

**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 side effects not listed in this leaflet. See section 4.

**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

**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 treat certain inflammatory disorders (autoimmune diseases).

**GAMMAGARD S/D is used for**

**Treatment of patients who do not have sufficient antibodies (replacement therapy). There are three 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

**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**

- if you are allergic to immunoglobulins or any of the other ingredients of this medicine (listed in section 6)
- 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. Your doctor will make sure that the rate at which GAMMAGARD S/D is infused is suitable for you.
- There may be a higher risk of side effects:
  - 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.
- 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, if you use oestrogens or have an indwelling vascular catheter. Your doctor will observe you closely if you have:
  - high blood pressure
  - low blood volume (hypovolaemia)
  - an increase in blood viscosity or have 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.

Your doctor will also take special care:

- if you have or have had problems with your kidneys or, if you receive medicines that may harm your kidneys (nephrotoxic medicines), as there is a very rare chance of acute kidney failure.

Please tell your doctor if you have a kidney disorder.

### **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.
- 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 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 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 conducted with GAMMAGARD S/D in pregnant or breast-feeding women.
- If you are breast-feeding, the antibodies of GAMMAGARD S/D can pass into the breast milk.
- The effects of GAMMAGARD S/D on fertility have not been established.

### **Driving and using machines**

There is no information on the effects of GAMMAGARD S/D on your ability to drive or use machines.

## **GAMMAGARD S/D contains glucose and sodium**

Tell your doctor if you are diabetic. GAMMAGARD S/D contains sugar (glucose), which could affect your blood sugar level.

This medicine contains 668 mg sodium (main component of cooking/table salt) in each bottle (10 g). This is equivalent to 34% of the recommended maximum daily dietary intake of sodium for an adult.

### **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 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.

### **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 difficult it becomes to move in the blood vessels. As a result, there will be less oxygen transferred to the vital organs, such as brain, lungs, etc. This could happen if you are a patient at risk, e.g. an elderly patient or a patient with kidney problems.

### **4. Possible side effects**

Like all medicines, GAMMAGARD S/D can cause side effects, although not everybody gets them.

#### Serious side effects

Infusions of medicines like GAMMAGARD S/D can occasionally result in serious, but rare, allergic reactions. You may experience a sudden fall in blood pressure and, in isolated cases, anaphylactic shock. Doctors are aware of these possible side effects and will monitor you during and after the initial infusions.

Typical signs or symptoms include feeling light-headed, dizzy or faint, skin rash and itchiness, swelling in the mouth or throat, difficulty breathing, wheezing, abnormal heart rate, chest pain, blueness of lips or fingers and toes, blurred vision.

Tell your doctor or nurse immediately if you notice any of these signs during the infusion.

The following side effects have been reported with GAMMAGARD S/D:

#### Common side effects (may affect up to 1 in 10 people):

- headache
- flushing
- nausea, vomiting
- fatigue, chills, fever.

#### Uncommon side effects (may affect up to 1 in 100 people):

- anxiety, agitation, feeling of tiredness, drowsiness or lack of energy
- blurred vision
- fast or irregular heart beats (palpitations)
- shortness of breath
- nose bleed
- diarrhoea, stomach pain or discomfort
- inflammation of the mucous membrane in the mouth
- itching, itchy rash (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, or generally feeling unwell
- redness, leaking or pain at the site of infusion
- pain
- increased blood pressure, or changes in blood pressure
- loss of appetite.

Frequency not known (cannot be estimated from the available data):

- Inflammation of brain membranes not caused by a bacterial infection (aseptic meningitis)
- destruction of red blood cells, decreased number of red blood cells, low blood platelet count
- swollen or painful lymph nodes
- allergic reaction
- restlessness, dizziness, tingling or numbness of the hands or feet
- tremors, seizures, migraine
- bleeding in the brain, stroke, fainting,
  - visual impairment, eye pain, increased sensitivity to light
- heart attack, fast heart beat, slow heart beat, high blood pressure, low blood pressure
- swelling or redness of veins, blood clots that develop in the artery, deep vein thrombosis, symptoms of which include a swelling, throbbing or cramping pain in the leg
- bluish colour of the skin, paleness, reduced oxygen levels in the blood
- cough, throat tightness, wheezing
- blockage of lung artery, build-up of fluid in the lung
- inflammation of the liver (hepatitis)
- redness of the skin, skin rash, allergic skin rash (allergic dermatitis)
- joint or muscle pain
- kidney failure
- unusual weakness
- swelling of body tissue (oedema)
- injection and infusion site reactions
- a sudden feeling of cold with shivering accompanied by a rise in temperature, often with excessive sweating
- positive result of Coombs test.

Side effects seen with similar medicines

The following side effects may occur after treatment with intravenous human immunoglobulins (medicines like GAMMAGARD S/D).

Common side effects (may affect up to 1 in 10 people), or uncommon side effects (may affect up to 1 in 100 people):

chills, headache, fever, vomiting, allergic reactions, nausea, joint pain, low blood pressure and moderate lower back pain.

Rare side effects (may affect up to 1 in 1,000 people):

a sudden fall in blood pressure, isolated cases of severe allergic reactions (anaphylactic shock), even if you have shown no reactions to previous infusions, eczema-like symptoms (transient cutaneous reactions).

Very rare side effects (may affect up to 1 in 10,000 people) or side effects which occur at an unknown frequency (i.e. cannot be estimated from available data):

temporary brain fever (reversible aseptic meningitis), temporary reduction of red blood cell count (reversible haemolytic anaemia/haemolysis), an increase in blood creatinine levels and kidney failure, blood clot formation in the veins (thromboembolic reactions), which may lead to heart attack, stroke, lung injury (pulmonary embolism), and deep vein thrombosis.

