Intragam® 10

Human Normal Immunoglobulin 10% (10 g/100 mL) solution for intravenous infusion

Product Information

Australia

NAME OF THE MEDICINE

Human Normal Immunoglobulin 10% (10 g/100 mL), solution for intravenous infusion.

DESCRIPTION

Intragam® 10 is a sterile, preservative free solution containing 10 g/100 mL of human plasma protein with a purity of at least 98% immunoglobulin G (IgG). At least 90% of the IgG consists of monomers and dimers (typically >96%). Aggregates are <3%. The distribution of the IgG subclasses closely resembles that found in normal human plasma (approximate mean ranges: 47.6–56.2% IgG_1, 41.5–49.5% IgG_2, 1.3–1.6% IgG_3, 0.9–1.3% IgG_4).

Intragam® 10 has a nominal osmolality of 350 mOsmol/kg and is approximately isotonic. The pH value of the ready-to-use solution is 4.25. Intragam® 10 contains 2.25 g of glycine in each 100 mL as a stabiliser which is a physiological non-essential amino acid. Intragam® 10 does not contain a carbohydrate stabiliser (e.g. sucrose, maltose) and contains no preservative. Intragam® 10 contains only trace amounts of IgA, typically <0.025 mg/mL. The maximum prekallikrein activator (PKA) levels are less than 28.6 IU/mL (typically ≤1.2 IU/mL).

Intragam® 10 is manufactured from human plasma collected by the Australian Red Cross Blood Service.

Intragam® 10 is manufactured by chromatographic fractionation. The manufacturing process contains three dedicated and complementary steps to reduce the possibility of pathogen transmission:

- pasteurisation (60°C for 10 hours)
- nanofiltration
- incubation at low pH.

PHARMACOLOGY

Pharmacodynamics

Intragam® 10 contains the IgG antibodies present in the donor population. It is prepared from pooled plasma collected from not fewer than 1000 donors. It has an IgG subclass distribution closely proportional to normal human plasma.

Intragam® 10 contains functionally intact IgG with a broad spectrum of antibodies against infectious agents. The IgG molecules have not been chemically or enzymatically modified and the Fc and Fab functions are retained.

Adequate doses of human normal immunoglobulin 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.

Pharmacokinetics

Intragam® 10 is immediately and completely bioavailable in the recipient's circulation after intravenous infusion. It is distributed relatively rapidly between plasma and extravascular fluid. After approximately 3 to 5 days, equilibrium is reached between the intra- and extravascular compartments.

The pharmacokinetic parameters for Intragam® 10 were established in a clinical study (see **CLINICAL TRIALS**) in patients with Primary Immunodeficiency Disease (PID). Nineteen patients (aged 18 to 69 years) participated in the pharmacokinetic assessment (see **Table 1**). The median half-life of Intragam® 10 in patients with PID was 34 days. This half-life may vary from patient to patient. IgG and IgG-complexes are broken down in cells of the reticuloendothelial system.

Table 1: Pharmacokinetic Parameters of Intragam® 10 in 19 PID patients

Parameter	Median (Range)
C_{max} (peak, g/L)	17.4 (11.9–21.4)
C_{min} (trough, g/L)	7.8 (4.9–11.3)
$t_{½}$ (days)	34.0 (25.0–50.6)

*C_{max}, maximum serum IgG concentration.
†C_{min}, trough (minimum) serum IgG concentration.
‡$t_{½}$, elimination half-life of IgG.

CLINICAL TRIALS

Treatment of Primary Immunodeficiency Disease (PID)

Intragam® P is CSL's 6% w/v intravenous immunoglobulin (IVIg) and parent product for Intragam® 10 which differs from Intragam® P only in formulation, concentration and additional pathogen removal step as part of the manufacturing process. The efficacy of Intragam® 10 in PID is confirmed by previous clinical trials conducted with Intragam® P, as the biological, pharmacokinetic and safety data showed no significant differences between the two products. Therefore, the following clinical trial information for Intragam® P supports the efficacy of Intragam® 10 in PID patients.

