1. NAME OF THE MEDICINAL PRODUCT

Omr-IgG-am™ 5%

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Human normal immunoglobulins 50 mg/ml. Solution for infusion.

Each bottle of 50 ml contains 2.5 g of human normal immunoglobulins.
Each bottle of 100 ml contains 5 g of human normal immunoglobulins.
Each bottle of 200 ml contains 10 g of human normal immunoglobulins.

Composition
Omr-IgG-am™ 5% is a sterile solution containing 5% protein (50 mg in 1 ml solution of which at least 95% is human normal immunoglobulin G as the active ingredient), 10% maltose and water for injections. The immunoglobulin A (IgA) content is ≤ 0.15 mg/ml.

Omr-IgG-am™ 5% does not contain sucrose. No preservatives are added.

Description
Omr-IgG-am™ 5% is manufactured from human plasma by Cohn (ethanol) fractionation (this step has been shown in literature to be a primary virus inactivation step). After a first ultra-/diafiltration, the product undergoes a second viral inactivation step by the solvent/detergent (TnBP/Triton-X-100), and a third viral inactivation step by nanofiltration at pH 4. **The manufacturing process includes a specific step to remove detectable thrombosis-generating agents** (see section 4.4 "Special warnings and precautions for use").

3. PHARMACEUTICAL FORM

Solution for infusion.
Omr-IgG-am™ 5% is a clear or slightly opalescent and colorless or pale yellow solution for intravenous infusion.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement therapy
- Primary immunodeficiency (patients with primary defective antibody synthesis such as agammaglobulinemia or hypogammaglobulinemia)
- Myeloma or Chronic Lymphocytic Leukemia (CLL) with severe secondary hypogammaglobulinemia and recurrent infections
- Children with congenital AIDS and recurrent infections

Immunomodulation
- Idiopathic Thrombocytopenic Purpura (ITP)
- Guillain-Barré syndrome
- Kawasaki disease

Allogenic Bone Marrow Transplantation

4.2 Posology and method of administration

- **Omr-IgG-am™ 5% should be infused intravenously at an initial rate of 0.01-0.02 ml/kg/min for 15 minutes.**
- **Infusion rate may increase gradually to a maximum of 0.08 ml/kg/min.**

Dosage
The dose and dosage regimen is dependent on the indication.
In replacement therapy, the dosage may need to be individualized for each patient, dependent on the pharmacokinetic and clinical response. The following dosage regimens are given as a guideline.

Replacement therapy
Replacement therapy in Primary Immunodeficiency
The dosage regimen should achieve a trough level of immunoglobulin G (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 depending on the circumstances (e.g., active infection) 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 weekly.
Trough levels should be measured every 6-12 months in order to adjust the dose and the dosage interval.

Replacement therapy in Myeloma or Chronic Lymphocytic Leukemia with severe secondary hypogammaglobulinemia and recurrent infections; replacement therapy in children with AIDS and recurrent infections
The recommended dose is 0.2-0.4 g/kg every three to four weeks.

Immunomodulation
Idiopathic Thrombocytopenic Purpura
For the treatment of an acute episode, 0.8-1 g/kg on day one, repeated on day three if necessary, or 0.4 g/kg daily for two to five days. The treatment can be repeated if relapse occurs. In the first treatment regimen, if an adequate increase in the platelet count is observed at 24 hours, the second dose of 1,000 mg/kg body weight may be withheld.
The high dose regimen (1,000 mg/kg x 1-2 days) is not recommended for individuals with expanded fluid volumes or where fluid volume may be a concern.

Guillain-Barré syndrome
0.4 g/kg/day for 3 to 5 days. Experience in children is limited.

