Package leaflet: Information for the user

Nuwiq 250 IU powder and solvent for solution for injection
Nuwiq 500 IU powder and solvent for solution for injection
Nuwiq 1000 IU powder and solvent for solution for injection
Nuwiq 1500 IU powder and solvent for solution for injection
Nuwiq 2000 IU powder and solvent for solution for injection
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Nuwiq 4000 IU powder and solvent for solution for injection
simoctocog 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 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 Nuwiq is and what it is used for

Nuwiq contains the active substance human recombinant coagulation factor VIII (simoctocog alfa). Factor VIII is necessary for the blood to form clots and stop bleeding. In patients with haemophilia A (inborn factor VIII deficiency), factor VIII is missing or not working properly.
Nuwiq replaces the missing factor VIII and is used for treatment and prevention of bleeding in patients with haemophilia A and can be used for all age groups.

2. What you need to know before you use Nuwiq

Do not use Nuwiq
- if you are allergic to the active substance simoctocog alfa or any of the other ingredients of this medicine (listed in section 6).

If you are unsure about this, ask your doctor.

Warnings and precautions
Talk to your doctor before using Nuwiq.

There is a rare chance that you may experience an anaphylactic reaction (a severe, sudden allergic reaction) to Nuwiq. You should be aware of the early signs of allergic reactions as they are listed in section 4 “Allergic reactions”.
If any of these symptoms occur, stop the injection immediately and contact your doctor.

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 Nuwiq, tell your doctor immediately.

Cardiovascular events
In patients with existing cardiovascular risk factors, substitution therapy with FVIII may increase the cardiovascular risk.

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.

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

Other medicines and Nuwiq
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.

Driving and using machines
Nuwiq has no influence on your ability to drive and use machines.

Nuwiq contains sodium
This medicine contains 18.4 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 0.92 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Nuwiq

Treatment with Nuwiq will be started by a doctor who is experienced in the care of patients with haemophilia A. Always use this medicine exactly as your doctor or nurse has told you. Check with your doctor or nurse if you are not sure.

Nuwiq is usually injected into a vein (intravenously) by your doctor or a nurse who are experienced in the care of patients with haemophilia A. You or someone else might also give your Nuwiq injection, but only after receiving adequate training.

Your doctor will calculate your dose of Nuwiq (in international units = IU) depending on your condition and body weight, and on whether it is used for prevention or treatment of bleeding. How often you need an injection will depend on how well Nuwiq is working for you. Usually, treatment for haemophilia A is a life-long treatment.

Prevention of bleeding
The usual dose of Nuwiq is 20 to 40 IU per kg body weight, given every 2 to 3 days. However, in some cases, especially in younger patients, more frequent injections or higher doses may be necessary.

Treatment of bleeding
The dose of Nuwiq 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 have the impression that the effect of Nuwiq 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.

Patients developing factor VIII inhibitors
If your plasma factor VIII fails to reach expected levels with Nuwiq, or if bleeding is not adequately controlled, it could be due to the development of factor VIII inhibitors. This will be checked by your doctor. You might need a higher dose of Nuwiq or a different product to control bleedings. Do not increase the total dose of Nuwiq to control your bleeding without consulting your doctor.

Use in children and adolescents
The way Nuwiq is used in children and adolescents does not differ from the way it is used in adults. Because factor VIII products may have to be given more often in children and adolescents, a central venous access device (CVAD) may need to be fitted. A CVAD is an external connector that allows access to the bloodstream through a catheter without injection through the skin.

If you use more Nuwiq than you should
No symptoms of overdose have been reported. If you have injected more Nuwiq than you should, please inform your doctor.

If you forget to use Nuwiq
Do not take a double dose to make up for a forgotten dose. Proceed with the next dose immediately and continue as advised by your doctor.

If you stop using Nuwiq
Do not stop using Nuwiq 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.

Please stop using this medicine immediately and seek urgent medical advice if:
- **you notice symptoms of allergic reactions**
  Allergic reactions may include rash, hives, urticaria (itchy rash), including generalized urticaria, swelling of lips and tongue, shortness of breath, wheezing, tightness of the chest, vomiting, restlessness, low blood pressure, and dizziness. These symptoms can be early symptoms of an anaphylactic shock. If severe, sudden allergic reactions (anaphylactic) occur (very rare: may affect up to 1 in 10,000 people), the injection must be stopped immediately and you must contact your doctor right away. Severe symptoms require prompt emergency treatment.

