Package leaflet: Information for the user

Gamunex® *10%*
100 mg/ml solution for infusion
human normal immunoglobulin (IVIg)

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 or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What *Gamunex® 10%* is and what it is used for

What *Gamunex®* 10% is

Gamunex® 10% contains human normal immunoglobulin (antibodies) as highly purified protein extracted from human plasma (part of the blood of donors). This medicine belongs to the group of medicines called intravenous immunoglobulins. These are used to treat conditions where the body's defence system against disease is not working properly.

What Gamunex® 10% is used for

Treatment of adults, children and adolescents (0-18 years) who do not have sufficient antibodies (replacement therapy) such as:

- Patients with primary immunodeficiency syndromes (PID), an inborn lack of antibodies
- Patients with acquired immunodeficiency (SID) with severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure or serum IgG level of <4 g/l

Treatment of susceptible adults, children and adolescents (0-18 years) who have been exposed to measles or are at risk of measles exposure and in whom active vaccination against measles is not indicated or not advised.

Treatment of adults, children and adolescents (0-18 years) with certain autoimmune disorders (immunomodulation). There are five groups:

- Primary immune thrombocytopenia (ITP), a condition where the number of platelets in the blood stream is greatly reduced. Platelets form an important part of the clotting process and a reduction in

their numbers may cause unwanted bleeding and bruising. The product is also used in patients at high risk of bleeding or prior to surgery to correct the platelet count.
- Guillain-Barré-Syndrome, where the immune system damages the nerves and hinders them from working properly.
- Kawasaki disease (in this case in conjunction with acetylsalicylic acid therapy), an illness in children where the blood vessels (arteries) in the body become enlarged.
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), a rare and progressive disease causing limb weakness, numbness, pain and fatigue.
- Multifocal motor neuropathy (MMN), a rare disease causing slowly progressive limb weakness without sensory loss.

Treatment of adults aged 18 years or older with:

- Severe acute exacerbations of myasthenia gravis. Myasthenia gravis is a disease that causes muscle weakness; exacerbations mainly affect swallowing, speaking and breathing.

2. What you need to know before you use *Gamunex® 10%*

Do not use *Gamunex® 10%*

- If you are allergic to human normal immunoglobulin or any of the other ingredients of this medicine (listed in section 6).
- If you do not have enough immunoglobulins of the type IgA in your blood and have developed antibodies to IgA.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using *Gamunex® 10%*.

Infusion reactions and hypersensitivity

Certain side effects may be related to the rate of infusion. The recommended infusion rate should therefore be followed (see "Information intended for healthcare professionals" at the end of this leaflet).

Certain side effects may occur more frequently:
- in case of high infusion rate,
- in patients with a complete lack of gammaglobulins or low gammaglobulin levels (agammaglobulinaemia or hypogammaglobulinaemia) with or without IgA deficiency,
- in patients who are receiving human normal immunoglobulin for the first time or, in rare cases, when the immunoglobulin product is switched or after a prolonged interval without treatment.

Potential complications can often be avoided by ensuring:
- that you are not hypersensitive to human immunoglobulin by having *Gamunex® 10%* initially infused slowly,
- that you are carefully monitored for any symptoms throughout the infusion period. In particular, if you are receiving human immunoglobulin for the first time, if you have been switched from a different immunoglobulin or if you have not received treatment for some time, you should be monitored for possible side effects during the first infusion and for one hour afterwards.

If side effects occur, the infusion rate should be reduced or the infusion should be suspended until the symptoms have disappeared. If the symptoms persist even after suspending the infusion, suitable treatment should be commenced. In the event of a shock reaction (anaphylactic shock with a severe fall in blood pressure), treatment with the product should be stopped immediately and the current standard medical treatment for shock should be implemented.

Patients with a kidney problem and other risk factors

Cases of kidney function disorders and acute kidney failure have been reported in connection with administration of intravenous immunoglobulins. You are particularly at risk if you have certain risk factors such as pre-existing impairment of kidney function (renal insufficiency), diabetes (diabetes mellitus) or a reduced blood volume (hypovolaemia). Other circumstances considered to be risk factors are if you are overweight or are being treated simultaneously with medicines that have harmful effects on the kidneys and/or if you are over the age of 65. The following precautions should be taken by you in any case:

- Please, drink enough to ensure adequate fluid intake prior to commencement of therapy,
- Your doctor should control your urine output and measure kidney function,
- Please, do not use simultaneously certain medicines that increase urine output (loop diuretics).

