SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

GammaQuin 160 g/l solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human normal immunoglobulin (SC/IMIg) 160 g/l*
* corresponding to human protein content of which at least 90% is IgG

One vial of 1 ml contains: 160 mg protein
One vial of 2 ml contains: 320 mg protein
One vial of 5 ml contains: 800 mg protein
One vial of 15 ml contains: 2400 mg protein

Distribution of IgG subclasses:
IgG_1 56%
IgG_2 39%
IgG_3 2%
IgG_4 3%

IgA max. 6 g/l

Hepatitis A antibody titer at least 100 IU/ml

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement therapy
Replacement therapy in adults and children in primary immunodeficiency syndromes such as:
- congenital agammaglobulinaemia and hypogammaglobulinaemia

- common variable immunodeficiency

- severe combined immunodeficiency

- IgG subclass deficiencies with recurrent infections

Replacement therapy in myeloma or chronic lymphatic leukaemia with severe secondary hypogammaglobulinemia and recurrent infections

Hepatitis A prophylaxis

- Hepatitis A prophylaxis in travellers who present less than 2 weeks before possible exposure, preferably in combination with vaccination.

  For long term hepatitis A prohylaxis active immunization is recommended.

- Hepatitis A prophylaxis in persons exposed less than 2 weeks previously.

Prevention or mitigation of measles
Within 1 week following exposure:
- following possible contact with a patient suffering from measles;
- in children less than one year old who are (have been) in contact with a measles patient

Passive immunisation can be considered for non-vaccinated individuals who have not yet had measles, who have been in contact with measles patients and for whom the disease itself and the associated complications could be dangerous.

4.2 Posology and method of administration

Posology

The dose and dosage regimen is 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. Administration of a loading dose of at least 0.2-0.5 g/kg (1.3 to 3.1 ml/kg) body weight 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 must be given by a physician or nurse.

It is recommended that the dose should be divided over multiple injection sites with the administration of a large dose (more than 5 ml).

4.3 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.

4.4 Special warnings and precautions for use

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

The recommended infusion rate stated under "4.2 Method of administration" 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 (see 4.2);

- 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.

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or (emerging) viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV and for non-enveloped viruses such as HAV and parvovirus B19.

There is reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to the

viral safety. One of the indications for GammaQuin is hepatitis A prophylaxis therefore GammaQuin has a high antibody titre for hepatitis A (100 IU/ml). Antibodies help preventing a hepatitis A infections.

It is strongly recommended that every time that GammaQuin is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

4.5 Interaction with other medicinal products and other forms of interaction

Live attenuated virus vaccines
Immunoglobulin administration may impair for a period of at least 6 weeks and up to 3 months the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella. After administration of this product, an interval of 3 months should elapse before vaccination with live attenuated virus vaccines In the case of measles this impairment may persist for up to 1 year. Therefore patients receiving measles vaccine should have their antibody status checked.

Interference with serological testing
After injection with immunoglobulin the transitory rise of the various passively transferred antibodies in the patients blood may result in misleading positive results in serological testing.

Passive transmission of antibodies to erythrocyte antigens, e.g. A, B,and D may interfere with some serological tests (reticulocyte count, haptoglobin and Coombs test).

4.6 Pregnancy and lactation

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given with caution to pregnant women and breast-feeding mothers. Clinical experience with immunoglobulins suggests that no harmful effects on the course of the pregnancy, on the foetus and on the neonate are to be expected.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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 on viral safety see 4.4.

4.9 Overdose

Consequences of an overdose are not known.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, for extravascular administration, ATC code: J06BA01.

Human normal immunoglobulin contains mainly immunoglobulin G (IgG) with a broad spectrum of antibodies against infectious agents.

Human normal immunoglobulin contains the IgG antibodies present in the normal population. It is usually prepared from pooled plasma from not fewer than 1000 donations. It has a distribution of immunoglobulin G subclasses closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low immunoglobulin G levels to the normal range.

5.2 Pharmacokinetic properties

With subcutaneous administration of human normal immunoglobulin, peak levels are achieved in the recipient's circulation after a delay of 4-6 days.

With intramuscular administration, human normal immunoglobulin is bioavailable in the recipient's circulation after a delay of 2-3 days.

IgG and IgG-complexes are broken down in the cells of the reticuloendothelial system.

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body. Animal experiments into the toxicity of a single administration are not relevant, since overdosage occurs at higher doses. Research into toxicity following repeated administration and into toxicity for the embryo or foetus is not feasible due to induction of, and disturbance by antibodies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycine, water for injections.

6.2 Incompatibilities

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

6.3 Shelf life

Two years.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.

6.5 Nature and contents of container

1 ml, 2 ml, 5 ml and 15 ml in vials (of glass type I) closed with a stopper (bromobutyl rubber) and sealed with an aluminium cap.

6.6 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 a 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.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

RVG 16941

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17 December 2012

10. DATE OF REVISION OF THE TEXT

Latest partial revision concerns section 4.4: 30-08-2016