

Package leaflet: Information for the user

GAMMAGARD S/D 5.0 g / 10.0 g Powder and solvent for solution for infusion Human normal immunoglobulin

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.

What is in this leaflet:

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

The information on Gammagard S/D in the following sections applies to both adults and children.

1. What GAMMAGARD S/D is and what it is used for

GAMMAGARD S/D belongs to a class of medications called immunoglobulins. These medicines contain human antibodies, which are present in human blood. Antibodies help your body to fight infections. Medicines like GAMMAGARD S/D are used if you do not have enough antibodies in your blood. These patients tend to get frequent infections. GAMMAGARD S/D can also be used if you need additional antibodies to cure certain inflammatory disorders (autoimmune diseases).

GAMMAGARD S/D is used for

Treatment of patients who do not have sufficient antibodies (replacement therapy). There are four groups:

1. Patients with inborn lack of antibodies (primary immunodeficiency syndromes (PID)) such as:
 - congenital agammaglobulinemia or hypogammaglobulinemia
 - common variable immunodeficiency
 - severe combined immunodeficiencies
 - Wiskott Aldrich syndrome
2. Patients with a lack of antibody production and recurrent infections (myeloma or chronic lymphocytic leukaemia with severe secondary hypogammaglobulinemia)
3. Children who suffer from inborn AIDS and get frequent infections
4. Premature children with low birth weight with a risk for getting infections.

Treatment of patients with certain inflammatory disorders (immunomodulation). There are three groups:

1. Patients who do not have enough blood platelets (idiopathic thrombocytopenic purpura, ITP). These patients may have a high risk of bleeding.
2. Patients with a disease that is associated with multiple inflammations of the nerves in the whole body (Guillain Barré syndrome)

3. Patients with a disease which results in multiple inflammations of several organs of the body (Kawasaki disease)

Treatment or prevention of infections after a bone marrow transplantation (allogeneic bone marrow transplantation)

2. What you need to know before you use GAMMAGARD S/D

Do NOT use GAMMAGARD S/D

You MUST NOT use GAMMAGARD S/D

- If you are allergic (hypersensitive) to immunoglobulins or any of the other ingredients of GAMMAGARD S/D. For other ingredients please refer to section 6. Contents of the pack and other information.
- If you have an immunoglobulin A deficiency. You may have antibodies against immunoglobulin A in your blood. However, GAMMAGARD S/D contains only very small amounts of immunoglobulin A (less than 3 micrograms/mL in a 5% solution).

Warnings and precautions

How long monitoring is required during the infusion

- You will be carefully observed during the infusion period with GAMMAGARD S/D to make sure that you do not suffer a reaction. Your doctor will make sure that the rate at which GAMMAGARD S/D is infused is suitable for you.
 - if GAMMAGARD S/D is administered at a fast rate,
 - if you suffer from a condition with low antibody levels in your blood (hypo- or agammaglobulinemia),
 - if you have not received this medicine before or
 - if there has been a long interval (e.g. several weeks) since you last received it.In such cases, you will be closely monitored during your infusion and for an hour after your infusion has stopped.
- If you have already received GAMMAGARD S/D recently, you will only be observed during and for at least 20 minutes after your infusion.

When slowing or stopping the infusion may be required

In rare cases your body will be sensitive to medicines containing antibodies. This may happen particularly if you suffer from immunoglobulin A deficiency. In these rare cases, you may get allergic reactions such as a sudden fall in blood pressure or shock even if you have already received treatment with medicines containing antibodies in the past.

If you develop any of the following side effects you must tell your doctor or nurse immediately:

- Sudden wheeziness, difficulty in breathing or tightness of the chest
- Headache
- Fever
- Swelling of the eyelids, face, lips or blood vessels
- Skin lumps or itchy red spots
- Itch all over the body.

Depending on your doctor's decision the rate of infusion can be slowed or the infusion can be stopped.

Special patient groups

Your doctor will take special care if you are overweight, elderly, diabetic, or immobilized or if you are using oestrogens or have an indwelling vascular catheter. Your doctor will observe you closely if you:

- suffer from high blood pressure
 - low blood volume (hypovolaemia)
 - increase in blood viscosity or from problems with your blood vessels (vascular diseases including cardiac output).
 - Excessive clotting or clotting disorders
- In these conditions, immunoglobulins may increase the risk of heart attack, stroke, lung embolism, or deep vein thrombosis although only in very rare cases. Tell your doctor if you are diabetic. GAMMAGARD S/D does not contain sucrose or maltose. A 5% solution of Gammagard SD contains 21.7 mg glucose per dose which could affect your blood sugar level.
- Your doctor will also take special care
 - if you have or had previously problems with your kidneys, or
 - if you receive medicinal products that may harm your kidney (nephrotoxic medicinal products), as there is a very rare chance of acute kidney failure. Please tell your doctor if you have a kidney disorder.
- The protein content can increase leading to higher viscosity of the blood.

