PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

THYMOGLOBULINE® 25 mg powder for solution for infusion.

Rabbit anti-human thymocyte immunoglobulin

Contains sugar alcohol: mannitol 50 mg.

Read all of this leaflet carefully before you are given THYMOGLOBULINE.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor, pharmacist, nurse or other health care provider.

What is in this leaflet

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

1. What THYMOGLOBULINE is and what it is used for

THYMOGLOBULINE belongs to a group of medicines called immunosuppressants (anti-rejection medicines). These medicines can help prevent the rejection of transplanted organs. They can also be used to treat other unwanted immune reactions.

THYMOGLOBULINE is an anti-human thymocyte globulin made from the blood of rabbits injected with cells from the human thymus gland. The immunoglobulins which it contains attach to and destroy some of the cells of your immune system in your body. These cells play a role in the rejection of transplanted organs or carry out other unwanted immune reactions.

- *Solid organ (kidney, pancreas, liver and heart) transplantation:*

THYMOGLOBULINE is used to prevent or treat the rejection of an organ transplant (kidney, pancreas, liver or heart transplant). THYMOGLOBULINE is usually used in combination with other immunosuppressants. When a patient receives an organ, the body's natural defence system will try to get rid of it (reject it). THYMOGLOBULINE modifies the body's defence mechanism and helps it accept the transplanted organ.

- *Aplastic anaemia:*

THYMOGLOBULINE can be used to treat aplastic anaemia, a serious condition in which your bone marrow can no longer produce enough blood cells. The most common cause of aplastic anaemia is from your immune system attacking and damaging the blood-forming stem cells in your bone marrow. THYMOGLOBULINE works by lowering certain cells within your body's immune system, to stop the damage of your blood-forming stem cells, thus giving your bone marrow a chance to produce blood cells.

- *Bone marrow or blood-forming stem cell transplantation:*

THYMOGLOBULINE is used to prevent or treat rejection of bone marrow or blood-forming stem cell transplantation (graft-versus-host syndrome). THYMOGLOBULINE works by lowering certain cells within your body's immune system, to stop your body attacking and rejecting the transplanted cells.

2. What you need to know before you receive THYMOGLOBULINE

THYMOGLOBULINE should not be administered to you if:

- You are allergic (hypersensitive) to anti-human thymocyte globulin, rabbits, or any of the other ingredients of THYMOGLOBULINE (see section 6).
- You have acute or chronic infections because THYMOGLOBULINE decreases your body's ability to fight infections.

Warnings and precautions

Tell your doctor or health care provider before being given THYMOGLOBULINE if:

- You have ever had an allergic reaction to animals or other medicines. Your doctor will monitor you closely and stop treatment if there are any signs of an allergic reaction to THYMOGLOBULINE (see section 4.8).
- You have any illnesses of the blood, such as thrombocytopenia (lower than normal number of platelets in your blood which may cause bleeding problems) or leucopenia (lower than normal white cells in your blood which may increase your risk for infection). Your dose will depend on the number of white blood cells or platelets in your blood which will be checked before, during and after treatment.
- You have a liver disease.
- You have any signs of an infection (e.g. unusual weakness or tiredness, loss of appetite, weight loss, fever, night sweats, chills and pains) (see section 4). THYMOGLOBULINE can lower the number of blood cells that help your body fight infections. This can make it easier for you to get sick from being around others who are ill. Your blood may need to be tested often.
- You have lowered immunity due to diseases such as HIV/AIDS, cancer, tuberculosis (TB), active skin allergies, including rash and eczema or recurring boils.

Take special care with THYMOGLOBULINE

- Using THYMOGLOBULINE may increase your risk of developing certain types of cancer, such as lymphoma (cancer of the lymph nodes). Talk with your doctor about your specific risk.
- Certain types of vaccines (live attenuated vaccines) are not recommended, while you are being treated with THYMOGLOBULINE (see Taking other medicines with THYMOGLOBULINE). Talk to your doctor before getting vaccinated while you are receiving THYMOGLOBULINE.
- THYMOGLOBULINE infusion may cause severe immune system reactions, including acute infusion-related reactions; allergic reactions and cytokine release syndrome (CRS) which may be fatal (see section 4).
- Human blood components (formaldehyde-treated red blood cells and thymus cells) are used in the manufacturing process for THYMOGLOBULINE. Standard measures to prevent infections resulting from the use of medicines prepared from human blood components include specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite these measures, when medicines prepared from human blood components are administered, the possibility of transmitting infective agents cannot be totally excluded. This risk also applies to unknown or emerging viruses and other pathogens (organisms that can cause disease).