The infusion rate in your case should be as low as possible and the immunoglobulin product should be used at the lowest feasible concentration. If a kidney function disorder occurs, your doctor will consider discontinuing the immunoglobulin treatment.

Haemolysis (abnormal breakdown of red blood cells)

It is commonly reported that immunoglobulins increase the risk of destruction of red blood cells (haemolysis) in both adults and children. If you were administered high doses of IVIg either on one day or over several days and are blood type A, B or AB and/or have an underlying inflammatory condition you may be at increased risk for red blood cell destruction (haemolysis).
In post-marketing reports it is observed that IVIg high-dose indications in children, particularly Kawasaki disease, are associated with an increased reporting rate of haemolytic reactions compared to other IVIg indications in children.
You should seek medical attention should you develop pallor (turn pale), lethargy (feeling weak), dark urine, shortness of breath or palpitations (fast heart rate).

Isolated cases of haemolysis-related kidney dysfunction/kidney failure with fatal outcome have occurred.

Information on safety with respect to infections

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,
- 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. The measures taken may be of limited value against non-enveloped viruses such as hepatitis A virus and/or parvovirus B19. Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections, possibly because the antibodies against these infections, which are contained in the product, are protective.

This medicinal product contains less than 1 mmol sodium (23 mg) per single dose (up to a maximum of 2g/kg), i.e. essentially ‘sodium free’.

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

Other medicines and *Gamunex® 10%*

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You should avoid the concomitant use of medicines that increase the excretion of water from your body (loop diuretics) during treatment with *Gamunex® 10%*.

Effects on vaccines: *Gamunex® 10%* may reduce the effectiveness of certain types of vaccines (live attenuated virus vaccines). In case of rubella, mumps and varicella a period of up to 3 months should elapse after receiving this medicine and before receiving these vaccines. In case of measles, the period is up to 1 year.

Pregnancy and breast-feeding

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

Dizziness or other reactions can sometimes occur and might affect the ability to drive and use machines. If this happens, you should wait for these to resolve before driving or operating machines.

3. How to use *Gamunex® 10%*

Gamunex® 10% is injected into your veins (intravenous administration) by your doctor. The dose that you will be given will depend on your illness and body weight and will be worked out by your doctor (please see section "Information intended for healthcare professionals" given at the end of this leaflet).
At the beginning of your infusion you will receive *Gamunex® 10%* at a slow rate. Depending on how comfortable you feel, your doctor may then gradually increase the infusion rate.

If you stop using *Gamunex® 10%*

If treatment with this medicine is stopped, your clinical condition may worsen. Please talk to the doctor in charge of your treatment if you wish to end treatment with this medicine prematurely.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

In rare and isolated cases, the following side effects have been reported with immunoglobulin preparations. **Seek medical care with no delay if any of the following side effects happen during or after the infusion:**

- A sudden fall in blood pressure and, in isolated cases, anaphylactic shock (which signs are rash, low blood pressure, quick or irregular heartbeat, wheezing, coughing, sneezing and difficulty breathing among others), even if you have shown no allergic reaction to previous administration.
- Cases of temporary non-infectious meningitis (which signs are headache, fear or intolerance of light, stiff neck).
- Cases of temporary reduction in the number of the red cells in the blood (reversible haemolytic anaemia/haemolysis).
- Cases of transient reactions of your skin.
- Increase in serum creatinine level (a test which measures your kidney function) and/or acute renal failure (which signs are low back pain, fatigue, decrease in the amount of urine).

- Thromboembolic reactions such as myocardial infarction (tight band around the chest with feeling like your heart is beating too fast), stroke (muscle weakness in the face, arm, or leg, trouble speaking or understanding others who are speaking), pulmonary embolism (shortness of breath, chest pain and fatigue), deep vein thromboses (pain and swelling in an extremity).
- Cases of transfusion related acute lung injury (TRALI) that causes hypoxia (lack of oxygen), difficulty in breathing, rapid breathing, bluish discolouration of skin or mucous membranes, fever and low blood pressure.

