

Package leaflet: Information for the user

ADYNOVI 250 IU / 5 ml powder and solvent for solution for injection
ADYNOVI 500 IU / 5 ml powder and solvent for solution for injection
ADYNOVI 1 000 IU / 5 ml powder and solvent for solution for injection
ADYNOVI 2 000 IU / 5 ml powder and solvent for solution for injection
ADYNOVI 3 000 IU / 5 ml powder and solvent for solution for injection

rurioctocog alfa pegol (pegylated recombinant human coagulation factor VIII)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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 any further questions, ask your doctor.
- 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What ADYNOVI is and what it is used for
2. What you need to know before you use ADYNOVI
3. How to use ADYNOVI
4. Possible side effects
5. How to store ADYNOVI
6. Contents of the pack and other information

1. What ADYNOVI is and what it is used for

ADYNOVI contains the active substance rurioctocog alfa pegol, pegylated human coagulation factor VIII. The human coagulation factor VIII has been modified to prolong its duration of action. Factor VIII is necessary for the blood to form clots and stop bleedings. In patients with haemophilia A (inborn lack of factor VIII), it is missing or not working properly.

ADYNOVI is used for the treatment and prevention of bleeding in patients from 12 years of age with haemophilia A (an inherited bleeding disorder caused by lack of factor VIII).

2. What you need to know before you use ADYNOVI

Do not use ADYNOVI

- if you are allergic to rurioctocog alfa pegol, octocog alfa or any of the other ingredients of this medicine (listed in section 6)
- if you are allergic to mouse or hamster proteins

If you are unsure about this, ask your doctor.

Warnings and precautions

It is important to keep a record of the batch number of your ADYNOVI. So, every time you get a new package of ADYNOVI, note down the date and the batch number (which is on the packaging after *Lot*) and keep this information in a safe place.

Talk to your doctor before using ADYNOVI.

There is a rare risk that you may experience an anaphylactic reaction (a severe, sudden allergic reaction) to ADYNOVI. 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 could be early symptoms of anaphylactic shock; additional symptoms may include extreme dizziness, loss of consciousness, and extreme difficulty in breathing.

If any of these symptoms occur, stop the injection immediately and contact your doctor. Severe symptoms, including difficulty in breathing and (near) fainting, require prompt emergency treatment.

If you suffer from cardiac disease, please inform your doctor, as there is an increased risk of blood clotting (coagulation) complications.

Patients developing factor VIII inhibitors

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 you or your child's bleeding is not being controlled with ADYNOVI, tell your doctor immediately.

Catheter-related complications

If you require a central venous access device (CVAD), risk of CVAD-related complications including local infections, presence of bacteria in the blood and catheter site thrombosis should be considered.

Children and adolescents

ADYNOVI can be used only in adolescents and adults (12 years and above). The listed warnings and precautions also apply to adolescents.

Other medicines and ADYNOVI

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

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine. Haemophilia A occurs only rarely in women. Therefore no experience regarding the use of ADYNOVI during pregnancy and breast-feeding is available.

Driving and using machines

ADYNOVI has no or negligible influence on the ability to drive or use machines.

ADYNOVI contains sodium

ADYNOVI contains up to 12.42 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 0.62 % of the recommended maximum daily dietary intake of sodium for an adult. Depending on your body weight and your dose of ADYNOVI, you could receive multiple vials. This should be taken into consideration if you are on a low salt diet.

3. How to use ADYNOVI

Treatment with ADYNOVI will be started and supervised by a doctor who is experienced in the care of patients with haemophilia A.

Your doctor will calculate your dose of ADYNOVI depending on your condition and body weight, and on whether it is used for prevention or treatment of bleeding. The frequency of administration will depend on how well ADYNOVI is working for you. Usually, the replacement therapy with ADYNOVI is a life-long treatment.

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

Prevention of bleeding

The usual dose of ADYNOVI is 40 to 50 IU per kg body weight, administered 2 times per week.

Treatment of bleeding

The dose of ADYNOVI is calculated depending on your body weight and the factor VIII levels to be achieved. The target factor VIII levels will depend on the severity and location of the bleeding.

If you think that the effect of ADYNOVI is insufficient, talk to 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.

Use in children and adolescents

ADYNOVI can be used only in adolescents and adults (12 years and above). The dose in adolescents is also calculated to body weight and is the same dose as for adults.

How ADYNOVI is given

ADYNOVI is usually injected into a vein (intravenously) by your doctor or nurse. You or someone else might also administer ADYNOVI as an injection, but only after receiving adequate training. Detailed instructions for self-administration are given at the end of this package leaflet.

