PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

OCTAGAM ®

Immunoglobulin Intravenous (Human) 10%

Solution for Infusion, 100 mg/mL, intravenous use

Prescription Medication, passive immunizing agent

Presentation sizes: 20 mL, 50 mL, 100 mL, 200 mL and 300 mL

ATC Code: JO6BA

Manufactured by:

OCTAPHARMA Pharmazeutika Produktionsges, m.b.H.
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and

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Date of Initial Authorization:
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May 19, 2022

Manufactured for:

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Submission Control Number: 253256

RECENT MAJOR LABEL CHANGES

1 Indications, 1.1 Pediatrics, 1.2 Geriatrics	04/2021
4.2 Recommended Dose and Dosage adjustments	04/2021
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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

OCTAGAM® (Immunoglobulin Intravenous 10% (Human)) is indicated for:

Replacement Therapy

Primary Immunodeficiency (PID) Syndromes including but not limited to

- Congenital agammaglobulinaemia and hypogammaglobulinaemia.
- Common variable immunodeficiency.
- Severe combined immunodeficiencies.

Secondary Immunodeficiency Syndromes (SID) including but not limited to

- Secondary hypo-gammaglobulinaemia in patients with chronic lymphocytic leukaemia (CLL), or multiple myeloma (MM) with recurrent infections.
- Children with congenital AIDS who have bacterial infections.

Immune Modulation

Immune thrombocytopenic purpura (ITP)

In patients at high risk of bleeding or prior to surgery to correct the platelet count. *Clinical data on pediatric patients (< 18 years old) is limited. (See CLINICAL TRIAL section).*

Neurological Conditions

Moderate to severe cases of Guillain-Barré Syndrome (GBS) in adults.

Dermatomyositis (DM) in adults.

1.1 Pediatrics

Treatment of primary and secondary immune deficiencies (age range 2-17 years):

Based on the data submitted and reviewed by Health Canada, the safety and efficacy of OCTAGAM® in pediatric patients with PID and SID has been established; therefore, Health Canada has authorized an indication for pediatric use. (See section 14 CLINICAL TRIALS, Table 3.

Treatment of Immune thrombocytopenic purpura:

Clinical data on pediatric patients (< 18 years old) with ITP is limited. (See section 14 CLINICAL TRIALS).

Treatment of GBS, and DM

The safety and effectiveness of OCTAGAM® has not been established in pediatric patients with GBS, CIDP and DM.

1.2 Geriatrics (> 65 years of age):

Clinical studies of OCTAGAM® in patients did not include sufficient numbers of subjects > 65 years to determine whether they respond differently from younger subjects.

2 CONTRAINDICATIONS

- OCTAGAM® is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGINAG.
- OCTAGAM® is contraindicated in any patient who has a history of an allergic reaction to any human immunoglobulin preparation or to any constituent of OCTAGAM®.
- OCTAGAM® is also contraindicated when an individual with an immunoglobulin A (IgA) deficiency, has known antibodies against IgA.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- There is clinical evidence of an association between the administration of immunoglobulins and thromboembolic events such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses.
- In general the risk factors for thromboembolic events include: obesity, advanced age, hypertension, diabetes mellitus, dermatomyositis, history of vascular disease or thrombotic episodes, acquired or inherited thrombophilic disorders, prolonged periods of immobilisation, severely hypovolemic patients, diseases which increase blood viscosity, hypercoagulable conditions, use of estrogens, indwelling central vascular catheters, and other cardiovascular risk factors.
- Thrombosis may occur even in the absence of known risk factors. (see 7 WARNING AND PRECAUTIONS – Thromboembolic events)

4 DOSAGE AND ADMINISTRATION

OCTAGAM ® is 10% Immunoglobulin (Human) Solution for Infusion 100 mg/mL for intravenous use only. OCTAGAM® should be administered under the supervision of a qualified health professional who is experienced in the use of immunomodulating agents and in the management of immunodeficiency syndromes. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

4.1 Dosing Considerations

As there are significant differences in the half-life of IgG among patients with primary immunodeficiencies, the frequency and amount of immunoglobulin therapy may vary from patient to patient. The proper amount can be determined by monitoring clinical response.

Patients should have adequate hydration prior to the infusion of OCTAGAM®. In patients at risk, OCTAGAM® should be administered at the minimum rate of infusion and dose practicable.

Risk factors should be identified, such as pre-existing renal insufficiency, diabetes mellitus, hypovolemia, overweight, concomitant nephrotoxic medications, or older age (> 65 years).

Patients should be observed for at least 20 minutes after administration.

4.2 Recommended Dose and Dosage Adjustment

Replacement therapy

Primary Immunodeficiencies

Doses between 100 and 600 mg/kg every 3 – 4 weeks are recommended. The aim of treatment is to maintain the IgG at levels greater than 500 mg/dL, or at a trough level of 350 mg/dL above baseline. A common practice is to start at 400 mg/kg at monthly intervals but give an extra dose at onset of therapy. After 3 months the pre-infusion IgG level is assessed and adjusted to a dose that maintains a trough level of 500 mg/dL.

The OCTAGAM® dose administered in clinical trials was 0.3 - 0.6 g/kg every 3 – 4 weeks.

Secondary Immunodeficiencies

The recommended dose is 0.2 - 0.4g/kg body weight every 3 – 4 weeks.

Immune modulatory treatment

Immune thrombocytopenic purpura (ITP)

OCTAGAM® to be administered at a total dose of 2 g/kg, divided into two doses of 1 g/kg (10mL/kg) given on 2 consecutive days. Treatment can be repeated if relapse occurs.

Neurological Conditions

Guillain-Barré Syndrome (GBS)

Information on the dose and duration of use of OCTAGAM® in GBS is based on data from a systematic review for IVIG; OCTAGAM® may be administered as a total dose of 2 g/kg (20 mL/kg) given in divided doses over 2-5 consecutive days.

Dermatomyositis (DM)

2 g/kg (20 mL/kg) divided in equal doses given over 2-5 consecutive days every 4 weeks.