The efficacy of Intragam® P was assessed in 35 subjects (age 6–76 years; 21 male) with PID, following the administration of monthly intravenous infusions of Intragam® P for six months. The dose of Intragam® P was individualised in the range 0.2 to 0.67 g/kg. The mean number of days of hospitalisation over the 6 month period was 2.8±9.0 and the mean number of days absent from work or school due to illness was 5.3±6.4. These figures were similar to historical data relating to other IVIgs.

Treatment of Idiopathic Thrombocytopenic Purpura (ITP)

The efficacy of Intragam® 10 was established in a multi-centre open-label clinical trial in patients with ITP, which was consistent with the results from the previous Intragam® P clinical trials. A total of 17 subjects aged 20 to 76 years with ITP and a platelet count of $<50 \times 10^9$/L were treated with 1 g/kg body weight of Intragam® 10 on each of two consecutive days (a total cumulative dose of 2 g/kg). A rise in platelet count to at least 50×10^9/L within 7 days after the first infusion was observed in 15 of the 17 subjects studied. The median time to achieve this platelet response was 4 days after the first infusion, and 71% of the subjects reached this response within four days (i.e. two days after the second infusion). For those subjects who responded, the median duration of platelet count $\geq 50 \times 10^9$/L was 17 days (range: 7 to >85 days).

Adverse events encountered during the Intragam® 10 clinical trials are outlined in **ADVERSE EFFECTS**.

Treatment of neurological disorders

There are several randomised controlled clinical trials demonstrating the efficacy and safety of the use of IVIg in the treatment of patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), Multifocal Motor Neuropathy (MMN) and Myasthenia Gravis (MG). Whilst the evidence for the efficacy of IVIg in the management of CIDP and acute exacerbations of MG is clear, data for the treatment of chronic MG and MMN is not as definitive. Clinical trials for the use of IVIg for MMN showed an increase in muscle strength but no impact on the disability scale.

The efficacy and safety of IVIg in the treatment of patients with stiff person syndrome and Lambert-Eaton Myasthenic Syndrome (LEMS) has only been demonstrated in a single randomised controlled clinical trial for each condition.

The adverse reactions reported in the literature for IVIg when used in CIDP, MMN, MG, LEMS and stiff person syndrome were consistent with those reported for other indications (see **ADVERSE EFFECTS**).

Intragam® 10 has similar characteristics to other IVIg products that have been used in the management of CIDP, MMN, MG, LEMS and stiff person syndrome.

INDICATIONS

Intragam® 10 is indicated for replacement IgG therapy in:

- Primary Immunodeficiency Diseases (PID)
- Symptomatic hypogammaglobulinaemia secondary to underlying disease or treatment.

Intragam® 10 is indicated for immunomodulatory therapy in:

- Idiopathic Thrombocytopenic Purpura (ITP), in adults or children at high risk of bleeding or prior to surgery to correct the platelet count
- Kawasaki disease
- Guillain-Barré Syndrome (GBS)
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- Multifocal Motor Neuropathy (MMN)
- Myasthenia Gravis (MG) in acute exacerbation (myasthenic crisis) or prior to surgery and/or thymectomy; as maintenance therapy for moderate to severe MG when other treatments have been ineffective or caused intolerable side effects
- Short-term therapy for severely affected nonparaneoplastic Lambert-Eaton Myasthenic Syndrome (LEMS) patients
- Treatment of significant functional impairment in patients who have a verified diagnosis of stiff person syndrome.

CONTRAINDICATIONS

Intragam® 10 is contraindicated in patients who have had a true anaphylactic reaction to human immunoglobulins (especially in patients with antibodies against IgA) or to the excipient glycine.

PRECAUTIONS

The recommended infusion rate of Intragam® 10 must be closely followed (see **DOSAGE AND ADMINISTRATION**). Certain severe adverse reactions may be related to the rate of infusion. Reactions to IVIg tend to be related to the infusion rate and are most likely to occur during the first hour of the infusion. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period. In case of adverse reaction, the rate of administration should be reduced or the infusion stopped to alleviate symptoms. Once a reaction has resolved, based on clinical judgement, the infusion may cautiously be recommenced at a slower rate.

