5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, for intravascular administration,

ATC-Code: J06B A02

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 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.
The mechanism of action in indications other than replacement therapy is not fully elucidated, but includes immunomodulatory effects.

Clinical Studies
In a prospective, open-label, multicentre phase III trial, the efficacy and safety of Octagam 10% [100 mg/ml] was studied in patients suffering from idiopathic (immune) thrombocytopenic purpura (ITP). Octagam 10% [100 mg/ml] was infused on 2 consecutive days at a dose of 1 gram/kg/day, and patients were observed for a period of 21 days and at a follow-up visit on Day 63 post-infusion. Haematology parameters were assessed on Days 2 to 7, 14 and 21.
A total of 31 subjects were included in the analysis; 15 were subjects with chronic ITP, 15 were newly-diagnosed, and 1 subject was incorrectly enrolled in the study (had no ITP) and was therefore excluded from the efficacy analysis.
In total, 25 subjects (83%) showed a clinical response. A higher clinical response rate was seen in the newly-diagnosed cohort (93%) than in the chronic ITP cohort (73%). In subjects with a response, the median time to platelet response was 2 days, with a range of 1 to 5 days.
In 24 subjects (77%), Octagam 10% [100 mg/ml] was given at the maximum allowed infusion rate of 0.06 mL/kg/min. Following a Protocol Amendment, 2 patients of the presented analysis received the product at a rate of 0.08 mL/kg/min which was uneventful in both cases. In the continuation of this on-going study, 22 subjects have been treated with the maximum allowed infusion rate of 0.12 mL/kg/min.
In 9 of 62 infusions (14.5%) treatment-related infusional AE were observed. The most common drug-related AE was headache, followed by tachycardia and pyrexia. There was no case of haemolysis related to the study drug. Pre-treatment to alleviate infusion-related intolerability was not given.

Paediatric population
No specific studies in the paediatric population were performed with Octagam 10%.
However, a prospective open-label phase III study was performed with Octagam 5% in 17 children/adolescent patients (median age 14.0 years, range 10.5 to 16.8) suffering from primary immunodeficiency disorders. Patients were treated for a period of 6 months. The clinical efficacy was satisfying, as the number of days with infections or fever, and the number of days out of school were low, and the type and severity of infections was comparable to those observed in the normal population. No severe infections leading to hospitalisation were observed. It is also noteworthy that the number of infectious episodes was lower, when IgG plasma levels were maintained around 6 g/L than when the IgG plasma levels were around 4 g/L.

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, after approximately 3-5 days equilibrium is reached between the intra- and extravascular compartments.
Human normal immunoglobulin has an average half life ranging from 26 to 41 days, as measured in immunodeficient patients. This half-life may vary from patient to patient, in particular in primary immunodeficiency. For Octagam 10%, no formal pharmacokinetic data in immunodeficient patients have been obtained.
IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

Paediatric population
No specific studies in the paediatric population were performed with Octagam 10%.
However, a prospective open-label phase III study was performed with Octagam 5% in 17 children/adolescent patients (median age 14.0 years, range 10.5 to 16.8) suffering from primary immunodeficiency disorders. Patients were treated for a period of 6 months.
During the treatment period, the average Cmax in steady state was 11.1 ± 1.9 g/L; the average trough level was 6.2 ± 1.8 g/L. The terminal half-life of total IgG was 36 ± 11 days with a median of 34 days. The volume of distribution for the total IgG was 3.7 ± 1.4 L and the total body clearance was 0.07 ± 0.02 L/day.

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body. Studies of repeated dose toxicity, genotoxicity, and toxicity to reproduction in animals are impracticable due to induction of and interference by developing antibodies to heterologous proteins. Since clinical experience provides no evidence for carcinogenic or mutagenic potential of immunoglobulins, no experimental studies in heterologous species were performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maltose
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf-life

2 years

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Do not freeze.
Keep the container in the outer carton in order to protect from light.
The product may be removed from the refrigerator for a single period of up to 9 months (without exceeding the expiry date) and stored at a temperature below 25°C. At the end of this period, the product should not be refrigerated again and should be disposed of. The date at which the product was taken out of the refrigerator should be recorded on the outer carton.

6.5 Nature and contents of container

Pack sizes:

2 g	in	20 ml
5 g	in	50 ml
10 g	in	100 ml
20 g	in	200 ml

Not all pack sizes may be marketed.

