PATIENT INFORMATION

What you need to know about ADVATE®

(OCTOCOG ALFA [RECOMBINANT HUMAN COAGULATION FACTOR VIII])

Your questions answered

You are receiving this booklet because you have been prescribed ADVATE.

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 or in the package leaflet.. You can also report side effects directly via the Yellow Card Scheme at 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.

This booklet is not a substitute for the Patient Information Leaflet that comes in your treatment pack. Please read the Patient Information Leaflet carefully.

This booklet has been produced by Takeda and is only intended for patients who have been prescribed ADVATE.

The information provided is not a substitute for professional and/or medical advice. Please talk to a healthcare professional for further advice.

Takeda

What's included in this booklet?

This booklet has been designed to answer any questions you may have about ADVATE factor VIII (FVIII) therapy. If you would like to know more, please speak to your consultant, nurse or haemophilia treatment centre.

What ADVATE is and what it is used for

ADVATE contains the active substance octocog alfa, human coagulation factor VIII produced by recombinant DNA technology. Factor VIII is necessary for the blood to form clots and stop bleeding.

ADVATE is used for the treatment and prevention of bleeding in patients of all age groups with haemophilia A (an inherited bleeding disorder caused by lack of factor VIII).

ADVATE is prepared without the addition of any human- or animal-derived protein in the entire manufacturing process.

How should I use ADVATE?

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

Your doctor will calculate your ADVATE dose for you. This dose will depend on your condition and body weight, and on whether you are using it to prevent bleeding (prophylaxis) or treatment of bleeding (on demand).

The frequency of administration will depend on how well ADVATE is working for you. Usually, the replacement therapy with ADVATE is a life-long treatment.

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

- **Prophylaxis**
  The ADVATE dose for prophylaxis is usually between 20 and 40 IU per kilogram of body weight, administered every 2 or 3 days. However, in some cases, especially in younger patients, more frequent infusions or higher doses may be necessary
- **Treating a bleed on demand**
  The ADVATE dose is calculated depending upon 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

Dose (IU) = body weight (kg) x desired factor VIII rise (% of normal) x 0.5

If you have the impression that the effect of ADVATE 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 (from 0 to 18 years of age)

For the treatment of bleeding the dosing in children does not differ from adult patients. For the prevention of bleeding in children under the age of 6, doses of 20 to 50 IU per kg body weight 3 to 4 times weekly are recommended. The administration of ADVATE in children (intravenously) does not differ from the administration in adults. A central venous access device (CVAD) may become necessary to allow frequent infusions of factor VIII products.

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, especially in children.

What is in your ADVATE pack?

Your pack will include your ADVATE vial, a vial containing 2 ml or 5 ml sterilised water for injections (solvent) and a BAXJECT II device for reconstitution.

May come with 2 mls or 5 mls sterilised water for injections		Comes with 5 mls sterilised water for injections			
					
250 IU	500 IU	1000 IU	1500 IU	2000 IU	3000 IU

Vials shown are for illustrative purposes only.

Do I need different amounts of water for different vial sizes?

Depending on the vial size you have been prescribed, ADVATE can be mixed with either 5 ml or 2 ml of sterilised water. You should only use the sterilised water for injections and the reconstitution device that are provided with each pack of ADVATE.

If you have any questions, please check with your consultant, nurse or haemophilia treatment centre.

How to prepare ADVATE

Prepare for your injection:

- Aseptic technique is required during preparation of the solution and administration
- Do not use after the expiry date stated on the labels and carton
- Do not use if the BAXJECT II device, its sterile barrier system or its packaging is damaged or shows any sign of deterioration as indicated by the symbol

- **Do not refrigerate** the solution after preparation
- ADVATE must not be mixed with other medicinal products or solvents

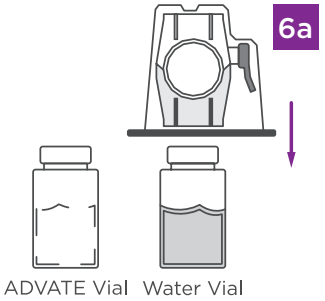
1. If the product is still stored in a refrigerator, take both the ADVATE powder and solvent vials from the refrigerator and let them reach room temperature (between 15 °C and 25 °C)
2. Wash your hands thoroughly using soap and warm water
3. Remove caps from powder and solvent vials
4. Cleanse stoppers with alcohol swabs
   - Place vials on a flat clean surface

After you have done these steps, follow the instructions on the next few pages to complete preparation of your ADVATE injection.

