PACKAGE LEAFLET

Package leaflet: Information for the user

Yimmugo 100 mg/mL solution for infusion
Human normal immunoglobulin (IVIg)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

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

What is in this leaflet

1. What Yimmugo is and what it is used for

Yimmugo
- belongs to the class of medicines called "human normal immunoglobulins". These medicines contain human antibodies, which are also present in your blood. Antibodies may help your body to prevent and overcome infections.

Yimmugo is used to treat adults, children, and adolescents (0–18 years) who do not have enough antibodies (replacement therapy):
1. Patients who are born with a lack of antibodies (primary immunodeficiency syndromes, PID)
2. Acquired lack of antibodies (secondary immunodeficiency syndrome, SID) in patients who suffer from severe or recurrent infections and ineffective antimicrobial treatment with either proven specific antibody failure or low immunoglobulin G level (< 4 g/L)

Yimmugo is also used to treat adults, children, and adolescents (0–18 years) with inflammatory disorders (immunomodulation) such as:
1. Patients with a lack of blood platelets (primary immune thrombocytopenia, ITP), who will have surgery in the near future or are at risk of bleeding
2. Patients with a disease that is associated with multiple inflammations of the peripheral nerves (Guillain-Barré syndrome)
3. Patients with a disease which causes inflammation of several organs of the body escpecially the blood vessels (Kawasaki's disease)
4. Patients with a chronic disease that is characterised by inflammation of the peripheral nerves. This disease causes muscle weakness and/or numbness mainly in the legs and upper limbs (Chronic inflammatory demyelinating polyneuropathy, CIDP)
5. Patients with a disease of the motor nerves characterized by slow progressive weakness of arms and legs (Multifocal motor neuropathy, MMN)

2. What you need to know before you use Yimmugo

Do not use Yimmugo
- if you are **allergic to human immunoglobulin** or any of the other ingredients of this medicine (listed in section 6)
- if you have an **insufficient amount of immunoglobulin A (IgA)**, especially if you have **antibodies against IgA in your blood**. This might lead to severe allgeric reaction (anaphylaxis)

Warnings and precautions

Before using this medicine:
Talk to your doctor, pharmacist or nurse before using Yimmugo if you:
- have an **active infection** or underlying **chronic inflammation**
- if you are **allergic** to immunoglobulins (see section "Do not use Yimmugo")
- have or had a **kidney disease**
- have received **medicines that may harm your kidneys**

In very rare cases immunoglobulins may increase the risk of heart attack, stroke, lung embolism, or deep vein thrombosis. Talk to your doctor, pharmacist or nurse, if you:
- are **overweight**, **elderly** or **diabetic**
- have **high blood pressure**, **low blood volume** (hypovolaemia) or **thicker blood than normal** (high blood viscosity)
- have been **bedridden** for a long time, have **problems with your blood vessels** (vascular diseases) or other **risks for thrombotic events** (blood clots)

In all of the above cases, your doctor will take special care of you.

Monitoring during and after the infusion is required, if you:
- have not received this medicine before or if there has been a long break (e.g. several weeks) since you last received it (monitoring after infusion: at least 1 hour by your doctor or nurse)
- have been given Yimmugo recently (monitoring after infusion: at least 20 minutes by your doctor or nurse)

Slowing or stopping of infusion may be required, if you:
- experience any symptoms during the infusion such as **headache, flushing, chills, muscle pain, wheezing, rapid heart rate, lower back pain, nausea** and **low blood pressure**. In rare cases these are signs of an **allergic reaction**. Another reason can be that the infusion rate might be too high and should be slowed (this is called an infusion-related reaction). **Tell your doctor immediately** about any symptoms appearing during infusion
- experience **severe difficulty breathing** (respiratory distress), **rapid breathing** (tachypnoe), abnormally low levels of oxygen in the blood (hypoxia) and **increased body temperature** (fever). These are symptoms of **transfusion-related acute lung injury** (TRALI). TRALI occurs in very rare cases after receiving immunoglobulins. This will lead to non-heart related accumulation of fluid in the air spaces of the lungs (non-cardiogenic pulmonary oedema). The symptoms typically appear 1 to 6 hours after receiving treatment. **Tell your doctor immediately** if you notice such reactions during the Yimmugo infusion. Your doctor will stop the infusion immediately.
- experience **fever**, **neck pain** and **headache**. These are symptoms of **aseptic meningitis syndrome** (AMS, inflammation of the membrane that covers the brain and spinal cord). AMS has been reported with immunoglobulin infusion. Stopping the immunoglobulin treatment resulted in remission of AMS within several days without further consequences. Your doctor can tell you more about the condition and its symptoms.