- **you notice that the medicine stops working properly (bleeding is not stopped or becomes frequent)**

For children and adolescents not previously treated with factor VIII medicines, inhibitor antibodies (see section 2) may form very commonly (more than 1 in 10 patients).
However for 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.

Common side effects may affect up to 1 in 10 people

Hypersensitivity, fever.

Uncommon side effects may affect up to 1 in 100 people
Tingling or numbness (paraesthesia), headache, dizziness, vertigo, dyspnoea, dry mouth, back pain, injection site inflammation, injection site pain, a vague feeling of bodily discomfort (malaise), haemorrhagic anaemia, non-neutralising antibody positive (in previously treated patients).

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.

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 Nuwiq

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

Store in a refrigerator (2°C – 8°C). Do not freeze. Store vial in the original package in order to protect from light.

Before the Nuwiq powder is reconstituted, it may be kept at room temperature (up to 25°C) for a single period not exceeding 1 month. Record the date from when you start to store Nuwiq at room temperature on the product carton. Do not store Nuwiq in the refrigerator again after it has been stored at room temperature.
Use the reconstituted solution immediately after reconstitution.

Do not use the medicine in case you notice visible signs of deterioration of the tamper proof of packaging especially of the syringe and/or the vial.

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 Nuwiq contains
Powder:
- The active substance is recombinant human coagulation factor VIII (simoctocog alfa).
  Each powder vial contains 250, 500, 1000, 1500, 2000, 2500, 3000 or 4000 IU of simoctocog alfa.
  Each reconstituted solution contains approximately 100, 200, 400, 600, 800, 1000, 1200 or 1600 IU/mL of simoctocog alfa.
- The other ingredients are sucrose, sodium chloride, calcium chloride dihydrate, arginine hydrochloride, sodium citrate dihydrate and poloxamer 188. See section 2, “Nuwiq contains sodium”.

Solvent:

Water for injections

What Nuwiq looks like and contents of the pack
Nuwiq is provided as powder and solvent for solution for injection. The powder is a white to off-white powder in a glass vial. The solvent is water for injections in a glass pre-filled syringe.
After reconstitution, the solution is clear, colourless and free from foreign particles.

Each pack of Nuwiq contains:
- 1 powder vial with 250, 500, 1000, 1500, 2000, 2500, 3000 or 4000 IU simoctocog alfa
- 1 pre-filled syringe with 2.5 mL water for injections
- 1 vial adapter
- 1 butterfly needle
- 2 alcohol swabs

Marketing Authorisation Holder and Manufacturer

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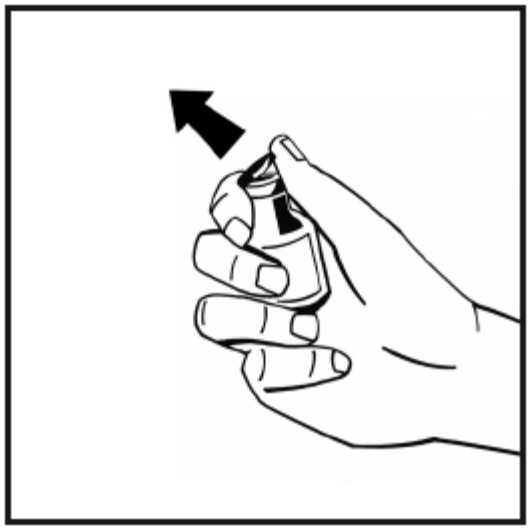
The following information is intended for healthcare professionals only:

On-demand treatment
The amount to be administered and the frequency of administration should always be oriented to the clinical effectiveness in the individual case.
In the 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.