Measles Exposure

Guidance for measles post-exposure prophylaxis has been provided by the National Advisory Committee on Immunization (NACI) and should be consulted.[1]

Individuals already receiving replacement IVIg at 400 mg/kg body weight or higher every month are considered protected against measles if the last dose of IVIG was received within three weeks prior to measles exposure. For patients receiving a dose below 400 mg/kg and/or when interval since last infusion is longer than 3 weeks administration of a single dose of 400 mg/kg bodyweight as soon as possible and within 6 days of exposure is recommended.

4.4 Administration

The product should be brought to room or body temperature before use and special caution should be exercised when OCTAGAM® is used for the first time.

It is recommended that OCTAGAM® should be intravenously administered initially at a rate of 1 mg/kg per minute (0.01 mL/kg per minute) for the first 30 minutes. If well-tolerated, the rate may be gradually increased to a maximum of 12 mg/kg per minute (0.12 mL/kg per minute). If side effects occur, the rate may be reduced, or the infusion interrupted until symptoms subside. The infusion may then be resumed at the rate, which is comfortable for the patient.

For patients at risk of renal dysfunction or thromboembolic events, administer OCTAGAM® at the minimum infusion rate practicable.

Patients with dermatomyositis are considered patients at increased risk for thromboembolic events and should therefore be carefully monitored and infusion rate should not exceed 0.04 ml/kg/min.

Certain severe adverse drug reactions may be related to the rate of infusion. Slowing or stopping the infusion usually allows the symptoms to disappear promptly.

Ensure that patients (especially those with pre-existing renal insufficiency) are not volume depleted. Patients should be observed for at least 20 minutes after administration. Discontinue OCTAGAM® liquid if renal function deteriorates.

OCTAGAM® should be inspected visually for particulate matter and discolouration prior to administration. Do not use non-homogenous solutions, or those that have a deposit. Because of the possibility of bacterial contamination, any remaining contents must be discarded. OCTAGAM® should be warmed up to room or body temperature before use.

Filtration of OCTAGAM® is not required.

Precautions:

OCTAGAM® should not be mixed with other medicinal products. A separate intravenous line should be used for the infusion. Do not use the product after expiry date.

[1] Tunis MC, Salvadori MI, Dubey V, Baclic O. Updated NACI recommendations for measles post-exposure prophylaxis, CCDR 2018; volume 44-9: 226-30

4.5 Missed Dose

A missed dose should be administered as soon as possible

5 OVERDOSAGE

Overdose may lead to fluid overload and hyperviscosity, particularly in the elderly and in patients with impaired renal function.

If you think you, or a person you are caring for, have taken too much OCTAGAM contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
intravenous	Solution for Infusion, 100 mg/mL	Maltose, Triton X-100, TNBP, Water for Injections

The following marketed dosage forms are available:

1 infusion bottle with 20 mL – 2 g protein

1 infusion bottle with 50 mL – 5 g protein

1 infusion bottle with 100 mL – 10 g protein

1 infusion bottle with 200 mL – 20 g protein

1 infusion bottle with 300 mL – 30 g protein

Each 100 mg/mL of OCTAGAM® contains the active ingredients: Immunoglobulin Intravenous (Human), one millilitre (mL) of solution contains 100 mg of protein of which ≥ 96% is gammaglobulin.

Quantitative composition:	**per mL**
Human normal immunoglobulin G (IgG)	100 mg
Maltose	90 mg
Triton X-100	5 µg
TNBP	1 µg
Water for injections	1 mL
IgA	≤ 0.4 mg

Each package contains 1 glass bottle of OCTAGAM® ready to use and the package leaflet.

6.1 Physical Characteristics

OCTAGAM® is a sterile, 10% liquid preparation of highly purified immunoglobulin G (IgG) derived from large pools of human plasma.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

General

This product is prepared from large pools of human plasma. Thus, there is a possibility it may contain causative agents of viral or other undetermined diseases, including theoretically, the variant Creutzfeld-Jakob disease (vCJD) agent that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses.

The viral safety of OCTAGAM® is ensured through a number of steps, such as the virus removal by cold-ethanol fractionation and solvent/detergent treatment which inactivates enveloped viruses such as HIV, hepatitis B (HBV) and hepatitis C (HCV) virus. In addition, prolonged pH4 incubation at 37°C inactivates both enveloped and non-enveloped viruses such as hepatitis A virus (HAV) and parvovirus B19. However, as with all products prepared from human blood or plasma, the risk of transmission of infectious agents cannot be fully excluded. There is also the possibility that unknown infectious agents may be present in such products. Individuals who receive infusions of blood or plasma products may develop signs and/or symptoms of some viral infections.

Carcinogenesis and Mutagenesis

Please refer to section 16 NON-CLINICAL TOXICOLOGY.

Driving and Operating Machinery

OCTAGAM® has no or negligible influence on the ability to drive and use machines. However, patients who experience adverse reactions during treatment should wait for these to resolve before driving or operating machines.

Hematologic

IVIG products, including OCTAGAM®, 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 and, rarely, haemolysis. Haemolytic anaemia can develop subsequent to IVIG therapy due to enhanced red blood cells (RBC) sequestration (see 8 ADVERSE REACTIONS). IVIG recipients should be monitored for clinical signs and symptoms of haemolysis.

Neutropenia/Leukopenia

A transient decrease in neutrophil count and/or episodes of neutropenia, sometimes severe, have been reported after treatment with IVIg.

Monitoring and Laboratory Tests

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 contained in OCTAGAM® as glucose. Accordingly, when administering OCTAGAM®, the measurement of blood glucose must be done with a glucose-specific method.

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.

Urine Glucose Testing: About 5% of intravenously administered maltose is excreted via the urine as glucose or maltose. Having this in mind, interference with both urine test methods can be expected.

Drug/Laboratory Test Interactions: IgG administration may impair the efficacy of live attenuated virus vaccines such as measles, mumps, rubella and varicella for at least six weeks, and possibly up to three months. In some cases, where large doses are given this period may be as long as one year.

After injection of IVIG, the transitory rise in the various passively transferred antibodies may result in misleading positive results in serological tests, e.g. CMV serology, Coombs Test, etc.

If signs and/or symptoms of haemolysis are present after IVIG infusion, appropriate confirmatory laboratory testing should be done (see 7 WARNINGS AND PRECAUTIONS).

Because of the potentially increased risk of thrombosis, baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronaemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies (see 7 WARNINGS AND PRECAUTIONS).

