ADYNOVATE®

Rurioctocog alfa pegol [Recombinant Coagulation Factor VIII (rch), PEGylated] powder for injection

Consumer Medicine Information

What is in this leaflet?

This leaflet answers some common questions about ADYNOVATE. 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 ADYNOVATE against the benefits they expect it will have for you.

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

Keep this leaflet.

You may wish to read it again.

What is ADYNOVATE used for?

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

ADYNOVATE contains the active substance rurioctocog alfa pegol, pegylated human recombinant coagulation factor VIII. The human coagulation factor VIII is produced by recombinant DNA technology and has been modified chemically to prolong its duration of action.

How does ADYNOVATE 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.

ADYNOVATE 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 ADYNOVATE

ADYNOVATE 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
- suffer from cardiac disease or if you have recently had major surgery
- are taking any prescription medicine or any other medicines purchased from a pharmacy, health food store or supermarket. Some medicines and ADYNOVATE may interfere with each other.

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

How ADYNOVATE is given

How much is given

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

The dose you receive will be based on:

- your 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):

ADYNOVATE 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. 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 white to off-white powder..

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.

Your medicine does not contain additives that would prevent the growth of bacteria once the powder is dissolved with sterile water. For this reason, each vial of ADYNOVATE is for single use only, in one patient only. Discard any residue.

How often is it given

Your doctor will tell you how often and what intervals ADYNOVATE is to be administered. Usually, a substitution therapy, such as ADYNOVATE is a lifetime treatment. Although no overdose adverse effect has been reported with ADYNOVATE, 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

ADYNOVATE 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 and 2000 IU (see, INSTRUCTION FOR USE).

ADYNOVATE 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 ADYNOVATE have been reported.

While you are being treated with ADYNOVATE

Discuss with your doctor the progress you have experienced after the treatment, especially during the first few days. As ADYNOVATE 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 ADYNOVATE treatment.

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

There is a rare adverse reaction known as "anaphylactic shock" may 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 ADYNOVATE reconstituted in 2 mL, the time to react to hypersensitivity reactions during an injection is further reduced. Therefore, caution is advised during injection of ADYNOVATE 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.

Common side effects

(may affect up to 1 in 10 people)

- headache
- nausea
- diarrhoea

Uncommon side effects

(may affect up to 1 in 100 people)

- flushing.
- hypersensitivity

Additional side effects in children

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

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.

Product descriptions

What ADYNOVATE looks like?

ADYNOVATE is a white to off-white friable powder in a single dose glass vial accompanied by a diluent (Sterile Water for Injection) in a glass vial for reconstitution. After reconstitution, the solution is clear, colourless and free from foreign particles.

ADYNOVATE 250, 500 and 1000 IU strengths may be supplied with either a 5 mL Sterile Water for Injection vial or a 2 mL Sterile Water for Injection vial. ADYNOVATE 2000 IU strength is only supplied with a 5 mL Sterile Water for Injection vial.

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

The package also contains a needle less transfer device.

What is in ADYNOVATE?

The active ingredient in ADYNOVATE is rurioctocog alfa pegol [Recombinant Coagulation Factor VIII (rch), PEGylated] produced by recombinant technology, which does not use any animal protein in cells culture media during the manufacturing process. Four strengths of ADYNOVATE are commercially available, from the lowest strength (250 IU) to the highest strength (2000 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 (7.8 mg), trometamol (6.1 mg), sodium chloride (26.3 mg), calcium chloride (1.2 mg), glutathione (0.4 mg), polysorbate 80 (0.5 mg) and mannitol (160 mg).

Storage

ADYNOVATE 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, ADYNOVATE may be stored at room temperature (up to 30°C) for a single period of up to 3 months; not to exceed the expiration date and then discarded. After ADYNOVATE has been stored at room temperature do not return product back to the refrigerator. Store in the original package in order to protect from light.

ADYNOVATE 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 ADYNOVATE concentrate vial or package and let the vial with the ADYNOVATE 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.

ADYNOVATE is supplied either with a BAXJECT II Hi-Flow or a BAXJECT III (preassembled) reconstitution device. Please refer to the instructions corresponding to the device supplied with your ADYNOVATE, as illustrated below.

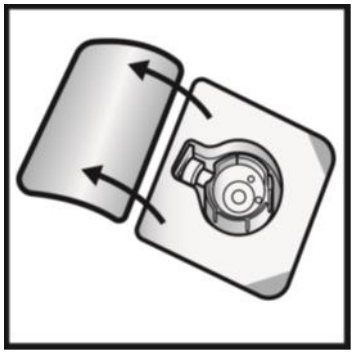
Using the BAXJECT II Hi-Flow Device:

For reconstitution use only the sterilised water for injections and the reconstitution device provided in the pack.

1. Use aseptic technique (clean and germ free) and a flat work surface during the reconstitution procedure.
2. Allow the vials of ADYNOVATE and diluent to reach room temperature before use.
3. Remove plastic caps from the ADYNOVATE and diluent vials.
4. Cleanse rubber stoppers with an alcohol wipe and allow to dry prior to use.

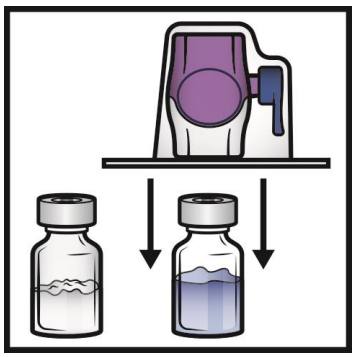
5. Open the BAXJECT II Hi-Flow device package by peeling away the lid, without touching the inside. (Figure A). Do not remove the device from the package.