Based on your condition, your doctor will decide the approporiate infusion rate, the duration of the treatment, whether the treatment with Yimmugo needs to be stopped and/or whether additional medical measures need to be initiated.

Effects on blood cells and blood tests
- This medicine can contain blood group antibodies. These can rarely increase the risk of red blood cell breakdown (haemolysis). Your doctor will monitor the clinical signs and symptoms of haemolysis and haemolytic anaemia.
- Low concentration of white blood cells (neutropenia) has been reported with immunoglobulins. This condition resolves spontaneously within 7 to 14 days. Your doctor can tell you more about the symptoms.
- Yimmugo can affect blood tests for a certain time. Tell your doctor about your treatment with Yimmugo prior to having any blood tests.

Information on safety with respect to infections
Yimmugo is made from human plasma (the liquid part of blood). When medicines are made from human blood or plasma, everything is done to prevent infective agents being passed on to patients through administration of these medicines. All blood donors are tested for viruses and infections. In addition, processing of the blood or plasma includes steps that can inactivate or remove viruses.

Despite these precautionary measures, when medicines prepared from human blood or plasma are given, the risk of passing on infections cannot be totally excluded.

The measures taken are considered effective for viruses such as:
- human immunodeficiency virus (HIV)
- hepatitis B virus (HBV)
- hepatitis C virus (HCV)
- hepatitis A virus (HAV)
- parvovirus B19

It is strongly recommended that every time you are given a dose of Yimmugo your doctor records the name and batch number of the product. The batch number provides information about the particular starting materials of your medicine. If necessary, a connection between you and the starting material used can thereby be made.

Children and adolescents
The special warnings and precautions for adults also apply to children and adolescents.

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

Yimmugo can reduce the effectiveness of some **vaccines** such as:
- **measles**
- **rubella**
- **mumps**
- **chicken pox**

You may have to wait up to 3 months before you can have some vaccines and up to a year before you can have a measles vaccine.

Please **avoid using loop diuretics** (medicines that make your kidney pass out more fluid) together with Yimmugo.

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 for advice before taking this medicine.
Your doctor will decide if Yimmugo may be used during pregnancy and breast-feeding.

Driving and using machines
Yimmugo has a minor influence on the ability to drive and use machines. If you experience reactions such as nausea or dizziness, you should wait for these to resolve before driving or using machines.

3. How to use Yimmugo

Dosage and method of administration
Yimmugo is intended only for administration via a vein (intravenous infusion). It is given to you by your doctor or nurse. Your doctor will decide the dose, frequency and infusion rate depending on your condition and your body weight. The product should be brought to room or body temperature before use.

At the start of treatment the infusion rate will be slow. Afterwards, if you feel well, your doctor or nurse may gradually increase the infusion rate.

Use in children and adolescents
Use in children and adolescents (0–18 years) is the same as that for adults.

If you miss an infusion
Please talk to your doctor about how to proceed.

If you receive more Yimmugo than you should
Your blood may become too thick (hyperviscous). This is more likely to happen in children or if you are elderly or have problems with your heart or kidneys. Make sure that you drink adequate fluids so you are not dehydrated and tell your doctor about any medical problems.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Possible side effects may be reduced or even avoided by slowing the infusion rate.

If you notice any of the following effects, tell your doctor immediately:
- rash
- itching
- wheezing
- difficulty breathing
- swelling of the eyelids, face, lips, throat or tongue
- extremely low blood pressure with symptoms like dizziness, confusion, fainting, fast pulse

This can be an allergic or in rare cases a serious allergic reaction (anaphylactic shock) or a hypersensitivity reaction.

The following side effects have been reported during controlled clinical trials with Yimmugo.
Frequencies given below have been calculated based on number of patients treated.