Other medicines and THYMOGLOBULINE

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

Tell your doctor if you are taking any other medicines (immunosuppressants) that could modify your body's defence system, such as azathioprine, ciclosporin, tacrolimus, mycophenolate mofetil or corticosteroids. This is because if the body's defence system is reduced too much, severe infections may occur. You may need different amounts of these medicines, or you may need to take different medicines. Your doctor will determine which medicines you need and calculate the dose most suitable for you.

Vaccinations: You must not be vaccinated during or soon after treatment with THYMOGLOBULINE without first discussing it with your doctor, as it may not be safe to do so. Vaccination may cause side effects (if it is a live attenuated vaccine) such as serious and potentially fatal infections, especially if you already have a compromised immune system.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other health care provider for advice before receiving THYMOGLOBULINE.

The safety of THYMOGLOBULINE during pregnancy and breastfeeding has not been established.

Due to the lack of information, THYMOGLOBULINE is not usually given to pregnant women unless it is absolutely necessary.

Do not breastfeed if you are receiving THYMOGLOBULINE because it may get into your breast milk and may affect your baby.

Driving and using machines

Do not drive or use any tools or machines as THYMOGLOBULINE may make you feel unwell, tired or dizzy.

THYMOGLOBULINE contains sodium

Each vial contains 4 mg of sodium (the main component of cooking/table salt).

3. How to receive THYMOGLOBULINE

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

You will not be expected to give yourself THYMOGLOBULINE. It will be given to you by a person who is qualified to do so, while you are in hospital.

The dose you are given is variable and depends on your ideal weight, which medical problem is being treated, and if you are being given any other medicines at the same time.
THYMOGLOBULINE will be given as an intravenous infusion at the specific dose calculated for you by your doctor and will be given for the following treatment periods:

Organ transplant

- *To prevent kidney, pancreas or liver transplant rejection:* for 2 to 9 days after transplantation.
- *To prevent heart transplant rejection:* for 2 to 5 days after transplantation.
- *To treat graft (organ) transplant rejection:* for 3 to 14 days.

Aplastic Anaemia

- *To treat severe aplastic anaemia*: every day for 5 days.

Graft-versus-host disease

- *To prevent rejection of transplanted bone marrow or blood-forming stem cells (graft-versus-host disease) in adults:* from day -4 to day -2 or -1 (before transplantation).
- *To treat rejection of transplanted bone marrow or blood-forming stem cells (graft-versus-host disease):* for 5 days.

THYMOGLOBULINE is given through a plastic tube (catheter) directly into your blood stream (intravenous infusion) over a period of at least 4 hours. The first dose may be given over a longer period of time. Your doctor or nurse will check you regularly while you receive your first dose because this is when you are more likely to get side effects. They will check your pulse and blood pressure, whether or not you have any rashes, that you can breathe easily and are alert.

Additional medications

Your doctor may give you some other medicines before, or at the same time as THYMOGLOBULINE. These medicines are used to avoid or treat possible side effects and could include:

- Medicine to reduce fever (like paracetamol).
- Corticosteroids (e.g. hydrocortisone) to prevent organ rejection and prevent side effects.
- Antihistamines (e.g. cetirizine) to prevent an allergic response.
- Heparin to reduce the risk of blood clots.

From time to time your doctor may also want you to have a blood test to monitor your blood cell count. The dose of THYMOGLOBULINE may be changed by your doctor if you have any side effects.

If you receive more THYMOGLOBULINE than you should

Since a health care provider will administer THYMOGLOBULINE, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you missed a dose of THYMOGLOBULINE

Since a health care provider will administer THYMOGLOBULINE, it is unlikely that the dose will be missed. THYMOGLOBULINE needs to be given on a fixed schedule. If you miss an appointment, call your doctor or health care provider for instructions.

4. Possible side effects

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

Some side effects, such as fever, rash and headache, and others affecting your pulse rate, blood pressure and breathing, as well as some allergic reactions, are more likely to occur with your first or second dose of THYMOGLOBULINE than with later doses.

Sometimes the effects of THYMOGLOBULINE may not occur until months after it is used. These delayed effects may include an increased risk of infections and of certain types of cancer.

