## 1. NAME OF THE MEDICINAL PRODUCT

Flebogamma 5% DIF solution for infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human normal immunoglobulin (IVIg)

One ml contains:
Human normal immunoglobulin …….. 50 mg
(purity of at least 97% of IgG)

Each vial of 10 ml contains: 0.5 g of human normal immunoglobulin
Each vial of 50 ml contains: 2.5 g of human normal immunoglobulin
Each vial of 100 ml contains: 5 g of human normal immunoglobulin
Each vial of 200 ml contains: 10 g of human normal immunoglobulin
Each vial of 400 ml contains: 20 g of human normal immunoglobulin

Distribution of the IgG subclasses (approx. values):
$IgG_1$ 66.6%
$IgG_2$ 28.5%
$IgG_3$ 2.7%
$IgG_4$ 2.2%

The maximum IgA content is 50 micrograms/ml.

Produced from the plasma of human donors.

Excipient with known effect:

One ml contains 50 mg of D-sorbitol.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for infusion.

The solution is clear or slightly opalescent and colourless or pale yellow.

Flebogamma DIF is isotonic, with an osmolality from 240 to 370 mOsm/kg.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**Replacement therapy in:**

**Primary immunodeficiency syndromes such as:**

**- congenital agammaglobulinaemia and hypogammaglobulinaemia**

**- common variable immunodeficiency**

**- severe combined immunodeficiency**

**- Wiskott Aldrich syndrome**

**Myeloma or chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections.**

**Children with congenital AIDS and recurrent infections.**

**Immunomodulation:**

**Idiopathic thrombocytopenic purpura (ITP), in children or adults at high risk of bleeding or prior to surgery to correct the platelet count.**

**Guillain Barré syndrome.**

**Kawasaki disease.**

**Allogeneic bone marrow transplantation.**

### 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.

Posology

The dose and dosage regimen is dependent on the indication.

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

*Replacement therapy in primary immunodeficiency syndromes*

The dosage regimen should achieve a trough level of IgG (measured before the next infusion) of at least 5 - 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 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 thrombocytopenic

There are two alternative treatment schedules:

0.8 - 1 g/kg given on day one, which may be repeated once within 3 days,

or 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.

Allogeneic bone marrow transplantation

Human normal immunoglobulin treatment can be used as part of the conditioning regimen and after the transplant.

For the treatment of infections and prophylaxis of graft versus host disease, dosage is individually tailored. The starting dose is normally 0.5 g/kg/week, starting seven days before transplantation and for up to 3 months after transplantation.

In case of persistent lack of antibody production, dosage of 0.5 g/kg/month is recommended until antibody level returns to normal.

The dosage recommendations are summarised in the following table:

| **Indication** | **Dose** | **Frequency** |
|---|---|---|
| Replacement therapy in primary immunodeficiency | - starting dose:<br>0.4 - 0.8 g/kg<br>- thereafter:<br>0.2 - 0.8 g/kg | every 2 - 4 weeks to obtain IgG trough level of at least 4 - 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 thrombocytopenic | 0.8 - 1 g/kg<br>or | on day 1, possibly repeated once within 3 days |
| | 0.4 g/kg/d | for 2 - 5 days |
| Guillain Barré syndrome | 0.4 g/kg/d | for 5 days |
| Kawasaki disease | 1.6 - 2 g/kg<br>or | in divided doses over 2 - 5 days in association with acetylsalicylic acid |
| | 2 g/kg | in one dose in association with acetylsalicylic acid |

*Paediatric population*

Flebogamma 5% DIF is contraindicated in children aged 0 to 2 years (see section 4.3).

The posology in children and adolescents (2 - 18 years) 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

Flebogamma 5% DIF should be infused intravenously at an initial rate of 0.01 - 0.02 ml/kg/min for the first thirty minutes. If well tolerated, (see section 4.4), the rate of administration may gradually be increased to a maximum of 0.1 ml/kg/min.

## 4.3 Contraindications

Hypersensitivity to the active substance (human immunoglobulins) or to any of the excipients (see sections 4.4 and 6.1).

Hereditary fructose intolerance (see section 4.4).

In babies and young children (aged 0 - 2 years) hereditary fructose intolerance (HFI) may not yet be diagnosed and may be fatal, thus, they must not receive this medicinal product.

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

**Sorbitol**

**Patients with rare hereditary fructose intolerance (HFI) must not be given this medicine unless strictly necessary.**

**Babies and young children (below 2 years of age) may not yet be diagnosed with hereditary fructose intolerance (HFI). Medicines (containing sorbitol/fructose) given intravenously may be life-threatening and should be contraindicated in this population unless there is an overwhelming clinical need and no alternatives are available.**

**A detailed history with regard to HFI symptoms has to be taken of each patient prior to being given this medicinal product.**

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.