Neurologic

A condition called aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with infusions of IVIGs, including OCTAGAM®. AMS usually begins within several hours to two days following treatment. The signs include severe headache (migraine-like), neck stiffness, drowsiness, fever, inability to stand bright light, painful eye movements, and nausea and vomiting. The condition usually reverses without ill effects when treatment is stopped. AMS may occur more frequently in association with high dose (2 g/kg) IVIG treatment. Patients with a history of migraine appear to be more susceptible to AMS. Preventive measures to avoid the occurrence of aseptic meningitis include careful risk/benefit evaluation in patients with history of migraine, premedication with analgesics with or without caffeine, proper hydration and maintenance of good fluid intake throughout treatment, and slow infusion rates.

Renal

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 medications, or over the age of 65.

While these reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IVIG products, those containing sucrose as a stabilizer accounted for a disproportionate share of the total number. OCTAGAM® does not contain sucrose.

In all patients, IVIG administration requires: adequate hydration prior to the initiation of the infusion of IVIG, monitoring of urine output, blood urea nitrogen (BUN), monitoring of serum creatinine levels, and avoidance of concomitant use of loop diuretics. In addition, the product should be administered at the minimum concentration and infusion-rate practicable. In case of renal impairment, IVIG discontinuation should be considered.

Respiratory

Transfusion-related acute lung injury (TRALI) has been rarely reported after treatment with IVIG products.

Sensitivity/Resistance

OCTAGAM® contains maltose, a disaccharide sugar, which is derived from corn. Anaphylactoid / anaphylactic reactions have been reported in association with infusion of other maltose / corn starch related products. Patients known to have corn allergies should either avoid using OCTAGAM® or be closely observed for signs and symptoms of acute hypersensitivity reactions.

In case of hypersensitivity, OCTAGAM® infusion should be immediately discontinued and appropriate treatment applied.

Thromboembolic events

There is clinical evidence of an association between the administration of immunoglobulins and thromboembolic events such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses.

Since thrombosis may occur in the absence of known risk factors, caution should be exercised in prescribing and administering immunoglobulins. The drug product should be administered at the minimum concentration available and at the minimum rate of infusion practicable. Patients should be adequately hydrated before administration.

Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia / markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. Patients at risk of hyperviscosity should be monitored for signs and symptoms of thrombosis and blood viscosity assessed appropriately (see 7 WARNINGS AND PRECAUTIONS: Monitoring and Laboratory Tests).

Risk factors for thromboembolic adverse events include: obesity, advanced age, hypertension, diabetes mellitus, dermatomyositis, history of vascular disease or thrombotic episodes, acquired or inherited thrombophilic disorders, prolonged periods of immobilisation, severely hypovolemic patients, diseases which increase blood viscosity, hypercoagulable conditions, use of estrogens, indwelling central vascular catheters, and cardiovascular risk factors. The potential risks and benefits of IVIG treatment should be weighed against those of alternative therapies for all patients for whom OCTAGAM® administration is being considered.

7.1 Special Populations

7.1.1 Pregnant Women

The safety of OCTAGAM® for use in human pregnancy and during lactation has not been established in controlled clinical trials and therefore should only be given with caution to pregnant woman and breast-feeding mothers.

7.1.2 Breast-feeding

Immunoglobulins are excreted into the milk and may contribute to the transfer of protective antibodies to the neonate. Octagam® should only be used in nursing women when the benefits outweigh the risk associated with its use.

7.1.3 Pediatrics

Pediatrics (2-17 years of age): the listed warnings and precautions apply both to adults and children.

7.1.4 Geriatrics

Geriatrics (> 65 years of age): the number of elderly patients (≥ 65 years of age) studied in clinical trials with OCTAGAM® is limited.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

In general, various minor allergic and hypersensitivity type of reactions and headache, chills, myalgia such as back or chest pain, fever, cutaneous reactions, and nausea may occasionally occur. Reactions to intravenous immunoglobulins tend to be related to the dose and the rate of infusion.

Replacement therapy:

The most common adverse reactions observed in clinical trial were: headache (15% of subjects) and nausea (7% of subjects).

Immune Thrombocytopenic Purpura

The most common adverse reactions observed in clinical trial were: headache (25% of subjects), pyrexia (15% of subjects) and increased heart rate (11% of subjects).

Dermatomyositis:

The most common adverse reactions observed in clinical trial were: headache (42% of subjects), pyrexia (19%), nausea (16%), vomiting (8%), myalgia (7%) chills (7%) and hypertension (6%).

The most serious adverse reaction observed with OCTAGAM® treatment during clinical trials were reported during the clinical trial in subjects with DM (study GAM10-08): muscle spasms and dyspnoea in 1 patient and loss of consciousness in 1 patient. Further 1 patient experienced deep vein thrombosis and pulmonary embolism (assessed as one TEE,) and 1 patient each experienced cerebrovascular accident, cerebral infarction, hypoesthesia, and pulmonary embolism. For risk factors for TEE see 7 WARNINGS AND PRECAUTIONS.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Study OCTA-06

This was a multiple-dose, open-label, multi-center study in patients with PID. The objectives were to assess the safety, pharmacokinetics, and therapeutic efficacy of OCTAGAM 5% as replacement therapy in PID. Forty-six patients received 654 infusions of OCTAGAM 5% (either 400–600 mg/kg every 28 days or 300–450 mg/kg every 21 days) for 12 months.

Nineteen patients (41%) experienced 71 treatment-related AEs (ADRs). The most common ADR was headache (7 patients, 15%; 18 events). The only other ADR that was reported by more than 2 patients was nausea (3 patients, 7%).

ADRs to OCTAGAM 5% were reported in association with 6% of the infusions. These included headache, injection site reaction, arthralgia, hypertension, palpitations, pruritus, pain in limb, and hypotension. The number of drug-related AEs per patient was approximately constant across all infusions.

Study GAM10-02

This was a prospective, open-label, single-arm, multi-center study 116 subjects with newly diagnosed or chronic ITP. Subjects received OCTAGAM® at a dose of 2 g/kg, administered daily as two 1 g/kg doses, given intravenously on 2 consecutive days. Fifty-four (47%) subjects received OCTAGAM® at the maximum infusion rate allowed (12 mg/kg/min [0.12 mL/kg/min]).