20 ml of solution in a 30 ml vial.
50 ml of solution in a 70 ml bottle.
100 ml of solution in a 100 ml bottle.
200 ml of solution in a 250 ml bottle.

The vials/bottles are made of type II glass closed with bromobutyl rubber stoppers.

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 to slightly opalescent and colourless to slightly yellow.
Do not use solutions that are cloudy or have deposits.
Any unused product or waste material should be disposed of in accordance with local requirements.
Due to the possibility of bacterial contamination, any remaining contents must be discarded.

7 NAME AND ADDRESS OF PHARMACEUTICAL COMPANY

7.1 Marketing authorisation holder

Pharmaniaga Marketing Sdn Bhd (118254-D)
No. 7, Lorong Keluli 1B,
Kaw. Perindustrian Bukit Raja Selatan,
Seksyen 7, 40000 Shah Alam,
Selangor Darul Ehsan, Malaysia.

7.2 Manufacturer

Octapharma Pharmazeutika Produktionsges.m.b.H., Vienna, Austria

8 DATE OF REVISION OF THE TEXT

July 2013

9 LEGAL CATEGORY

For prescription only.

SUMMARY OF PRODUCT CHARACTERISTICS
(Instructions for use)

1 NAME OF THE MEDICINAL PRODUCT

OCTAGAM 10%, solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Human normal immunoglobulin (IVIg)* 100 mg/ml
* corresponding to the total protein content of which at least 95% is human Immunoglobulin G

Distribution of IgG subclasses:

IgG_1	ca. 60%
IgG_2	ca. 32%
IgG_3	ca. 7%
IgG_4	ca. 1%

Maximum IgA content: 400 micrograms/ml

Each vial of 20 ml contains 2g of human normal immunoglobulin.
Each vial of 50 ml contains 5g of human normal immunoglobulin.
Each vial of 100 ml contains 10g of human normal immunoglobulin.
Each vial of 200 ml contains 20g of human normal immunoglobulin.

Produced from plasma of human donors.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
The liquid preparation is clear to slightly opalescent and colourless to slightly yellow. The pH of the liquid preparation is 4.5 – 5.0, the osmolality is ≥ 240 mosmol/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Replacement therapy in adults, and children and adolescents (0-18 years) 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.
- Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation (HSCT).
- Congenital AIDS with recurrent bacterial infections

Immunomodulation in adults, and children and adolescents (0-18 years) 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.

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 dose 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.

Hypogammaglobulinaemia in patients after allogeneic haematopoietic stem cell transplantation
- The recommended dose is 0.2-0.4 g/kg every three to four weeks. The trough levels should be maintained above 5g/l.

Primary immune thrombocytopenia
There are two alternative treatment schedules:
- 0.8-1g/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 injection
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
Hypogammaglobulinaemia (< 4 g/l) in patients after allogeneic haematopoietic stem cell transplantation	0.2 - 0.4 g/kg	every 3 - 4 weeks to obtain IgG trough level above 5g/l.
Immunomodulation:		
Primary immune thrombocytopenia	0.8 - 1 g/kg 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 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
The posology in children and adolescents (0-18 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
For intravenous use.
Octagam 10% [100 mg/ml] should be infused intravenously at an initial rate of 0.01 mL/kg body weight per minute for 30 minutes. If well tolerated (see Section 4.4), the rate of administration may gradually be increased to a maximum of 0.12 mL/kg/ body weight per minute.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients of Octagam 10% [100 mg/ml] (see Section 4.4).
Hypersensitivity to human immunoglobulins, especially in patients with antibodies against IgA.

4.4 Special warnings and precautions for use
This medicinal product contains 90 mg of maltose per ml as an excipient. 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. Also, cases of true hypoglycaemia may go untreated if the hypoglycaemic state is masked by falsely elevated glucose readings (see Section 4.5). For acute renal failure see below.
Certain severe adverse drug reactions 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.

Certain adverse reactions may occur more frequently:
- in case of high rate of infusion
- 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

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 to 0.02 mL/kg body weight per minute);
- 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 to Octagam 10% [100 mg/ml] 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.

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.

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

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.

This medicinal product contains not more than 0.03 mmol (or 0.69 mg) sodium per ml. To be taken into consideration by patients on a controlled sodium diet.

Hypersensitivity
True hypersensitivity reactions are rare. They can occur in patients with anti-IgA antibodies.
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.

