# AUSTRALIAN PRODUCT INFORMATION - OCTAGAM® 10% (HUMAN NORMAL IMMUNOGLOBULIN, 100 MG/ML, SOLUTION FOR INTRAVENOUS INFUSION)

## 1. NAME OF THE MEDICINE

Human Normal Immunoglobulin

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Octagam® 10% contains 100 mg/mL of human normal immunoglobulin with a purity of at least 95% immunoglobulin G (IgG), and a broad spectrum of antibodies against infectious agents. It is composed of the following distribution of IgG subclasses (approx.. values):

| | |
|---|---|
| $IgG_1$ | 60% |
| $IgG_2$ | 32% |
| $IgG_3$ | 7% |
| $IgG_4$ | 1% |

Octagam® 10% contains ≤ 3% polymers. Monomer and dimer content is ≥ 90%.

The human immunoglobulin A (IgA) content is ≤ 0.4 mg/mL. Octagam 10% is contraindicated in patients with IgA deficiency (for further details, refer to section 4.3 Contraindications).

Octagam® 10% contains all the IgG activities, which are present in the normal population. It is prepared from pooled plasma from more than 3,500 donors.

For a full list of excipients, see section 6.1 List of Excipients.

## 3. PHARMACEUTICAL FORM

Solution for intravenous infusion.

The solution is clear or slightly opalescent.

## 4. CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

Replacement therapy in:

- Primary immunodeficiency syndromes:
  - congenital agammaglobulinaemia and hypogammaglobulinaemia
  - common variable immunodeficiency
  - severe combined immunodeficiencies
  - Wiskott Aldrich syndrome
- Myeloma or chronic lymphocytic leukaemia with severe secondary hypogammaglobulinaemia and recurrent infections.

- Children with congenital Acquired Immune Deficiency Syndrome (AIDS) who have repeated bacterial infections.

Immunomodulation

- Idiopathic thrombocytopenic purpura, in adults or children with a high risk of bleeding or prior to surgery to correct the platelet count.
- Guillain Barré syndrome
- Kawasaki disease

Allogeneic bone marrow transplantation

## 4.2 DOSE AND METHOD OF ADMINISTRATION

### Dose

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

***Replacement therapy in primary immunodeficiency syndromes:***

- The dosage regimen should achieve a trough level of IgG (measured before the next infusion) of at least 4 – 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, followed by at least 0.2 g/kg every three weeks.
- The dose required to achieve a trough level of 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 2 to 4 weeks.
- Trough levels should be measured in order to adjust the dose and dosage interval.

***Replacement therapy in myeloma or chronic lymphatic leukaemia with severe secondary hypogammaglobulinaemia 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.

***Idiopathic Thrombocytopenic Purpura:***

- For the treatment of an acute episode, 0.8 - 1 g/kg on day one, which may be repeated once within 3 days, or 0.4 g/kg daily for two to five days.
- The treatment can be repeated if relapse occurs.

***Guillain Barré syndrome:***

- 0.4 g/kg/day for 3 to 7 days. Experience in children is limited.

***Kawasaki disease:***

- 1.6 - 2 g/kg should be administered in divided doses over two to five days or 2 g/kg as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid.

***Allogeneic Bone Marrow Transplantation:***

- Human normal immunoglobulin treatment can be used as part of the conditioning regimen and after the transplant. For the treatment of infections and prophylaxis of graft versus host disease, dosage is individually tailored.
- The starting dose is normally 0.5 g/kg/week, starting seven days before transplantation and for up to 3 months after transplantation.
- In the case of persistent lack of antibody production, dosage of 0.5 g/kg/month is recommended until antibody level returns to normal.

The dosage recommendations are summarised in Table 1 below.

