Octagam has a broad spectrum of antibodies against various infectious agents (e.g. antibody titer for streptococcus and hepatitis B-antigen is established at 3 times the initial plasma pool), corresponding to those pathogens endemic in Europe and North America.

5.2 Pharmacokinetic properties

OCTAGAM is immediately and completely bioavailable in the patient's circulation after intravenous administration. It is distributed relatively rapidly between plasma and extravascular fluid, after 3-5 days equilibrium is reached between the intra- and extravascular compartments.

OCTAGAM has a half life of about 26-34 days (as measured in immunodeficient patients). This half-life may vary from patient to patient, in particular in primary immunodeficiency. Immunoglobulin G (IgG) and IgG-complexes are broken down in cells of the reticuloendothelial system.

5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body. In animals, acute toxicity testing is of no relevance and higher doses result in overloading. Repeated dose toxicity testing and embryo-foetal toxicity studies are impracticable due to induction of and interference with antibodies. Effects of the product on the immune system of the newborn have not been studied.

Since clinical experience provides no hint for tumorigenic or mutagenic effects of immunoglobulins, experimental studies, particularly in heterologous species, are not considered necessary.

6 PHARMACEUTICAL PARTICULARS

6.1 Excipients

Maltose

Aqua ad inj.

6.2 Incompatibilities

Octagam must not be mixed with other medicinal drugs.

6.3 Shelf-life

24 months

6.4 Special precaution for storage

The product should not be stored and transported above +25°C.

Keep container in the outer carton in order to protect from light.

Do not use after expiry date. Do not freeze.

From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user. Any remaining contents must be discarded.

6.5 Nature and contents of container

The infusion bottles are made of glass type II, Ph.Eur. closed with bromobutyl rubber stoppers.

Pack sizes:

1 infusion bottle with 2.5 g (50 ml)
1 infusion bottle with 5 g (100 ml)
1 infusion bottle with 10 g (200 ml)

6.6 Instructions for use and handling

The product should be brought to room or body temperature before use.

Do not use non-homogenous solutions, or those which have a deposit.

Any remaining contents must be discarded.

7 NAME AND ADDRESS OF PHARMACEUTICAL COMPANY

Marketing authorisation holder and Manufacturer:

OCTAPHARMA Pharmazeutika Produktionsges.m.b.H.
Oberlaaer Strasse 235
A-1100 Vienna
Austria

Distributed in Lebanon by: MPC

phone +961.1.545544
www.MPC-pharma.com

Reg. numbers: 405919 (2.5 g / 50 ml), 405920 (5 g / 100 ml), 405921 (10 g / 200 ml)

8 DATE OF REVISION OF THE TEXT

November 2003

9 LEGAL CATEGORY

For prescription only.

2010385-02

INSTRUCTIONS FOR USE

(Summary of product characteristics)

1 NAME OF THE MEDICINAL PRODUCT

OCTAGAM®

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Active ingredients

Human immunoglobulin for intravenous use

2.2 Quantitative composition:

1 ml solution contains:

Protein 50 mg
of which ≥ 95% is human Immunoglobulin G
IgA ≤ 0.1 mg

Distribution of IgG subclasses:

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

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Solution for infusion

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

4.1.1 Replacement therapy in:

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

- Children with congenital AIDS and recurrent bacterial infections.

4.1.2 Immunomodulatory effect:

- Idiopathic thrombocytopenic purpura (ITP) in children or adults at high risk of bleeding or prior to surgery to correct the platelet count.
- Guillain Barré syndrome
- Kawasaki disease
- Allogeneic bone marrow transplantation

4.2 Posology and method of administration

4.2.1 Posology

The dose and dosage regimen is dependant on the indication.

In replacement therapy the dosage may need to be individualised for each patient dependant on the pharmacokinetic 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 depending on the clinical circumstances (e.g. active infection), followed by at least 0.2 g/kg every three weeks.
- The dose required to achieve a trough level of 6 g/l is 0.2-0.8 g/kg/month. The dosage interval when steady state has been reached varies from 2 - 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 3 to 4 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:
- 1.6-2.0 g/kg should be administered in divided doses over two to five days. Patients should receive concomitant treatment with acetylsalicylic acid.

Allogeneic Bone Marrow Transplantation:
- Intravenous immunoglobulin treatment is used as part of the conditioning regimen and after 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.

4.2.2 Method of administration

OCTAGAM should be infused intravenously at an initial rate of 1 ml/kg/hour. If well tolerated, the rate of administration may gradually be increased to a maximum of 5 ml/kg/hour.