In clinical trials performed with *Gamunex® 10%* the following side effects have been observed:

The following side effects were common (may affect up to 1 in 10 infusions):

- headache
- fever

The following side effects were uncommon (may affect up to 1 in 100 infusions):

- dizziness
- urticaria (hives, redness, skin itching)
- pruritus (itching)
- rash
- nausea
- vomiting
- high blood pressure
- throat inflammation
- cough
- blocked nose
- wheezing
- joint pain
- back pain
- flu like illness
- fatigue
- chills
- asthenia (weakness)
- muscle pain

The following side effects were rare (may affect up to 1 in 1,000 infusions):

- haemolytic anaemia (destruction of red blood cells)
- shortness of breath
- sinusitis
- peeling of skin
- anxiety
- haemoglobin decreased
- impaired digestion
- contusion
- flushing
- musculoskeletal stiffness
- palmar erythema (reddening of the palms)
- aphonia (inability to produce voice)
- white blood cell count decreased
- dermatitis (inflammation of the skin) or contact dermatitis
- abdominal pain
- diarrhoea
- low blood pressure
- neck pain

- musculoskeletal pain
- chest pain
- malaise
- injection site reaction
- urethritis (painful or difficult urination)
- viral upper respiratory tract infection (illnesses caused by an acute infection which involves the upper respiratory tract including the nose, sinuses, throat)
- lymphocytosis (increase in the number of a particular type of white blood cells)
- hypersensitivity (allergic reaction)
- sensitivity of eyes to light
- hypertensive crisis (acute increased blood pressure)
- hyperaemia (increase of blood flow)
- haemoglobinuria (protein transporting oxygen in blood is found in abnormally high concentrations in the urine)
- blood pressure increased
- free haemoglobin present (haemoglobin circulating outside of red blood cells)
- red blood cell sedimentation rate increased (increased rate of settlement of red blood cells in a test tube)

What countermeasures should be taken if side effects occur?

If side effects occur, the infusion rate should be reduced or the infusion should be suspended until the signs of the effects have disappeared. If the signs persist even after suspending the infusion, suitable treatment should be initiated.

In the event of a severe hypersensitivity reaction with a fall in blood pressure and dyspnoea to the point even of a severe generalised allergic reaction (anaphylactic shock), use of this medicine should be ceased immediately and appropriate countermeasures should be initiated.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system: Yellow Card Scheme; website: 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 *Gamunex® 10%*

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 carton and the vial. The shelf life is 3 years.

Store in a refrigerator (2 - 8°C). Do not freeze. Keep the vial in the outer carton.

The product may be stored in its outer carton for a one-off period of up to 6 months at room temperature (not above 25°C). In that case, the shelf life of the product expires after 6 months, irrespective of the original expiry date. The new expiry date must be noted on the outer carton.The new expiry date must be no later than the printed expiry date, however. Subsequent refrigeration is not possible.
Once the individual container has been opened, the content must be used immediately. Any remainder must be discarded. Further storage, even in a refrigerator, is not permitted on account of possible microbial contamination.

6. Contents of the pack and other information

What G*amunex*® *10%* contains

The active substance is human normal immunoglobulin (IVIg). One ml of this medicine contains 100 mg protein with an IgG content of at least 98% in water for injections.

One vial of 10 ml contains: 1 g of human normal immunoglobulin
One vial of 50 ml contains: 5 g of human normal immunoglobulin
One vial of 100 ml contains: 10 g of human normal immunoglobulin
One vial of 200 ml contains: 20 g of human normal immunoglobulin
One vial of 400 ml contains: 40 g of human normal immunoglobulin

The percentage of IgG subclasses is approximately 62.8% (IgG_1), 29.7% (IgG_2), 4.8% (IgG_3), 2.7% (IgG_4).

The maximum IgA content is 84 micrograms/ml.

The other ingredients are glycine and water for injection.

What *Gamunex*® *10%* looks like and contents of the pack

Gamunex® *10%* is a solution for infusion. The solution is clear to slightly opalescent and colourless or pale yellow.
Gamunex®*10%* is available in pack sizes of 10 ml, 50 ml, 100 ml, 200 ml and 400 ml. The carton contains a vial made of glass with a stopper (chlorobutyl), a tear-off hanger label and a package leaflet.