Table 1: Dosage recommendations

| Indication | Dose | Frequency of injection |
|---|---|---|
| Replacement therapy in primary immunodeficiency | Starting dose:<br>0.4 - 0.8 g/kg<br><br>Thereafter:<br>0.2 - 0.8 g/kg | every 2 - 4 weeks to obtain IgG trough level of at least 4 - 6 g/L |
| Replacement therapy in secondary immunodeficiency | 0.2 - 0.4 g/kg | every 3 - 4 weeks to obtain IgG trough level of at least 4 - 6 g/L |
| Children with AIDS | 0.2 – 0.4 g/kg | every 3 - 4 weeks |
| Immunomodulation:<br>Idiopathic Thrombocytopenic Purpura | 0.8 - 1 g/kg<br><br>or<br><br>0.4 g/kg/day | on day 1, possibly repeated once within 3 days<br><br><br><br>for 2-5 days |
| Guillain Barré syndrome | 0.4 g/kg/day | for 3-7 days |
| Kawasaki syndrome | 1.6 - 2 g/kg<br>or<br>2 g/kg | in several doses for 2 - 5 days in association with acetylsalicylic acid<br><br>in one dose in association with acetylsalicylic acid |
| Allogeneic bone marrow transplantation:<br>- 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 IgG levels return to normal |

**Method of administration**

Octagam® 10% should be infused intravenously at an initial rate of 0.6 to 1.2 mL/kg/hour for 30 minutes. If well tolerated, the rate of administration may gradually be increased to a maximum of 7.2 mL/kg/hour.

If large volumes are administered, the product should be warmed to room or body temperature before use.

The solution should be clear or slightly opalescent. Do not use solutions which are cloudy or have deposits.

Octagam® 10% does not contain an antimicrobial agent. Once the container has been opened the contents should be used immediately. Product is for single use in one patient only.

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.

Any unused product should be disposed of in accordance with Section 6.6 Special precautions for disposal.

## 4.3 CONTRAINDICATIONS

Hypersensitivity to homologous immunoglobulins, especially in very rare cases of IgA deficiency, when the patient has antibodies against IgA. Octagam® 10% is contraindicated in any patient who has a history of an allergic reaction to any human normal immunoglobulin preparation or to any constituent of octagam® 10%.

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Certain severe adverse drug reactions may be related to the rate of infusion. The recommended infusion rate must be closely followed (see Section 4.2 Dose and method of administration). Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.

Certain adverse reactions may occur more frequently:

- with a high infusion rate
- in patients with hypo- or agammaglobulinaemia, with or without IgA deficiency
- 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 patient are:

- are not sensitive to human normal immunoglobulin by initially infusing the product slowly (0.6 to 1.2 mL/kg/hour).
- carefully monitored for any symptoms throughout the infusion period. In particular, patients naive to human normal immunoglobulin, patients switched from an alternative intravenous human normal immunoglobulin (IVIg) product to octagam® 10% 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.

If allergic or anaphylactic-type reactions occur, the infusion should be stopped immediately and appropriate treatment instituted. In case of shock, the current medical standards for shock-treatment should be observed.

**Hypersensitivity and anaphylactic reactions**

True hypersensitivity reactions are rare. They can occur in very seldom cases of IgA deficiency with anti-IgA antibodies.

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.

**Thromboembolic events**

Arterial and venous thromboembolic events have been reported in association with octagam®, particularly in those with known risk factors (see Section 4.8 Adverse effects). The pathogenesis of thromboembolic events associated with IVIg´s is assumed to be multifactorial. A relative increase in blood viscosity from the high influx of immunoglobin and/or the presence of procoagulant factors in the immunoglobulin solution are two possible mechanisms. There was an increased rate of thromboembolic events reported in 2010 associated with octagam®. The unexpected presence of factor XIa appeared to be the main cause for the thromboembolic events. Corrective measures in the manufacturing process of octagam® have been implemented. Arterial thromboembolic events included myocardial infarction and stroke. Most arterial thromboembolic events occurred during octagam® infusion or within the first 24 hours post infusion. Venous thromboembolic events included deep vein thromboses and pulmonary embolism. Most venous thromboembolic events occurred within 72 hours post octagam® infusion.