Information on the source material of GAMMAGARD S/D

GAMMAGARD S/D is made from human plasma (the liquid part of blood). When medicines are made from human blood or plasma, a number of 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. Manufacturers of these products also include 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 for the manufacture of GAMMAGARD S/D 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 and parvovirus B19. GAMMAGARD S/D also contains certain antibodies that can prevent an infection with hepatitis A virus and parvovirus B19.

Other medicines and GAMMAGARD S/D

Tell your doctor or pharmacist

- if you are taking, have recently taken or might take any other medicines or
- if you have received a vaccination during the last six weeks.

The infusion of immunoglobulins like GAMMAGARD S/D may impair the effect of some live virus vaccines such as measles, rubella, mumps and chicken pox. Therefore, after receiving these medicines you may have to wait up to 3 months before receiving your live-attenuated virus vaccine. You may have to wait for up to 1 year after receiving immunoglobulins before you receive your measles vaccine.

Effects on blood tests

GAMMAGARD S/D contains a wide variety of different antibodies, some of which can affect blood tests. If you have a blood test, please inform the person taking your blood or your doctor that you have received GAMMAGARD S/D.

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 pharmacist for advice before taking this medicine. Your doctor will decide if GAMMAGARD S/D may be used during pregnancy and breast-feeding.
- No clinical trials have been made with GAMMAGARD S/D in pregnant or breast-feeding women.
- If you are breast-feeding, the antibodies of GAMMAGARD S/D can be found in the breast milk.

Driving and using machines

There is no information on the effects of GAMMAGARD S/D on the ability to drive or operate a heavy machine. Patients may experience reactions (for example dizziness or nausea) during the treatment with GAMMAGARD S/D, which might affect the ability to drive and use machines. If this happens, you should wait until the reactions have disappeared.

GAMMAGARD S/D contains glucose

Tell your doctor if you are diabetic. GAMMAGARD S/D contains maximum of 0.4g/g glucose, which could affect your blood sugar level and should be taken into account in patients with diabetes mellitus. GAMMAGARD S/D contains 0.85 mg/ml sodium (*up to 9.77g sodium per dose.*). This needs to be taken into account in patients on low sodium diet.

3. How GAMMAGARD S/D is given

GAMMAGARD S/D is intended for intravenous administration (infusion into a vein). It is given to you by your doctor or nurse. Dosage and frequency of the infusion will vary depending on your condition and your body weight.

At the beginning of your infusion you will receive GAMMAGARD S/D at a slow rate. Dependent on how comfortable you are, your doctor may then gradually increase the infusion rate.

Use in children

The same indications, dose and frequency of infusion as for adults apply for children (age 0 to 18).

If you are given more GAMMAGARD S/D than you should

If you get more GAMMAGARD S/D than you should, your blood may become too thick (hyperviscous). The thicker the blood becomes, the more difficultly will it move in the vessels of your body. As a result, there will be less oxygen transferred to the vital organs, such as brain, lungs, etc. This could particularly happen when you are a patient at risk, e.g. an elderly patient or a patient having problems with your heart or your kidneys. Be sure that you take adequate fluids so you are not dehydrated and notify your physician if you are known to have medical problems.

4. Possible side effects

Like all medicines, GAMMAGARD S/D can cause side effects, although not everybody gets them. However, possible side effects may be reduced by slowing the infusion rate.

- Occasionally general reactions with intravenous human immunoglobulin have been experienced such as
 - chills, headaches, fever, low blood pressure,
 - vomiting, nausea (feeling sick),
 - allergic reactions,
 - joint pain, moderate lower back pain.
 - **The following side effects occur rarely**
 - cases of a sudden fall in blood pressure,
 - cases of eczema-like symptoms (transient cutaneous reactions) characterized by redness, skin swelling, itching and dryness.
 - **The following side effects occur very rarely**
 - single cases of allergic reactions (anaphylactic shock), even in patients who have shown no reactions to previous infusions,
 - cases of temporary meningitis (reversible aseptic meningitis),
 - isolated cases of temporary decrease of red blood cells (reversible haemolytic anaemia/haemolysis).
 - Impairment of kidney function (increase in blood creatinine content) and kidney failure has also been observed.
 - Blood clot formation in the veins (deep vein thrombosis) resulting in heart attack, stroke, lung defects (pulmonary embolism), have been reported which may be related to the infusion of immunoglobulins.

