Patient Information Leaflet

SCHEDULING STATUS

S4

IMMUNATE 250 I.U. POWDER AND SOLVENT FOR SOLUTION FOR INJECTION

IMMUNATE 500 I.U. POWDER AND SOLVENT FOR SOLUTION FOR INJECTION

IMMUNATE 1 000 I.U. POWDER AND SOLVENT FOR SOLUTION FOR INJECTION

Human coagulation factor VIII

Sugar Free

Read all of this leaflet carefully before you using IMMUNATE.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, nurse or other health care provider.
- IMMUNATE has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

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

1. What IMMUNATE is and what it is used for

What IMMUNATE is

IMMUNATE is a coagulation factor VIII / von Willebrand factor complex made from human plasma. The coagulation factor VIII in Immunate replaces the factor VIII which is lacking or is not functioning properly in haemophilia A. Haemophilia A is a sex-linked, hereditary blood coagulation defect due to reduced factor VIII levels. This results in severe bleeding in joints, muscles and inner organs, either spontaneously or as a

consequence of accidental or surgical traumata. The administration of Immunate temporarily corrects the factor VIII deficiency and reduces the bleeding tendency.

In addition to its role as a factor VIII protecting protein, von Willebrand factor (VWF) mediates platelet adhesion to sites of vascular injury and plays a role in platelet aggregation.

What IMMUNATE is used for

IMMUNATE is used Treatment and prevention of bleeding in patients with congenital factor VIII deficiency or acquired factor VIII deficiency (haemophilia A, haemophilia A with factor VIII inhibitor, acquired factor VIII deficiency due to spontaneous development of factor VIII inhibitor).

Immunate is also used for the treatment of bleeding in patients with Von Willebrand's disease with factor VIII deficiency.

2. What you need to know before you use IMMUNATE

Do not use IMMUNATE

- if you are allergic to human coagulation factor VIII 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

Special care should be taken with IMMUNATE

<u>When allergic reactions occur:</u>

- There is a rare chance that you may experience an anaphylactic reaction (a severe, sudden allergic reaction) to Immunate. You should be aware of the early signs of allergic reactions such as flush, rash, hives, wheals, generalised itching, swelling of lips, eyelid and tongue, dyspnoea, wheezing, chest pain, tightness in the chest, general feeling of being unwell, dizziness, faster heart beat and low blood pressure. 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/infusion immediately and contact your doctor. Severe symptoms, including difficulty in breathing and (near) fainting, require immediate emergency treatment.

When monitoring is required:

- Your doctor may wish to carry out tests to ensure that your current dose is sufficient to reach and maintain adequate factor VIII or von Willebrand levels.

When bleeding is still occurring:

- 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 IMMUNATE, tell your doctor immediately.

  If you have von Willebrand's disease, especially type 3, you may develop neutralizing antibodies (inhibitors) to von Willebrand factor. Your doctor may wish to carry out tests to confirm this. Von Willebrand factor inhibitors are antibodies in the blood that block the von Willebrand factor you are using. This makes von Willebrand factor less effective in controlling bleeding.

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, the testing of each donation and pools of plasma for signs of virus/infections, and the inclusion of 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 virus and hepatitis C virus, and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B 19

infection may be serious for pregnant women (foetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

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

It is strongly recommended that every time you receive a dose of Immunate the name and batch number of the medicine are recorded in order to maintain a record of the batches used.

IMMUNATE contains blood group isoagglutinins (anti-A and anti-B). If you have blood group A, B, or AB, haemolysis may occur following repetitive administration at short intervals or following administration of very large doses.

Children and adolescents

The product should be used with caution in children less than 6 years of age, who have limited exposure to factor VIII products, as there is limited clinical data available for this patient group.

Other medicines and IMMUNATE

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

No interactions of IMMUNATE with other medicinal products have been reported.

IMMUNATE must not be mixed with other medicinal products or solvents, except the enclosed Sterilised Water for Injections, prior to administration as this might impair the efficacy and safety of the product. It is advisable to flush implanted venous access with an appropriate solution, e.g. physiological saline solution, prior to and after infusion of IMMUNATE.

IMMUNATE with food and drink

There are no specific recommendations as to when IMMUNATE should be administered with regard to meals.

Pregnancy, breast-feeding and fertility

There is no experience regarding the use of IMMUNATE during pregnancy, breast-feeding and fertility as haemophilia A is rare in women. IMMUNATE should be used during pregnancy and lactation only if clearly indicated. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

There is no information on the effects of IMMUNATE on the ability to drive and use machines.

IMMUNATE contains sodium

250 IU and 500 IU pack size:

IMMUNATE contains 9,8 mg of sodium (main component of cooking/table salt) in each vial. This is equivalent to 0,5 % of the recommended maximum daily dietary intake of sodium for an adult.

1 000 IU pack size :

IMMUNATE contains 19,6 mg of sodium (main component of cooking/table salt) in each vial. This is equivalent to 1 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use IMMUNATE

Do not share medicines prescribed for you with any other person.

Your therapy should be under the supervision of a doctor experienced in the treatment of haemostatic disorders.