Caution should be exercised in prescribing and infusing IVIg in patients with pre-existing risk factors for arterial and venous thromboembolic events such as obesity, smoking, advanced age, hypertension, diabetes, a history of atherosclerosis/vascular disease or thrombotic events, hyperlipidaemia, multiple cardiovascular risk factors, impaired cardiac output, pregnancy and the puerperium, oestrogen-containing hormone replacement therapy or oral contraceptive, acquired or inherited thrombophilic disorders, prolonged periods of immobilisation, hypovolemia, surgery, central venous catheterisation, active malignancy and/or known or suspected hyperviscosity.

The potential risks and benefits of IVIg´s, including octagam® should be weighed against those of alternative therapies for all patients for whom IVIg administration is being considered. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronaemia/markedly high triglycerides, or monoclonal gammopathies. Patients should be monitored closely for signs and symptoms of thromboembolism, particularly during and for 72 hours after octagam® infusion. Rapid rates of IVIg infusion may be a risk factor for thromboembolic events. The recommended infusion rate should not be exceeded. For patients judged to be a risk of developing thromboembolic events, administer octagam® at the minimum rate of infusion practicable. The decision to take antithrombotic prophylactic measures is a clinical

decision that requires a careful assessment of individual patients underlying risk factors.

**Renal dysfunction**

Cases of renal dysfunction, acute renal failure, osmotic nephrosis and death 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, sepsis, overweight, concomitant nephrotoxic medicinal products or age over 65.

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

In case of renal impairment, IVIg discontinuation should be considered.

While the 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 stabiliser accounted for a disproportionate share of the total number. In patients at risk, the use of IVIg products not containing sucrose may be considered.

In all patients, IVIg administration requires:

- adequate hydration prior to the infusion of IVIg
- monitoring of urine output
- monitoring of serum creatinine levels
- avoidance of concomitant use of loop diuretics

**Aseptic meningitis syndrome**

Aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with IVIg treatment. The syndrome usually begins within several hours to two days following IVIg treatment. It is characterised by symptoms and signs including severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, and nausea and vomiting. Cerebrospinal fluid (CSF) studies are frequently positive with pleocytosis up to several thousand cells per cu.mm, predominantly from the granulocytic series, and elevated protein levels up to several g/L. Patients exhibiting such symptoms and signs should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. It appears that patients with a history of migraine may be more susceptible. Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae.

**Haemolysis**

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 and, rarely, haemolysis. Haemolytic anaemia can develop subsequent to IVIg therapy due to enhanced RBC sequestration (see Section 4.8 Adverse effects). IVIg recipients should be monitored for clinical signs and symptoms of haemolysis.

In patients with a normal acid base compensatory mechanism, the acid load delivered by the largest dose of the preparation would be neutralised by the buffering capacity of whole blood alone, even if the dose were to be infused instantaneously. In patients with limited or compromised acid base compensatory mechanisms including neonates, consideration should be given to the effect of the additional acid load that the preparation might present.

**Transmissible agents**

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses.

Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV).

The manufacturing process for octagam® 10% includes a three stage viral inactivation/removal process, which includes two dedicated viral inactivation steps (solvent/detergent treatment followed by incubation at low pH at 37°C for 24-26 hours) and a cold ethanol fractionation process, which also contributes to viral removal/inactivation.

Viral removal and inactivation procedures performed during the manufacturing process may be of limited value against non-enveloped viruses such as hepatitis A virus or parvovirus B19.

Parvovirus B19 infection may be serious for pregnant women (foetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia).

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.

The manufacturing process was investigated for the capacity to decrease the amount of an experimental agent of transmissible spongiform encephalopathy (TSE), considered as a model for the vCJD and CJD agents. The manufacturing process of octagam® 10% has been shown to decrease the amount of this experimental model agent. The TSE reduction step is the precipitation and separation of fraction I+III.

Vaccination for patients in receipt of medicinal products made from human plasma should be considered where appropriate.

It is strongly recommended that every time octagam® 10% 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 use**

The safety of octagam® 10% for paediatric use has not been established in controlled clinical trials.

