**Package leaflet: Information for the user**

# Thymoglobuline® 25 mg powder for solution for infusion

rabbit anti-human thymocyte immunoglobulin

genzyme
A SANOFI COMPANY

**Read all of this leaflet carefully before you are given this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- This medicine will be given to you by a doctor or nurse in hospital.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**



## 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 made by injecting human thymus cells into rabbits. It contains immunoglobulins (antibodies) which 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.

**Kidney and Heart Transplantation**
Thymoglobuline is used in patients who have had a kidney or heart transplant, to prevent the rejection of a kidney or a heart transplant. It is also used to treat the rejection of a kidney transplant in patients who are resistant to treatment with corticosteroids. Thymoglobuline is a type of drug known as an immunosuppressant (anti-rejection drug) and 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.

## 2. What you need to know before you are given Thymoglobuline

**You should not be given Thymoglobuline :**
- if you are allergic to anti–human thymocyte globulin, rabbits or any of the other ingredients of this medicine (listed in section 6).
- if you have a severe infection because Thymoglobuline decreases your body's ability to fight infections.

**Warnings and precautions**
Talk to your doctor or nurse before you are given Thymoglobuline.
Thymoglobuline may not be suitable for you:
- 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.
- if you have any blood disorders, such as lower than normal platelets in your blood (thrombocytopenia) or lower than normal white cells in your blood (leucopenia).The dose you will be given will depend on the number of white blood cells or platelets in your blood which will be checked before, during and after treatment.

During treatment with Thymoglobuline, your doctor will carry out regular blood tests and other tests to monitor your health. Because of the way this medicine works, it could affect your blood and other organs.

Human blood components are used in the manufacturing process for Thymoglobuline. 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. Also during manufacturer of Thymoglobuline, steps have been included during processing of the blood that can inactivate or remove the viruses. Despite these measures, when medicines prepared from human blood components 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, hepatitis C virus and for the non-enveloped Hepatitis A and parvovirus B19 viruses.

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**Other medicines and Thymoglobuline**
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines or any other **anti-rejection** medicine (immunosuppressants), such as azathioprine or corticosteroids. This is because, if the body's defense system is reduced too much, severe infections may occur. It may also increase the risk of developing cancer in the future.

**Vaccinations**
Do not have any vaccination during or soon after treatment with Thymoglobuline without first discussing it with your doctor as it may cause side effects or may not work because your immune system cannot respond to it.

**Thymoglobuline with food and drink and alcohol**
It is unlikely that eating and drinking will affect your medicine.

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or nurse for advice before taking this medicine. This is because Thymoglobuline should not be given to pregnant women unless it is absolutely necessary as the effects are unknown.
**Do not** breastfeed while you are being given Thymoglobuline. This is because it may get into your breast milk and may affect the baby.

**Driving and using machines**
**Do not** drive or operate with machinery while being treated with Thymoglobuline.

## 3. How Thymoglobuline is given

Your medicine will be given to you by a doctor or nurse in a hospital. Thymoglobuline is given through a plastic tube (catheter) directly into your blood stream (intravenous infusion) over a period of at least 6 hours. The first dose may be given over a longer period of time.
The dose you will be given will depend on your weight (unless you are obese when it will depend on your ideal weight), which medical problem you are being treated for, and if you are being given any other medicines at the same time.

To **prevent** kidney rejection: The recommended dose is between 1 and 1.5 mg of Thymoglobuline for every kilogram of weight every day for 3 to 9 days.
To **prevent** heart rejection: The recommended dose is between 1 and 2.5 mg of Thymoglobuline for every kilogram of weight for 3 to 5 days.
To **treat** kidney rejection in patients resistant to corticosteroids: The recommended dose is 1.5 mg of Thymoglobuline for every kilogram of weight every day for 7 to 14 days. There are no data in children for rejection of kidney transplantation.

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 for rashes, check your pulse, blood pressure and breathing. From time to time your doctor may also want you to have a blood test to monitor your blood cell count. If your white blood cell count is low, your doctor may also administer medicines to prevent or treat infections; if your platelet counts are low, your doctor may give you a platelet transfusion.

The dose of Thymoglobuline may be changed by your doctor if you have any side effects.

**Other medicines your doctor may give you**
Your doctor may give you some other medicines before, or at the same time as Thymoglobuline. These medicines are used to prevent, or treat possible side effects and could include:
- Antipyretics (like paracetamol) to reduce fever
- 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

**If you are given more Thymoglobuline than you should have**
It is unlikely you will be given more Thymoglobuline than you should, as you will be closely checked by your doctor or nurse during your treatment. If this does happen you may get a lower than normal platelet cell count (thrombocytopenia) or lower than normal white cell count (leucopenia). This can cause fever, chills, sore throat, mouth ulcers and bleeding or bruising more easily than normal.

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.
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.