Certain adverse reactions may occur more frequently:

- with a higher infusion rate
- in patients with hypo- or agammaglobulinemia 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:

- patients are not sensitive to human normal immunoglobulin by first infusing the product slowly (1 mL/min)
- patients are carefully monitored for any symptoms throughout the infusion period
- reducing the infusion rate in patients who are naive to Intragam® 10 or who are at increased risk of adverse events.

True hypersensitivity reactions to immunoglobulins are rare. They can occur in patients with anti-IgA antibodies, such as those with IgA deficiency. Intragam® 10 should be used with caution in patients with a known allergy to constituents of the preparation. Intragam® 10 contains traces of IgA which seldomly may provoke anaphylaxis in IgA deficient patients 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. In case of anaphylactic reaction, the infusion should be stopped immediately.

Cases of renal dysfunction and acute renal failure have been reported in patients receiving IVIg therapy. Risk factors may include: pre-existing renal insufficiency, diabetes mellitus, hypovolemia, concomitant nephrotoxic medicinal products, sepsis, paraproteinaemia, being overweight or aged over 65 years. The majority of cases of renal dysfunction and acute renal failure have been associated with the use of those IVIg products containing sucrose as a stabiliser. There is no sucrose in Intragam® 10. The formulation enables the same dose to be delivered within a reduced infusion volume compared to Intragam® P. In case of renal impairment, IVIg discontinuation should be considered. The following precautions should be followed for all patients:

- ensuring adequate hydration prior to the initiation of Intragam® 10
- monitoring of urine output
- monitoring of serum creatinine levels
- avoidance of concomitant loop diuretics.

In patients at risk for renal failure, IVIg products should be administered at the minimum rate of infusion and dose practicable.

There is clinical evidence of an association between IVIg administration and thromboembolic events which is assumed to be related to a relative increase in blood viscosity through the high influx of immunoglobulin in at-risk patients. Caution should be exercised when prescribing and infusing IVIg for patients with pre-existing risk factors for thrombotic events such as advanced age, oestrogen use, in-dwelling vascular catheters, a history of venous or arterial thrombosis, acquired or inherited hypercoagulable states, cardiovascular risk factors (including history of atherosclerosis and/or impaired cardiac output), prolonged periods of immobilisation, severe hypovolaemia, hyperviscosity (including cryoglobulins, fasting chylomicronaemia and/or high triglyceride levels, and monoclonal gammopathies. Reports have included cases of thrombophlebitis. In case of thromboembolic adverse reaction, the benefit and risk of treatment should be assessed before IVIg therapy is continued.

In patients at risk for thromboembolic adverse reactions, IVIg products should be administered at the minimum rate of infusion and dose practicable, and these individuals should be monitored for thrombotic complications. Consideration should also be given to measurement of baseline blood viscosity in individuals at risk for hyperviscosity.

Aseptic Meningitis Syndrome (AMS) has been reported in association with IVIg treatment. It has been hypothesised that IVIg-associated AMS is the severe presentation of a continuum that begins with the more common adverse event of headache. The AMS 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, predominantly from the granulocytic series, and elevated protein levels. Patients exhibiting such symptoms and signs should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. AMS may occur more frequently in association with high dose (2 g/kg) IVIg treatment. Discontinuation of IVIg treatment has resulted in remission of AMS within several days without sequelae.

Patients with a history of AMS, migraine or frequent headaches may be more susceptible to the syndrome. For these patients the following precautions should be taken:

- assessment of hydration status and ensuring adequate hydration prior to commencement of infusion of Intragam® 10
- administration of a pre-medication (e.g. paracetamol/ paracetamol & codeine) if needed prior to each infusion of Intragam® 10 (e.g. if headache present)
- administration of the minimum dose at the minimum rate practicable.

IVIg products can contain blood group antibodies which may act as haemolysins and induce *in vivo* coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction (Coombs test) and, rarely, haemolysis. Haemolytic anaemia can develop subsequent to IVIg therapy due to enhanced red blood cells (RBC) sequestration. Patients at increased risk for haemolysis following treatment with immunoglobulin include those with blood groups A, B, or AB, or who have underlying associated inflammatory conditions. Also at risk are patients receiving high cumulative doses of immunoglobulin over the course of several days. IVIg recipients should be monitored for clinical signs and symptoms of haemolysis, particularly those patients at increased risk. If these occur, appropriate laboratory testing should be undertaken.