Of the 238 temporally associated AEs reported for 92 subjects, the investigators judged 129 (54%) (in 62 patients) to be at least possibly related to the infusion of OCTAGAM®. Most of the AEs related to the infusion of OCTAGAM® were mild (n=105, 81%), 24 were moderate, and none was severe. The most common temporally associated AEs judged by the investigators to be “at least possibly” related to the infusion were headache (25% of subjects), pyrexia (15% of subjects), and increased heart rate (11% of subjects).

Guillain-Barré Syndrome (GBS)

There is limited information from clinical trials for OCTAGAM® in CIDP and GBS. However, adverse reactions in both indications are expected to be comparable to those observed in ITP patients, due to the similar mechanism of action for immunoglobulin solutions in these conditions and because the recommended doses for CIDP and GBS is the same as the initial loading dose in ITP (2 g/kg).

Study GAM10-08

In a prospective, double-blind, randomized, placebo-controlled multicenter study a total of 95 adult patients with DM were enrolled. In the First Period (16 weeks), 47 patients received 2 g/kg OCTAGAM® and 48 patients received placebo (0.9% saline solution) every 4 weeks for 4 infusion cycles. In the following 24-week open label Extension Period, a total of 91 patients received further 6 infusions cycles of OCTAGAM® treatment every 4 weeks.

One infusion cycle comprised of all infusions administered over 2-5 days. During the whole study 91 patients received a total of 664 infusion cycles with OCTAGAM® (First Period 189 infusion cycles; Extension Period: 475 infusion cycles).

During the whole study, 62 patients (65.3%) who received OCTAGAM® experienced 282 adverse drug reactions (ADR) that were considered related to the study drug, the majority of which were mild in intensity (207/282). During the First Period, 30 patients (57.7%) who received OCTAGAM® and 11 patients (22.9%) who received placebo reported 113 and 38 related ADR respectively. The most commonly reported adverse reactions by the patients who received OCTAGAM® were headache, pyrexia, nausea, vomiting, myalgia, chills and hypertension.

During the whole study a total of 351 infusional adverse events (AE during infusion or within 72h after end of infusion cycle) were reported in 76 patients (80.0%) who received OCTAGAM®.

No patients who received placebo reported any related serious adverse reaction. Seven (7) patients who received OCTAGAM® reported at least one related serious adverse reaction, including muscle spasms, dyspnoea, deep vein thrombosis, pulmonary embolism, loss of consciousness, cerebrovascular accident, cerebral infarction, and hypoaesthesia.

A total of 6 patients (6.3%) who received OCTAGAM® reported 8 thromboembolic events (TEEs): pulmonary embolism (3), deep vein thrombosis (2), cerebrovascular accident (1), cerebral infarction (1), and hypoaesthesia (1). Of these 2 events (pulmonary embolism and deep vein thrombosis) in 1 patient were assessed as not related. No patients who received

placebo reported any TEE.

Premedication for infusions was given to 21.3% of patients in the OCTAGAM® group. The most common type of premedications were analgesics and systemic antihistamines given to 6.3% of patients each.

Intravascular hemolysis due to a Hemolytic transfusion reaction would be suspected if all of the following criteria were fulfilled: a positive direct Coombs' test result, a drop in hemoglobin of 2 g/dL or greater, a drop in serum haptoglobin to below the lower limit of normal, and a rise in serum Lactate dehydrogenase from baseline. No patient met the criteria for a hemolytic transfusion reaction. No deaths were reported.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

In the ITP study (GAM10-02), there were no significant changes in haematological parameters (haemoglobin, haematocrit, red and white blood cells) over the study period, other than platelets.

Five patients had clinically relevant, transient increases in ASAT and ALAT. These changes were judged to be possibly related to OCTAGAM® in 2 patients and unrelated in 3 patients.

Nine patients had a negative direct Coombs test at baseline but subsequently became positive after treatment. Of these, haemolysis was documented in a single patient but was judged by the investigator to be unrelated to the study drug. In this individual patient, an episode of severe bleeding unrelated to study drug may have caused or contributed to aggravation of the ITP-related anaemia that was pre-existing at study enrolment; the remaining 8 patients had no clinical signs of haemolysis.

In the DM study (GAM10-08), the laboratory results, hematology, clinical chemistry, and viral markers, did not indicate any safety concerns. Changes to a clinically significant value were observed only for a small proportion of patients. Thirteen (13) patients (27.7%) had a negative direct Coombs' test at baseline and became positive at the end of study. From Baseline to Week 16, there were no shifts of Coombs' test from negative to positive in the patients who received placebo.

8.5 Post-Market Adverse Reactions

The following ADRs have been identified during post-approval use of OCTAGAM (any strength). Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency.

System Organ Class (MedDRA Terminology)	Reported ADRs
Blood and lymphatic system disorders	Leukopenia, lymphopenia, haemolytic anaemia.
Immune system disorders	hypersensitivity; anaphylactic shock; anaphylactic reaction; anaphylactoid reaction; angioneurotic edema; face edema.
Metabolic and nutritional disorders	fluid overload; (pseudo)hyponatraemia.
Psychiatric disorders	confusional state; agitation; anxiety; nervousness.
Nervous system disorders	Headache; cerebrovascular accident; meningitis aseptic; loss of consciousness; speech disorder; migraine; dizziness; hypoesthesia; paraesthesia; photophobia; tremor
Eye disorder	visual impairment; blurred vision
Cardiac disorders	myocardial infarction; angina pectoris; bradycardia; tachycardia; palpitations; cyanosis.
Vascular disorders	thrombosis; circulatory collapse; peripheral circulatory failure; phlebitis; hypotension; hypertension; pallor.