4.3 Contraindications

Hypersensitivity to homologous immunoglobulins, especially in the very rare cases of IgA deficiency when the patient has antibodies against IgA.

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.

4.4 Special warnings and special precautions for use

Certain severe adverse drug reactions may be related to the rate of infusion. The recommended infusion rate given under "4.2 Method of administration" 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 IgG for the first time
- in patients with hypo- or agammaglobulinaemia, with or without IgA deficiency
- in rare cases, when the immunoglobulin product is switched
- in patients when treatment has been stopped for more than eight weeks.

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.

Potential complications can often be avoided by ensuring:
- that patients are not sensitive to human normal immunoglobulin by first injecting the product slowly (0.016 ml/kg/min);
- that patients are carefully monitored for any symptoms throughout the infusion period; in particular, patients naive to human normal immunoglobulin, patients switched from an alternative immunoglobulin to OCTAGAM or when treatment has been stopped for more than eight weeks 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.

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, age over 65, hypovolemia, overweight or concomitant nephrotoxic medicinal products).
In all patients, intravenous immunoglobulin 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

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, those containing sucrose as a stabiliser accounted for a disproportionate share of the total number. In patients at risk, the use of IGIV products that do not contain sucrose may be considered.

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 side effects.

In case of shock, treatment should follow the guidelines for shock therapy.
In patients with cerebrovascular or cardiovascular diseases or other vascular risk factors, immunoglobulins should be administered with care, particularly if high doses are used, due to potential increases in plasma viscosity. It is advisable to measure the blood viscosity of patients at risk.

When medicinal products prepared from human blood are administrated, infectious diseases due to transmission of infective agents cannot be totally excluded. This also applies to pathogens of hitherto unknown nature.

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The risk of transmission of infective agents is however reduced by:
- selection of donors by a medical interview and screening of donations for the three major pathogenic viruses: HIV, HCV and HBV.
- The plasma pools are tested for HCV genomic material (nucleic acids).
- Removal/inactivation procedures included in the production process have been validated using model viruses and are considered effective for HIV, HCV and HBV.

The viral removal/inactivation procedures are effective against lipid-enveloped viruses, but may be of limited value against non-enveloped viruses such as hepatitis A virus or parvovirus B19.

4.5 Interaction with other medicinal products

Live attenuated vaccines

Immunoglobulin administration may impair for a period of at least 6 weeks and up to 3 months the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella. After administration of this product, an interval of 3 months should elapse before vaccination with live attenuated virus vaccines. In the case of a measles, this impairment may persist for up to 1 year. Therefore patients receiving measles vaccine should have their antibody status checked.

Interference with serological testing

After injection of immunoglobulin the various passively transferred antibodies in the patients 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 (reticulocyte count, haptoglobin and Coombs tests).

Interference with glucose tests

Octagam contains Maltose which could interfere with blood and urinary glucose tests.

4.6 Pregnancy and lactation

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. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy on the foetus or the neonate are to be expected. 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

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

Adverse reactions such as chills, headache, fever, nausea, vomiting, allergic reactions, arthralgia, changes in blood pressure and moderate low back pain may occur occasionally.

Rarely human normal immunoglobulin may cause a 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, isolated cases of reversible haemolytic anaemia / haemolysis, reversible transient increases in liver transaminases and rare cases of regressive cutaneous reactions (often eczema-like) have been observed with IVIG.

Increase in creatininemia and/or acute renal failure have been observed (see 4.4 Special warnings and special precautions for use).

Thrombotic events have been reported in the elderly, in patients with signs of cerebral or cardiac ischemia, and in overweight and overly volume depleted patients (see 4.4 Special warnings and special precautions for use).

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: Immunoglobulin G (human),
ATC-Code: J06 BA02
OCTAGAM contains mainly ≥ 95 % immunoglobulin G (IgG) with a broad spectrum of antibodies against various infectious agents. IgA content ≤ 0.1s mg/ml.
Opsonisation and neutralisation of microbes and toxins has been documented.
OCTAGAM contains all the IgG activities which are present in the normal population.
It is prepared from pooled plasma from not fewer than 3500 donations.

OCTAGAM has a distribution of IgG-subclasses:

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

which are closely proportional to that in native human plasma. Adequate doses of this medicinal product may restore abnormally low IgG level to the normal range.

The mechanism of action in idiopathic thrombocytopenic purpura is not fully elucidated. The IgG-molecules have not been chemically or enzymatically modified. The antibody activities are fully functional. Octagam contains ≤ 3.0 % polymers. Monomer and dimer is ≥ 90 %.