Below is a list of side effects that some patients reported when GAMMAGARD S/D was tested in clinical trials and side effects reported during post-market phase:

- Very common side effects (seen in more than 1 in every 10 patients): none
- Common side effects (seen in less than 1 in every 10 patients):
Headache, flushing, nausea, vomiting, fatigue, chills, fever
- Uncommon side effects (seen in less than 1 in every 100 patients):
Flu, anxiety, agitation, abnormal drowsiness, vision blurred, sensation of irregular beating of the heart, shortness of breath, nosebleed, diarrhoea, upper abdominal pain, stomach discomfort, inflammation in the mouth, itching, hives, cold sweat, excessive sweating, back pain, muscle cramp, pain in extremity, chest pain, chest discomfort, feeling abnormal, feeling cold, feeling hot, flu-like illness, infusion site redness, leaking at infusion site, infusion site pain, feeling or being sick, pain, high blood pressure, blood pressure fluctuation, loss of appetite
- Frequency not known (cannot be estimated from available data) for:
Inflammation of brain membranes not caused by a bacterial infection, destruction of red blood cells, decreased number of red blood cells, decreased number of blood platelets, swollen lymph nodes, all severity degrees of allergic reactions including allergic shock, restlessness, dizziness, abnormal skin sensation, involuntary trembling, seizures, bleeding in the brain, (transient) stroke, migraine, loss of consciousness, dislike of light, visual disturbance, eye pain, occlusion of central eye blood vessel, heart attack, bluish colour of the skin, increased heart rate, reduced heart rate, high blood pressure, paleness, low blood pressure, inflammation of veins, occlusion of blood vessels, cough, throat tightness, reduced oxygen level in blood, overbreathing, wheezing, airway spasm, occlusion of blood vessels in the lung, fluid in the lung, disturbed digestion, abdominal pain, inflammation of the liver (not transmissible), redness of the skin, skin eruptions, inflammation of the skin, allergic swelling of deep skin layers, joint and muscle pain, failure of the kidney, general weakness, swelling of body tissue, injection and infusion site reactions, chills, positive result of Coombs test

Reporting of 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store GAMMAGARD S/D

- Keep out of the sight and reach of children.
- Do not use GAMMAGARD S/D 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.
- Do not use if particulate matter or discolouration is observed.
- Do not store above 25°C.
- Do not freeze.

6. Contents of the pack and other information

What GAMMAGARD S/D contains

- The active substance of GAMMAGARD S/D is human normal immunoglobulin. GAMMAGARD S/D may be reconstituted with Sterilized Water for Injections to a 5% (50 mg/mL) solution or a 10% (100 mg/mL) solution of protein. At least 90 % of the protein is immunoglobulin G (IgG).
- The other ingredients are human albumin, glycine, sodium chloride and glucose monohydrate, macrogol, hydrochloric acid, sodium hydroxide.

What GAMMAGARD S/D looks like and contents of the pack

GAMMAGARD S/D is a freeze-dried, white or very faint yellow powder, substantially free of foreign visible particles.. GAMMAGARD S/D is available in pack sizes of 5.0 g, and 10.0 g.

GAMMAGARD S/D 5.0 g, and 10.0 g: Each package contains

- a 5.0 g or 10.0 g powder vial,
- 96 mL or 192 mL of Sterilized Water for Injections,
- a sterile transfer device and
- a sterile administration set with filter.

Marketing Authorisation Holder and Manufacturer

Manufacturer:	Marketing Authorisation Holder:
Baxalta Belgium	Baxalta Innovations GmbH
Manufacturing S.A.,	
Boulevard Rene Branquart 80,	Industriestrasse 67
B-7860 Lessines, Belgium.	A-1221 Vienna, Austria

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The following information is intended for healthcare professionals only

Special Precautions for Storage

When reconstitution is performed aseptically outside of a sterile laminar airflow hood, administration should begin as soon as possible, but not more than 2 hours after reconstitution. When reconstitution is performed aseptically in a sterile laminar airflow hood, the reconstituted product may be stored under constant refrigeration (2-8°C), for up to 24 hours. If these conditions are not met, sterility of the reconstituted product cannot be maintained. Partially used vials should be discarded.

