GAMMAPLEX®

Solution for Infusion

1. NAME OF THE MEDICINAL PRODUCT

Gammaplex®

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Gammaplex 5 % w/v, solution for infusion.

Human normal immunoglobulin (IVIg)
One ml contains: Human normal immunoglobulin 50 mg (purity of at least 95% IgG).

Each 2.5 g vial of 50 ml contains: 2.5 g of human normal immunoglobulin.
Each 5 g vial of 100 ml contains: 5 g of human normal immunoglobulin.
Each 10 g vial of 200 ml contains: 10 g of human normal immunoglobulin.

Distribution of the IgG subclasses (approximate values):

IgG1	62 %
IgG2	31 %
IgG3	6 %
IgG4	1 %

The maximum IgA content is 10 micrograms/ml.

Produced from the plasma of human donors.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gammaplex is a colourless sterile solution for intravenous infusion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement therapy in adults, and children and adolescents in:

- Primary immunodeficiency syndromes with impaired antibody production (see section 4.4)
- Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed
- Hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation
- Congenital AIDS with recurrent bacterial infections

Immunomodulation in adults, and children and adolescents in:

- Primary immune thrombocytopenia (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count
- Guillain Barré syndrome
- Kawasaki disease

4.2 Posology and method of administration

Replacement therapy should be initiated and monitored under the supervision of a physician experienced in the treatment of immunodeficiency. Treatment at home should be similarly supervised, with the patient fully assessed and trained in hospital prior to self-infusion at home.

Posology

The dose and dose regimen is dependent on the indication.

In replacement therapy the dose may need to be individualised for each patient dependent on the pharmacokinetic and clinical response. The following dose regimens are given as a guideline.

Replacement therapy in primary immunodeficiency syndromes
The dose regimen should achieve a trough level of IgG (measured before the next infusion) of at least 5 to 6 g/l. Three to six months are required after the initiation of therapy for equilibration to occur. The recommended starting dose is 0.4 - 0.8 g/kg given once, followed by at least 0.2 g/kg given every three to four weeks.

The dose required to achieve a trough level of 5-6 g/l is of the order of 0.2 - 0.8 g/kg/month. The dosage interval when steady state has been reached varies from 3 - 4 weeks.
Trough levels should be measured and assessed in conjunction with the incidence of infection. To reduce the rate of infection, it may be necessary to increase the dosage and aim for higher trough levels.

Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia, in whom prophylactic antibiotics have failed; hypogammaglobulinaemia and recurrent bacterial infections in plateau phase multiple myeloma patients who have failed to respond to pneumococcal immunisation; congenital AIDS with recurrent bacterial infections
The recommended dose is 0.2 - 0.4 g/kg every three to four weeks.

Primary immune thrombocytopenia
There are two alternative treatment schedules:

- 0.8 - 1 g/kg given on day one; this dose may be repeated once within 3 days
- 0.4 g/kg given daily for two to five days.

The treatment can be repeated if relapse occurs.

Guillain Barré syndrome
0.4 g/kg/day over 5 days.

Kawasaki Disease
1.6 - 2.0 g/kg should be administered in divided doses over two to five days or 2.0 g/kg as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid.

The dosage recommendations are summarised in the following table:

Indication	Dose	Frequency of injections
Replacement therapy in primary immunodeficiency	-starting dose: 0.4 - 0.8 g/kg - thereafter: 0.2 - 0.8 g/kg	every 3 - 4 weeks to obtain IgG trough level of at least 5 - 6 g/l
Replacement therapy in secondary immunodeficiency	0.2 - 0.4 g/kg	every 3 - 4 weeks to obtain IgG trough level of at least 5 - 6 g/l
Congenital AIDS	0.2 - 0.4 g/kg	every 3 - 4 weeks
Immunomodulation: Primary immune thrombocytopenia	 0.8 - 1 g/kg or 0.4 g/kg/day	 on day 1, possibly repeated once within 3 days for 2 - 5 days
Guillain Barré syndrome	0.4 g/kg/day	for 5 days
Kawasaki disease	1.6 - 2 g/kg or 2 g/kg	in divided doses over 5 days in association with acetylsalicylic acid in one dose in association with acetylsalicylic acid

Paediatric population
The posology in children and adolescents 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.