**Effects on laboratory tests**

*Interference with serological testing*

After injection of human normal immunoglobulin the transitory rise of 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 or D may interfere with some serological tests for red cell allo-antibodies, for example the antiglobulin test (e.g. Coombs Test), reticulocyte count and haptoglobin.

*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® 10% as glucose. This may result in falsely elevated glucose readings 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% 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.

## 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

*Live attenuated virus vaccines*

Human normal 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.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

**Effects on fertility**

No data are available

**Use in pregnancy**

The safety of octagam ® 10% 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. Clinical experience with human normal

immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the neonate are to be expected.

**Use in lactation**

Immunoglobulins are excreted into the milk and may contribute to the transfer of protective antibodies to the neonate.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

There is no indication that human normal immunoglobulins may impair the ability to drive and use machines.

## 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

In general, various allergic and hypersensitivity type of reactions and headache, chills, back pain, chest pain, fever, cutaneous reactions, vomiting, arthralgia, low blood pressure and nausea may occasionally occur. Reactions to IVIg tend to be related to the dose and rate of infusion.

The following adverse effects (Table 2) have been identified in clinical trials with octagam® (5 and 10%). Within each frequency grouping, undesirable effects are presented in the internationally agreed order.

Table 2: Adverse effects observed in clinical trials with octagam®

| **MedDRA Coded** | **Common (≥1% - <10%)** | **Uncommon (≥0.1% - <1%)** |
|---|---|---|
| Immune system disorders | hypersensitivity | |
| Nervous system disorders | headache | dizziness |
| Cardiac disorders | tachycardia | |
| Vascular disorders | hypertension | hypotension |
| Gastrointestinal disorders | nausea<br>vomiting | |
| Skin and subcutaneous tissue disorders | eczema | |
| Musculoskeletal and connective tissue disorders | | back pain |
| General disorders and administration site conditions | fever<br>fatigue<br>chills<br>injection site reaction | chest pain<br>hot flush |
| Investigations | hepatic enzymes increased | |

Cases of reversible aseptic meningitis, isolated cases of reversible haemolytic anaemia/haemolysis and rare cases of transient cutaneous reactions, have been observed with human normal immunoglobulin.

Increase in serum creatinine level and/or acute renal failure have been observed (see Section 4.4 Special warnings and precautions for use).

Very rarely, thromboembolic reactions such as myocardial infarction, stroke, pulmonary embolism, deep vein thrombosis have been observed. For further information, see Section 4.4 Special warnings and precautions for use.

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.

Table 3 lists adverse effects that have been identified during post-approval use of octagam® (5% and 10%). Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency.

Table 3: Adverse effects observed from post marketing experience

| **MedDRA Coded** | **Adverse Reactions** |
|---|---|
| Blood and lymphatic system disorders | Leucopenia, haemolytic anemia |
| Immune system disorders | Hypersensitivity, anaphylactic shock, anaphylactic reaction, anaphylactoid reaction, angioneurotic edema, face edema |
| Metabolic and nutritional disorders | Fluid overload |
| Psychiatric disorders | Agitation |
| Nervous system disorders | Headache, cerebrovascular accident, meningitis aseptic, migraine, dizziness, paraesthesia |
| Cardiac disorders | Myocardial infarction, tachycardia, palpitations, cyanosis |
| Vascular disorders | Hypotension, thrombosis, peripheral circulatory failure, hypertension |
| Respiratory, thoracic and mediastinal disorders | Respiratory failure, pulmonary embolism, pulmonary oedema, bronchospasm, dyspnea, cough |
| Gastrointestinal disorders | Nausea, vomiting, diarrhea, abdominal pain |
| Skin and subcutaneous tissue disorders | Eczema, urticaria, rash, rash erythematous, dermatitis, exfoliative dermatitis, pruritus, alopecia |
| Musculoskeletal and connective tissue disorders | Back pain, arthralgia, myalgia, pain in extremity |
| Renal and urinary disorders | Renal failure acute |
| General disorders and administration site conditions | Fatigue, injection site reaction, pyrexia, chills, chest pain, hot flush, flushing, hyperhidrosis, malaise |
| Investigations | Hepatic enzymes increased, blood glucose false positive |

For information on viral safety, see Section 4.4 Special warnings and precautions for use.

### Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

## 4.9 OVERDOSE

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

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: immune sera and immunoglobulins: immunoglobulins, normal human, solution for intravenous infusion.

ATC-Code: J06B A02

### Mechanism of action

Octagam® 10% has a distribution of IgG-subclasses closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low IgG levels to the normal range.

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

### Clinical trials

Octagam® 10% is a human normal immunoglobulin solution ready for intravenous administration (IVIg) developed as a new strength of the essentially similar octagam® 5%. Having in mind that both products have similar biochemical characteristics, it is reasonable to conclude that both products are equally efficacious. No differences concerning the efficacy of octagam® 10% are to be expected. Nevertheless efficacy data are presented, derived from an ongoing study in patients suffering from ITP.

In a prospective, open-label, multicentre phase III trial (GAM10-02), the efficacy and safety of octagam® 10% was studied in patients suffering from idiopathic (immune) thrombocytopenic purpura (ITP). Octagam® 10% was infused on 2 consecutive days at a dose of 1 g/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.

In agreement with national health agencies, a descriptive interim analysis has been performed following the completion of 31 subjects. The final analysis of results will be presented in subsequent study reports. From 31 subjects included in the interim 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 (defined as an increase in platelets to at least 50 x $10^9$ /L within 7 days after treatment). 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% 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. These administrations were not related to a higher incidence of adverse reactions.

In 9 of 62 infusions (14.5%) treatment related AEs 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.

### 5.2 PHARMACOKINETIC PROPERTIES

**Absorption**

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

**Distribution**

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

**Metabolism**

Human normal immunoglobulin has an average half-life ranging of 26 to 41 days, as measured in immunodeficient patients. This half-life may vary from patient to patient, in particular in primary immunodeficiency.

**Excretion**

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

### 5.3 PRECLINICAL SAFETY DATA

**Genotoxicity**

Clinical experience provides no evidence for genotoxic potential of human normal immunoglobulin.

**Carcinogenicity**

Clinical experience provides no evidence for genotoxic potential of human normal immunoglobulin.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 LIST OF EXCIPIENTS

Maltose
Human immunoglobulin A (IgA)
Tributyl phosphate
Octoxinol 10
Water for Injections

### 6.2 INCOMPATIBILITIES

Octagam® 10% must not be mixed with other medicinal products.

## 6.3 SHELF LIFE

Shelf life is 2 years.

## 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C to 8°C (Refrigerate. Do not freeze).

Protect from light.

Do not use after expiry date.

Once removed from refrigeration, the product may be stored below 25°C for a single period of 9 months. In this case the product expires at the end of the 9-month period - the new date of expiry should be noted on the outer carton. The product may not be returned to refrigerated storage after storage below 25°C.

Octagam® 10% doesn't contain any antimicrobial agent. It must, therefore, be used immediately after opening; any remaining contents must be discarded (refer to Section 6.6 Special precautions for disposal).

## 6.5 NATURE AND CONTENTS OF CONTAINER

The primary container is made of type II glass closed with a bromobutyl rubber stopper. Each container contains 100 mg/mL solution for infusion.

The product is supplied in the following vial sizes:

1 injection vial with 20 mL

1 infusion bottle with 50 mL

1 infusion bottle with 100 mL

1 infusion bottle with 200 mL

## 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

## 6.7 PHYSICOCHEMICAL PROPERTIES

**Chemical structure**

No data available

**CAS number**

None assigned

# 7. MEDICINE SCHEDULE (POISONS STANDARD)

S4

## 8. SPONSOR

Octapharma Australia Pty. Ltd.
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## 9. DATE OF FIRST APPROVAL

11 November 2009

## 10. DATE OF REVISION

11 January 2021

### SUMMARY TABLE OF CHANGES

| Section changed | Summary of new information |
|---|---|
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| | |
| | |