If any of the following happens, tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, tongue or throat, which may cause difficulty in swallowing or breathing or fainting.
- Raised itchy rash.
- Stomach pain.

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

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Frequent:

- Blood test results showing low counts of certain types of white blood cells or low platelet counts.
- Bleeding or bruising more easily than normal.
- Infection (symptoms may include fever, chills, sore throat, mouth ulcers).
- A serious infection called sepsis, including symptoms such as difficulty breathing, low blood pressure, fast heart rate and mental confusion.
- Shortness of breath, difficulty breathing, wheezing or coughing.
- Irregular or fast heartbeat.
- Abnormal cell growths (including cancerous and non-cancerous).

Less frequent:

- Infusion-associated reactions such as fever, chills, difficulty breathing, nausea, vomiting, diarrhoea, high or low blood pressure, discomfort, tiredness, decreased oxygen saturation, rash or headaches.
- Serum sickness, which is an illness caused by antibodies against THYMOGLOBULINE and may cause rash, itching, urticaria (itchy, red welts), joint pains, kidney problems and swollen lymph nodes.
- Formation of blood clots throughout the body (disseminated intravascular coagulation), blocking small blood vessels. Symptoms may include chest pain, shortness of breath, leg pain, problems speaking, or problems moving parts of your body.
- Unusual bleeding or formation of blood clots (coagulopathy).
- Inflammation of veins under the skin with the formation of blood clots in the vein (thrombophlebitis).
- Increase in some liver enzymes in your blood (transaminases).
- Liver injury (liver failure), symptoms may include yellowing of the skin or eyes, pain in the upper right abdomen, feeling sick (nausea) or being sick (vomiting) or sleepiness.
- Oral thrush (creamy white, sore patches in your mouth or on your tongue) or viral infections such as cold sores and fever blisters around the mouth and on the face or genitals.
- Severe cytokine release syndrome has been associated with symptoms such as low blood pressure, swelling of the lungs, difficulty breathing, heart attack, palpitations and/or death.
- Lymphoproliferative disorder which causes excessive formation of lymphocytes (a certain type of white blood cell). Symptoms include fever, inflammation and soreness of the throat, swollen lymph glands, enlarged spleen or liver, and/or abnormal liver function resulting in yellowing of the skin, mucous membranes, and whites of the eyes (jaundice).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor as soon as possible if you notice any of the following:

Frequent:

- Fever.
- Shivering.
- Pain at the infusion site.
- Feeling sick (nausea) or being sick (vomiting).
- Dizzy or feeling faint.
- Muscle or joint pain.
- Rash and itching.
- Headache.
- Diarrhoea.
- Low blood pressure.

These side effects may be mild and go away on treatment with other medicines. They may also be reduced by changing the dose of THYMOGLOBULINE or increasing the period of time over which it is given.

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. This includes any possible side effects not listed in this leaflet. You can report any side effects directly to Sanofi's Pharmacovigilance Unit at za.drugsafety@sanofi.com (email) or 011 256 3700 (tel).

You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form" found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

5. How to store THYMOGLOBULINE

Your medicine will be stored in a hospital by a doctor or nurse, according to the following storage requirements:

- Store all medicines out of reach of children.
- Unopened vials are stored at or between 2 °C – 8 °C (in a refrigerator).
- Do not freeze. Protect from light.

The doctor or nurse will check that the product has not passed its expiry date before preparation.

THYMOGLOBULINE will not be used if particles are present in the vial which do not disappear when the vial is rotated.

6. Contents of the pack and other information

What THYMOGLOBULINE contains

The active substance is 25 mg of rabbit anti-human thymocyte immunoglobulin per vial.

The other ingredients are mannitol, glycine and sodium chloride (salt).

What THYMOGLOBULINE looks like and contents of the pack

THYMOGLOBULINE is a creamy white powder supplied in a vial (10 mL, type 1 glass) equipped with a stopper (chlorobutyl).

Each vial is packed in a carton box.

Before THYMOGLOBULINE is used it is mixed with 5 mL of sterile water for injection to make a limpid or slightly opalescent, colourless or pale yellow solution. Each 1 mL solution contains 5 mg rabbit anti-human thymocyte immunoglobulin (25 mg/5 mL). This solution is then mixed with a sodium chloride or glucose solution before it can be administered.

Holder of Certificate of Registration

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