**Tell your doctor immediately if you notice:**
- A raised itchy rash
- Difficulty in breathing
- Stomach pain
- Swelling of the face, tongue or throat

Sometimes, receiving a Thymoglobuline infusion may cause the following additional side effects. **You should tell your doctor as soon as possible if you have any of the following:**
- Difficulty breathing, wheezing or coughing
- Feeling or being sick
- Dizzy or feeling faint
- Tiredness
- Joint pain
- Headache
- Bleeding or bruising more easily than normal
- Irregular or fast heartbeat
- Symptoms of infection such as fever, chills, sore throat, mouth ulcers

During or after treatment with Thymoglobuline, some patients experience a temporary increase in certain liver function tests (laboratory tests which indicate how well your liver is functioning). Generally, there are no symptoms and the liver function tests return to normal without treatment.

The side effects listed below were recorded during a clinical study. This does not necessarily mean that all were caused by Thymoglobuline.

**Very common side effects** (may affect more than 1 in 10 people):
- Low white blood cell count; low platelet count
- Fever
- Infection
- Low count of red blood cells (anaemia)

**Common side effects** (may affect more than 1 in 100 people):
- Diarrhoea, difficulty swallowing, nausea, vomiting
- Shivering
- Serum sickness, which is an illness caused by antibodies against Thymoglobuline causing rash, itching, urticaria (itchy, red welts), joint pains, kidney problems and swollen lymph nodes and which develops within 6-21 days. Serum sickness is usually mild and goes away without treatment or with a short course of corticosteroids
- Muscle pain
- Growths (including cancerous and non-cancerous)
- Shortness of breath
- Itchiness, rash
- Low blood pressure
- Increase in some liver enzymes in your blood

**Uncommon side effects** (may affect more than 1 in 1,000 people):
- Liver injury (liver failure)

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.

**Frequency not known** (frequency cannot be estimated from the available data)
- Increased bilirubin in the blood (elevation of laboratory parameter)

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. These events have sometimes been associated with a fatal outcome.

If you are receiving Thymoglobuline with other medicines which suppress your immune system, you may be more susceptible to infections.

Talk to your doctor if you are concerned about any of these side effects or if there is anything you do not understand.

**Reporting side effects**
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed below. By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Ireland
HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2;
Tel: +353 1 6764971; Fax: +353 1 6762517. www.hpra.ie;
Email: medsafety@hpra.ie

Malta
ADR Reporting www.medicinesauthority.gov.mt/adrportal

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**The following information is intended for healthcare professionals only:**

Each vial of Thymoglobuline is intended for single use only.

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

Depending on the daily dose, reconstitution of several vials of Thymoglobuline powder might be needed. Determine the number of vials to be used and round up to the nearest vial. Using aseptic technique, reconstitute the powder with 5 ml of sterile water for injections to obtain a solution containing 5 mg protein per ml.

The solution should be clear or slightly opalescent. Reconstituted medicine should be inspected visually for particulate matter and discolouration. Do not use vials exhibiting particles or discolouration. Immediate use of reconstituted medicine is recommended.

**Preparation of Thymoglobuline Infusion (Use Aseptic Technique)**
Withdraw the required volume of the reconstituted solution from the Thymoglobuline vials. Add the daily dose to an infusion solution (0.9% sodium chloride or 5% glucose solution) so as to obtain a total infusion volume of 50 to 500 ml (usually 50 ml/vial). The medicine should be administered on the same day. The use of a 0.22 µm in–line filter is recommended. Any unused medicine or waste material should be disposed of in accordance with local requirements. For additional information about the medicine, please consult the SmPC or contact the local representative.

## 5. How to store Thymoglobuline

Your medicine will be stored in a hospital by a doctor or nurse, out of the sight and reach of children.
The unopened vials of Thymoglobuline will be stored in a refrigerator (2 – 8 °C).
The doctor or nurse will check that the medicine has not passed its expiry date before preparation.

## 6. Contents of the pack and other information

**What Thymoglobuline contains**
The active substance is: 25 mg of rabbit anti-human thymocyte immunoglobulin.
The other ingredients are: mannitol, glycine, sodium chloride (salt).
Thymoglobuline may also contain residues of polysorbate, from the manufacturing process.

**What Thymoglobuline looks like and contents of the pack**
Thymoglobuline is supplied in a glass vial containing a white powder.
Before it is used it is mixed with 5 millilitres (ml) of sterile water to make a liquid. Each millilitre (ml) contains 5 mg of rabbit anti-human thymocyte immunoglobulin. This liquid is then mixed with a sodium chloride or glucose solution so that it can be given slowly (infused) into your bloodstream through a plastic tube (catheter) in a large vein.

**Marketing Authorisation Holder and Manufacturer**
Marketing Authorisation Holder :
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Marketing Authorisation numbers:
UK: PL 12375/0021
Ireland: PA 611/3/1
Malta: MA 596/00201

**This medicinal product is authorised in the Member States of the EEA under the following names:**
Ireland: Thymoglobuline 25 mg powder for solution for infusion
Malta: Thymoglobuline 25 mg, powder for solution for infusion
Slovenia: Thymoglobuline 25 mg, powder for solution for infusion
UK: Thymoglobuline 25 mg powder for solution for infusion

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| Date: | 04 APR 2019 |
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| Printing Cols: | Black, |
| Non-Printing Cols: | Dieline |
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