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 before 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 summarized in the following table

Indication	Dose	Frequency of Injections
Replacement Therapy		
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
Myeloma or Chronic Lymphocytic Leukemia	0.2-0.4 g/kg	Every 3-4 weeks to obtain IgG trough level of at least 5-6 g/L
Children with AIDS	0.2-0.4 g/kg	Every 3-4 weeks
Immunomodulation		
Idiopathic Thrombocytopenic Purpura	0.8-1.0 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 3-5 days
Kawasaki disease	1.6-2 g/kg or 2 g/kg	In divided doses for 2-5 days in association with acetylsalicylic acid In one dose in association with acetylsalicylic acid
Allogenic Bone Marrow Transplantation		
Treatment of infections and prophylaxis of graft-versus-host disease	0.5 g/kg	Every week from day 7 up to 3 months after transplantation
Persistent lack of antibody production	0.5 g/kg	Every month until antibody levels return to normal

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Omr-IgG-am™ 5% is contraindicated in individuals who are known to have anaphylactic or severe systemic response to intramuscular or intravenous immunoglobulin preparations or to any of the excipients.
As with other immunoglobulin preparations, **Omr-IgG-am™ 5%** should not be given to patients with antibodies to IgA or selective IgA deficiency.

4.4 Special warnings and precautions for use

Any vial that has been entered should be used promptly. Partially used vials should be discarded. Do not use if turbid.
Solutions which have been frozen should not be used.

Adequate hydration prior to the initiation of IVIg infusion is required.
Potential complications can often be avoided by ensuring that patients:
- Are not sensitive to human immunoglobulin by initially injecting the product slowly.
- Are carefully monitored for any symptoms throughout the infusion period. In particular, patients naive to human 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 order to detect potential adverse signs. All other patients should be observed for at least 20 minutes after administration.

Certain severe adverse drug reactions may be related to the rate of infusion; therefore, recommended infusion rate given under section 4.2 "Posology and method of administration" must be closely followed.

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

Patients naive to immunoglobulin G (IgG)
Patients naive to immunoglobulin G (IgG) usually experience a higher frequency of events than those well maintained on regular therapy. The recommended infusion rate given under section 4.2 "Posology and method of administration" must be closely followed and patients must be closely monitored and carefully observed for any symptoms throughout the infusion period, and for 1 hour after the first infusion. In case of adverse reactions, either the rate of administration must be reduced or the infusion stopped until symptoms disappear.
If severity of reactions persists after discontinuation of the infusion, appropriate treatment is recommended.
In case of anaphylactic reaction or shock, treatment should follow the guidelines for shock therapy. Epinephrine should be available for the treatment of any acute, anaphylactoid reactions.

Patients with agammaglobulinemia or extreme hypogammaglobulinemia
Patients with agammaglobulinemia or extreme hypogammaglobulinemia who have not received immunoglobulin therapy within the preceding 8 weeks may be at risk of developing inflammatory reactions upon the infusion of human immunoglobulins. These reactions are manifested by a rise in temperature, chills, nausea and vomiting, and appear to be related to the rate of infusion.

Hypersensitivity
True 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

IVIg is not indicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern.
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.

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, systemic lupus erythematosus, 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 with the above risk factors, creatinine levels should be measured for 3 days after intravenous immunoglobulin infusion. In patients at risk of 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.

Hemolysis
Heightened awareness of the potential for hemolysis is recommended in individuals receiving immunoglobulin products, particularly those who are determined to be at increased risk.
Patients at increased risk for hemolysis following treatment with immunoglobulins include those with non-O blood group types, those who have undergone major histocompatibility conditions, and those receiving high cumulative doses of immunoglobulins over the course of several days.
Patients receiving immunoglobulin products should be monitored for clinical signs and symptoms of haemolysis, particularly those at increased risk.
Clinical symptoms and signs of hemolysis include fever, chills and dark urine. If these occur, appropriate laboratory tests should be obtained.
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.

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 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 immunoglobulins, 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).

Thromboembolic events
Despite the new step to remove detectable thrombosis-generating agents, 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 thrombosis which is assumed to be related to a relative increase in blood viscosity through the high influx of immunoglobulin in at-risk patients. Care should be used when immunoglobulin products are given to individuals determined to be at increased risk of thrombosis.

Caution should be exercised in prescribing and infusing IVIg in obese patients and in patients with pre-existing risk factors for thromboembolic events (such as acquired or hereditary hypercoagulable states, prolonged immobilization, in-dwelling vascular catheters, advanced age, estrogen use, hypertension, diabetes mellitus and a history of venus or arterial thrombosis, cardiovascular risk factors (including history of atherosclerosis and/or impaired cardiac output) and hyperviscosity (including cryoglobulins, fasting chylomicronemia and/or high triglyceride levels, and monoclonal gammopathies), vascular disease or thrombotic episodes, acquired or inherited thrombophilic disorders, or patients with prolonged periods of immobilisation, severe hypovolemia, or with diseases which increase blood viscosity).
Patients at risk for thrombosis should receive immunoglobulin products at the slowest infusion rate practicable, and these individuals should be monitored for thrombotic complications. Consideration should also be given to measurement of baseline blood viscosity in individuals at risk for hyperviscosity.