If you use more ADYNOVI than you should

Always use ADYNOVI exactly as your doctor has told you. You should check with your doctor if you are not sure. If you inject more ADYNOVI than recommended, tell your doctor as soon as possible.

If you forget to use ADYNOVI

Do not inject a double dose to make up for a forgotten dose. Proceed with the next injection as scheduled and continue as advised by your doctor.

If you stop using ADYNOVI

Do not stop using ADYNOVI without consulting your doctor.

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

4. Possible side effects

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

If **severe, sudden allergic reactions** (anaphylactic) occur, the injection **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.

For patients who have received previous treatment with Factor VIII (more than 150 days of treatment) inhibitor antibodies (see section 2) may form uncommonly (less than 1 in 100 patients). If this happens your medicine may stop working properly and you 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)

Headache

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

Nausea

Diarrhoea

Rash

Dizziness

Hives

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

Flushing, allergic reaction (hypersensitivity)

Factor VIII inhibitors (for patients who have received previous treatment with Factor VIII (more than 150 days of treatment))

Increase in some type of white blood cells

Infusion reaction

Redness of the eye

Adverse drug reaction of the skin

Side effects with unknown frequency (frequency cannot be estimated from the available data)

Potentially life-threatening reactions (anaphylaxis)

Additional side effects in children

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

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store ADYNOVI

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 label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

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

During the shelf life the powder vial may be kept at room temperature (up to 30 °C) for a single period not exceeding 3 months. In this case, this medicine expires at the end of this 3-month period or the expiry date printed on the product vial, whichever is earlier. Please record the end of the 3-month storage at room temperature on the outer carton. The product may not be returned to refrigerated storage after storage at room temperature. Do not refrigerate the solution after preparation.

Use the product within 3 hours once the powder is completely dissolved.

The product is for single use only. Discard any unused solution appropriately.

Do not throw away any medicines via waste water 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 ADYNOVI contains

- The active substance is ruriotocog alfa pegol (pegylated human coagulation factor VIII produced by recombinant DNA technology). Each powder vial contains nominally 250, 500, 1 000, 2 000 or 3 000 IU ruriotocog alfa pegol.
- The solvent vial contains 5 ml of water for injections.
- The other ingredients are mannitol, trehalose dihydrate, histidine, glutathione, sodium chloride, calcium chloride dihydrate, tris(hydroxymethyl)aminomethane and polysorbate 80. See Section 2 “ADYNOVI contains sodium”.

What ADYNOVI looks like and contents of the pack

ADYNOVI is provided as a powder and solvent for solution for injection (powder for solution for injection). The powder is a white to off-white crumbly powder. The solvent is a clear, colourless solution. After reconstitution, the solution is clear, colourless and free from foreign particles.

Marketing Authorisation Holder

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This leaflet was last revised in July 2023.

Instructions for preparation and administration

ADYNOVI must not be mixed with other medicinal products or solvents.

It is strongly recommended that every time ADYNOVI is administered, the name and batch number of the product are recorded. Peel-off labels are provided on the blister.

Instructions for reconstitution

- Do not use after the expiry date stated on the labels and carton.
 - Do not use if the lid is not completely sealed on the blister
 - Do not refrigerate the solution after preparation.
1. If the product is still stored in a refrigerator, take the sealed blister (contains powder and solvent vials preassembled with the system for reconstitution) from the refrigerator and let it reach room temperature (between 15 °C and 25 °C).
 2. Wash your hands thoroughly using soap and warm water.
 3. Open the ADYNOVI blister by peeling away the lid. Remove the BAXJECT III system from the blister.
 4. Place the powder vial on a flat surface with the solvent vial on top (Figure 1). The solvent vial has a blue stripe. Do not remove the blue cap until instructed in a later step.
 5. With one hand holding the powder vial in the BAXJECT III system, press down firmly on the solvent vial with the other hand until the system is fully collapsed and the solvent flows down into the powder vial (Figure 2). Do not tilt the system until the transfer is complete.
 6. Verify that the solvent transfer is complete. Swirl gently until all material is dissolved (Figure 3). Be sure that the 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.