*Precautions for use*
Potential complications can often be avoided by ensuring that patients:
- are not sensitive to human normal immunoglobulin by initially administering the product slowly (at an initial rate of 0.01 - 0.02 ml/kg/min)
- are carefully monitored for any symptoms throughout the infusion period. In particular, patients naive 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 during the first infusion and for the first hour after the first infusion in a controlled healthcare setting in order to detect potential adverse signs and to ensure that emergency treatment can be administered immediately should problems occur. 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 IVIg infusion

- monitoring of urine output
- monitoring of serum creatinine levels
- avoidance of concomitant use of loop diuretics (see 4.5)

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

Infusion-related 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 active 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, and 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. Flebogamma DIF does not contain sucrose, maltose or glucose.

Aseptic meningitis syndrome (AMS)

AMS 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 (CSF) 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 (RBC) with immunoglobulin, causing a positive direct antiglobulin reaction (Coombs' test) and, rarely, haemolysis. Haemolytic anaemia can develop subsequent to IVIg therapy due to enhanced 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 IVIg. 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 after 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 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 viral safety.

It is strongly recommended that every time that Flebogamma DIF 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.

Sodium content

This medicinal product contains less than 7.35 mg sodium per 100 ml, equivalent to 0.37% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Paediatric population
It is recommended to monitor vital signs when administering Flebogamma DIF to paediatric patients.

## 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 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

It is expected that the same interactions than those mentioned for the adults may be presented by 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. 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

The safety of this medicinal product for use in breast-feeding mothers has not been established in controlled clinical trials and therefore should only be given with caution to breast-feeding mothers. Immunoglobulins are excreted into human milk. No negative effects on the breastfed newborns/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, such as dizziness, associated with Flebogamma DIF. 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)

For safety information with respect to transmissible agents, see section 4.4.

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 ($\geq$1/10)
- common ($\geq$1/100 to <1/10)
- uncommon ($\geq$1/1,000 to <1/100)
- rare ($\geq$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.

**Source of the safety database from clinical trials and post-authorisation safety studies in a total of 128 patients exposed to Flebogamma 5% DIF (with a total of 1318 infusions)**

| MedDRA System Organ Class (SOC) | Adverse reaction | Frequency per patient | Frequency per infusion |
|---|---|---|---|
| Infections and infestations | Nasopharyngitis | Uncommon | Uncommon |
| Immune system disorders | Hypersensitivity | Uncommon | Rare |
| Psychiatric disorders | Abnormal behaviour | Uncommon | Rare |
| Nervous system disorders | Migraine | Uncommon | Rare |
| | Headache | Very Common | Common |
| | Dizziness | Common | Uncommon |
| Cardiac disorders | Tachycardia | Common | Common |
| | Cardiovascular disorder | Uncommon | Rare |
| Vascular disorders | Hypertension | Common | Uncommon |
| | Diastolic hypertension | Common | Uncommon |
| | Systolic hypertension | Uncommon | Uncommon |
| | Hypotension | Common | Common |
| | Diastolic hypotension | Common | Common |
| | Blood pressure fluctuation | Uncommon | Rare |
| | Flushing | Uncommon | Rare |
| Respiratory, thoracic and mediastinal disorders | Bronchitis | Common | Uncommon |
| | Dyspnoea | Uncommon | Rare |
| | Asthma | Uncommon | Rare |
| | Epistaxis | Uncommon | Rare |
| | Productive cough | Uncommon | Uncommon |
| | Cough | Uncommon | Rare |
| | Wheezing | Common | Uncommon |
| | Laryngeal pain | Uncommon | Rare |
| | Nasal discomfort | Uncommon | Rare |
| Gastrointestinal disorders | Diarrhoea | Common | Uncommon |
| | Vomiting | Common | Uncommon |
| | Abdominal pain upper | Common | Uncommon |
| | Abdominal pain | Common | Uncommon |
| | Nausea | Common | Uncommon |
| Skin and subcutaneous tissue disorders | Rash pruritic | Uncommon | Uncommon |
| | Dermatitis contact | Uncommon | Rare |
| | Urticaria | Common | Uncommon |
| | Pruritus | Uncommon | Uncommon |
| | Rash | Uncommon | Rare |
| | Hyperhidrosis | Uncommon | Rare |
| Musculoskeletal and connective tissue disorders | Arthralgia | Common | Uncommon |
| | Myalgia | Common | Uncommon |
| | Back pain | Common | Uncommon |