Aseptic meningitis syndrome (AMS)
An aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with immunoglobulin intravenous (human) treatment. The syndrome usually begins within several hours to two days after infusion. It is characterised by symptoms and signs including severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, nausea and vomiting. Cerebrospinal fluid studies are frequently positive with pleocytosis up to several thousand cells per mm³, predominantly from the granulocytic series, and protein levels rising up to several hundred mg/dL. Patients exhibiting such symptoms and signs should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. AMS may occur more frequently in association with high-dose (2g/kg) immunoglobulin intravenous (human) treatment.
Discontinuation of immunoglobulin intravenous (human) treatment has resulted in remission of AMS within several days without sequelae.

Transmissible agents
Products made from plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by effective donor screening, testing for the presence of certain current virus infections, by inactivating and/or removing certain viruses. Despite these measures, such products can still potentially transmit diseases. Because this product is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent.
It is strongly recommended that every time that **Omr-IgG-am™ 5%** is administered to a patient, the name and batch number of the product be recorded in order to maintain a link between the patient and the batch of the product. For this purpose a sticker with the batch identification will be added to each **Omr-IgG-am™ 5%** vial.

See section 4.5 "Interactions with other medicinal products and other forms of interaction" for information regarding blood glucose testing.

4.5 Interaction with other medicinal products and other forms of interaction

Live attenuated 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.

Interference with serological testing
Passive transmission of antibodies to erythrocyte antigen, e.g., A,B or D, may interfere with some serological tests, e.g., Coomb's test, haptoglobin, reticulocyte count.

Blood glucose testing
Omr-IgG-am™ 5 % contains maltose which can be misinterpreted as glucose by certain types of blood glucose testing systems (e.g., by systems based on GDH-PQQ or glucose dye oxidoreductase methods). Due to the potential for falsely elevated glucose readings, only testing systems that are glucose-specific should be used to test or monitor blood glucose levels in patients receiving maltose-containing parenteral products, including **Omr-IgG-am™ 5%.**
The product information of the blood glucose testing system, including that of the test strips, should be carefully reviewed to determine if the system is appropriate for use with maltose-containing parenteral products. If any uncertainty exists, contact the manufacturer of the testing system to determine if the system is appropriate for use with maltose-containing parenteral products. The interference of maltose in blood glucose assays may result in falsely elevated glucose readings and, consequently, in the inappropriate administration of insulin, resulting in life-threatening hypoglycaemia and death.

4.6 Pregnancy and breast-feeding

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 after 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 to be expected.

Breast-feeding
Immunoglobulins are excreted into the milk and may contribute to protecting the neonate from pathogens which have a mucosal portal of entry.

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 **Omr-IgG-am™ 5%.** Patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

4.8 Undesirable effects

Adverse reactions
During or shortly after the application of intravenous immunoglobulins minor side effects such as headache, chills, dizziness, fever, vomiting, allergic reactions, nausea, arthralgia, low blood pressure and moderate back pain may occur occasionally. Dyspnea and tachycardia may occur more frequently and require medical attention. Reversible aseptic meningitis and nephrotoxicity have occurred rarely.
Rarely, immunoglobulins may cause a fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no sensitivity to previous administration.
Slowing or stopping the infusion should allow the symptoms to disappear promptly. Thereafter, the infusion may be started again using a lower infusion rate. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period. Allergic and anaphylactic reactions necessitate immediate cessation of the infusion. Less severe reactions may be controlled with glucocorticoids and/or antihistamines. When severe reactions occur, treatment as a rule must be initiated according to current guidelines. For this purpose, see the recommendations given in the following table.