System Organ Class (MedDRA Terminology)	Reported ADRs
Respiratory, thoracic and mediastinal disorders	respiratory failure; pulmonary embolism; pulmonary edema; bronchospasm; hypoxia; dyspnoea; cough.
Gastrointestinal disorders	nausea; vomiting; diarrhoea; abdominal pain.
Skin and subcutaneous tissue disorders	eczema; skin exfoliation; urticaria; rash; rash erythematous; dermatitis; pruritus; alopecia; erythema.
Musculoskeletal and connective tissue disorders	back pain; arthralgia; myalgia; pain in extremity; neck pain; muscle spasms; muscular weakness; musculoskeletal stiffness.
Renal and urinary disorders	renal failure acute; renal pain.
General disorders and administration site conditions	fatigue; pyrexia; injection site reaction; chills; chest pain; edema; influenza like illness; hot flush; flushing; feeling cold; feeling hot; hyperhidrosis; malaise; chest discomfort; asthenia; lethargy; burning sensation

System Organ Class (MedDRA Terminology)	Reported ADRs
Investigations	hepatic enzymes increased; blood glucose false positive; hemoglobin decreased
Injury, poisoning and procedural complications	transfusion-related acute lung injury

Thromboembolic events, such as myocardial infarction, stroke, pulmonary embolism, and deep vein thromboses, have been reported, and may be serious or even fatal depending on the site and type of thrombosis.

Cases of aseptic meningitis have been reported; however, no fatal cases observed.

Acute renal failure has been observed. In most cases it was mild, but may be serious in elderly patients, patients with diabetes, and patients with pre-existing renal disease.

Heamolytic anemia / haemolysis have been observed. In most cases it is mild and self-limited.

9 DRUG INTERACTIONS

No formal studies of drug interactions have been performed.

Human IVIG should not be mixed with other medicinal products, including IVIG from other manufacturers. A separate intravenous line should be used for the infusion. Interactions with other drugs are unknown.

The infusion line may be flushed before and after administration of OCTAGAM® with either normal saline or 5% dextrose in water.

IgG administration may impair the efficacy of live attenuated virus vaccines such as measles, mumps, rubella and varicella for at least six weeks, and possibly up to three months. In some cases, where large doses are given, this period may be as long as one year.

Components used in the packaging of OCTAGAM® are latex-free.

9.4 Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established

9.7 Drug-Laboratory Test Interactions

OCTAGAM® contains maltose which can be misinterpreted as glucose by certain types of blood glucose testing systems. 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 OCTAGAM®. (see 7 WARNINGS AND PRECAUTIONS).

After injection of IVIG, the transitory rise in the various passively transferred antibodies may result in misleading positive results in serological tests, e.g. CMV serology, Coombs Test, etc.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

In the treatment of PID and SID, OCTAGAM® temporarily replaces/supplements the measured deficiency in plasma IgG levels thereby restoring immune competence.

The mechanism of action of IVIGs in the treatment of ITP is not fully understood. One possible mechanism may be the inhibition of the elimination of autoantibody-reacted platelets from the blood circulation by IgG-induced Fc-receptor blockade of phagocytes. Another proposed mechanism is the down-regulation of platelet autoantibody-producing B cells by anti-idiotypic antibodies in IVIG.

The mechanism of action of OCTAGAM® in the treatment of CIDP, GBS and DM has not been fully elucidated but since all three conditions are thought to be autoimmune, modulation or interference with such processes is probable.

10.2 Pharmacodynamics

OCTAGAM® contains mainly immunoglobulin G (IgG) with a broad spectrum of antibodies against various infectious agents reflecting the IgG activity found in the donor population. OCTAGAM®, which is prepared from pooled material from not less than 3500 donors, has an IgG subclass distribution similar to that of native human plasma. Adequate doses of IVIG can restore abnormally low IgG level to the normal range.

10.3 Pharmacokinetics

The pharmacokinetics of OCTAGAM® has not been formally studied in ITP patients nor in DM patients.

Several clinical studies were specifically designed to examine the pharmacokinetics of OCTAGAM 5% after single or repeated doses in PID patients.

Table 1 provides an overview of these studies. The reported half-lives ranged from 36 to 40 days. Several factors such as the endogenous production, the actual catabolism rate, the underlying disease or inter-patient variability help to explain the wide range observed for terminal half-lives.

Table 1: Pharmacokinetic Studies with OCTAGAM 5% in PID patients

Study No. (Protocol) Design	No. of Patients Age Gender	Diagnosis Inclusion/ Exclusion Criteria	Treatment Dose Regimen	Pharmacokinetics Data
OCTA-06 Open label	14 Patients 10 to 70 years 8 males 6 females	Primary immunodeficiency disease, IVIG therapy at steady dose for ≥ 3 months, trough serum IgG level ≥ 400 mg/dL above baseline, no history of anaphylactic reactions to blood or blood-derived products, no demonstrable antibodies to IgA	OCTAGAM 5% 400-600 mg/kg IV every 21 or 28 days for 12 months	$t_{½}$ 40.7 ± 17.0 Days C_{max} 16.7 mg/mL AUC 7,022 ± 1,179 mg*h/mL
X (GAM-04) Open label	17 patients 10 to 17 years 15 males 2 females	Primary immuno-deficiency syndromes; IgG titre ≤ 3 g/L; no history of anaphylactic reactions to immunoglobulins	OCTAGAM 5% 200 to 400 mg/kg IV every 3 weeks for 6 months	$t_{½}$ 35.9 ± 10.8 Days $C_{ss\ max}$ 11.1 ± 1.9 g/L AUC_{ss} 160.1 ± 43.6 g • day/L Clearance 0.07 ± 0.02 L/day Volume of distribution: 3.7 ± 1.4 L
I (None) Open label	12 patients 22 to 66 years 4 males 8 females	Primary, severe hypogamma-globulinemia, under treatment with IgG so plasma concentration > 4 g/L, no increased liver enzymes, no HIV	Single dose of OCTAGAM 5% 400 mg/kg IV	$t_{½}$ 30.7 days ± 4.0

After intravenous infusion, peak levels of OCTAGAM 5% are obtained within 30 minutes in Primary Immune Deficiency patients. Due to the distribution of IVIG between intra-and extravascular compartments, serum IgG levels drop by about 40 to 50% during the first week following intravenous administration.

High concentrations of IVIG and hyper-metabolism associated with fever and infection may shorten the half-life.

For detailed data on efficacy, please refer to section 14 CLINICAL TRIALS.

Special Populations and Conditions

No specific pharmacokinetic studies have been performed in patients at increased risk, such as elderly subjects or patients with renal or hepatic impairment.

11 STORAGE, STABILITY AND DISPOSAL

Store at +2 °C to +8 °C for 36 months from the date of manufacture. Within this shelf-life the product may be stored up to 9 months at ≤ 25°C. After the storage at ≤ 25°C the product must be used or discarded.

Do not freeze. Protect from exposure to light.

