PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

GammaQuin, 160 g/l, solution for injection
Human normal immunoglobulin

Read all of this leaflet carefully before you start using this medicine.
- 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. Do not pass it on to others. This medicine may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT GAMMAQUIN IS AND WHAT IT IS USED FOR

What is GammaQuin?
GammaQuin is a solution for injection which contains human normal immunoglobulin. Immunoglobulins are antibodies and normal constituents of human blood and they protect you from infections. GammaQuin contains immunoglobulins that are present in a normal population. GammaQuin is used to raise antibody levels in your blood when the antibody level is too low or if you need additional antibodies in certain diseases. The administration of antibodies can also have an effect in case of a disrupted immune system. GammaQuin can also be used to prevent infection with the hepatitis A virus or to reduce the symptoms of the hepatitis A disease. The hepatitis A virus may induce hepatitis in humans.

What is GammaQuin used for?

* congenital (primary immunodeficiency),or acquired immune disorders without known cause (idiopathic immune deficiency), with which infections may repeatedly occur. In that case, the body may create too little (or in some cases, absolutely no) immunoglobulin G (antibodies) or there is an absence of one or multiple types of immunoglobulin G (subclass deficiencies).
This involves the following illnesses:
- congenital complete agammaglobulinaemia and hypogammaglobulinaemia
- common variable immunodeficiency
- severe combined immunodeficiency's
- IgG subclass deficiencies with recurrent infections
(in healthy people the immunoglobulin G antibody (or IgG) occurs in so-called subdivisions (subclasses) of immunoglobulin G1, immunoglobulin G2, immunoglobulin G3 and immunoglobulin G4. In some persons, one or more of these subclasses fail to be produced, which may cause infections to occur repeatedly).

* - to prevent hepatitis A, or to make the illness subside within 2 week after you came into contact with the hepatitis A virus, as with contacts between relatives or within a family, contacts in a military connection and contact in other circumstances in which people live and work together closely.
- to prevent hepatitis A, if you plan to travel to an area where hepatitis A occurs frequently.

* to prevent measles or to reduce symptoms of illness within one week after exposure to the measles virus, and when at least one of the following situations apply:
  - you have not been vaccinated with a measles vaccine and it may be dangerous for you to get the measles. This will be determined by your physician.
  - children younger than 12 months who have not been vaccinated with a measles vaccine and for whom it may be dangerous to get the measles.

2. WHEN ARE YOU ALLOWED TO USE GAMMAQUIN OR DO YOU HAVE TO BE EXTRA CAREFUL?

Do not use GammaQuin

- if you are allergic (hypersensitive) to human normal immunoglobulin or any of the other ingredients of GammaQuin such as glycine. This applies also for patients who are missing another type of antibody, namely immunoglobulin A (IgA-deficiency) and have antibodies against immunoglobulin A. However, in this last case your physician may decide to administer GammaQuin (see below **"Take special care with GammaQuin"**).
- into a blood vessel.
- into a muscle if you suffer from any bleeding disorders. In that case GammaQuin should be administered under the skin (subcutaneous).

Take special care with GammaQuin

Tell your doctor if you have any other illnesses.

Tell your doctor if any of the following situations apply to you to you, because these can be risk factors during the treatment with GammaQuin.

- diabetes (abnormally high glucose levels in the blood)
- a history of vascular disease or thrombotic episodes (formation of a blood clot in a blood vessel)
- high blood pressure
- overweight
- diseases which increase blood viscosity (thickness)
- hypovolaemia (decrease in the circulating amount of blood)
- advanced age (over 65 years)
- if you experienced a prolonged period of immobilization

Thromboembolic events including myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism have been associated with the use of immunoglobulins.
Contact you doctor immediately if you experience symptoms like shortness of breath, chest pain, pain and swelling of a limb, weakness or numbness on one side of your body after administration of GammaQuin.
Before administration of GammaQuin sufficient hydration should be ensured.

- GammaQuin may induce a severe hypersensitivity reaction (anaphylactic shock) in persons that have no immunoglobulin A (IgA deficiency) and who have antibodies against immunoglobulin A. A hypersensitivity reaction may also occur in patients who have demonstrated hypersensitivity to previous use of blood or blood products. In these cases, if strictly necessary, GammaQuin must be administered under the careful supervision of a physician.

- In case of an anaphylactic shock, administration must be stopped immediately.
When you receive GammaQuin for the first time you must be monitored for at least 20 minutes after the administration of GammaQuin.

- Prevention to hepatitis A is recommended if you are going to countries where hepatitis A frequently occurs. GammaQuin gives short-term protection against the hepatitis A virus. This involves an injection with antibodies against the hepatitis A virus (passive immunisation). Passive immunisation is not needed in

persons that have already had a hepatitis A infection. Your physician can investigate this by having your blood examined for antibodies against the hepatitis A virus.
A long-lasting protection against the hepatitis A virus is only obtained after vaccination with the hepatitis A vaccine. This causes the human body itself to form antibodies after the introduction of inactivated hepatitis A virus. This is recommended for persons that plan to visit an area where hepatitis A frequently occurs.