Reconstitution - use aseptic technique:

After reconstitution only clear or slightly opalescent and colourless or pale yellow solutions are to be administered.

5.0 g, 10.0 g Sizes

Bring GAMMAGARD S/D and Sterilized Water for Injections (solvent) to room temperature. This temperature needs to be maintained until dissolution is complete.

A. 5% Solution:

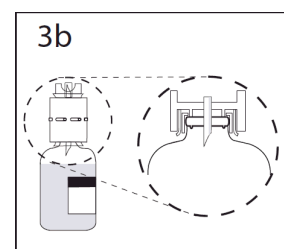
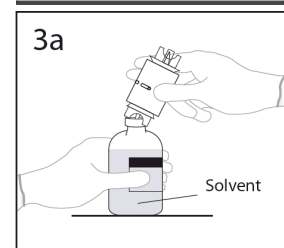
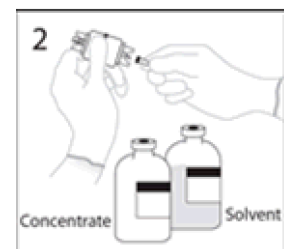
1. Remove bottle caps and clean stoppers with germicidal solution.
2. Remove spike cap from one end of the transfer device.

Do not touch spike.

- 3a. Place the solvent vial on a flat surface. Use exposed end of transfer device to spike solvent vial through centre of the stopper.

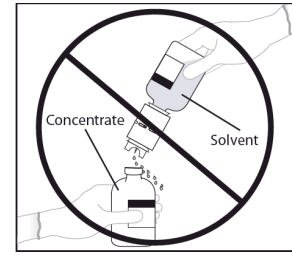
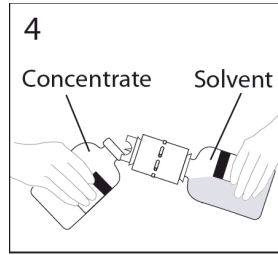
Caution: Failure to insert spike into centre of the stopper may result in dislodging of the stopper.

- 3b. Ensure that the collar collapses fully into the device by pushing down on the transfer device firmly. While holding onto transfer device, remove remaining spike cover. Do not touch spike.



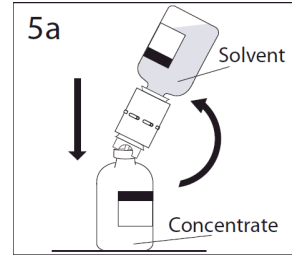
4. Hold solvent bottle with attached transfer device at an angle to the concentrate bottle to prevent spilling the solvent.

Note: Do not hold solvent bottle upside down, for this can lead to solvent spillage.

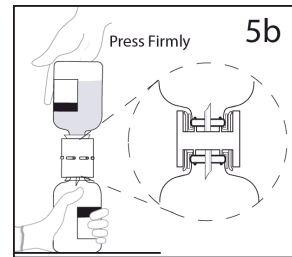


- 5a. Spike concentrate bottle through the centre of the stopper while **quickly inverting the solvent vial** to avoid spilling out solvent.

CAUTION: Failure to insert the spike into the centre of the stopper may result in dislodging of the stopper and loss of vacuum.

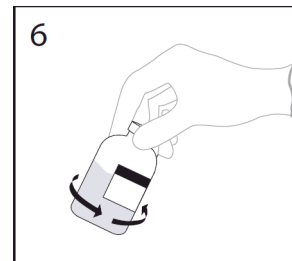


- 5b. Ensure that the collar collapses fully into the device by pushing down on the solvent bottle firmly.



6. After transfer of solvent is complete, remove transfer device and empty solvent bottle. Immediately swirl the concentrate bottle gently to thoroughly mix contents.

CAUTION: Do not shake. Avoid foaming. Discard transfer device after single use.



B. 10% Solution:

1. Remove bottle caps and clean stoppers with germicidal solution.
2. To prepare a 10% solution, it is necessary to remove half of the volume of solvent. Table 2 indicates the volume of solvent that should be **removed from the vial** before attaching the transfer device to produce a 10% concentration. Using aseptic technique, withdraw the unnecessary volume of solvent using a sterile hypodermic syringe and needle. Discard the filled syringe and the needle.
3. Using the residual solvent in the solvent vial, follow steps 2-6 as previously described in A.