Do not use after expiry date. Because of the possibility of bacterial contamination, any remaining contents must be discarded.

Human IVIG should not be mixed with other medicinal products. A separate intravenous line should be used for the infusion.

12 SPECIAL HANDLING INSTRUCTIONS

Any unused product or waste material should be disposed of in accordance with local requirements for blood products.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	OCTAGAM®, Immunoglobulin Intravenous (Human) 10%
Chemical name:	Immunoglobulin G (Human)
Molecular formula and molecular mass:	not applicable
Structural formula:	not applicable
Physicochemical properties:	The molecular weights range from 146 to 170 kD. Immunoglobulins have a common structure with four polypeptide chains. Two heavy chains and two non-glycosylated light chains. Human IgG is divided in four subclasses IgG_1, IgG_2, IgG_3 and IgG_4 due to minor differences in the amino sequence. The isoelectric point varies between 5.0 and 9.5
Pharmaceutical standard:	WHO. ATC 02 J06BA / Immunoglobulin G (Human)

Product Characteristics:

OCTAGAM® is prepared by cold-ethanol fractionation of donated human fresh frozen plasma. Each preparation is made from a pool of at least 3,500 donations of human fresh frozen plasma. Viral inactivation is accomplished by a solvent detergent (S/D) method and a specific pH 4 treatment. The pH 4 treatment also reduces anti-complementary activity and aggregation of the IgG polymers. Residual S/D reagents are removed by oil extraction (TNBP) and C18 chromatography (Triton X-100) before sterile filtration. Residual ethanol is removed via ultra-/diafiltration. A second ultra-/diafiltration step removes all ions such as sodium and increases the protein content to approximately 10%. The whole manufacturing process is carried out at a low pH in order to maintain the nativity of the IgG molecules.

After addition of maltose the 10% IgG solution is sterile filtered and filled into siliconized glass vials. The final product is salt free and no dilution with saline solution is needed prior to its administration.

Viral Inactivation

OCTAGAM® is double virus inactivated. Two established processes are incorporated into the manufacturing process, namely the S/D method and a specific pH4 treatment.

The S/D method, developed by the New York Blood Center, has been validated using both real and model viruses and in various chimpanzee tests. Among others, the effective inactivation of experimentally added HIV viruses, hepatitis non-A, non-B viruses (Hutchinson strain), HBV and HCV has been demonstrated.

14 CLINICAL TRIALS

Efficacy and Safety Studies

Study in ITP

Table 2 summarizes the clinical study that has been completed in patients with ITP.

Table 2: Results of Clinical Studies in ITP Patients

Study No. (Protocol) Design	Dosage, route of administration and duration	Number of Subjects Gender (Age range)	Primary Endpoint	Results
GAM10-02 Open label	OCTAGAM® 1g/kg per day on 2 consecutive days, given IV	116 patients 42 male, 74 female (17–88 years)	Response rate: Increase in platelet count to ≥ 50 x 10^9/L within 7 days after treatment	Overall response rate of 80%.

According to original trial design and endpoint definition the clinical response (i.e. increase in platelets to at least 50 x 109/L within 7 days) was 82% in chronic ITP patients.

The results of Study GAM10-02 were re-analysed post-hoc after using the following revised definitions of “clinical response”.

Definition of “Clinical Response”	**# (%) of chronic ITP patients with “Clinical Response”**
Standard efficacy endpoint: •Increase of platelet count to ≥50 x 10^9/L within 7 days	53/65 (81.5%)
Additional Post Hoc analyses conducted outside the original study design showed the following results:	
Post Hoc re-analysis 1: • Increase of platelet count to ≥50x10^9/L within 7 days • No prohibited medication • No start or increase in dose of Etamsylate during first 7 days • No withdrawal from the study within the first 7 days • Regression of bleeding	49/65 (75.4%)
Post Hoc re-analysis 2: • Increase of platelet count to ≥50x10^9/L within 7 days • No prohibited medication • No Etamsylate* • No withdrawal from the study within the first 7 days • Regression of bleeding	37/66 (56.1%)

* Etamsylate is a synthetic haemostatic drug that was used exclusively in study sites in Poland and the Czech Republic. It was not a forbidden therapy in Study GAM10-02 and has no effect on platelet counts. A sub-analysis did not show a positive confounding effect on bleeds by Etamsylate (39% of subjects who received Etamsylate had no bleeds at study day 3 versus 63% of subjects who did not receive Etamsylate).

In Study GAM10-02, 14 subjects experienced SAEs. All SAEs except one (headache) were unrelated to study drug. Five out of 14 subjects were ITP recurrences. Two patients were hospitalised for reasons other than ITP and thrombocytopenia was detected by routine laboratory testing. In 8 subjects ITP recurrences were reported as non-serious AEs. Only one case of ITP recurrence led to study withdrawal. Safety data from clinical trials can be found in PART I – 8.2 Clinical Trial Adverse Reactions.

Studies in PID

Table 3 summarizes the 4 clinical studies that have been completed in patients with PID.

Table 3: Results of Clinical Studies in PID Patients

Study No. (Protocol) Design	**Dosage, route of administration and duration**	**Number of Subjects Gender (Age range)**	**Primary Endpoint**	**Associated value and statistical significance for drug at specific dosages**
OCTA-06 Open label	OCTAGAM 5% 400- 600 mg/kg IV every 28 days or 300 to 450 mg/kg IV every 21 days for 12 months	46 patients 28 male, 18 female (6 to 74 years)	Primary = serious infections per year Secondary = days work/school missed, hospitalizations, physician/ER visits, other infections	Serious infection rate = 0.115 infections/patient/year (98% confidence interval 0.033 - 0.279). Numbers of days patients missed work/school, were hospitalized, and visited physician or ER were each 1.5% or fewer of study days.
X (GAM-04) Open label	OCTAGAM 5% 200 to 400 mg/kg IV every 3 weeks for 6 months	17 patients 15 male, 2 female (10 to 17 years)	Number of days out of school, with infections, on antibiotics, and in hospital; frequency and type of infections	Type and severity of infections similar to normal population; no severe infections leading to hospitalization; low number of days out of school, with infection, and with fever
V (GAM/III/D) Open label	OCTAGAM 5% 300 mg/kg IV monthly for 6 months	10 patients 7 male, 3 female (2.5 to 9 years)	Trough levels of IgG and subclasses after third injection, number and severity of infections	Effective in maintaining trough levels and reducing incidence of infections; no severe infection and 5 patients completely free of infection
I (None) Open label	Single dose of OCTAGAM 5% 400 mg/kg IV	12 patients 4 male, 8 female (20 to 66 years)	Serum levels and half-life of IgG and IgG subclasses	Significant increase in IgG; half-life comparable to other products (30.7 ± 4.0 days)

ER = emergency room, PID = primary immunodeficiency disease

Study in Dermatomyositis (DM)

Table 4 Summarizes the clinical study that has been completed in patients with DM.