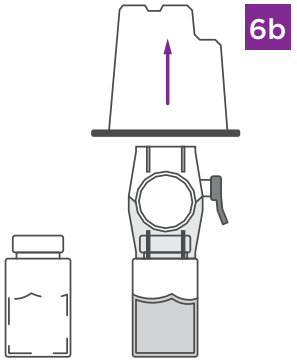
Connect sterilised water vial

5. **Open the package of BAXJECT II** device by peeling away the paper lid without touching the inside
   - **Do not remove the device from the package**

6. **Turn** the package over and **insert the clear plastic spike through the solvent stopper**



- **Grip** the package at its edge and pull the package off BAXJECT II
- **Do not remove the blue cap from the BAXJECT II device**

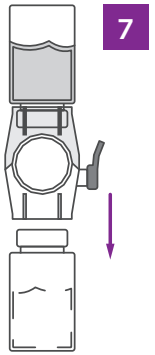


How to prepare ADVATE

Connect ADVATE vial

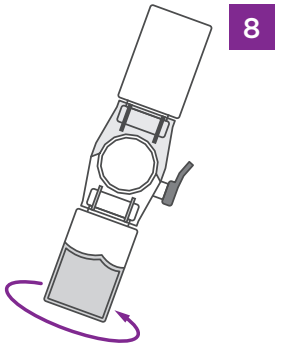
7 With BAXJECT II attached to the solvent vial, **invert** the system so that the solvent vial is on top of the device

- **Insert** the white plastic spike through the ADVATE powder stopper. The vacuum will draw the solvent into the ADVATE powder vial



8 **Swirl** gently until all ADVATE is dissolved

- **Be sure** that the ADVATE powder is completely dissolved, otherwise not all reconstituted solution will pass through the device filter. ADVATE dissolves rapidly (usually in less than 1 minute). After reconstitution the solution should be clear, colourless and free from foreign particles
- Inspect the prepared solution for particulate matter and discoloration prior to administration (it should be clear, colourless and free from foreign particles). **Do not use** if the solution is not fully clear or not completely dissolved

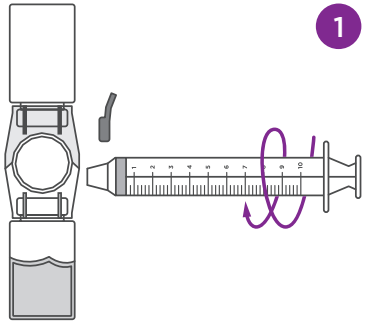


If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the national reporting system: Yellow Card Scheme www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

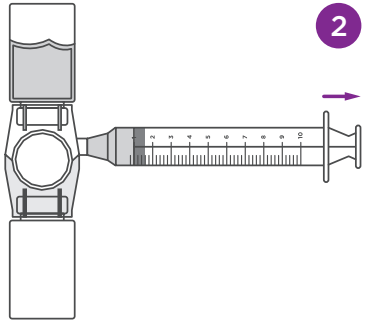
How to inject ADVATE

For administration the use of a luer-lock syringe is required



1 **Remove** the blue cap from BAXJECT II

- **Do not draw air into the luer lock syringe**
- **Connect** the syringe to BAXJECT II



2 **Invert** the system (the vial with the reconstituted solution has to be on top)

- **Draw** the reconstituted solution into the syringe by pulling the plunger back slowly

3 **Disconnect** the syringe

4 **Attach** a butterfly needle to the syringe and inject the reconstituted solution into a vein. The solution should be administered slowly, at a rate that you are comfortable with. Do not exceed 10 ml per minute

5 **Discard** any unused solution appropriately

Do not try to administer the injection unless you have received special training from your doctor or nurse

The information provided is not a substitute for professional and/or medical advice. Please consult a healthcare professional or your haemophilia treatment centre for further advice.

It is strongly recommended that every time you administer ADVATE, the name and batch number of the product are recorded.

If you are having any difficulties reconstituting ADVATE, please contact your haemophilia team in the first instance. Alternatively, contact us at Takeda: e-mail: medinfoemea@takeda.com or telephone: +44 (0)3333 000 181.

How do I store ADVATE?

Keep ADVATE out of the sight and reach of children

Do not use ADVATE after the expiry date, which is stated on the label after EXP. The expiry date refers to the last day of that month

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

Do not freeze

During its shelf life, ADVATE may be kept at room temperature (up to 25°C) for a single period no longer than 6 months. In this case, ADVATE expires at the end of this 6 month period or the expiry date printed on your vial, whichever is earlier

Please record the end of the 6 months storage at room temperature on the end of the product carton

Do not return ADVATE to refrigerated storage after storage at room temperature

Keep the ADVATE vial in the outer carton in order to protect from light until you need to use it

ADVATE is for single use only. Discard any unused solution appropriately

Once ADVATE is completely dissolved, use the solution immediately

Do not refrigerate the ADVATE solution after it has been mixed

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

What do I need to know now that I've been prescribed ADVATE?