Immediate measures to be taken in case of intolerable reactions:

Clinical symptoms	Measures
Subjective complaints (backache, nausea, etc.)	Stop infusion
Skin symptoms (flush, urticaria, etc.)	Antihistamines
Tachycardia, moderate drop in blood pressure (below 90 mm Hg systolic)	Glucocorticoids i.v. (100-500 mg prednisolone)
Dyspnea shock	Dopamine continuous infusion (2-4 µg/kg/min) high doses of glucocorticoids i.v. (up to 1 g prednisolone [water-soluble]), oxygen, volume expander, possibly increased diuresis using furosemide in case of normovolaemia, control of acid base balance and electrolytes (if necessary, correct).
Persistent normovolaemic shock	Dopamine dosage up to a maximum of 10 µg/kg/min possibly in combination with noradrenaline.

When medicinal products prepared from human blood or plasma are administered, infectious diseases due to transmission of infective agents cannot be totally excluded. This also applies to pathogens of hitherto unknown nature.
To reduce the risk of transmission of infective agents, selection of donors and donations by suitable measures is performed, plasma pools are tested, and removal and/or inactivation procedures are included in the production process.
The **Omr-IgG-am™ 5%** manufacturing process contains three virus inactivation steps: Cohn fractionation (ethanol), solvent/detergent treatment (TnBP +Triton-X-100) and nanofiltration at pH 4.

The following viruses have been included in the viral safety assessment:
- Type 1 human immunodeficiency virus (HIV-1) (enveloped RNA) (AIDS)
- Pseudorabies virus (PRV) (enveloped DNA, model for herpes)
- Bovine viral diarrhoeal virus (BVDV) (enveloped RNA, model for HCV)
- Hepatitis A virus (HAV) (naked RNA)
- Encephalomyocarditis virus (EMCV) (naked RNA) (model for HAV)
- Theiler's mouse encephalomyelitis virus (TMEV) (naked RNA, model for HAV)
- Minute virus of mice (MVM) (naked DNA, model for parvovirus B-19)

Log reduction of infective agents during the **Omr-IgG-am™ 5%** manufacturing process:

Virus	HIV-1	PRV	BVDV	HAV	EMCV	TMEV	MVM
Cohn	Not done	Not done	>4.55	Not done	4.19	Not done	4.14
S/D step	>4.01	>4.0	>5.74	1.76	Not done	Not done	Not done
Nanofiltration	>5.18	>5.03	>5.49	>7.31	Not done	1.73	1.51

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 adverse reaction, adverse reactions are presented in order of decreasing seriousness.
Frequencies for post-marketing reported reactions are estimated from the available data.

MedDRA System Organ Classification (SOC) according to the sequence:	Adverse Reaction	Frequency per patient	Frequency per infusion
Blood and lymphatic system disorders	leukopenia	uncommon	uncommon
Immune system disorders	hypersensitivity	very common	common
Nervous system disorders	headache	very common	common
Cardiac disorders	tachycardia	uncommon	uncommon
Vascular disorders	hypertension	common	uncommon
Gastrointestinal disorders	nausea vomiting	common common	uncommon uncommon
Musculoskeletal and connective tissue disorders	back pain	common	uncommon
General disorders and administration site conditions	fever fatigue injection site reaction chills chest pain	common common common common uncommon	uncommon uncommon uncommon uncommon uncommon
Investigations	hepatic enzymes increased	common	uncommon

The following reactions have been reported from post-marketing experience with **Omr-IgG-am™ 5%.**
Frequencies for post-marketing reported reactions cannot be estimated from the available data.