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.

It is recommended that the name and batch number of the product are recorded every time the product is administered to a patient.

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

Pathogen safety

This product is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses and theoretically Creutzfeldt-Jakob Disease (CJD) agents. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain infectious agents and by testing for the presence of certain pathogen markers. In addition, three dedicated pathogen reduction steps are included in the manufacturing process of Intragam® 10 to reduce the possibility of pathogen transmission including pasteurisation (heating at 60°C for 10 hours), nanofiltration and incubation at low pH. The current procedures applied in the manufacture of this product are effective against enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV) viruses, and the non-enveloped viruses hepatitis A (HAV) and parvovirus B19. In addition, Intragam® 10 contains specific antibodies directed against parvovirus B19.

Despite these measures, there remains the potential that such products may transmit disease. There is also the possibility that other known or unknown infectious agents may be present in such products. Vaccination of patients in receipt of plasma-derived therapeutics should be considered where appropriate.

Effects on fertility

No fertility studies have been conducted with Intragam® 10.

Use in pregnancy

No animal reproduction studies have been conducted with Intragam® 10. Intragam® 10 should be given to pregnant women only if clearly indicated.

Table 2: Causally related adverse drug reactions (ADRs) observed in clinical studies with Intragam® 10

System organ class	Very common (≥10%)	Common (≥1% and <10%)
Nervous system disorders	Headache Lethargy Migraine* Dizziness*	-
Gastrointestinal disorders	Nausea Vomiting*	Abdominal pain*
General disorders and administration site reactions	Infusion site pain* Pyrexia Pain	-
Musculoskeletal and connective tissue disorders	Arthralgia Myalgia Musculoskeletal stiffness*	-
Infections and infestations	Meningitis aseptic*	-
Skin and subcutaneous tissue disorders	Pruritus	Rash*
Vascular disorders	Hot flush	-
Immune system disorders	-	Hypersensitivity*
Respiratory, thoracic and mediastinal disorders	-	Dyspnoea*

* These adverse events were only observed in the clinical study for the treatment of ITP.

An embryofetal development study in which rats were infused IV with the excipient glycine 945 mg/kg/day on gestation days 6–17 showed no adverse effects.

Use in lactation
No lactation studies have been conducted with Intragam® 10. Immunoglobulins are excreted in breast milk and may contribute to the transfer of protective antibodies to the neonate.

Paediatric use
The use of Intragam® 10 in the paediatric population has not been established in clinical studies.

Use in the elderly
Clinical studies of Intragam® 10 did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently to younger subjects.

Genotoxicity
No genotoxicity studies have been conducted with Intragam® 10.

Carcinogenicity
No carcinogenicity studies have been conducted with Intragam® 10.

Effect on laboratory tests
After immunoglobulin infusion the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing.

Passive transmission of antibodies to erythrocyte antigens (e.g. A, B, D) may interfere with some serological tests for red cell allo-antibodies (e.g. Coombs test), reticulocyte count and haptoglobin.

INTERACTIONS WITH OTHER MEDICINES
Immunoglobulin infusion may impair the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella for a period of at least six weeks and up to three months. After infusion of Intragam® 10, an interval of three months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to one year. Therefore patients receiving measles vaccine should have their antibody status checked. Additionally, immunoglobulins should not be administered for at least two weeks after these vaccines are given.

The interaction of Intragam® 10 with other medicines has not been established.

ADVERSE EFFECTS
Two clinical studies with Intragam® 10 were performed, one study of 19 patients with PID and one study of 19 patients with ITP.

Based on their pharmacological plausibility and as known class effects of IVIg products, adverse reactions reported in the studies are summarised and categorised according to the MedDRA System organ class and frequency in **Table 2** (very common (≥10% patients), or common (≥1% and <10% patients)).

Adverse events (AEs) reported by two or more patients (>10%) in the studies, ***irrespective of causal relationship to the product***, are presented in **Table 3**.

General effects associated with intravenous immunoglobulins
True hypersensitivity reactions to IVIg products, such as urticaria, angioedema, bronchospasm, or a sudden drop in blood pressure, have been observed in patients. In isolated cases immunoglobulins may cause anaphylactic shock, even when the patient has shown no known hypersensitivity to previous administration (see **PRECAUTIONS**). Should an anaphylactic reaction to Intragam® 10 develop, the infusion should be stopped immediately and appropriate treatment initiated.