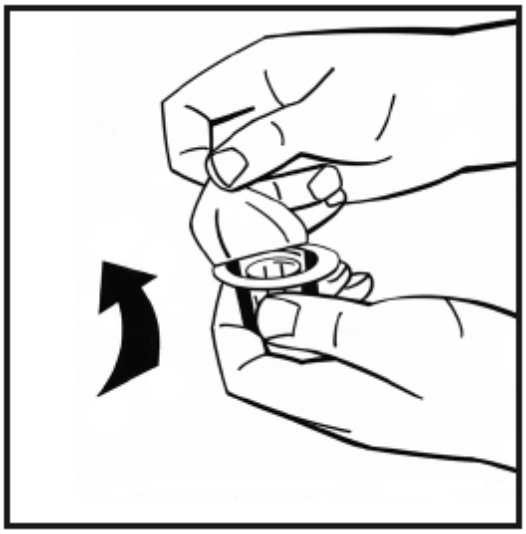
Degree of haemorrhage/ Type of surgical procedure	**Factor VIII level required (%) (IU/dL)**	**Frequency of doses (hours)/ Duration of therapy (days)**
Haemorrhage		
Early haemarthrosis, muscle bleeding or oral bleeding	20–40	Repeat every 12 to 24 hours. At least 1 day, until the bleeding episode as indicated by pain is resolved or healing is achieved.
More extensive haemarthrosis, muscle bleeding or haematoma	30–60	Repeat infusion every 12 to 24 hours for 3 to 4 days or more until pain and acute disability are resolved.
Life threatening haemorrhages	60–100	Repeat infusion every 8 to 24 hours until threat is resolved.
Surgery		
Minor surgery including tooth extraction	30–60	Every 24 hours, at least 1 day, until healing is achieved.
Major surgery	80–100 (pre- and postoperative)	Repeat infusion every 8–24 hours until adequate wound healing, then therapy for at least another 7 days to maintain a factor VIII activity of 30% to 60% (IU/dL).

INSTRUCTIONS FOR PREPARATION AND ADMINISTRATION

1. Allow the solvent syringe (water for injections) and the powder in the closed vial to reach room temperature. You can do this by holding them in your hands until they feel as warm as your hands. Do not use any other way to heat the vial and pre-filled syringe. This temperature should be maintained during reconstitution.
2. Remove the plastic flip-off cap from the powder vial to expose the central portions of the rubber stopper. Do not remove the gray stopper or metal ring around the top of the vial.

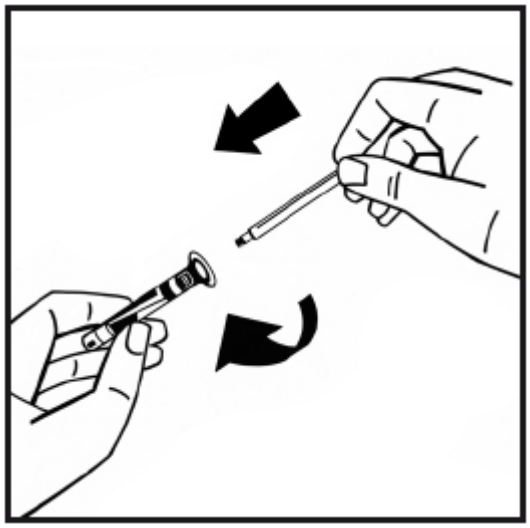


3. Wipe the top of the vial with an alcohol swab. Allow the alcohol to dry.
4. Peel back the paper cover from the vial adapter package. Do not remove the adapter from the package.

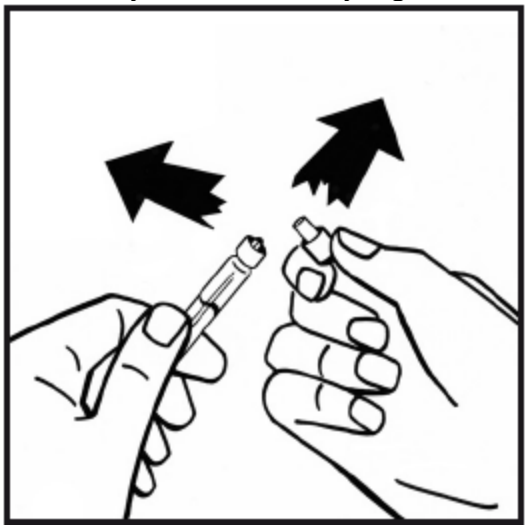


5. Place the powder vial on an even surface and hold it. Take the adapter package and place the vial adapter over the centre of the rubber stopper of the powder vial. Press down firmly the adapter package until the adapter spike penetrates the rubber stopper. The adapter snaps to the vial when done.