### Reporting 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. Website: [www.mhra.gov.uk/yellowcard](http://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 GAMMAGARD S/D is stored**

Keep 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. The expiry date refers to the last day of that month.

Do not store above 25°C.

Do not freeze.

Keep the bottle in the outer carton in order to protect from light.

Do not use this medicine if the solutions are cloudy or have deposits.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

## **6. Contents of the pack and other information**

### **What GAMMAGARD S/D contains**

- The active substance is human normal immunoglobulin. GAMMAGARD S/D may be reconstituted with 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.

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

GAMMAGARD S/D is a freeze-dried, white or very faint yellow powder. 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 bottle,
- 96 mL or 192 mL of Water for Injections,
- a sterile transfer device and
- a sterile administration set with filter.

Not all pack sizes may be marketed.

### **Marketing Authorisation Holder and Manufacturer**

#### **Marketing Authorisation Holder**

Baxalta Innovations GmbH  
Industriestrasse 67  
A-1221 Vienna  
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**Manufacturer**

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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 bottles should be discarded.

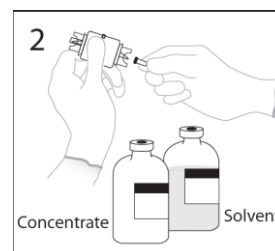
**Reconstitution - use aseptic technique:**

**5.0 g, 10.0 g Sizes**

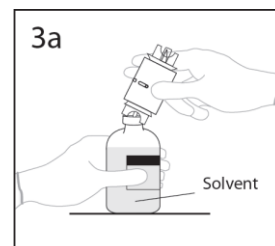
Bring GAMMAGARD S/D and Water for Injections (solvent) to room temperature. This temperature needs to be maintained until dissolution is complete.

**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 bottle on a flat surface. Use exposed end of transfer device to spike solvent bottle through centre of the stopper.

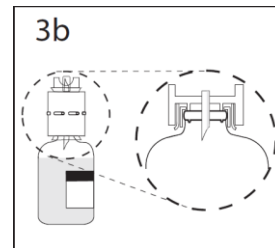


**Caution: Failure to insert spike into centre of the**

**stopper may result in dislodging of the stopper.**

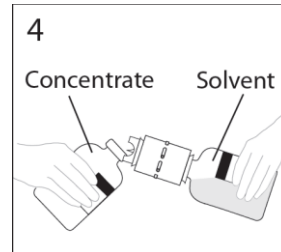
3b. Ensure that the collar collapses fully into the device by pushing down on the transfer device firmly.

While holding onto transfer device, remove remaining spike cover. Do not touch spike.



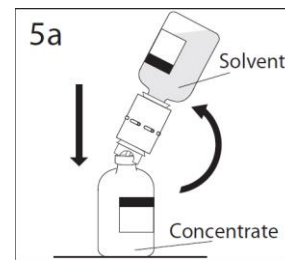
4. Hold solvent bottle with attached transfer device at an angle to the concentrate bottle to prevent spilling the solvent.

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

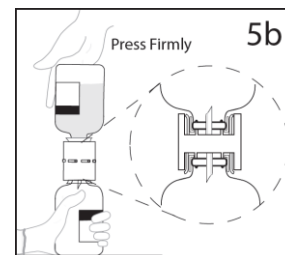


5a. Spike concentrate bottle through the centre of the stopper while **quickly inverting the solvent bottle** to avoid spilling out solvent.

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



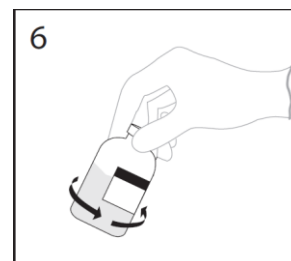
5b. Ensure that the collar collapses fully into the device by pushing down on the solvent bottle firmly.



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 bottle** 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 needle.
3. Using the residual solvent in the solvent bottle, follow steps 2-6 as previously described in A.



**TABLE 2**

**Required Solvent Volume to be Removed**

Concentration	5.0 g bottle	10.0 g bottle
5%	<b>Do not remove any solvent for reconstitution of 5% Solution</b>	
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. Do not use solutions that are cloudy or have deposits. Reconstituted products should be inspected visually for particulate matter and discolouration prior to administration.
- Any unused product or waste material should be disposed of in accordance with local requirements.

**Method of Administration**

GAMMAGARD S/D 5% (50 mg/mL) should be infused intravenously at an initial rate of 0.5 mL/kg body weight (BW)/hour. 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. 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

<b>Indication</b>	<b>Dose</b>	<b>Frequency of Injections</b>
<p>Replacement therapy in primary immunodeficiency</p> <p>Replacement therapy in secondary immunodeficiency</p> <p>Children with AIDS</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>every 2 – 4 weeks to obtain IgG trough level of at least 4 – 6 g/L</p> <p>every 3 – 4 weeks to obtain IgG trough level of at least 4 – 6 g/L</p> <p>every 3 - 4 weeks</p>
<p><b>Immunomodulation:</b></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 consecutive 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>
<p><b>Allogeneic bone marrow transplantation:</b></p> <p>- Treatment of infections and prophylaxis of graft versus host disease</p> <p>- Persistent lack of antibody production</p>	<p>0.5 g/kg BW</p> <p>0.5 g/kg BW</p>	<p>every week from day –7 up to 3 months after transplantation</p> <p>every month until antibody levels return to normal</p>