Method of administration

For intravenous use.

Gammaplex should be infused intravenously, at an initial rate of 0.01 - 0.02 ml/kg/minute (0.6 - 1.2 ml/kg/hour) for 15 minutes. If well tolerated (see section 4.4), the rate of administration may be increased to 0.04 ml/kg/minute (2.4 ml/kg/hour) for 15 minutes, then to 0.06 ml/kg/minute (3.6 ml/kg/hour) for 15 minutes, followed by a maximum of 0.08 ml/kg/minute (4.8 ml/kg/hour).

4.3 Contraindications

Hypersensitivity to the active substance (human immunoglobulins) or to any of the excipients listed in section 6.1 (see section 4.4).
Hereditary fructose intolerance (see section 4.4).
Babies and young children (see section 4.4).
Patients with selective IgA deficiency who developed antibodies to IgA, as administering an IgA-containing product can result in anaphylaxis.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Fructose

This medicinal product contains 50 mg of sorbitol per ml as an excipient. Patients with rare hereditary problems of fructose intolerance should not take this medicine. In babies and young children hereditary fructose intolerance may not yet be diagnosed, as they may not yet have been exposed to fructose-containing foods such as fruit or sucrose and infusion of sorbitol may be fatal. Therefore, babies and young children who have not been exposed to fructose containing foods or sucrose should not receive this medicine until it is known whether they can metabolise fructose.

In other patients, in case of inadvertent administration and suspicion of fructose intolerance, the infusion has to be stopped immediately, normal glycaemia has to be re-established and organ function has to be stabilised by means of intensive care.

Precautions for use

Potential complications can often be avoided by ensuring that patients:

- are not sensitive to human normal immunoglobulin by initially injecting the product slowly (0.01 – 0.02 ml/kg/min)
- are carefully monitored for any symptoms throughout the infusion period. In particular, patients naïve to human normal immunoglobulin, patients switched from an alternative IVIg product or when there has been a long interval since the previous infusion, should be monitored at the hospital 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.

In all patients, IVIg administration requires:

- adequate hydration prior to the initiation of the infusion of IVIg
- monitoring of urine output
- monitoring of serum creatinine levels
- avoidance of concomitant use of loop diuretics (see section 4.5).

In case of adverse reaction, either the rate of administration must be reduced or the infusion stopped. The treatment required depends on the nature and severity of the adverse reaction.

Infusion reaction

Certain adverse reactions (e.g. headache, flushing, chills, myalgia, wheezing, tachycardia, lower back pain, nausea, and hypotension) may be related to the rate of infusion. The recommended infusion rate given under section 4.2 must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.

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 there has been a long interval since the previous infusion
- in patients with an untreated infection or underlying chronic inflammation

Hypersensitivity

Hypersensitivity reactions are rare.

Anaphylaxis can develop in patients:

- with undetectable IgA who have anti-IgA antibodies
- who had tolerated previous treatment with human normal immunoglobulin

In case of shock, standard medical treatment for shock should be implemented.

Thromboembolism

There is clinical evidence of an association between IVIg administration and thromboembolic events such as myocardial infarction, cerebral vascular accident (including stroke), pulmonary embolism and deep vein thromboses which is assumed to be related to a relative increase in blood viscosity through the high influx of immunoglobulin in at-risk patients. Caution should be exercised in prescribing and infusing IVIg in obese patients and in patients with pre-existing 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 immobilisation, severely hypovolaemic patients, patients with diseases which increase blood viscosity).

In patients at risk for thromboembolic adverse reactions, IVIg products should be administered at the minimum rate of infusion and dose practicable.

Acute renal failure

Cases of acute renal failure have been reported in patients receiving IVIg therapy. In most cases, risk factors have been identified, such as pre-existing renal insufficiency, diabetes mellitus, hypovolaemia, overweight, concomitant nephrotoxic medicinal products or age over 65.

Renal parameters should be assessed prior to infusion of IVIG, particularly in patients judged to have a potential increased risk for developing acute renal

failure, and again at appropriate intervals. In patients at risk for acute renal failure, IVIg products should be administered at the minimum rate of infusion and dose practicable. In case of renal impairment, IVIg discontinuation should be considered.
While reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IVIg products containing various excipients such as sucrose, glucose and maltose, those containing sucrose as a stabiliser accounted for a disproportionate share of the total number. In patients at risk, the use of IVIg products that do not contain these excipients may be considered. Gammaplex does not contain sucrose, maltose or glucose.