Figure A



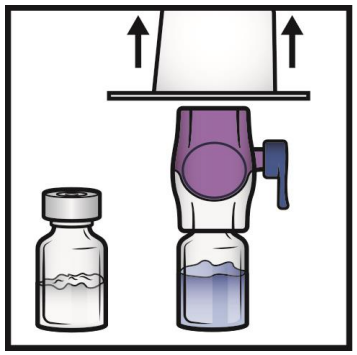
6. Turn the package over. Press straight down to fully insert the clear plastic spike through the diluent vial stopper. (Figure B)

Figure B



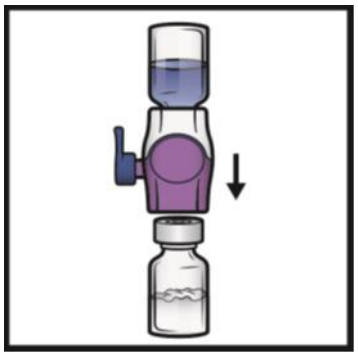
7. Grip the BAXJECT II Hi-Flow package at its edge and pull the package off the device. (Figure C). Do not remove the blue cap from the BAXJECT II Hi-Flow device. Do not touch the exposed purple plastic spike.

Figure C



8. Turn the system over so that the diluent vial is on top. Quickly insert the purple plastic spike fully into the ADYNOVATE vial stopper by pushing straight down. (Figure D). The vacuum will draw the diluent into the ADYNOVATE vial.

Figure D



9. Swirl gently until ADYNOVATE is completely dissolved. Do not refrigerate after reconstitution.

Figure E

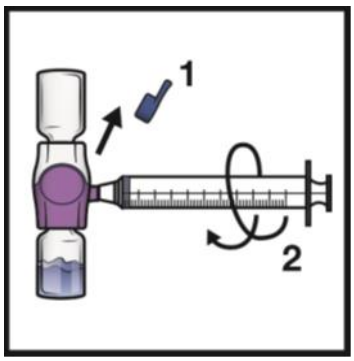
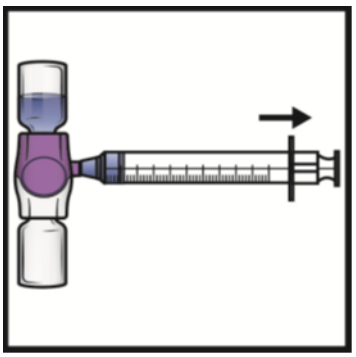


Figure F



Using the BAXJECT III system

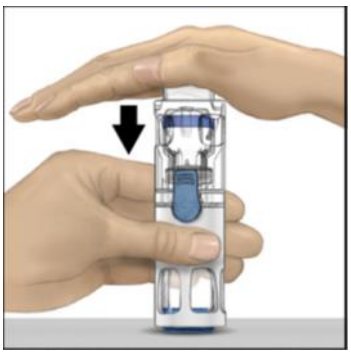
Do not use if the lid is not completely sealed on the blister

1. If the product is still stored in a refrigerator, take the sealed blister (contains powder and diluent vials preassembled with the system for reconstitution) from the refrigerator and let it reach room temperature.
2. Wash your hands thoroughly using soap and warm water.
3. Open the ADYNOVATE package by peeling away the lid. Remove the BAXJECT III system from the blister.
4. Place ADYNOVATE on a flat surface with the diluent vial on top. (Fig 1). The diluent vial has a blue stripe. Do not remove the blue cap until instructed in a later step.

Figure 1

5. With one hand holding ADYNOVATE in the 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 ADYNOVATE vial. (Fig 2).Do not tilt the system until the transfer is complete.

Figure 2



6. Verify that the diluent transfer is complete. Swirl gently until all material is dissolved. (Fig 3)

Figure 3

Be sure that the ADYNOVATE powder is completely dissolved, otherwise not all reconstituted solution will pass through the device filter. The product dissolves rapidly (usually in less than 1 minute). After reconstitution the solution should be clear, colourless and free from foreign particles.

Administration

- Visually inspect the reconstituted ADYNOVATE solution for particulate matter and discoloration prior to administration.
- The appearance of ADYNOVATE is clear and colourless.
- Do not use if particulate matter or discoloration is observed.
- Administer ADYNOVATE as soon as possible, but no later than 3 hours after reconstitution.

Administration Steps:

1. Remove the blue cap from the BAXJECT II Hi-Flow / BAXJECT III device. Connect the syringe to the BAXJECT II Hi-Flow / BAXJECT III device. Use of a Luer-lock syringe is recommended. Do not inject air.
2. Turn the system upside down (ADYNOVATE vial now on top). Draw the factor concentrate into the syringe by pulling the plunger back slowly.
3. Disconnect the syringe; attach a suitable needle and inject intravenously as instructed under Administration by bolus injection. If a patient is to receive more than one vial of ADYNOVATE, the contents of multiple vials may be drawn into the same syringe.

   A separate BAXJECT II Hi-Flow device is required to reconstitute each vial of ADYNOVATE with the diluent.
4. Administer ADYNOVATE over a period of less than or equal to 5 minutes (maximum infusion rate 10 mL per min).

Sponsor

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AUST R 273517 (ADYNOVATE 250 IU)

AUST R 278727 (ADYNOVATE 500 IU)

AUST R 278728 (ADYNOVATE 1000 IU)

AUST R 278729 (ADYNOVATE 2000 IU)

This leaflet was prepared in December 2017.