Very common (may occur in more than 1 in 10 patients**)**
- headache

Common (may occur in up to 1 in 10 patients)
- dizziness
- tiredness (fatigue), chills, fever
- nausea, abdominal or oral pain
- increased blood pressure, positive Coombs test result
- skin reaction
- back pain, pain in arms and legs
- difficulty breathing (dyspnoea), pain in the mouth and throat (oropharyngeal pain)

- decreased number of white blood cells (neutropenia), decreased number of red blood cells (haemolysis)
- difficulty balancing (vertigo), ringing in the ears (tinnitus)
- allergic/anaphylactic reaction
- confusion
- flushing

Immunoglobulin preparations in general may cause the following additional side effects (in decreasing frequency):
- vomiting, joint pain and low blood pressure
- decrease in the number of red blood cells due to a breakdown of these cells in the blood vessels ((reversible) haemolytic reactions) and haemolytic anaemia requiring transfusion
- a sudden fall in blood pressure and, in isolated cases, anaphylactic shock
- temporary skin reactions (including cutaneous lupus erythematosus)
- formation of blood clots which may enter your circulation (thromboembolic reactions) causing heart attack (myocardial infarction), stroke, clots in the blood vessels of the lung (pulmonary embolism), blood clots in a vein (deep vein thrombosis)
- cases of temporary acute inflammation of the protective membranes covering the brain and spinal cord (reversible aseptic meningitis)
- cases of blood test results which indicate that kidney function is impaired and/or sudden kidney failure
- cases of Transfusion Related Acute Lung Injury (TRALI) see also section "Warnings and precautions"

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 also report side effects directly via the Yellow Card Scheme at: 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.

5. How to store Yimmugo

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

Do not use this medicine after the expiry date which is stated on the label and carton after EXP.

Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original package in order to protect from light.
Yimmugo may be kept at room temperature (up to 25°C) for a single period **not exceeding 6 months**. Record the date from when you start to store Yimmugo at room temperature on the product carton. Do not store Yimmugo in the refrigerator again after it has been stored at room temperature.

Yimmugo is for single use.

Yimmugo should be used immediately after opening.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Do not use this medicine if the solution is cloudy or contains 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 Yimmugo contains

- The active substance is human normal immunoglobulin
  1 mL contains 100 mg human normal immunoglobulin (purity of at least 96% IgG). The IgG subclass distribution is approx. 62% IgG1, 32% IgG2, 4% IgG3 and 1% IgG4. The maximum IgA content is 500 micrograms/mL.
- The other ingredients are: glycine, polysorbate 80 and water for injections.

What Yimmugo looks like and contents of the pack

Yimmugo is a solution for infusion. The solution should be clear or slightly opalescent and colourless to pale yellow.
50 mL, 100 mL or 200 mL of solution in a vial (Type II glass) with a stopper (bromobutyl) and a flip off cap (plastic).

Pack with 1 vial with 50 mL, 100 mL or 200 mL solution.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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<u>The following information is intended for healthcare professionals only</u>:

<u>Dosage</u>
The dosage recommendations are summarised in the following table:

Indication	**Dose**	**Frequency of infusions**
<u>Replacement therapy</u>:		
Primary immunodeficiency syndromes	Starting dose: 0.4–0.8 g/kg Maintenance dose: 0.2–0.8 g/kg	 every 3–4 weeks
Secondary immunodeficiencies (as defined in section 1)	0.2–0.4 g/kg	every 3–4 weeks
<u>Immunomodulation</u>:		
Primary immune thrombocytopenia	0.8–1 g/kg or 0.4 g/kg/d	on day 1, possibly repeated once within 3 days for 2–5 days
Guillain Barré syndrome	0.4 g/kg/d	for 5 days

Kawasaki's disease	2 g/kg	in one dose in association with acetylsalicylic acid
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	Starting dose: 2 g/kg Maintenance dose: 1 g/kg	 in divided doses over 2–5 days every 3 weeks in divided doses over 1–2 days
Multifocal Motor Neuropathy (MMN)	Starting dose: 2 g/kg Maintenance dose: 1 g/kg or 2 g/kg	 in divided doses over 2–5 consecutive days every 2–4 weeks or every 4–8 weeks in divided doses over 2–5 days

Method of administration
Intravenous use.
Yimmugo should be infused intravenously at an initial rate of not more than 0.3 mL/kg/h for 30 minutes. See section 2. In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. If well tolerated, the infusion rate can be gradually increased to a maximum of 2 mL/kg/h for the first infusion. For subsequent infusions, if well tolerated, the infusion rate can be gradually increased to a maximum of 6 mL/kg/h.

Replacement Therapy:
In patients who have tolerated the infusion rate of 6 mL/kg/h well, the rate may be gradually increased to a maximum of 8 mL/kg/h.

Incompatibilities
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products, nor with any other IVIg products.