Aseptic meningitis syndrome (AMS)
Aseptic meningitis syndrome has been reported to occur in association with IVIg treatment.
The syndrome usually begins within several hours to 2 days following IVIg treatment. Cerebrospinal fluid studies are frequently positive with pleocytosis up to several thousand cells per mm^3, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dl.
AMS may occur more frequently in association with high-dose (2 g/kg) IVIg treatment.
Patients exhibiting such signs and symptoms should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis.

Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae.

Haemolytic anaemia
IVIg products can contain blood group antibodies which may act as haemolysins and induce *in vivo* coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction (Coombs' test) and, rarely, haemolysis. Haemolytic anaemia can develop subsequent to IVIg therapy due to enhanced red blood cells (RBC) sequestration. IVIg recipients should be monitored for clinical signs and symptoms of haemolysis (See section 4.8.).

Neutropenia/Leukopenia

A transient decrease in neutrophil count and/or episodes of neutropenia, sometimes severe, have been reported after treatment with IVIgs. This typically occurs within hours or days after IVIg administration and resolves spontaneously within 7 to 14 days.

Transfusion related acute lung injury (TRALI)

In patients receiving IVIg, there have been some reports of acute non-cardiogenic pulmonary oedema [Transfusion Related Acute Lung Injury (TRALI)].

TRALI is characterised by severe hypoxia, dyspnoea, tachypnoea, cyanosis, fever and hypotension. Symptoms of TRALI typically develop during or within 6 hours of a transfusion, often within 1-2 hours. Therefore, IVIg recipients must be monitored for and IVIg infusion must be immediately

stopped in case of pulmonary adverse reactions. TRALI is a potentially life-threatening condition requiring immediate intensive-care-unit management.

Interference with serological testing

After the administration of immunoglobulin, the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing.

Passive transmission of antibodies to erythrocyte antigens, e.g. A, B, D may interfere with some serological tests for red cell antibodies for example the direct antiglobulin test (DAT, direct Coombs' test).

Transmissible agents

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 human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) and for the non-enveloped hepatitis A (HAV) and parvovirus B19 viruses.

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.

It is strongly recommended that every time that Gammaplex 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.

Paediatric population

This medicinal product contains 50 mg of sorbitol per ml as an excipient. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Special precautions should be taken with babies and young children because this fructose intolerance may not yet be diagnosed and may be fatal.

Home therapy

Gammaplex must only be used by patients themselves at home after thorough training in hospital by a qualified health care professional, expert in infusion of IVIg products. The patient should first be stabilised on the product under supervision in hospital.

4.5 Interactions 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 medicinal 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.

Loop diuretics

Avoidance of concomitant use of loop diuretics.

Paediatric population

There are no known interactions that are specific to the paediatric population or any subset of the paediatric population.

4.6 Fertility, pregnancy and lactation

Pregnancy

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. IVIg products have been shown to cross the placenta, increasingly during the third trimester. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are expected.

Breast-feeding

Immunoglobulins are excreted into human milk. No negative effects on the breastfed new-borns/infants are anticipated.

Fertility

Clinical experience with immunoglobulins suggests that no harmful effects on fertility are to be expected.

4.7 Effects on ability to drive and use machines

The ability to drive and operate machines may be impaired by some adverse reactions associated with Gammaplex. Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions caused by human normal immunoglobulins (in decreasing frequency) encompass (see also Section 4.4):

- chills, headache, dizziness, fever, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate low back pain.