| MedDRA System Organ Class (SOC) | Adverse reaction | Frequency per patient | Frequency per infusion |
|---|---|---|---|
| | Neck pain | Uncommon | Rare |
| | Pain in extremity | Uncommon | Rare |
| | Muscle spasms | Uncommon | Rare |
| Renal and urinary disorders | Urinary retention | Uncommon | Rare |
| General disorders and administration site conditions | Pyrexia | Very Common | Common |
| | Chest pain | Uncommon | Rare |
| | Oedema peripheral | Uncommon | Rare |
| | Chills | Common | Uncommon |
| | Rigors | Common | Uncommon |
| | Pain | Common | Uncommon |
| | Asthenia | Uncommon | Rare |
| | Injection site reaction | Common | Uncommon |
| | Infusion site erythema | Uncommon | Rare |
| | Infusion site extravasation | Uncommon | Rare |
| | Injection site pruritus | Uncommon | Rare |
| | Infusion site inflammation | Uncommon | Rare |
| | Injection site swelling | Uncommon | Rare |
| | Injection site oedema | Uncommon | Rare |
| | Infusion site pain | Uncommon | Rare |
| | Injection site pain | Uncommon | Rare |
| Investigations | Blood pressure increased | Uncommon | Rare |
| | Blood pressure systolic increased | Common | Uncommon |
| | Blood pressure systolic decreased | Uncommon | Uncommon |
| | Body temperature increased | Common | Uncommon |
| | Alanine aminotransferase increased | Uncommon | Rare |
| | Coombs test positive | Common | Uncommon |
| Injury, poisoning and procedural complications | Infusion related reaction | Uncommon | Uncommon |

Description of selected adverse reactions

The most reported post-marketing ADRs received since the product was authorised for both concentrations were chest pain, flushing, blood pressure increased and decreased, malaise, dyspnoea, nausea, vomiting, pyrexia, back pain, headache and chills.

Paediatric population

The safety results for 29 paediatric patients (those ≤ 17 years old) included in the PID studies were evaluated. It was observed that the proportion of headache, pyrexia, tachycardia and

hypotension in children was higher than in adults. Assessment of vital signs in clinical trials of the paediatric population did not indicate any pattern of clinically relevant changes.

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 (www.health.gov.il) according to the National Regulation by using an online form https://sideeffects.health.gov.il

### 4.9 Overdose

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

Paediatric population

Information on overdose in children has not been established with Flebogamma DIF. However, as in adult population, overdose may lead to fluid overload and hyperviscosity as with any other intravenous immunoglobulins.

## 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 1000 donors. 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, but includes immunomodulatory effects. A significant increase in median platelet levels was achieved in a clinical trial in chronic ITP patients (64,000/µl) although it did not reach normal levels.

Three clinical trials were performed with Flebogamma DIF, two for replacement therapy in patients with primary immunodeficiency (one in both adults and in children above 10 years

and another in children between 2 to 16 years) and another for immunomodulation in adult patients with immune thrombocytopenic purpura.

## 5.2 Pharmacokinetic properties

Absorption
Human normal immunoglobulin is immediately and completely bioavailable in the recipient's circulation after intravenous administration.

Distribution
It is distributed relatively rapidly between plasma and extravascular fluid, after approximately 3 - 5 days equilibrium is reached between the intra- and extravascular compartments.

Elimination
Flebogamma 5% DIF has a half-life of about 30 - 32 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*

No differences of the pharmacokinetic properties are expected in the paediatric population.

## 5.3 Preclinical safety data

Single dose toxicity studies were carried out in rats and mice. The absence of mortality in the non-clinical studies performed with Flebogamma DIF with doses up to 2500 mg/kg, and the lack of any confirmed relevant adverse sign affecting respiratory, circulatory and central nervous system, of the treated animals support the safety of Flebogamma DIF.

Repeated dose toxicity testing and embryo-foetal toxicity studies are impracticable due to induction of, and interference with antibodies. Effects of the product on the immune system of the newborn have not been studied.

# 6. PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

D-sorbitol
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 indicated on the packaging materials.

## 6.4 Special precautions for storage

Do not store above 30 ºC.
Do not freeze.

## 6.5 Nature and contents of container

10 ml, 50 ml, 100 ml, 200 ml or 400 ml solution in a vial (type II glass) with stopper (chloro-butyl-rubber).

Pack size: 1 vial

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

The product should be brought at room temperature (no more than 30 ºC) 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

Instituto Grifols, S.A.
Can Guasc, 2 - Parets del Vallès
08150 Barcelona - Spain

# 8. LICENSE HOLDER

Medici Medical Ltd.
3 Hamachshev St.

Netanya 4250713 – Israel

## 9. MARKETING AUTHORISATION NUMBER(S)

121-04-29877-00

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