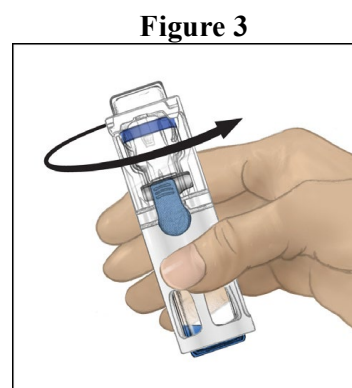
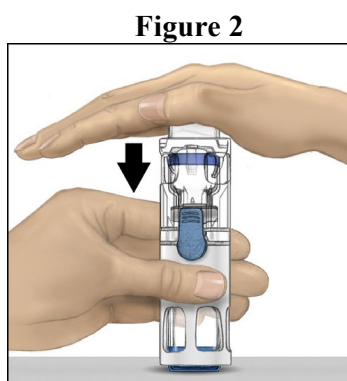
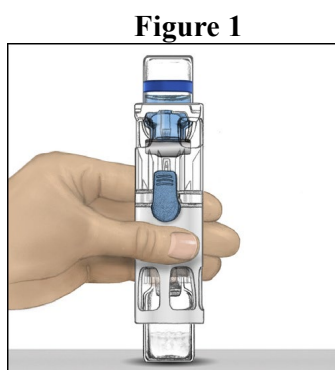
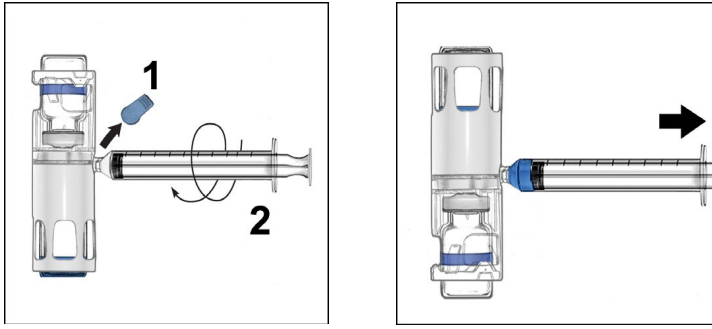


Figure 4

Figure 5



Instructions for injection

Antiseptic technique (clean and low-germ conditions) is required during administration.

Important note:

- Inspect the prepared solution for particulate matter and discolouration prior to administration (the solution should be clear, colourless and free from particles).
Do not use if the solution is not fully clear or not completely dissolved.
1. Remove the blue cap from BAXJECT III (Figure 4). **Do not draw air into the syringe.** Connect the syringe to BAXJECT III. Use of a Luer-lock syringe is recommended.
 2. Turn the system upside down (powder vial now on top). Draw the reconstituted solution into the syringe by pulling the plunger back slowly (Figure 5).
 3. Disconnect the syringe; attach a butterfly needle to the syringe and inject the reconstituted solution into a vein. The solution should be administered slowly, at a rate as determined by the patient's comfort level, not to exceed 10 ml per minute. (See section 4 "Possible side effects").
 4. Discard any unused solution appropriately.

The following information is intended for healthcare professionals only:

On demand treatment

In case of the following haemorrhagic events, factor VIII activity should not fall below the given plasma activity level (in % of normal or IU/dl) in the corresponding period. The following table can be used to guide dosing in bleeding episodes and surgery.

Table 1: Guide for dosing in bleeding episodes and surgery

Degree of haemorrhage/type of surgical procedure	Factor VIII level required (% or IU/dl)	Frequency of doses (hours)/duration of therapy (days)
Haemorrhage		
Early haemarthrosis, muscle bleeding or oral bleeding.	20 – 40	Repeat injections every 12 to 24 hours. At least 1 day, until the bleeding episode, as indicated by pain, is resolved or healing is achieved.
More extensive haemarthrosis, muscle bleeding or haematoma	30 – 60	Repeat injections every 12 to 24 hours for 3 – 4 days or more until pain and acute disability are resolved.
Life threatening haemorrhages.	60 – 100	Repeat injections every 8 to 24 hours until threat is resolved.
Surgery		

<i>Minor</i> Including tooth extraction.	30 – 60	Every 24 hours at least 1 day, until healing is achieved.
<i>Major</i>	80 – 100 (pre- and postoperative)	Repeat injections every 8 to 24 hours until adequate wound healing, then continue therapy for at least another 7 days to maintain a factor VIII activity of 30% to 60% (IU/dl).

Prophylaxis

For long term prophylaxis, the recommended dose is 40 to 50 IU of ADYNOVI per kg bodyweight twice weekly in 3 to 4 day intervals. Adjustments of doses and administration intervals may be considered based on achieved FVIII levels and individual bleeding tendency.

Paediatric population

On demand treatment dosing in paediatric patients (12 to 18 years of age) is the same as for adult patients. Prophylactic treatment for patients from 12 to <18 years is the same as for adult patients. The long-term safety of ADYNOVI in children below 12 years has not yet been established. Adjustments of doses and administration intervals may be considered based on achieved FVIII levels and individual bleeding tendency.