- reversible haemolytic reactions; especially in those patients with blood groups A, B, and AB and (rarely) haemolytic anaemia requiring transfusion
- (rarely) a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.
- (rarely) transient cutaneous reactions (including cutaneous lupus erythematosus - frequency unknown)
- (Very rarely) thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism, deep vein thromboses.
- cases of reversible aseptic meningitis
- cases of increased serum creatinine level and/or occurrence of acute renal failure
- cases of Transfusion Related Acute Lung Injury (TRALI)

Tabulated list of adverse reactions

The table presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level).
Frequencies have been evaluated according to the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Frequency of Adverse Reactions (ADRs) in clinical studies with Gammaplex

MedDRA System Organ Class (SOC)	**Adverse reaction**	**Frequency per patient**	**Frequency per infusion**
Metabolism and nutrition disorders	Fluid retention, dehydration	Common	Uncommon
	Decreased appetite, iron deficiency	Uncommon	Rare
Psychiatric disorders	Insomnia	Uncommon	Rare
Nervous system disorders	Headache	Very common	Common
	Dizziness	Common	Uncommon
	Migraine, paraesthesia	Uncommon	Uncommon
	Hypoaesthesia, lethargy	Uncommon	Rare
Ear and labyrinth disorders	Vertigo	Common	Uncommon
	Tinnitus	Uncommon	Rare
Cardiac disorders	Palpitations, tachycardia	Common	Uncommon

Vascular disorders	Hypertension	Common	Common
	Hypotension	Common	Uncommon
	Thrombosis, hot flush	Uncommon	Rare
Respiratory, thoracic and mediastinal disorders	Nasal congestion	Common	Uncommon
	Bronchospasm	Uncommon	Uncommon
	Epistaxis, pharyngolaryngeal pain	Uncommon	Rare
	Transfusion related acute lung injuries (TRALI)	Not Known	Not Known
Gastrointestinal disorders	Vomiting, nausea, diarrhoea, abdominal pain	Common	Uncommon
	Abdominal distension, constipation, stomatitis	Uncommon	Rare
Skin and subcutaneous tissue disorders	Urticaria	Uncommon	Uncommon
	Erythema multiforme, pruritus	Uncommon	Rare
	Cutaneous lupus erythematosus	Not Known	Not Known
Musculoskeletal, connective tissue disorders and bone disorders	Myalgia	Common	Common
	Arthralgia, muscle spasms, back pain, neck pain	Common	Uncommon
	Pain in extremity	Uncommon	Uncommon
	Musculoskeletal stiffness	Uncommon	Rare
General disorders and administration site conditions	Pyrexia	Very common	Common
	Fatigue	Common	Common
	Chills, chest discomfort/ pain, asthenia, infusion site reaction, infusion site erythema, pain	Common	Uncommon
Investigations	Coombs' direct test positive, anaemia/haemoglobin decreased	Common	Uncommon
	Anti-erythrocyte antibody positive, white blood cell count increased, urinary haemosiderin positive, gastric pH decreased	Uncommon	Rare

Description of selected adverse reactions

None of the reported adverse reactions to Gammaplex warrant separate description.

Paediatric population

Of the 50 patients in the clinical study of Gammaplex in primary immunodeficiency (GMX01), seven were aged less than 18 years (age range 9 to 17 years). A separate paediatric clinical study of Gammaplex in primary immunodeficiency (GMX04) treated 25 patients aged less than 18 years (age range 3 to 16 years). Of the 35 patients in the clinical study of Gammaplex in chronic immune thrombocytopenia (ITP) (GMX02), three were aged less than 18 years (age range 6 to 17 years). The frequency, type and severity of adverse reactions in children are similar to those in adults.

Other special populations

Certain patient groups may be at increased risk of hypersensitivity reactions, thromboembolism or acute renal failure. Caution should be exercised when infusing IVIg in obese patients or those with advanced age, hypertension, diabetes mellitus, history of vascular disease or thrombotic episodes, acquired or inherited thrombophilic disorders, prolonged periods of immobilisation, severe hypovolaemia, diseases which increase blood viscosity, pre-existing renal insufficiency or those receiving concomitant nephrotoxic medicinal products; see section 4.4 for details.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il
Additionally, you should also report to Kamada LTD to email address: pharmacovigilance@kamada.com

4.9 Overdose

Overdose may lead to fluid overload and hyperviscosity, particularly in patients at risk, including elderly patients or patients with cardiac or renal impairment (see section 4.4).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, for intravascular administration, ATC code: J06BA02.
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 1,000 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.

The mechanism of action in indications other than replacement therapy is not fully elucidated.

GMX01

A phase III, multicentre, non-randomized, open-label study in 50 predominantly adult subjects with primary immunodeficiency diseases (PID), where Gammaplex was infused at a dose of 300 to 800 mg/kg every 21 or 28 days, concluded that Gammaplex was well tolerated and efficacious and therefore suitable for the management of subjects with PID. There were no serious acute bacterial infections during the 12 months of treatment, and the most commonly reported adverse reactions were headache (18 patients), nausea (6 patients), pyrexia (6 patients) and fatigue (6 patients).