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 hypovolemic 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, hypovolemia, overweight, concomitant nephrotoxic medicinal products or age over 65.
In case of renal impairment, IVIg discontinuation should be considered. While these 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 not containing such excipients may be considered.
In patients at risk for acute renal failure, IVIg products should be administered at the minimum rate of infusion and dose practicable.

Aseptic meningitis syndrome (AMS)
Aseptic meningitis syndrome has been reported to occur in association with IVIg treatment. Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae. 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 mm3, 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.

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.)

Interference with serological testing
After injection 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 HIV, HBV and HCV.
The measures taken may be of limited value against non-enveloped viruses such as HAV and parvovirus B19.
There is a 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 Octagam 10% [100 mg/ml] 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
There are no specific or additional warnings or precautions applicable for the paediatric population.

4.5 Interaction with other medicinal products and other forms of interactions
In order to infuse any product that may remain in the infusion tubing at the end of the infusion the tubing may be flushed with either 0.9% saline or 5% dextrose solution.

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.

Blood Glucose Testing
Some types of blood glucose testing systems (for example, those based on the glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase methods) falsely interpret the maltose (90 mg/ml) contained in Octagam 10% [100 mg/ml] as glucose. This may result in falsely elevated glucose readings during an infusion and for a period of about 15 hours after the end of the infusion and, consequently, in the inappropriate administration of insulin, resulting in life-threatening or even fatal hypoglycemia. Also, cases of true hypoglycemia may go untreated if the hypoglycemic state is masked by falsely elevated glucose readings. Accordingly, when administering Octagam 10% [100 mg/ml] or other parenteral maltose-containing products, the measurement of blood glucose must be done with a glucose-specific method.
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.
Paediatric population
There were no specific or additional interactions observed for 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 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.
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 Octagam 10% [100 mg/ml]. 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
In general, various allergic and hypersensitivity type of reactions and headache, dizziness, chills, back pain, chest pain, fever, cutaneous reactions, vomiting, arthralgia, low blood pressure and nausea may occasionally occur. Reactions to intravenous immunoglobulins tend to be related to the dose and the rate of infusion.
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.
Cases of reversible aseptic meningitis and rare cases of transient cutaneous reactions have been observed with human normal immunoglobulin. Reversible haemolytic reactions have been observed in patients, especially those with blood groups A, B, and AB. Rarely, haemolytic anaemia requiring transfusion may develop after high dose IVIg treatment (see also Section 4.4).
Increase in serum creatinine level and/or acute renal failure have been observed.
Very rarely: Thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism, deep vein thromboses.
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. For safety 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 (≥ 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).
The frequencies given in the following table are derived from clinical studies that were conducted with Octagam 5% (columns named „common" and „uncommon") and from postmarketing experience with Octagam 5% (column named „very rare"). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

MedDRA 8.1 Coded	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1,000 to < 1/100	Very Rare < 1/10,000
Blood and lymphatic system disorders			leukopenia; haemolytic anaemia
Immune system disorders	hypersensitivity		anaphylactic shock; anaphylactic reaction; anaphylactoid reaction; angioneurotic oedema; face oedema
Psychiatric disorders			agitation
Nervous system disorders	headache		cerebrovascular accident; meningitis aseptic; migraine; dizziness; paraesthesia
Cardiac disorders			myocardial infarction; tachycardia; palpitations; cyanosis
Vascular disorders			thrombosis; peripheral circulatory failure; hypotension; hypertension
Respiratory, thoracic and mediastinal disorders			respiratory failure; pulmonary embolism; pulmonary oedema; bronchospasm; dyspnoea; cough
Gastrointestinal disorders	nausea		vomiting; diarrhoea; abdominal pain
Skin and subcutaneous tissue disorders		eczema;	urticaria; rash; rash erythematous; dermatitis; pruritus; alopecia
Musculoskeletal and connective tissue disorders		back pain	arthralgia; myalgia
Renal and urinary disorders			renal failure acute
General disorders and administration site conditions	fever; fatigue; injection site reaction	chills; chest pain	hot flush; flushing; hyperhidrosis; malaise
Investigations			hepatic enzymes increased; blood glucose false positive

Description of selected adverse reactions
For description of selected adverse events, see Section 4.4
Paediatric population
In clinical studies with Octagam most adverse reactions observed in children were graded as mild and many of them responded to simple measurements such as reduction of the infusion rate or temporary discontinuation of the infusion. With respect to the type of adverse reaction, all were recognised for IVIG preparations. The most frequent adverse reaction observed in the paediatric population was headache.

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.