor VIII level and post-operative bruise.

Related to central venous access devices (CVAD)

catheter-related infection, systemic infection and local blood clot at the catheter site.

Side effects with unknown frequency

Potentially life-threatening reactions (anaphylaxis) and other allergic reactions (hypersensitivity), general disorders (tiredness, lack of energy).

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

Other adverse effects that may occur include irregular heartbeats, chest pain, chest discomfort, tremors, fainting, abdominal pain, chills and eye inflammation.

Product descriptions

What ADVATE looks like?

It is a white to cream colour powder in a single dose glass vial accompanied by Sterile Water for Injection in glass vial for reconstitution. ADVATE 250, 500, 1000, 1500 IU strengths may be supplied with either a 5 mL Sterile Water for Injection vial (grey cap) or a 2mL Sterile Water for Injection vial (clear colourless cap). ADVATE 2000, 3000 and 4000 IU strengths are only supplied with either a 5 mL Sterile Water for Injection vial (grey cap).

ADVATE must always be reconstituted with the Sterile Water for Injection vial supplied in the same carton.

Below is summarised what strengths of ADVATE are available, which strengths can be reconstituted with the 2 mL vial of sterile water for injection, and how to differentiate the packaging of the 2 mL and 5 mL Sterile Water for Injection configurations.

ADVATE with 5 mL Sterile Water for Injection vial is available in the following strengths (IU) 250, 500, 1000, 1500, 2000, 3000, 4000 with a grey WFI vial cap:

It is supplied in a yellow background carton.

ADVATE with 2 mL Sterile Water for Injection vial is available in the following strengths (IU), 250, 500, 100, 1500 with a clear, colourless WFI vial cap:

It is supplied in a purple background carton.

The package also contains a needle less transfer device.

What is in ADVATE?

The active ingredient in ADVATE is Octocog alfa [antihaemophilic factor VIII Recombinant Coagulation Factor VIII (rhc)] produced by recombinant technology, which does not use any animal protein in cells culture media during the manufacturing process. Seven strengths of ADVATE are commercially available, from the lowest strength (250 IU) to the highest strength (4000 IU). The amounts of each component of the excipients in all strengths are the same.

The amounts in 2 mL or 5 mL of the reconstituted solution are as follows: trehalose (40 mg), histidine (8 mg), trometamol (6 mg), sodium chloride (26.5 mg), calcium chloride (1.3 mg), glutathione in reduced form (0.4 mg), polysorbate 80 (0.5 mg), mannitol (160 mg).

How to store ADVATE

ADVATE is a protein preparation, therefore it should be stored at 2°C - 8°C in a refrigerator for the duration of its shelf life: do not freeze as it may damage the water for injection vial. In case it is needed for ambulatory use, ADVATE may be stored at below 25°C (room temperature) for a single period of up to 6 months and then discarded. After ADVATE has been stored at room temperature it should not be refrigerated. Store in the original package in order to protect from light.

ADVATE does not contain antimicrobial preservation. Therefore:

- use within 3 hours after reconstitution
- do not refrigerate preparation after reconstitution
- discard any unused solution appropriately
- do not use the product with a torn packaging or any sign of deterioration such as discolouration.

Where can you get more information?

You can get more information from your doctor or pharmacist.

INSTRUCTIONS FOR USE

(For intravenous use only)

IMPORTANT:

Contact your doctor or local Haemophilia Treatment Centre if you experience any problems with this procedure. These instructions are intended only as a visual aid for those patients who have been instructed by their doctor or haemophilia centre on the proper way to self-infuse the product.

Do not attempt to self-infuse unless you have been taught how by your doctor or haemophilia centre.

In a quiet place, prepare a clean surface and gather all the materials you will need for the infusion. Check the expiration date on the ADVATE concentrate vial or package and let the vial with the ADVATE concentrate and the Sterile Water for Injection EP (diluent) warm up to room temperature. Wash your hands and put on clean exam gloves. If self-infusing at home the use of gloves is optional.

ADVATE is supplied either with a BaxJect II or a BaxJect III (pre-assembled) reconstitution device. Please refer to the instructions corresponding to the device supplied with your ADVATE, as illustrated below:

Reconstitution using BAXJECT II device:

ADVATE with 5 mL Diluent

ADVATE with 2 mL Diluent

1. After washing your hands and putting on gloves, remove caps from the factor concentrate and diluent to expose the centres of the rubber stoppers.
2. Disinfect the stoppers with an alcohol swab (or other suitable solution suggested by your doctor of haemophilia centre) by rubbing the stoppers firmly for several seconds and allow to dry prior to use. Place the vials on a flat surface.
3. Open the BAXJECT II device package by peeling away the lid without touching the inside of the package. The BAXJECT II device remains in the package at this time. Do not remove the device from the package.
4. Turn the package with the device upside down and place it over the top of the diluent vial. Fully insert the clear plastic spike of the BAXJECT II device into the centre of the diluent vial's stopper by pushing straight down. Grip the package at its edge and pull it off the device. After removing the packaging be careful not to touch the white plastic exposed spike. Do not remove the blue cap from BAXJECT II device.