Adverse reactions (such as chills, headache, fever, vomiting, nausea, arthralgia, changes in blood pressure or moderate lower back pain) or allergic-type reactions (such as flushing, pruritis, lethargy, restlessness, tachycardia, tingling, tissue swelling, wheezing or shortness of breath) may occur occasionally with the use of IVIg products.

Other general types of reactions that may occur include: malaise, abdominal pain, chest-tightness, facial flushing or pallor, erythema, hot sensations, respiratory difficulty, non-urticarial skin rash, cutaneous vasculitis, or infusion/injection site reactions (such as pain, swelling, erythema, pruritis or rash at the site).

Some patients may develop delayed adverse reactions to IVIg products such as: nausea, vomiting, chest pain, rigors, dizziness, aching legs or arthralgia. These adverse reactions occur after the infusion has stopped but usually within 24 hours.

Cases of reversible AMS (see **PRECAUTIONS**), isolated cases of reversible haemolytic anaemia/haemolysis (see **PRECAUTIONS**), and cases of transient cutaneous reactions, have been reported with IVIg treatment. Neutropenia has been reported in rare instances. Increase in serum creatinine level and/or acute renal failure (see **PRECAUTIONS**) have been observed.

Mild and moderate elevations of serum transaminases (AST, ALT, gamma GT) have been observed in a small number of patients given IVIg. Such changes were transient and not associated with the transmission of hepatitis.

Very rarely, thrombotic reactions such as myocardial infarction, stroke, pulmonary embolism and deep vein thromboses have been associated with IVIg treatment (see **PRECAUTIONS**).

Table 3: Adverse events occurring in two or more patients (>10%) in at least one of the clinical studies with Intragam® 10, *irrespective of causality*

MedDRA System organ class Preferred term	PID Patients N=19 n (%)	ITP Patients N=19 n (%)
Infections and infestations		
Upper respiratory tract infection	8 (42.1%)	0
Lower respiratory tract infection	7 (36.8%)	0
Gastroenteritis	5 (26.3%)	0
Sinusitis	5 (26.3%)	0
Viral infection	2 (10.5%)	0
Meningitis aseptic	0	2 (10.5%)
Nervous system disorder		
Headache	7 (36.8%)	14 (73.7%)
Lethargy	4 (21.1%)	2 (10.5%)
Dizziness	0	2 (10.5%)
Migraine	0	2 (10.5%)
Gastrointestinal disorders		
Nausea	3 (15.8%)	9 (47.4%)
Vomiting	0	6 (31.6%)
Diarrhoea	3 (15.8%)	1 (5.3%)
Musculoskeletal and connective tissue disorders		
Osteopenia	4 (21.1%)	0
Arthralgia	2 (10.5%)	3 (15.8%)
Myalgia	2 (10.5%)	0
Osteoporosis	2 (10.5%)	0
Musculoskeletal stiffness	0	2 (10.5%)
Pain in extremity	0	2 (10.5%)
General disorders and administration site conditions		
Fatigue	0	3 (15.8%)
Pyrexia	2 (10.5%)	1 (5.3%)
Infusion site pain	0	2 (10.5%)
Pain	2 (10.5%)	0
Respiratory, thoracic and mediastinal disorders		
Cough	4 (21.1%)	0
Injury, poisoning and procedural complications		
Animal bite	0	2 (10.5%)
Contusion	0	2 (10.5%)
Procedural pain	0	2 (10.5%)
Vascular disorders		
Hot flush	3 (15.8%)	0
Eye disorders		
Conjunctivitis	2 (10.5%)	0
Skin and subcutaneous tissue disorders		
Pruritus	2 (10.5%)	0

DOSAGE AND ADMINISTRATION

Dosage

The dosage recommendations are summarised in **Table 4***.

Administration

CAUTION: This product does not contain an antimicrobial preservative. It must, therefore, be used immediately after opening the bottle. Any unused solution should be discarded appropriately. Use in one patient on one occasion only. Do not use if the solution has been frozen.