What if I forget my ADVATE infusion?

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.

What if I stop using ADVATE?

Do not stop using ADVATE without consulting your doctor.

What if I take too much ADVATE?

Always take ADVATE exactly as your doctor has told you. You should check with your doctor if you are not sure. If you inject more ADVATE than recommended, tell your doctor or haemophilia treatment centre as soon as possible.

What are the possible side effects of using ADVATE?

Like all medicines, ADVATE can cause side effects, although not everybody gets them. **Very common side effects** that may affect more that 1 in 10 people are factor VIII inhibitors (for children not previously treated with factor VIII medicines). **Common side effects** that may affect up to 1 in 10 people are:

- headache
- fever

Uncommon side effects that may affect up to 1 in 100 people include: factor VIII inhibitors (for patients who have received previous treatment with factor VIII [more than 150 days of treatment]), dizziness, flu, fainting, abnormal heartbeat, red itchy bumps on the skin, chest discomfort, injection site bruise, injection site reaction, itching, increased sweating, unusual taste in the mouth, hot flushes, migraines, memory impairment, chills, diarrhoea, nausea, vomiting, shortness of breath, sore throat, infection of the lymphatic vessels, whitening of skin, eye inflammation, rashes, excessive sweating, foot and leg swelling, reduced percentage of red blood cells, increase in a type of white blood cells (monocytes), and pain in the upper abdomen or lower chest.

Side effects with unknown frequency (frequency cannot be estimated from the available data) potentially life-threatening reactions (anaphylaxis) and other allergic reactions (hypersensitivity), general disorders (tiredness, lack of energy).

Additional side effects in children

Other than the development of inhibitors in previously untreated paediatric patients (PUPs), and catheter-related complications, no age-specific differences in side effects were noted in the clinical studies.

How do I report any side effects?

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in the package leaflet. You can also report side effects directly via the national reporting system listed below:

Yellow Card Scheme

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.

What if I have a sudden allergic reaction?

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.

What if I have surgery?

Side effects include 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.

What if I have a central venous access device (CVAD)?

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

What if I haven't been treated with factor VIII medicines before?

For children not previously treated with factor VIII medicines, inhibitor antibodies may form and are very commonly occurring in more than 1 in 10 people; however patients who have received previous treatment with factor VIII (more than 150 days of treatment) the risk is uncommon (less than 1 in 100 people).

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.

What do I need to know before I use ADVATE?

Do not use ADVATE

- if you are allergic to octocog alfa or any of the other ingredients of this medicine
- if you are allergic to mouse or hamster proteins

If you are unsure about this, ask your doctor.

Warnings and precautions

Talk to your doctor before using ADVATE. You should tell your doctor if you have been previously treated with factor VIII products, especially if you developed inhibitors, since there might be a higher risk that it happens again. Inhibitors are blocking antibodies against factor VIII that reduce the efficacy of ADVATE to prevent or control bleeding. Development of inhibitors is a known complication in the treatment of haemophilia A. If your bleeding is not controlled with ADVATE, tell your doctor immediately.

There is a rare risk that you may experience an anaphylactic reaction (a severe, sudden allergic reaction) to ADVATE. 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, stop the injection immediately and contact your doctor. Severe symptoms, including difficulty in breathing and (near) fainting, require prompt emergency treatment.

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 ADVATE, tell your doctor immediately.

Children and adolescents

The listed warnings and precautions apply to both adults and children (from 0 to 18 years of age).

Other medicines and ADVATE

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

Pregnancy and breastfeeding

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

ADVATE has no influence on your ability to drive or to use machines.

ADVATE contains sodium

This medicine contains 0.45 mmol sodium (10 mg) per vial. To be taken into consideration by patients on a controlled sodium diet.

Misapplication of ADVATE

Misapplication (injection into the artery or outside the vein) should be avoided as mild, short-term injection site reactions, such as bruising and redness, may occur.

Recording your progress

When you start on ADVATE, it's important that you keep a record of when you have your injections and of any bleeds. To do this you should use Haemtrack online, on paper, or the Haemtrack phone app. You will also need to have regular blood tests to check your factor trough levels and test for factor VIII inhibitors.

Where can I find more information?

For further information please see the leaflet that comes in the ADVATE pack or contact your haemophilia treatment centre.

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