Marketing Authorisation Holder and Manufacturer

Marketing authorisation holder:
Grifols Deutschland GmbH
Colmarer Straße 22
60528 Frankfurt
Germany

Manufacturer:
Instituto Grifols S.A.
Can Guasc 2, Parets del Vallès
08150 Barcelona
Spain

This medicinal product is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under following names:

Austria, Belgium, Cyprus, Ireland, Germany, Luxembourg, Netherlands, Poland, Portugal, United Kingdom (Northern Ireland): **Gamunex 10% 100mg/ml**
Czech Republic, Denmark, Finland, France, Hungary, Italy, Norway, Slovakia, Spain, Sweden**: Gamunex 100 mg/ml**
Greece**: Gaminex 10% 100 mg/ml**

This leaflet was last revised in July 2022.

The following information is intended for healthcare professionals only

Use only clear or slightly opalescent and colourless or pale yellow solutions for infusion that are free of particles – do not shake. Prior to infusion, bring Gamunex® 10% up to room or body temperature (possibly in a water bath at a temperature no higher than 37°C).

The vials are supplied with a hanger label (Fig. 1). After inserting the infusion set (Fig. 2), invert the vial and fold back the loop section of the label (Fig. 3). **Use firm finger pressure** to create a ***crease*** on each side where the loop section joins the rest of the label (Fig. 4). Suspend the vial from the infusion stand by the resulting loop (Fig. 5).

Fig. 1

Fig. 2

Fig. 3

Fig. 4

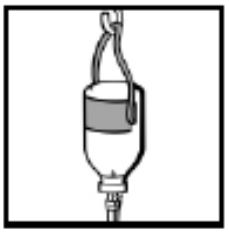

Fig. 5

Posology and method of administration

The dose and dose regimen are dependent on the indication.
The dose may need to be individualised for each patient dependent on the clinical response. Dose based on body weight may require adjustment in underweight or overweight patients. The following dose regimens are given as a guideline.

The dosage recommendations are summarised in the following table:

Indication	Dose	Frequency of Infusions
Replacement therapy		
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	0.2 - 0.4 g/kg	every 3 - 4 weeks
Measles pre/post exposure prophylaxis:		
Post-exposure prophylaxis in susceptible patients	0.4 g/kg	As soon as possible and within 6 days, possibly to be repeated once after 2 weeks to maintain the measles antibody serum level > 240 mIU/ml
Post-exposure prophylaxis in PID/SID patients	0.4 g/kg	In addition to maintenance therapy, given as an extra dose within 6 days of exposure
Pre-exposure prophylaxis in PID/SID patients	0.53 g/kg	If a patient receives a maintenance dose of less than 0.53 g/kg every 3–4 weeks, this dose should be increased once to at least 0.53 g/kg.
Immunomodulation:		

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 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
Severe acute exacerbations of myasthenia gravis	2 g/kg	administered over 2 consecutive days (dose of 1 g/kg per day)

Method of administration

For intravenous use.
Human normal immunoglobulin should be infused intravenously at an initial rate of 0.6 - 1.2 ml/kg/hr for 0.5 hr. In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. If well tolerated, the rate of administration may gradually be increased to a maximum of 4.8 - 8.4 ml/kg/hr.

Paediatric population

The posology in children and adolescents (0-18 years) is not different to that of adults as the posology for each indication is given by body weight and adjusted to the clinical outcome of the above mentioned conditions.

Gamunex® 10% must not be mixed with other solutions for infusion and other medicines. If dilution is necessary prior to infusion, 50 mg/ml *glucose solution may be used for this purpose.*
Do not dilute with saline solutions

Simultaneous administration of Gamunex® 10% and heparin through a single lumen delivery device must be avoided.
Gamunex® 10% infusion lines can be flushed with 50 mg/ml glucose or with sodium chloride solution (9 mg/ml) and should not be flushed with heparin.

Heparin Lock through which Gamunex® 10% was administered should be flushed with 50 mg/ml glucose or sodium chloride solution (9 mg/ml) and should not be flushed with heparin.