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Instructions for Home Treatment

Please read all the instructions and follow them carefully!
Wilate is reconstituted in the supplied solvent and injected intravenously.

Instructions for reconstitution:

1. Warm the Powder and Solvent in the closed vials up to room temperature. This temperature should be maintained during reconstitution. If a water bath is used for warming, care must be taken to avoid water coming into contact with the rubber stoppers (latex-free) or the caps of the vials. The temperature of the water bath should not exceed +37°C.
2. Remove the caps from the powder vial and the solvent vial and clean the rubber stoppers with an alcohol swab.
3. Remove the protective cover from the short end of the double-ended needle, making sure not to touch the exposed tip of the needle.
   Then perforate the centre of the solvent vial rubber stopper with the vertically held needle.
   In order to withdraw the fluid from the solvent vial completely, the needle must be introduced into the rubber stopper in such a way that it just penetrates the stopper and is visible in the vial.
4. Remove the protective cover from the other, long end of the double-ended needle, making sure not to touch the exposed tip of the needle.
   Hold the solvent vial upside-down above the upright powder vial and quickly perforate the centre of the concentrate vial rubber stopper with the needle. The vacuum inside the concentrate vial draws in the solvent.

5. Remove the double-ended needle with the empty solvent vial from the powder vial, then slowly rotate the vial until the concentrate is completely dissolved. Wilate dissolves quickly at room temperature to a clear solution.

The solution is clear to slightly opalescent. If the concentrate fails to dissolve completely or an aggregate is formed, the preparation must not be used.

Instructions for injection:

As a precautionary measure, the patients pulse rate should be measured before and during the FVIII injection. If a marked increase in the pulse rate occurs the injection speed must be reduced or the administration must be interrupted.

1. After the powder has been reconstituted in the manner described above, remove the protective cover from the filter needle and perforate the rubber stopper of the concentrate vial.
2. Remove the cap of the filter needle and attach the syringe.
3. Turn the vial with the attached syringe upside-down and draw the solution up into the syringe.
4. Clean the intended injection site with an alcohol swab.
5. Remove the filter needle from the syringe and attach the butterfly infusion needle to the syringe instead.
6. Inject the solution intravenously at a slow speed of 2–3 ml/minute.

Any unused product or waste material should be disposed of in accordance with local requirements.

Wilate must not be mixed with other medicinal products or administered simultaneously with other intravenous preparation in the same infusion set.

Only the provided injection/infusion sets can be used because treatment failure can occur as a consequence of FVIII/VWF adsorption to the internal surfaces of some infusion equipment.

PACKAGE LEAFLET: INFORMATION FOR THE USER
Wilate 500, 500 IU FVIII/500 IU VWF,
powder and solvent for solution for injection
Wilate 1000, 1000 IU FVIII/1000 IU VWF,
powder and solvent for solution for injection
Human coagulation factor VIII/human von Willebrand factor

Read all of this leaflet carefully before you start using this medicine.
- Please keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Wilate is and what it is used for

Wilate belongs to the pharmacotherapeutic group of medicines called clotting factors and contains human blood coagulation factor VIII (FVIII) and von Willebrand factor (VWF). Together these two proteins are involved in blood clotting.

Von Willebrand disease
Wilate is used to treat and prevent bleeding in patients with von Willebrand disease (VWD), which in fact is a family of related diseases. All types of VWD are inborn, where bleeding can go on for longer than expected. This is either due to a lack of VWF in the blood or due to VWF that does not work the way it should.

Haemophilia A
Wilate is used to treat and prevent bleeding in patients with haemophilia A. This is a condition in which bleeding can go on for longer than expected. It is due to an inborn lack of FVIII in the blood.

2. Before you use Wilate

Do not use Wilate
- if you are allergic (hypersensitive) to human blood coagulation factor VIII, von Willebrand factor or any of the other ingredients of Wilate.

Take special care with Wilate
- Any medicine, such as Wilate, which is prepared from human blood (containing proteins) and which is injected into a vein (administered intravenously) can cause allergic reactions. Please pay attention to early signs of allergic reactions (hypersensitivity), such as hives, skin rash, tightness of the chest, wheezing, low blood pressure, or anaphylaxis (when any or all of the above symptoms develop rapidly and are intense).
  If these symptoms occur, stop the injection immediately and contact your doctor.
- When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections. The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B (HBV) virus and hepatitis C virus (HCV), and for the non-enveloped hepatitis A virus (HAV). The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (infection of the baby) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or abnormal breakdown of red blood cells).
- It is strongly recommended that every time you receive a dose of Wilate the name and the batch number of the product are recorded in order to maintain a record of the batches used.

Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly/repeatedly receive human plasma-derived FVIII/VWF products.

Von Willebrand disease (VWD)
- Please see section 4. (Von Willebrand disease (VWD)) for side effects related to the treatment of VWD.

Haemophilia A
- Please see section 4. (Haemophilia A) for side effects related to the treatment of haemophilia A.

Taking other medicines
Although no influences on Wilate from other medicinal products are known, please tell your doctor or pharmacist if you are taking or have recently taken any other medicines (including medicines obtained without a prescription).
Please do not mix Wilate with any other medicines during the injection.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before using Wilate.

Important information about some of the ingredients of Wilate
This medicinal product contains up to 2.55 mmol sodium (58.7 mg) per dose for 500 IU FVIII and VWF/vial and up to 5.1 mmol sodium (117.3 mg) per dose for 1000 IU FVIII and VWF/vial. To be taken into consideration if you are on a controlled sodium diet.