If it appears to be turbid or to contain any sediment, it must not be used and the bottle should be returned unopened to the Australian Red Cross Blood Service.

Intragam® 10 should be administered through a standard intravenous infusion giving set. Allow the preparation to reach room temperature before use. Intragam® 10 should be administered separately from intravenous fluids (other than normal saline) or medications the patient might be receiving.

Intragam® 10 may be infused undiluted or diluted with up to 2 parts of 0.9% saline. The infusion should be commenced at the rate of 1 mL per minute. After 15 minutes the rate may be gradually increased to a maximum of 3 to 4 mL per minute over a further 15 minutes. Infusion rates higher than recommended may increase the incidence of headache. Consideration should be given to reducing the rate of infusion in patients naive to Intragam® 10, patients switching from an alternative IVIg, patients who have not received IVIg for a long time, elderly patients and in patients with pre-existing renal disease (see **PRECAUTIONS**).

OVERDOSE

Overdose with immunoglobulin products may lead to fluid overload and hyperviscosity, particularly in the elderly and in patients with renal impairment.

PRESENTATION AND STORAGE CONDITIONS

The following presentations in **Table 5** are registered for Intragam® 10.

Intragam® 10 is packaged in latex free materials. Store at 2°C to 8°C (Refrigerate. Do not freeze). Once removed from refrigeration, store below 25°C and use within 3 months. Protect from light.

Do not use after the expiry date.

NAME AND ADDRESS OF THE SPONSOR

CSL Behring (Australia) Pty Ltd
ABN 48 160 734 761
189–209 Camp Road
Broadmeadows VIC 3047
Australia

POISON SCHEDULE OF THE MEDICINE

S4

DISTRIBUTED BY

Australian Red Cross Blood Service

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

1 April 2011

DATE OF MOST RECENT AMENDMENT

17 July 2015

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Table 4: Dosage recommendations

Indication	Dose	Frequency of infusion
Replacement therapy†		
Primary or secondary immunodeficiency	0.2 to 0.8 g IgG/kg	Every 3 to 4 weeks to achieve IgG serum level of at least 5 g/L
Immunomodulatory therapy‡		
Idiopathic thrombocytopenic purpura	Maximum cumulative dose of 2 g IgG/kg	Over 2 to 5 days
Guillain-Barré Syndrome (GBS)	0.4 g IgG/kg	Daily for 5 days
Kawasaki disease	1.6 to 2 g IgG/kg or 2 g IgG/kg	In divided doses over 2 to 5 days in association with acetylsalicylic acid As a single dose in association with acetylsalicylic acid
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	Induction: 2 g IgG/kg	In divided doses over 2 to 5 days
	Maintenance: 0.4–1 g/kg	Every 2 to 6 weeks
Multifocal Motor Neuropathy (MMN)	Induction: 2 g IgG/kg	In divided doses over 2 to 5 days
	Maintenance: 0.4–2 g/kg	Every 2 to 6 weeks
Myasthenia Gravis (MG)	Prior to surgery or during myasthenic crisis Induction: 1–2 g IgG/kg	In divided doses over 2 to 5 days
	Maintenance: 0.4–1 g/kg	Every 4 to 6 weeks
Lambert-Eaton Myasthenic Syndrome (LEMS)	Induction: 2 g IgG/kg	In divided doses over 2 to 5 days
	Maintenance: 0.4–1 g/kg	Every 2 to 6 weeks
Stiff person syndrome	Induction: 2 g IgG/kg	In divided doses over 2 to 5 days
	Maintenance: 1–2 g/kg	Every 4 to 6 weeks

* The optimal dose and frequency of administration of Intragam® 10 must be determined for each patient.

† Adjustment of both dose and infusion interval is empirical and should be based on the patient's clinical state and the pre-infusion IgG level.

‡ Adjustment of both dose and infusion interval is empirical and should be based on the patient's clinical state.

Table 5: Presentations

Amount of IgG (g)	Volume of solution (mL)	Vial size (mL)
2.5	25	50
5	50	50
10	100	100
20	200	250

Note that not all presentations may be available.

Version: PI 7:00

Intragam® 10

Human Normal Immunoglobulin 10% (10 g/100 mL), solution for intravenous infusion.