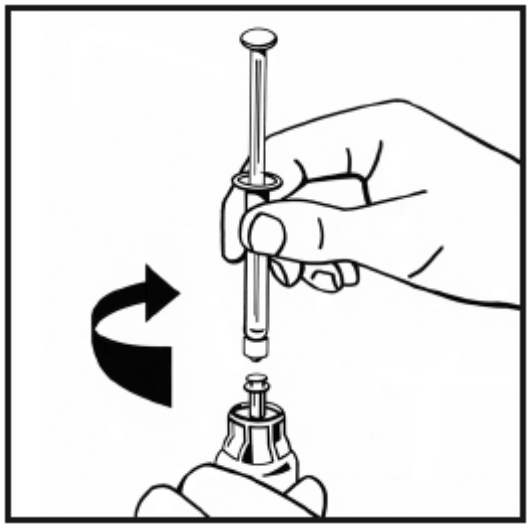
6. Peel back the paper cover from the pre-filled syringe package. Hold the plunger rod at the end and do not touch the shaft. Attach the threaded end of the plunger rod to the solvent syringe plunger. Turn the plunger rod clockwise until a slight resistance is felt.



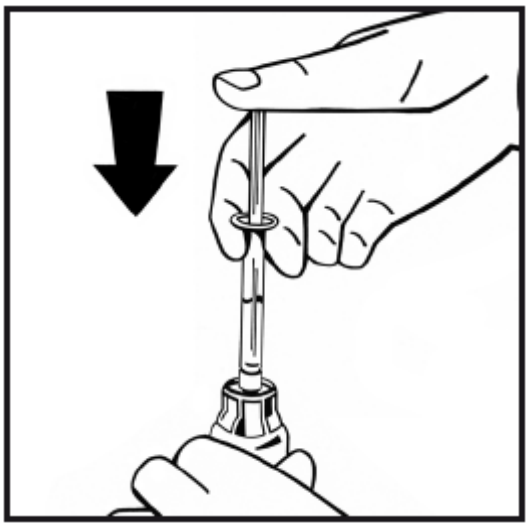
7. Break off the tamper-proof plastic tip from the solvent syringe by snapping the perforation of the cap. Do not touch the inside of the cap or the syringe tip. In case the solution is not used immediately close the filled syringe with the tamper-proof plastic tip for storage.



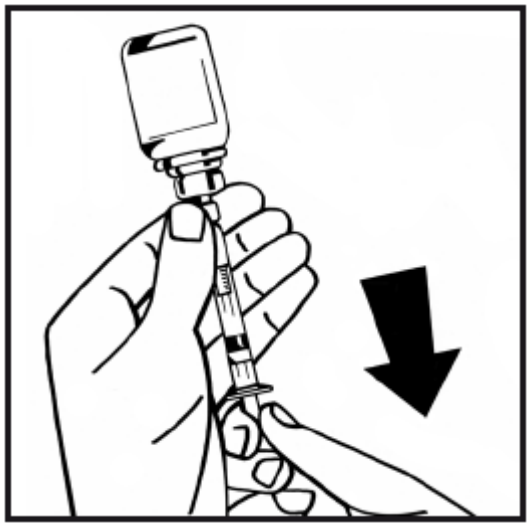
8. Remove the adapter packaging and discard.
9. Firmly connect the solvent syringe to the vial adapter by turning clockwise until resistance is felt.



10. Slowly inject all solvent into the powder vial by pressing down the plunger rod.



11. Without removing the syringe, gently move or swirl the vial in circles a few times to dissolve the powder. Do not shake. Wait until all the powder dissolves completely.
12. Visually inspect the final solution for particles before administration. The solution should be clear and colourless, practically free from visible particles. Do not use solutions that are cloudy or have deposits.
13. Turn the vial attached to the syringe upside down, and slowly draw the final solution into the syringe. Make sure that the entire content of the vial is transferred to the syringe.



14. Detach the filled syringe from the vial adapter by turning counter clockwise and discard the empty vial.
15. The solution is now prepared for immediate use. Do not refrigerate.
16. Clean the chosen injection site with one of the provided alcohol swabs.
17. Attach the provided infusion set to the syringe.
    Insert the needle of the infusion set into the chosen vein. If you have used a tourniquet to make the vein easier to see, this tourniquet should be released before you start injecting the solution. No blood must flow into the syringe due to the risk of formation of fibrin clots.
18. Inject the solution into the vein at a slow speed, not faster than 4 mL per minute.

If you use more than one vial of powder for one treatment, you may use the same injection needle again. The vial adapter and the syringe are for single use only.