3. How to use Wilate

Wilate should be injected into a vein (administered intravenously) after reconstitution with the supplied solvent. Treatment should be started under medical control.

Dosage
Your doctor will advise you about your individual dosage and the frequency with which you should use Wilate. Always use Wilate exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

If you use more Wilate than you should
No symptoms of overdose with human FVIII or VWF have been reported. However, the recommended dosage should not be exceeded.

If you forget to take Wilate
Do not take a double dosage to make up for a forgotten dosage.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible Side Effects

Like all medicines, Wilate can cause side effects, although not everybody gets them.
- Even though **uncommon**, hypersensitivity or allergic reactions have been observed. These may include:
  burning and stinging at the infusion site, chills, flushing, headache, hives (urticaria), low blood pressure (hypotension), tiredness (lethargy), sickness (nausea), restlessness, increase of heart rate (tachycardia), tightness of the chest, feeling of pins and needles (tingling), vomiting, wheezing, sudden swellings in various parts of the body (angiooedema).
  If you suffer from any of the above-mentioned symptoms, please inform your doctor.
  You should stop using Wilate and see your doctor immediately, if you experience symptoms of angiooedema, such as:
  - swollen face, tongue or throat (pharynx)
  - difficulties to swallow
  - hives and difficulties to breath
- On **rare** occasions, fever has been observed.
- In **very rare** cases, hypersensitivity may lead to a severe allergic reaction called anaphylaxis (when any or all of the above symptoms develop rapidly and are intense), which may include shock. In case of an anaphylactic shock, treatment using the current medical recommendations for shock is essential.

Von Willebrand disease (VWD)
- When using a FVIII-containing VWF product to treat VWD, the continued treatment may cause an excessive rise in FVIII in the blood. This may increase the risk that your blood flow will be disturbed (thrombosis).
  If you are a patient with known clinical or laboratory risk factors, you have to be checked for early signs of thrombosis. Prevention (prophylaxis) of thrombotic events should be decided by your doctor, according to the current recommendations.
- Patients with VWD (especially type 3 patients) may develop inhibitors (neutralising antibodies) to VWF during the treatment with VWF. In these **very rare** cases inhibitors can stop Wilate working properly.
  In case your bleeding continues, your blood has to be tested for these inhibitors.
  Inhibitors may increase the risk of suffering severe allergic reactions (anaphylactic shock). If you suffer an allergic reaction, you should be tested for the presence of inhibitors.

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Once inhibitors have been found in your blood, please contact a physician with experience in the care of patients with bleeding disorders. In patients with high amounts of inhibitors, another kind of treatment might be useful and should be considered.

Haemophilia A
- When using FVIII products to treat patients with haemophilia A, the formation of inhibitors (neutralising antibodies) to FVIII is a known complication. In these rare cases inhibitors can stop Wilate working properly and bleeding may continue. Please contact a specialised haemophilia centre if Wilate does not stop your bleeding. Regular blood tests will be performed during treatment to test for these inhibitors.

Inhibitors may increase the risk of suffering severe allergic reactions (anaphylactic shock). If you suffer an allergic reaction, you should be tested for the presence of inhibitors.

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

There are insufficient data to recommend the use of Wilate in previously untreated patients.

The experience of treatment with Wilate in children less than 6 years of age is limited.

For information on viral safety see section 2. (Take special care with Wilate).

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

5. How to store Wilate

Keep out of the reach and sight of children.

Store powder and solvent vial in a refrigerator (2°C – 8°C).

Do not freeze.

Keep the vials in the outer carton to protect from light.

Do not use Wilate after the expiry date stated on the label.

Wilate can be stored at room temperature (max. +25°C) for 6 months. In this case the shelf-life expires 6 months after the product has been taken out of the refrigerator for the first time. The new shelf-life has to be noted on the outer carton by you.

The powder should be dissolved only directly before injection. The stability of the solution has been demonstrated for 12 hours at room temperature. Nevertheless, to

prevent contamination, the solution should be used immediately and on one occasion only. Any unused product or waste must be disposed of correctly.

6. Further information

What Wilate contains
- The active substances are human coagulation factor VIII and human von Willebrand factor
- The other ingredients are sodium chloride, glycine, sucrose, sodium citrate and calcium chloride. Solvent: water for injections with 0.1% Polysorbate 80

What Wilate looks like and contents of the pack
Freeze-dried powder: white or pale yellow powder or crumbly solid
Reconstituted solution: should be clear or slightly opalescent

Wilate is supplied as a powder and solvent for solution for injection. It comes in 2 pack sizes:
- Wilate 500, 500 IU FVIII and 500 IU VWF, powder and solvent for solution for injection, contains nominally 500 IU human coagulation factor VIII and 500 IU human von Willebrand factor per vial. The product contains approximately 100 IU/ml human coagulation factor VIII and 100 IU/ml human von Willebrand factor when reconstituted with 5 ml of Water for Injections with 0.1% Polysorbate 80 (Solvent).
- Wilate 1000, 1000 IU FVIII and 1000 IU VWF, powder and solvent for solution for injection, contains nominally 1000 IU human coagulation factor VIII and 1000 IU human von Willebrand factor per vial. The product contains approximately 100 IU/ml human coagulation factor VIII and 100 IU/ml human von Willebrand factor when reconstituted with 10 ml of Water for Injections with 0.1% Polysorbate 80 (Solvent).

Content of the package
1 vial with freeze-dried powder
1 vial with solvent
1 equipment pack with the following medical devices:
1 disposable syringe
1 transfer set (1 double-ended needle and 1 filter needle)
1 infusion set
2 alcohol swabs