Required Solvent Volume to be Removed		
	5.0 g	10.0 g
Concentration	bottle	bottle
5 %	Do not remove any solvent for reconstitution of 5 % solution	

10 %	48 mL	96 mL
Administration – use aseptic technique		

5.0 g, 10.0 g Sizes

Follow the direction insert for use, which accompanies the administration set provided in each package. If another administration set is used, ensure that the set contains a similar filter.

Instructions for Handling and Disposal

- Total dissolution should be obtained within 30 minutes.
- The product should be brought to room or body temperature before use.
- Reconstituted material should be a clear to slightly opalescent and colourless to pale yellow solution. Reconstituted products should be inspected visually for particulate matter and discolouration prior to administration. Solutions that are cloudy or have deposits should not be used.
- Any unused product or waste material should be disposed of in accordance with local requirements.
- Discard transfer device after single use only.

Method of Administration

For intravenous use.

It is recommended that antecubital veins be used for GAMMAGARD S/D 10% solutions, if possible. This may reduce the likelihood of the patient experiencing discomfort at the infusion site.

GAMMAGARD S/D 5% (50 mg/mL) should be infused intravenously at an initial rate of 0.5 mL/kg body weight (BW)/hour. In general, it is recommended that patients beginning therapy with GAMMAGARD SD or switching from one IVIG brand to another be started at a lower rate and then advanced to the maximal rate if they have tolerated several infusions at intermediate rates of infusion. If well tolerated, the rate of administration may gradually be increased to a maximum of 4 mL/kg BW/hour.

Patients who tolerate GAMMAGARD S/D 5% solutions at 4 mL/kg BW/hour can be infused with the 10% concentration starting at 0.5 mL/kg BW/hour. When switching from the 5% solution to the 10% solution, the rate of the 10% solution should be initially reduced to keep the rate of IgG protein administered comparable.

If no adverse effects occur, the rate can be increased gradually up to a maximum rate of 8 mL/kg BW/hour.

Special Precautions

- Any infusion-related adverse events should be treated by lowering the infusion rate or by stopping the infusion.
- It is recommended that every time GAMMAGARD S/D is administered, the name and batch number of the product is recorded.

Incompatibilities

GAMMAGARD S/D must not be mixed with other medicinal products.

It is recommended that GAMMAGARD S/D be administered separately from other medicinal products that the patient may be receiving.

Dosage Recommendations

Indication	Dose	Frequency of Injections
<p>Replacement therapy in primary immunodeficiency</p> <p>Replacement therapy in secondary immunodeficiency</p> <p>congenital AIDS</p> <p>Hypogammaglobulinaemia (< 4 g/l) in patients after allogeneic haematopoietic stem cell transplantation</p> <p>- Treatment of infections and prophylaxis of graft versus host disease</p> <p>- Persistent lack of antibody production</p>	<p>- starting dose: 0.4 – 0.8 g/kg BW</p> <p>- thereafter: 0.2 – 0.8 g/kg BW</p> <p>0.2 – 0.4 g/kg BW</p> <p>0.2– 0.4 g/kg BW</p> <p>0.2 – 0.4 g/kg</p>	<p>every 3 – 4 weeks to obtain IgG trough level of at least 5 – 6 g/L</p> <p>every 3 – 4 weeks to obtain IgG trough level of at least 5 – 6 g/L</p> <p>every 3 - 4 weeks</p> <p>every 3 – 4 weeks to obtain IgG trough level above 5g/l</p> <p>every week from day –7 up to 3 months after transplantation</p> <p>every month until antibody levels return to normal</p>
<p>Immunomodulation:</p> <p>Idiopathic thrombocytopenic purpura</p> <p>Guillain Barré syndrome</p> <p>Kawasaki disease</p>	<p>0.8 – 1 g/kg BW</p> <p>or</p> <p>0.4 g/kg BW/day</p> <p>0.4 g/kg BW/day</p> <p>1.6 – 2 g/kg BW</p> <p>or</p> <p>2 g/kg BW</p>	<p>on day 1, possibly repeated once within 3 days</p> <p>for 2 – 5 days</p> <p>for 5 days</p> <p>in several doses for 2 – 5 days in association with acetylsalicylic acid</p> <p>in one dose in association with acetylsalicylic acid</p>