   Please note that the connection of the two vials should be done expeditiously to close the open fluid pathway created by the first insertion of the spike to the diluent vial.
5. Quickly turn over the diluent vial with the BAXJECT II device, place on top of the vial containing the factor concentrate and fully insert the white plastic spike into the factor concentrate vial's stopper by pushing straight down. The vacuum will draw the diluent into the factor concentrate vial.
6. Swirl the factor concentrate gently and continuously with the BAXJECT II attached until it is completely dissolved.

   Do not shake.

   Check to make sure the factor concentrate is completely dissolved. The solution should be clear and colourless in appearance.
7. Remove the blue cap from the BAXJECT II device. Connect the syringe to the BAXJECT II device. DO NOT INJECT AIR.
8. Turn the system over so that the factor concentrate solution vial is on top. Withdraw the factor concentrate solution into the syringe by pulling back the plunger slowly. Disconnect the syringe, leaving the BAXJECT II device connected. Attach the infusion needle to the syringe using at winged infusion set, if available. Point the needle up and remove any air bubbles by gently tapping the syringe with your finger and slowly and carefully pushing the air out of the syringe. Dispose of the used BAXJECT II system in your hard-walled Sharps container without taking it apart.

Reconstitution using BAXJECT III device:

1. Open the ADVATE package by peeling away the lid. Remove the ADVATE in the BAXJECT III system from the package and verify that the expiration date on the label has not passed and the potency unit number is same as expected.
2. Place the ADVATE on a flat surface with the diluent vial on top. The diluent vial has a blue stripe.

   Do not remove the blue cap until instructed in a later step.
3. With one hand holding the ADVATE in a BAXJECT III system, press down firmly on the diluent vial with the other hand until the system is fully collapsed and the diluent flows down into the ADVATE vial. Both vials will move into the housing when pressed.

   Do not remove the blue cap until instructed in a later step.
4. Swirl the ADVATE in the BAXJECT III system gently and continuously until the ADVATE is completely dissolved.

   Do not shake. Do not refrigerate after reconstitution.

   Inspect the ADVATE solution for particulate matter and discoloration prior to administration. The solution should be clear and colorless in appearance. If not, do not use the solution and notify your healthcare provider immediately.
5. Take off the blue cap from the BAXJECT III system and connect the syringe.

   Be careful to not inject air into the ADVATE in the BAXJECT III system.
6. Turn over the ADVATE in the BAXJECT III system so that the vial containing the ADVATE solution is on top. Draw the ADVATE solution into the syringe by pulling back the

plunger slowly. If the solution does not draw into the syringe, be sure that both vials are pressed firmly together. The contents of more than one vial may be drawn into a single, appropriately sized syringe if you are using more than one vial of ADVATE.

7. Disconnect the syringe from the system. Attach the infusion needle to the syringe using a winged (butterfly) infusion set, if available. Point the needle up and remove any air bubbles by gently tapping the syringe with your finger and slowly and carefully pushing air out of the syringe and needle.

Administration of reconstituted Advate

1. If receiving more than one vial of ADVATE the contents of multiple vials may be drawn into the same syringe.

   Please note that the BAXJECT II or III reconstitution device is intended for use with a single vial of ADVATE and Sterile Water for Injection only, therefore reconstituting and withdrawing a second vial into the syringe requires a second BAXJECT II or III reconstitution device.

2. Apply a tourniquet and prepare the injection site by wiping the skin well with an alcohol swab (or other suitable solution suggested by your doctor or haemophilia centre).

3. Insert the needle into the vein and remove the tourniquet. Infuse the factor concentrate.

   Do not infuse any faster than 10mL per minute.

   Remove the needle from the vein and apply pressure with sterile gauze to the infusion site for several minutes.

   Do not recap the needle after the infusion, and do not dispose in ordinary household trash. Place it with the used syringe in a hard-walled Sharps container for proper disposal.

4. After the infusion remove the peel-off label from the factor concentrate vial (for BAXJECT II) or from the blister label (for BAXJECT III) and place in your factor log book. Clean up any spilled blood with a freshly prepared mixture of 1 part bleach and 9 parts water, soap and water, or any household disinfecting solution.

5. Do not reuse syringes and needles. Place them in a puncture resistant disposable container, or otherwise dispose of them as directed by your doctor. Likewise, discard any unused solution as directed by your doctor.

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(ADVATE 500 IU)

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(ADVATE 1000 IU)

AUST R 100387

(ADVATE 1500 IU)

AUST R 136204

(ADVATE 2000 IU)

AUST R 150366

(ADVATE 3000 IU)

AUST R 214709

(ADVATE 4000 IU)