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

Dosage for prevention of bleeding

If you are using IMMUNATE to prevent bleeding, your doctor will calculate the dose for you. He/she will do this according to your particular needs. The usual dose will be between 20 to 40 IU factor VIII per kg of body

weight, administered at intervals of 2 to 3 days. However, in some cases, especially in younger patients, shorter dose intervals or higher doses may be necessary.

If you have the impression that the effect of Immunate is insufficient, talk to your doctor.

Dosage for treatment of bleeding

If you are receiving IMMUNATE for treatment of bleeding, your doctor will calculate the dose for you. He/she will do this according to your particular needs.

Your doctor will tell you how long your treatment with IMMUNATE will last. Do not stop treatment early because 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. If you have the impression that the effect of IMMUNATE is too strong or too weak, tell your doctor or pharmacist.

Dosage in von Willebrand's disease

Your doctor will control haemorrhages following the guidelines given for haemophilia A.

Route and/or method of administration

IMMUNATE is administered into a vein (intravenously) after preparing the solution with the solvent provided.

Follow the directions given by your doctor closely.
For reconstitution use only the administration set provided in the pack because treatment failure can occur as a consequence of human coagulation factor VIII adsorption to the internal surfaces of some infusion equipment.

IMMUNATE is to be reconstituted immediately before administration. The solution should then be used straight away as it does not contain preservatives.

Reconstitution of the powder to prepare a solution for injections

Use Aseptic Technique as described below

Lyophilised Powder for injection

1. Warm the unopened vial containing the solvent (Sterilised Water for Injections) to room temperature (maximum 37 °C).
2. Remove protective caps from the concentrate vial and solvent vial (fig. A) and cleanse the rubber stoppers of both.
3. Place and press the undulated rim of the transfer set onto the solvent vial (fig. B).
4. Remove protective covering from the other end of the transfer set taking care not to touch the exposed end.
5. Invert the transfer set with the attached solvent vial over the concentrate vial and insert the free needle through the rubber stopper of the concentrate vial (fig. C). The solvent will be drawn into the concentrate vial by vacuum.
6. After approximately one minute, disconnect the two vials by removing the transfer set with the attached solvent vial from the concentrate vial (fig. D). Since the preparation dissolves easily, only gently - if at all - agitate the concentrate vial. DO NOT SHAKE THE CONTENTS OF THE VIAL. DO NOT INVERT THE CONCENTRATE VIAL UNTIL READY TO WITHDRAW CONTENTS.
7. After reconstitution, the prepared solution should be inspected visually for particulate matter and discoloration prior to administration. However, even when the reconstitution procedure is strictly followed, a few small particles may occasionally be visible. The enclosed filter set will remove particles and the labelled potency will not be reduced.

Administration: Use Aseptic Technique as described below

1. To prevent stopper-derived rubber particles from being administered with the medicinal product (risk of microembolism), use the enclosed filter set. To withdraw the dissolved preparation, fit the filter set onto the enclosed disposable syringe and insert it through the rubber stopper (fig. E).
2. Disconnect the syringe for a moment from the filter set. Air will enter into the concentrate vial and any foam will collapse. Then draw the solution into the syringe through the filter set (fig. F).
3. Disconnect the syringe from the filter set and slowly inject the solution intravenously (maximum rate of injection: 2 ml per minute) with the enclosed winged infusion set (or the enclosed disposable needle).

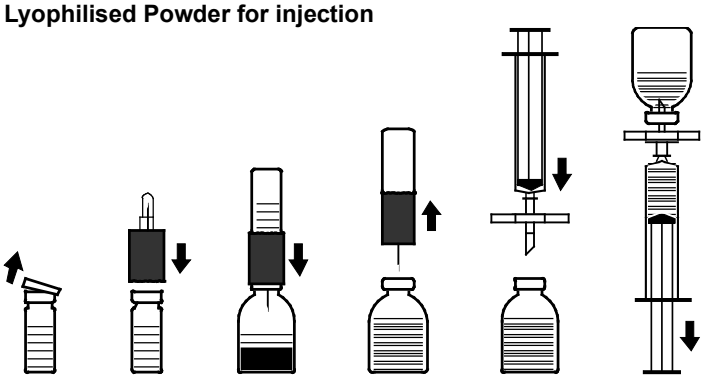


fig. A fig. B fig. C fig. D fig. E fig. F

All unused solution, empty vials and used needles and syringes must be discarded appropriately.

The administration of IMMUNATE should be documented, and the lot number recorded. A detachable documentation label is attached to each vial.

Frequency of administration

Your doctor will tell you how often and at what intervals IMMUNATE is to be administered. He/she will do this according to the effectiveness in your individual case.

If you use more IMMUNATE than you should

- No symptoms of overdose with coagulation factor VIII have been reported. If you have any doubts, please consult your doctor.
- Thromboembolic events may occur.
- Haemolysis may occur in patients with blood group A, B, or AB.

If you forget to use IMMUNATE

- Do not take a double dose to make up for a forgotten dose.
- Proceed with the next regular administration immediately and continue at regular intervals as advised by your doctor.