Study No. (Protocol) Design	Dosage, route of administration and duration	Number of Subjects Gender (Age range)	Primary Endpoint	Associated value and statistical significance for drug at specific dosages
GAM10-08 Double-blind, randomized, placebo-controlled	OCTAGAM® 2 g/kg divided in equal doses given over 2-5 consecutive days every 4 weeks	95 patients 24 male, 71 female (22 to 79 years)	Primary: proportion of responders at week 16 compared vs placebo	Octagam®: 78.72% Placebo: 43.75% Difference: 34.97% (95% CI: 16.70, 53.24; p=0.0008)

In a double-blinded, randomized, placebo-controlled study, 95 adults with DM (67 definite DM and 28 probable DM) were enrolled and randomized. 47 patients received Octagam and 48 received placebo in an initial 16-week, double-blinded First Period, followed by a 6-month, open-label Extension Period, during which all patients who were eligible to continue (91 in total) received OCTAGAM® every 4 weeks.

A responder was defined as a subject with an improvement of ≥20 points on the Total Improvement Score (TIS based on six Core Set Measures including: Manual Muscle Testing MMT-8, Physician Global Disease Activity (GDA), Extramuscular Activity, Patient GDA, Health Assessment Questionnaire (HAQ), and Muscle Enzymes: Aldolase, Creatine Kinase, ALAT, ASAT, LDH).

Table 4 shows the proportion of responders (improvement of ≥20 points on the TIS) in the Octagam® and the placebo groups, and the difference in responder rate between the two groups at Week 16.

Table 5 TIS - Proportion of responders by Improvement Category at Week 16

Total Improvement Score (TIS) Response Category	Octagam 10% N=47 Number (%) of Subjects	Placebo N=48 Number (%) of Subjects	Difference in responder proportion Octagam 10% – placebo Point Estimate [95% CI]
At Least Minimal Improvement (TIS ≥ 20) (Primary Efficacy Endpoint)	37 (78.7%)	21 (43.8%)	34.97% [16.70%, 53.24%] p-value = 0.0008*
At Least Moderate Improvement (TIS ≥ 40)	32 (68.1%)	11 (22.9%)	45.17% [27.31%, 63.03%]
At Least Major Improvement (TIS ≥ 60)	15 (32.0%)	4 (8.3%)	23.58% [8.13%, 39.03%]

*Cochran-Mantel-Haenszel Test; CI = Confidence interval

Efficacy was further supported by an improvement in the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) total activity score, with a mean decrease of 9.4 (SD: 10.5) points from baseline to Week 16 in the OCTAGAM® group versus 1.2 (SD: 7.0) point in the placebo group.

Safety data from clinical trials can be found in section PART I – 8.2 Clinical Trials Adverse Reactions.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

A systematic review of the use of similar IVIGs in the treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) concluded that IVIG was an effective treatment and comparable to other treatments such as Plasma Exchange and high-dose Corticosteroids[2].

Use of OCTAGAM 5% in CIDP was reviewed in a 47 person case series conducted in France. Though no conclusions on efficacy could be reached due to the retrospective nature of the study design, there were no unexpected safety signals. The OCTAGAM 5% doses used were quite variable but approximated to the recommendation found in the systematic review ie 2g/kg initially and 1g/kg every 3 weeks for 24 weeks.

[2] Eftimov F, Winer JB, Vermeulen M, de HR, van S, I. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy. The Cochrane database of systematic reviews. 2013;12:CD001797

Guillain-Barré Syndrome (GBS)

Support for the use of OCTAGAM® in the treatment of moderate to severe cases of GBS in adults when used in the first two weeks of disease onset, comes from a systematic review of clinical trials providing moderate quality of evidence[3].

16 NON-CLINICAL TOXICOLOGY

IgG is a normal constituent of the human organism and obtained from human plasma. No toxicity studies have been performed with the final drug product, because volume overload would occur long before a toxicologically relevant dose is reached in animals. Repeated dose toxicity studies, reproduction and development toxicity studies with heterologous IgG preparations are impracticable due to the induction of, and the interference with antibodies.

Since clinical experience does not provide any evidence of tumorigenic or mutagenic effects of IgG, experimental studies, especially on heterologous species, are not considered to be necessary.

OCTAGAM®'s preclinical evaluation, therefore focused on evaluation of its safety with respect to impurities that are derived from the manufacturing process. The level of impurities is controlled by the manufacturing process specifications on raw materials, by in-process controls, and by the final product specification. Tri-N-butyl phosphate (TNBP) and Octoxynol are used as S/D reagents for virus inactivation. A study program to evaluate the toxicological effect of these compounds. Both compounds are of low toxicity in the low residual concentrations in OCTAGAM® and have not raised any safety concerns or signs of intolerance.

[3] Hughes RA, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barre syndrome. Cochrane Database SystRev. 2012;7:Art. No. CD002063-DOI: 10.1002/14651858.CD002063.pub5

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

OCTAGAM®

Immunoglobulin Intravenous (Human) 10%

Read this carefully before you start taking OCTAGAM® and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about OCTAGAM®**.**

Serious Warnings and Precautions

- Thromboembolic events such as heart attack, stroke, and obstructions of a deep vein e.g. in the calves or of a blood vessel in the lung (pulmonary embolism) may occur with administration of human immunoglobulin intravenous (IVIG) products.
- Thromboembolic events occur more commonly in patients with pre-existing risk factors for thromboembolism receiving IVIG products.

  In general the risk factors for thromboembolic events include: obesity, advance age, hypertension, diabetes mellitus, previous events of heart attack, stroke, and obstructions of a deep vein etc., prolonged periods of immobilisation, intake of certain hormones (e.g. the pill).
- Thrombosis may occur however even in the absence of known risk factors.