Using other medicines

Please tell your doctor or pharmacist if you are taking, or have recently taken, any other medicines, including medicines obtained without a prescription.

GammaQuin weakens the effect of certain vaccines. This is in particular is true for vaccines against measles, mumps, varicella (chicken pox) and rubella (German measles). Inform your physician if you have been vaccinated in the past 3 to 4 weeks, or will shortly be vaccinated (within 3 months after administration of GammaQuin).

No information is available concerning possible interactions between GammaQuin and other medicinal products.

Effects on blood tests

The use of GammaQuin may influence the results of certain blood tests.

Using GammaQuin with food and drink

No effects of food and drink on the use of GammaQuin are known.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

The safety of this medicinal product for use during pregnancy or breast-feeding has not been investigated. To date, the use of immunoglobulins, such as GammaQuin, during pregnancy or while breastfeeding has never led to harmful effects. Immunoglobulins are transferred to the new-born infants through breast milk and contribute to the new-born infant’s defences. You are advised to contact your physician if you are pregnant, while breastfeeding or if you want to become pregnant.

Driving and using machines

No effects on ability to drive or use machines have been observed.

Special warnings and special precautions for use

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. 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 are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped viruses hepatitis A virus and 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.

<u>Batch number control:</u>

It is strongly recommended that every time you receive a dose of GammaQuin the name and batch number (Lot:) of the product are recorded in order to maintain a record of the batches used.

3. HOW TO USE GAMMAQUIN

Always use GammaQuin exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Instructions for use
Administration of GammaQuin should be performed by a physician. GammaQuin may be self administered at home when you have been trained sufficiently.

GammaQuin must be injected deep into the muscle (intramuscular) usually in the upper arm or buttock. Before GammaQuin is administered, make sure the vial is at body temperature. It is recommended dividing the dose over multiple injection sites while administrating a large dose (more than 5 ml) in the muscle.

In the case of immune disorders, when it is necessary to administer a high dose, GammaQuin is administered under the skin (subcutaneous) with a so-called “infusion pump”. The physician may also administer GammaQuin subcutaneously in patients with a special tendency towards spontaneous, sometimes long lasting, haemorrhages. The infusion speed is 2-3 ml/hour; this can be increased if you tolerate it well.
A light cloudiness or a small amount of precipitate may occur during the storage period. This causes no objection to the administration of this product.

If you use more GammaQuin than you should
The risks of overdosing with GammaQuin are not known. Consult your doctor if you have taken more GammaQuin then prescribed.

If you forget to use GammaQuin
Do not take a double dose to make up for a forgotten dose. Contact your doctor what to do.

If you stop using GammaQuin
Contact your doctor or pharmacist, if you wish to stop using GammaQuin.

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

4. POSSIBLE SIDE EFFECTS

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

Adverse reactions such as chills, headache, fever, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate low back pain may occur occasionally.

Rarely human normal immunoglobulins may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.

Local reactions at infusion site: swelling, soreness, redness, induration, local heat, itching, bruising and rash.

With intramuscular administration, local pain and tenderness can be observed at the injection site.

For information about virus safety, please refer to chapter 2, section ‘Special warnings and special precautions for use’.

5. HOW TO STORE GAMMAQUIN

Keep out of the reach and sight of children.

Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original package in order to protect from light.

Do not use GammaQuin after the expiry date which is stated on the label and the carton after EXP:. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. CONTENT OF THE PACKING AND FURTHER INFORMATION

What GammaQuin contains

- The active substance is human normal immunoglobulin 160 g/l (at least 90% is immunoglobulin G).
- The other ingredients are glycine and water for injections.
- The maximal IgA content is 6 g/l.

What GammaQuin looks like and contents of the pack

GammaQuin is available in four pack sizes containing160 mg/1 ml, 320 mg/2 ml, 800 mg/5 ml and 2400 mg/15 ml of protein. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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Plesmanlaan 125
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This leaflet was last updated in August 2016.

The following information is intended for medical or healthcare professionals only:

Therapeutic indications

- Replacement therapy
- Hepatitis A prophylaxis
- Measles prophylaxis or mitigation

See section 1 of this package leaflet for an explanation of these indications.

Posology and method of administration

Posology

The dose and dosage regimen are dependent on the indication.

Replacement therapy

The product should be administered via the subcutaneous route.

Treatment should be initiated and monitored under the supervision of a physician experienced in the treatment of immunodeficiency.

The dosage may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. The following dosage regiments are given as a guideline:

The dosage regimen using the subcutaneous route should achieve a sustained level of IgG. A loading dose of at least 0.2-0.5 g/kg (1.3 to 3.1 ml/kg) may be required. After steady state IgG levels have been attained, maintenance doses are administered at repeated intervals to reach a cumulative monthly dose of the order of 0.4-0.8 g/kg (2.5 to 5 ml/kg).

Trough levels should be measured in order to adjust the dose and dosage interval.

Hepatitis A prophylaxis

The product should be administered via the intramuscular route.