Consumer Medicine Information

What is in this leaflet

This leaflet answers some common questions about Intragam® 10. It does not take the place of talking to your doctor. It does not contain all the available information about Intragam® 10.

All medicines have risks and benefits. Your doctor has weighed the benefits of you receiving Intragam® 10 against the possible risks.

If you have any concerns about receiving this medicine, ask your doctor. Follow your doctor's advice even if it is different from what this leaflet says.

Please read this leaflet carefully and keep it as you may need to read it again.

The information in this leaflet is subject to change. Please check with your doctor whether there is any new information about this medicine that you should know since you were last treated.

What Intragam® 10 is used for

Your medicine is Intragam® 10, a solution for intravenous infusion. Intragam® 10 contains human immunoglobulins and is manufactured from human plasma (the liquid component of blood) collected by the Australian Red Cross Blood Service. Immunoglobulins are also called antibodies and are a type of protein found in the blood. Immunoglobulins are produced by your body's immune system to fight infections caused by bacteria and viruses. If you do not have enough antibodies you may not be able to fight off diseases.

Your doctor may have prescribed Intragam® 10 for another reason. Ask your doctor if you have any questions about why Intragam® 10 has been prescribed for you.

Before you are given Intragam® 10

Tell your doctor if you have, or have had, any of the following medical conditions:

- allergy to human immunoglobulin products or to glycine. Some of the symptoms of an allergic reaction may include rash, itchiness, swelling of the lips and tongue, shortness of breath.
- allergies to any other medicines, or if you have ever had an allergic reaction to an injection
- a condition that causes low antibody levels in your blood (e.g. immunoglobulin A (IgA) deficiency, hypogammaglobulinaemia or agammaglobulinaemia with or without immunoglobulin A deficiency)
- a history of heart, or blood vessel disease, or blood clots, have thick blood, have been immobile for some time. Also tell the doctor what medicine you are using as some medicines, such as those that contain the hormone estrogen (for example, birth control pills), may increase your risk of developing a blood clot.
- high blood pressure
- diabetes
- kidney problems or kidney disease
- a history of severe headaches or migraine
- any other medical conditions.

It is also important that you tell your doctor if you:

- have blood group A, B or AB
- are pregnant, intending to become pregnant or are breast-feeding
- have had any vaccination within the last two weeks
- are dehydrated
- are taking any other medicines, including herbal or complementary medicines.

How Intragam® 10 is given

Your doctor will determine the dose(s) of Intragam® 10 that you will receive. Intragam® 10 is administered as an intravenous infusion (an injection given slowly into a vein).

While you are taking Intragam® 10

This medicine is not expected to affect your ability to drive a car or operate machinery.

Please inform your doctor if you are planning to have a vaccination. Intragam® 10 may impair the effect of some virus vaccines such as measles, mumps, rubella and chicken pox for a period of at least 6 weeks, and up to 3 months. After receiving this medicine, a period of 3 months should be allowed before vaccination with some virus vaccines. In the case of measles vaccine, this effect may last for up to 1 year, so if you are going to receive a measles vaccine you should have your measles antibody status checked.

Things you must do:

- If you experience any of the effects listed in the side effects section of this leaflet or any other abnormal signs after treatment, tell your doctor immediately.
- If you are about to be started on any new medicine, remind your doctor that you have been given Intragam® 10. Tell any other doctors, dentists, and pharmacists who treat you that you have been given this medicine.
- If you are about to have any blood tests, tell your doctor that you have been given this medicine. It may interfere with the results of some tests.

Things to be careful of:

- If having an infusion makes you feel light headed, dizzy or faint, be careful when getting up from a sitting or lying position. Getting up slowly may help.
- Some patients may develop delayed reactions to Intragam® 10. These reactions occur after the infusion has stopped but usually within 24 hours.

Side effects

Tell your doctor as soon as possible if you do not feel well while you are being given Intragam® 10, even if you do not think how you feel is connected with your medicine.

Along with their intended effects, medicines occasionally cause unwanted effects (side effects) in some people, some of which are serious. Side effects are more common with the first dose of Intragam® 10. Different people may react differently to similar doses of the same product. This applies to Intragam® 10. Most minor side effects are related to the rate of infusion and disappear when the rate is slowed down.