If you stop using IMMUNATE

Do not make a decision to stop using IMMUNATE 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, IMMUNATE can cause side effects, although not everybody gets them.

Not all side effects reported for IMMUNATE are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking IMMUNATE, please consult your health care provider for advice.

Serious side effects possible with human plasma derived factor VIII products

Allergic reactions, which may in some cases progress to severe and potentially life-threatening reactions (anaphylaxis), have been observed rarely. Therefore you should be aware of the early signs of allergic reactions such as flush, rash, hives, wheals, generalised itching, swelling of lips and tongue, dyspnoea (difficulty in breathing), wheezing (impaired breathing in and/or out due to constriction of the air passages), tightness in the chest, low blood pressure, drop in blood pressure, general feeling of being unwell, and dizziness. These symptoms may be early signs of an anaphylactic shock. If allergic or anaphylactic reactions occur, stop the injection/infusion immediately and inform your doctor. Severe symptoms require immediate emergency treatment.

For children not previously treated with factor VIII medicines, inhibitor antibodies (see section 2) may form very commonly (more than 1 in 10 patients); 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 patients). If this happens you 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.

The formation of neutralising antibodies (inhibitors) to von Willebrand factor is a known complication in the treatment of patients with von Willebrand’s disease. If you develop neutralising antibodies (inhibitors), this can manifest itself as an insufficient clinical response (bleeding is not controlled with an appropriate dose) or as allergic reaction. In these cases, it is recommended to contact a specialised haemophilia centre.

If you have blood group A, B or AB, haemolysis may occur following the administration of large doses.

These are all very serious side effects. If you have them, you may have had a serious reaction to IMMUNATE. You may need urgent medical attention or hospitalisation.

Side effects reported with the use of IMMUNATE

Very common (may affect more than 1 in 10 people)

- Factor VIII inhibition (for children not previously treated with factor VIII medicines).

Uncommon (may affect up to 1 in 100 people)

- Hypersensitivity
- Factor VIII inhibition (for patients who have received previous treatment with factor VIII (more than 150 days of treatment)).

Not known (frequency cannot be estimated from the available data)

- Coagulopathy (inability to form clots)
- Restlessness
- Paraesthesia (tingling or pricking sensation)
- Dizziness
- Headache
- Conjunctivitis (pink eye)
- Tachycardia (rapid heartbeat)
- Palpitations (feeling one's heartbeat)
- Hypotension (low blood pressure)
- Flushing
- Pallor (Pale appearance)
- Dyspnoea (shortness of breath)
- Cough
- Vomiting
- Nausea
- Urticaria (nettle rash on the entire body)
- Rash

- Pruritus (itching sensation)
- Erythema (redness of the skin)
- Hyperhidrosis (excessive sweating)
- Neurodermatitis (itchy or scratchy skin)
- Myalgia (muscle pain)
- Chest pain
- Chest discomfort
- Oedema (fluid retention)
- Pyrexia (fever)
- Chills
- Burning and stinging at the injection site injections site reactions
- Pain

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med_Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. Additionally, suspected adverse reactions can be reported to AE.southafricassa@takeda.com or on the 24 hours contact number: 082 525 3040. By reporting side effects, you can help provide more information on the safety of IMMUNATE

5. How to store Immunate

Keep this medicine out of the sight and reach of children.

Store and transport refrigerated (2 °C-8 °C). Do not freeze.

Store in the original package in order to protect from light.

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.

During the shelf life, IMMUNATE may be kept at room temperature (up to 25 °C) for a single period not exceeding 6 months. Please record the beginning of storage at room temperature on the product carton.

After storage at room temperature, IMMUNATE must not be put back into the refrigerator but is to be used immediately or to be discarded.

Do not use this medicine if you notice that the reconstituted product solution is turbid or has deposits.

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 IMMUNATE contains

Powder

- IMMUNATE contains approximately 50 IU/ml (250 IU pack size) or 100 IU/ml (500 IU and 1000 IU pack size) of human coagulation factor VIII and at least 25 U/ml (250 IU pack size) or 50 U/ml (500 IU and 1000 IU pack size) of von Willebrand factor when reconstituted with 5 ml (250 IU and 500 IU pack size) or 10 ml (1000 IU pack size) of Sterilised Water for Injection.
- The other ingredients are human albumin, glycine, sodium chloride, sodium citrate, lysine monohydrochloride and calcium chloride.

Solvent

- Sterilised water for injections

What IMMUNATE looks like and contents of the pack

Powder and solvent for solution for injection.

White or pale yellow powder or friable solid.

IMMUNATE is available in sizes of 250 IU, 500 IU and 1000 IU, to be dissolved in 5 ml (250 IU and 500 IU pack size) or 10 ml (1000 IU pack size) of Sterilised Water for Injections. Both powder and solvent come in single dose glass vials (powder: surface-treated soda lime silica glass, hydrolytic type II; solvent: neutral glass, hydrolytic type I) closed by either halogenobutyl rubber or fluoro-resin laminated butyl rubber stoppers. Each pack also includes a kit for reconstitution and injection comprising a transfer/filter set, a disposable syringe, a disposable needle, and a winged infusion set.

Holder of Certificate of Registration

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