- Short term Hepatitis A prophylaxis in travellers who present less than 14 days before possible exposure.

GammaQuin with a minimum antibody content for HAV of 100 IU/ml can be given in combination with Hepatitis A vaccine.

The table below can serve as a guideline:

Body weight	**Duration of stay ≤ 1 month**	**Duration of stay ≤ 6 weeks**	**Duration of stay ≤ 3 months**
	0.02 ml/kg	0.03 ml/kg	0.06 ml/kg
< 25 kg	1 ml	1 ml	2 ml
25 - 50 kg	1 ml	2 ml	3 ml
50 - 80 kg	2 ml	4 ml	5 ml
> 80 kg	2 ml	4 ml	5 ml

- **Hepatitis A prophylaxis** in persons exposed less than 2 weeks previously: 0.003-0.004 g/kg (0.02 ml/kg) body weight administered intramuscularly.

Measles

The product should be administered intramuscularly.

For prevention or mitigation, the dosage is 0.25 ml per kilogram of body weight. A dose of 0.5 ml per kilogram of body weight should be administered to a non-immunised, also immunocompromised child that has been exposed to measles.
The product should be administered as soon as possible, and no later than 1 week after exposure.

Method of administration:

Depending on the indication, human normal immunoglobulin should be administered via the subcutaneous (replacement therapy) or intramuscular (hepatitis A and measles prophylaxis) route.

Subcutaneous infusion for home treatment should be initiated by a physician experienced in the guidance of patients for home treatment. The patient will be instructed in the use of a syringe driver, infusion techniques, the keeping of a treatment diary and measures to be taken in case of severe adverse events.

GammaQuin may be injected into sites such as the abdomen, thigh, upper arm and lateral hip. It is recommended to use an initial administration speed of 2-3 ml per hours per pump. The infusion rate can be increased, if the patient can tolerate it. The optimal speed differs per patient and depends on what the patient tolerates. The maximally reported speed is 25 ml per hour. More that one pump can be used simultaneously.

Intramuscular injection
See section 3 of this package leaflet.

Contraindications

Hypersensitivity to any of the components.

GammaQuin must not be given intravenously.

GammaQuin must not be administered intramuscularly in cases of severe thrombocytopenia and in other disorders of haemostasis.

Special warnings and precautions for use

If GammaQuin is accidentally administered into a blood vessel, patients could develop shock.

The recommended infusion rate should be adhered to. Patients should be closely monitored and carefully observed for any adverse events throughout the infusion period.

Certain adverse reactions may occur more frequently in patients who receive human normal immunoglobulin for the first time or, in rare cases, when the human normal immunoglobulin product is switched or when treatment has been stopped for more than eight weeks.

True hypersensitivity reactions are rare. They can particularly occur in the very rare cases of IgA deficiency with anti-IgA antibodies and these patients should be treated with caution.

Rarely, human normal immunoglobulin can induce a fall in blood pressure with anaphylactic reaction, even in patients who had tolerated previous treatment with human normal immunoglobulin.

Potential complications can often be avoided by ensuring that:

- patients are not sensitive to human normal immunoglobulin, by first injecting the product slowly;

- patients are carefully monitored for any symptoms throughout the infusion period. In particular, patients naïve to human normal immunoglobulin, patients switched from an alternative product or when there has been a long interval since the previous infusion should be monitored during the first infusion and for the first hour after the first infusion, in order to detect potential adverse signs. All other patients should be observed for at least 20 minutes after administration.

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. In case of shock, standard medical treatment should be administered.

Thromboembolism

Arterial and venous thromboembolic events including myocardial infarction, stroke, deep venous thrombosis and pulmonary embolism have been associated with the use of immunoglobulins. Patients should be sufficiently hydrated before use of immunoglobulins. Caution should be exercised in patients with preexisting risk factors for thrombotic events (such as advanced age, hypertension, diabetes mellitus and a history of vascular disease or thrombotic episodes, patients with acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilization, severely hypovolemic patients, patients with diseases which increase blood viscosity). Patients should be informed about first symptoms of thromboembolic events including shortness of breath, pain and swelling of a limb, focal neurological deficits and chest pain and should be advised to contact their physician immediately upon onset of symptoms.

For the transmission of infections: see ‘Special warnings and special precautions for use’ at section 2 of this package leaflet.

Incompatibilities

This medicinal product must not be mixed with other medicinal products.

Special precautions for disposal and other handling

The product should be brought to room or body temperature before use.
For subcutaneous administration of GammaQuin an infusion needle for subcutaneous administration is used. The site where the needle is injected is the abdomen (please note that the needle should be at least 4 cm off the umbilicus) or in the thigh. To shorten the time of infusion 2 needles can be placed, by using one pump through a Y-line, or 2 pumps.

When using GammaQuin, attention should be paid that the needle is not injected in the blood vessel.

A light cloudiness or a small amount of precipitation may occur during the storage period. This causes no objection to the administration of this product.

Any unused product or waste material should be disposed of in accordance with local requirements.