If you are over 65 years you may have an increased chance of experiencing a side effect.

Do not be alarmed by the following lists of possible side effects. You may not experience any of them. If you have any questions, ask your doctor.

Tell your doctor if you notice any of the following:

This list includes the more common side effects of Intragam® 10. They are usually mild and short-lived.

- headache
- nausea
- lethargy
- pain in a joint
- vomiting
- pain in a muscle
- infusion site pain
- fever
- dizziness
- paleness of skin
- migraine
- musculoskeletal stiffness
- constipation
- itchiness
- pain in the abdomen
- rash.

If you experience any of the following, tell your doctor immediately or go to Accident and Emergency at your nearest hospital:

- severe headache
- neck stiffness
- drowsiness
- fever
- inability to stand bright light
- painful eye movements
- tingling, numbness or weakness on one side of the body
- pain/tenderness, swelling/discolouration of an arm or leg
- shortness of breath
- chest pain
- skin becoming yellow
- dark urine.

This list includes very serious side effects. You may need urgent medical attention or hospitalisation if you experience any of these side effects.

Other side effects not listed above may also occur in some people. Some of these side effects may not cause symptoms and may only be found when your doctor does tests from time to time to check your progress.

Important information about some of the ingredients in Intragam® 10

When medicines are made from human blood or plasma, processes are used to prevent infections being passed from the blood/plasma donor to the person receiving the medicine. These processes include careful selection of the people who donate blood and plasma to make sure that those who might be carrying infections are excluded. In addition, each donation and pools of donations are tested for indicators of virus/virus infection(s).

Manufacturers of these medicines also include steps in the processing of blood or plasma that inactivate or remove viruses. Despite these processes, when medicines are prepared from human blood or plasma, the possibility of passing on an infection cannot be totally ruled out. Unknown or new viruses or other types of infection could also be passed on.

However, the measures taken in the manufacture of this medicine are considered effective for enveloped viruses such as human immunodeficiency virus, hepatitis B virus, and hepatitis C virus, and for the non-enveloped viruses hepatitis A and B19 virus (B19V).

There is reassuring clinical experience regarding the lack of hepatitis A or B19V infections with immunoglobulins. The antibodies which are in Intragam® 10 may make an important contribution to limiting the possibility an infection could also be passed on.

Please discuss the risks and benefits of this product with your doctor.

If you receive too much (overdose)

As Intragam® 10 is given to you under the supervision of your doctor or trained medical professional, it is very unlikely that you will receive an overdose. If you experience any side-effects, tell your doctor immediately.

Further information

Intragam® 10 can only be obtained on a doctor's prescription. This leaflet does not contain all the available information about Intragam® 10. If you require further information about Intragam® 10 and your treatment generally, or if you have any questions or are not sure about something in this leaflet, consult your doctor.

Storing Intragam® 10

You will normally be given this medicine in hospital. You will probably not need to keep any bottles of Intragam® 10. However, if you have to keep this medicine at home it should be stored refrigerated (2°C to 8°C) but not frozen. Once removed from refrigeration, store below 25°C and use within 3 months.

It should be protected from light and should not be used after the expiry date shown on the label.

Product description

What it looks like

Intragam® 10 is a clear colourless solution provided in glass vials.

Ingredients

In each vial of Intragam® 10 is a sterile solution containing 10% plasma proteins of which at least 98% are immunoglobulins. Intragam® 10 does not contain any preservatives. Intragam® 10 is packaged in latex free materials.

The amount of active ingredient in each vial is shown in the table below:

Amount of Immunoglobulin (g)	Volume in vial (mL)
2.5	25
5	50
10	100
20	200

Manufacturer

Intragam® 10 is manufactured in Australia by:

CSL Behring (Australia) Pty Ltd
ABN 48 160 734 761
189–209 Camp Road
Broadmeadows VIC 3047
Australia

Distributor

Australian Red Cross Blood Service

Date of most recent amendment

July 2015

Australian Register Numbers

25 mL: AUST R 162486
50 mL: AUST R 162487
100 mL: AUST R 162488
200 mL: AUST R 162489

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