What is OCTAGAM® used for?

OCTAGAM® is used for:

- Immune thrombocytopenic purpura (ITP) patients at high risk of bleeding or prior to surgery to correct the platelet count.
- patients who need antibody replacement therapy due to primary or secondary immune deficiency.
- adult patients who suffer from moderate to severe Guillain-Barré Syndrome (GBS).
- adult patients who suffer from Dermatomyositis (DM)

How does OCTAGAM® work?

OCTAGAM® is known as antibody replacement therapy, because it replaces the missing and much-needed IgG antibodies in people who have low levels of these infection-fighting proteins ie. PID/SID patients.

The mechanism of action in ITP, GBS and DM is not fully understood but includes modulatory effects of the immune system.

What are the ingredients in OCTAGAM®?

Medicinal ingredients: Immunoglobulin Intravenous (Human), 10%

Non-medicinal ingredients: Maltose, Triton X-100, TNBP, Water for Injections, IgA

OCTAGAM® comes in the following dosage forms:

OCTAGAM® is a 100 mg/mL solution for intravenous infusion and comes in the following dosage forms:

- 1 infusion bottle with 20 mL
- 1 infusion bottle with 50 mL
- 1 infusion bottle with 100 mL
- 1 infusion bottle with 200 mL
- 1 infusion bottle with 300 mL

Do not use OCTAGAM® if:

- You have a history of an allergic reaction to any human immunoglobulin/antibody preparation or if you are allergic to any of the other components of the preparation.
- You have immunoglobulin A (IgA) deficiency, with known antibodies against IgA. Octagam® contains trace amounts of IgA (average 106 µg/mL in a 10% solution).

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take OCTAGAM®. Talk about any health conditions or problems you may have, including if you:

- recently have heart disease or have had blood clots.
- are pregnant or nursing.
- have the following risk factors: kidney disease, diabetes mellitus, seriously dehydrated, overweight, take kidney damaging medications or are over the age of 65.
- are allergic to the immunoglobulins or to any of the nonmedicinal ingredients.
- have a history of allergy to corn products.
- use any device to measure blood or urine glucose, as the maltose in this product may interfere with these measurements.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with OCTAGAM®:

- There is no known drug interaction to OCTAGAM®. OCTAGAM® administration may slow the protection of live attenuated viral vaccines such as measles, mumps, rubella and varicella for at least six weeks, and possibly up to three months or longer.
- The infusion line may be flushed before and after administration of OCTAGAM® with either normal saline or 5% dextrose in water.
- Components used in the packaging of OCTAGAM® are latex-free.

How to take OCTAGAM®:

- OCTAGAM® will be given to you by a healthcare professional in a healthcare setting.
- OCTAGAM® should be inspected visually for particulate matter and discolouration prior to administration. Do not use non-homogenous solutions, or those that have a deposit.
- OCTAGAM® should be brought to room or body temperature before administration.
- OCTAGAM® should not be mixed with other products.
- Filtration of OCTAGAM® is not required.

Usual dose:

Your doctor will determine the dose(s) of OCTAGAM® that you are to receive as an infusion, which is an injection given slowly in a vein. The dose you receive will depend on your clinical situation and disease, but the following are a generally accepted starting doses of OCTAGAM®:

Immune modulatory treatment in

- ITP: 2 g/kg body weight divided into two doses of 1 g/kg (10 mL/kg) given on two consecutive days.
  Treatment can be repeated if relapse occurs.
- GBS: The usual starting dose of OCTAGAM® - 2 g/kg body weight given in divided doses over 2 to 5 consecutive days.
- Dermatomyositis (DM): 2 g/kg body weight given in divided doses over 2 to 5 consecutive days every 4 weeks.

Replacement therapy in

- PID/SID - 100 to 600 mg/kg body weight, every 3 to 4 weeks.

Overdose:

Overdose is possible in patients that are overweight, elderly, or those with impaired kidney function.

Missed Dose:

A missed dose should be given as soon as possible.

What are possible side effects from using OCTAGAM®?

These are not all the possible side effects you may have when taking OCTAGAM®. If you experience any side effects not listed here, tell your healthcare professional.

Hypersensitivity (such as changes in blood pressure, difficulty breathing a blue discoloration of the skin or mucous membranes, fast heart rate, skin reactions - rash/itching/hives), headache, increased blood pressure, nausea, fever, chills, blurred vision, dizziness, tremor, increased heart rate, vomiting, pain in extremity, back pain, chest pain, muscle pain, muscle spasms, joint pain, difficulty breathing, fatigue, injection site reactions, weakness, swelling of extremities, abdominal pain, diarrhea, flushing, cough, feeling unwell.

In rare cases, treatment with IVIG can also result in the following rare but serious symptoms. Tell your doctor immediately if you have any of the following symptoms.

- Severe headache with nausea, vomiting, neck stiffness, fever, and sensitivity to light. These could be signs of a temporary and reversible, non-infectious swelling of the membranes surrounding the brain and spinal cord (aseptic meningitis).
- Pain, swelling, warmth, redness, or a lump in your legs or arms, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body, sudden confusion, or trouble speaking. These could be signs of a blood clot.
- Hives, swelling of the lips, tongue or throat, difficulty breathing, faintness, nausea, vomiting. These could be signs of an allergic reaction. Allergic reactions are rare, but can induce an anaphylactic shock, even in patients who had tolerated the previous treatments.
- Fatigue, weakness, dizziness, headache, dark urine, jaundice and/or paleness. These may be symptoms of hemolytic anemia, a condition where you have not enough red blood cells.

If you have a troublesome symptom or side effect that is not listed here or if a side effect becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store refrigerated (+2 °C to +8 °C) for up to 36 months. Within this shelf-life the product may be stored up to 9 months at ≤ 25°C. After the storage at ≤ 25°C the product must be used or discarded.

Do not freeze. Protect from light. Discard any remaining contents after use. Do not use after expiry date.

Keep out of reach and sight of children.

If you want more information about OCTAGAM®:

- Talk to your healthcare professional

- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website http://www.octapharma.ca, or by calling 1-888-438-0488.

This leaflet was prepared by Octapharma Pharmazeutika Produktionsges.m.b.H

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