MedDRA System Organ Classification (SOC) according to the sequence:	Adverse Reaction (Preferred Term Level)	Frequency
Blood and lymphatic system disorders	haemolytic anaemia	not known
Immune system disorders	anaphylactic shock anaphylactic reaction anaphylactoid reaction angioedema face oedema	not known not known not known not known not known
Metabolic and nutritional disorders	fluid overload (pseudo) hyponatraemia	not known not known
Psychiatric disorders	confusional state agitation anxiety nervousness	not known not known not known not known
Nervous system disorders	cerebrovascular accident meningitis aseptic loss of consciousness speech disorder migraine dizziness hypoaesthesia paraesthesia photophobia tremor	not known not known not known not known not known not known not known not known not known not known
Eye disorders	visual impairment	not known
Cardiac disorders	myocardial infarction angina pectoris bradycardia palpitations cyanosis	not known not known not known not known not known
Vascular disorders	thrombosis circulatory collapse peripheral circulatory failure phlebitis hypotension pallor	not known not known not known not known not known not known
Respiratory, thoracic and mediastinal disorders	respiratory failure pulmonary embolism pulmonary oedema bronchospasm hypoxia dyspnoea cough	not known not known not known not known not known not known not known
Gastrointestinal disorders	diarrhoea abdominal pain	not known not known
Skin and subcutaneous tissue disorders	skin exfoliation urticaria rash rash erythematous dermatitis pruritus alopecia erythema	not known not known not known not known not known not known not known not known
Musculoskeletal and connective tissue disorders	arthralgia myalgia pain in extremity neck pain muscle spasms muscular weakness musculoskeletal stiffness	not known not known not known not known not known not known not known
Renal and urinary disorders	renal failure acute renal pain	not known not known
General disorders and administration site conditions	oedema influenza-like illness hot flush flushing feeling cold feeling hot hyperhidrosis malaise chest discomfort asthenia lethargy burning sensation	not known not known not known not known not known not known not known not known not known not known not known not known
Investigations	blood glucose false positive	not known

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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

4.9 Overdose

See section 4.2 "Posology and method of administration".

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

As human normal immunoglobulin, the product contains mainly IgG having a broad spectrum of antibodies against various infectious agents (viruses and bacteria) currently prevalent in the population.
Opsonization and neutralization of micro-organisms and toxins have been documented.
Omr-IgG-am™ 5% contains all the immunoglobulin G activities which are present in the normal population. It is prepared from pooled source material from not fewer than 1,000 prescreened donors.
The product has a distribution of IgG sub-classes closely proportional to that of normal human plasma.

Adequate doses of this medicinal product may restore abnormally low IgG levels to the normal range.
The mechanism of action in idiopathic thrombocytopenic purpura is not fully elucidated, but includes immunomodulatory effects.

5.2 Pharmacokinetic properties

Absorption
Human normal immunoglobulin I.V. 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 an equilibrium is reached between the intra- and extravascular compartments.

Elimination
Human normal immunoglobulin I.V.has a half life of between 26 and 32 days.This half life may vary from patient to patient, in particular in primary immunodeficiency.
Immunoglobulin G (IgG) and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body.

In animals, single-dose toxicity testing is of no relevance and higher doses result in fluid overloading. 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.
Since clinical experience provides no indication of tumorigenic or mutagenic effects of immunoglobulins, experimental studies, particularly in heterologous species, are not considered necessary.
Virus inactivation of **Omr-IgG-am™ 5%** has been carried out using solvent/detergent (SD) method with tri-n-butyl phosphate (TnBP) and Triton-X-100. These SD reagents are removed during the purification process. At the doses at which **Omr-IgG-am™ 5%** is administered, no toxic effects have occurred with these reagents in animal studies of single-dose and repeated-dose toxicity, and of reproduction toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maltose	100 mg/ml
Water for injections	q.s.1 ml

6.2 Incompatibilities

Omr-IgG-am™ 5% should not be mixed with other medicinal products nor with any other IVIg products. A separate intravenous line should be used for the infusion.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25˚C, protected from light. Do not freeze!
Do not use if the solution is turbid. Use immediately after opening. For single use.

Keep out of reach and sight of children.

6.5 Nature and contents of container

Omr-IgG-am™ 5% is available in the following package sizes:

Package size	Contents	Package type	Container
Omr-IgG-am 2.5 g	50 ml	BOTTLE GLASS TYPE II	70 ml infusion bottle
Omr-IgG-am 5 g	100 ml	BOTTLE GLASS TYPE I	100 ml infusion bottle
Omr-IgG-am 5 g	100 ml	BOTTLE GLASS TYPE II	100 ml infusion bottle
Omr-IgG-am 10 g	200 ml	BOTTLE GLASS TYPE II	250 ml infusion bottle

7. MARKETING AUTHORIZATION HOLDER

Omrix Biopharmaceuticals LTD.
14 Einstein St., Nes Ziona, 7610601
Israel

8. MARKETING AUTHORIZATION NUMBER

127-54-30698-00

Revised in May 2025 according to MOHs guidelines.