GMX02

A later phase III, open-label, multicentre clinical study investigating the safety and efficacy of Gammaplex infused at a dose of 1 g/kg/day for two consecutive days in 35 subjects with chronic immune thrombocytopenic purpura (ITP) showed Gammaplex to be an effective treatment, and hence its efficacy in immunomodulation. The most commonly reported adverse reactions were headache (10 patients), vomiting (6 patients) and pyrexia (5 patients).

<u>Paediatric population</u>

Study GMX01 above, comprised predominantly of adult subjects with PID and included seven patients aged less than 18 years (9-17 years inclusive). There were no reports of serious adverse reactions in any of the paediatric subjects.

Study GMX02 above in ITP included three subjects aged less than 18 years (6-17 years inclusive). One of the paediatric subjects (aged six years) experienced a serious adverse reaction (headache, with vomiting and dehydration).

GMX04

A phase III, multicentre, non-randomized, open-label paediatric study in 25 children and adolescent subjects (aged 3-16 years inclusive) with primary immunodeficiency diseases (PID), where Gammaplex was infused at a dose of 300 to 800 mg/kg every 21 or 28 days, concluded that Gammaplex was well tolerated and efficacious in children with PID.
There were two serious acute bacterial infections reported during the 12 months of treatment, and the most commonly reported adverse reactions were headache (8 patients), hypotension (4 patients), pyrexia (3 patients) and tachycardia (3 patients).

5.2 Pharmacokinetic properties

Human normal immunoglobulin is immediately and completely bioavailable in the recipient's circulation after intravenous administration. It is distributed relatively rapidly between plasma and extravascular fluid, and after approximately 3 - 5 days equilibrium is reached between the intra- and extravascular compartments. Human normal immunoglobulin has a half-life of about 31.3 days (range 21.1 days to 42.7 days). This half-life may vary from patient to patient, in particular in primary immunodeficiency.

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

Paediatric population

Pharmacokinetic data is available from 25 paediatric patients across the two PID studies: GMX01 (2/50 patients were included in the paediatric PK analysis) and GMX04 (23/25 patients were included in the PK analysis). At steady state Gammaplex was shown to have a median half-life in children of 35.5 days (range 24.2 to 76.2 days).

5.3 Preclinical safety data

Immunoglobulins are normal constituents of human plasma and therefore toxicity testing in heterologous species is of no relevance. Gammaplex contains highly purified immunoglobulins and has been tested in non-clinical haemodynamic monitoring studies. There was no evidence of effects on blood pressure or heart rate at infusion rates similar to those used clinically. At higher infusion rates of approximately 2- to 7-fold those used clinically, a hypertensive effect was found. No other preclinical studies have been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol
Glycine
Sodium Chloride

Sodium Acetate Trihydrate
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products, nor with any other IVIg products.

6.3 Shelf-life

The expiry date of the product is as indicated on the packaging materials, if stored unopened in the dark at temperatures between 2ºC and 25ºC. Gammaplex should be used immediately after opening (see section 4.2).

6.4 Special precautions for storage

Gammaplex should be stored at temperatures between 2ºC and 25ºC in its carton.

Do not freeze.

Do not use after the expiry date printed on the label. The conditions of expired or incorrectly stored product cannot be guaranteed. Such product may be unsafe and should not be used.

6.5 Nature and contents of container

Gammaplex is a sterile colourless liquid immunoglobulin G supplied as 2.5 g, 5 g and 10 g doses. The product is contained in a clear glass bottle with an integral sling, closed with a stopper and over-sealed with a tamper-evident cap.

6.6 Special precautions for disposal and other handling

The product should be brought to room or body temperature before use.
The solution should be clear or slightly opalescent and colourless or pale yellow. 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.

7. MANUFACTURER

Bio Products Laboratory Limited (BPL)
Dagger Lane
Elstree
WD6 3BX
United Kingdom.

8. LICENSE HOLDER

Kamada Ltd., Beit Kama, Israel

9. LICENSE NUMBER

145-40-33225

Revised in September 2020