IMMUNE GLOBULIN INTRAVENOUS (HUMAN) (Systemic)

Introduction

VA CLASSIFICATION (Primary/Secondary)¾IM402/AM900; BL900; CV900; XX000
Commonly used brand name(s):Gamimune N 10%; Gamimune N 10% S/D; Gamimune N 5%; Gamimune N 5% S/D; Gammagard S/D; Gammagard S/D 0.5 g; Gammar-P IV; Iveegam; Polygam S/D; Sandoglobulin; Venoglobulin-I; Venoglobulin-S.
Other commonly used names are IGIV and IVIG .

Note: For a listing of dosage forms and brand names by country availability, see Dosage Forms section(s).

Category

Immunizing agent (passive); platelet count stimulator (systemic); anti-Kawasaki disease (systemic); antibacterial (systemic); antiviral (systemic); antipolyneuropathy agent.

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Note: The Food and Drug Administration (FDA) has approved specific brands of immune globulin intravenous (IGIV) preparations for specific indications 5.

However, although IGIV preparations vary slightly, they are generally thought to be therapeutically equivalent and usually are selected on the basis of cost and convenience 24, 52, 54.

Most physicians use IGIV preparations interchangeably (see Pharmacology/Pharmacokinetics) 20, 24, 52.

Immunodeficiency, primary (treatment)¾IGIV is indicated for the treatment of patients with primary immunodeficiency syndromes, such as congenital agammaglobulinemia (X-linked agammaglobulinemia), hypogammaglobulinemia, common variable immunodeficiency, X-linked immunodeficiency with hyperimmunoglobulin M, severe combined immunodeficiency, and Wiskott-Aldrich syndrome, to replace or boost immunoglobulin G (IgG) 1, 2, 3, 4, 5.

The beneficial effect of IGIV in the prophylactic management of these patients has been well documented 1, 6, 48.

The use of IGIV in IgG subclass deficiencies remains controversial and at present is recommended only for those patients who also demonstrate a deficiency in the ability to form antibodies against a variety of polysaccharide and protein antigens 1.

Thrombocytopenic purpura, idiopathic (treatment)¾IGIV is indicated for the treatment of idiopathic thrombocytopenic purpura (ITP) when a rapid rise in the platelet count is required, such as prior to surgery, to control excessive bleeding, or to defer or avoid splenectomy 1, 5, 7, 8.

Not all patients will respond, however, and, if the platelet increment does occur, it may be transient. This treatment should not be considered curative, although remissions have occurred 20.

Kawasaki disease (treatment adjunct)¾IGIV in conjunction with aspirin is indicated for the treatment of Kawasaki disease 1, 5, 6.

Treatment with IGIV within the first 10 days of illness significantly reduces the prevalence of coronary artery abnormalities 9.

In addition, IGIV has been shown to decrease the prevalence of giant coronary artery aneurysms (i.e., those with an internal diameter of > 8 mm) that are associated with the highest morbidity and mortality rates in Kawasaki disease 9.

Leukemia, chronic lymphocytic (treatment adjunct)¾IGIV is indicated for the prevention of recurrent bacterial infections in patients with hypogammaglobulinemia associated with B-cell chronic lymphocytic leukemia (CLL) 1, 5.

Transplantation, bone marrow (treatment adjunct)¾IGIV is indicated to prevent the risk of acute graft-versus-host disease, associated interstitial pneumonia (infectious or idiopathic), and infections (e.g., cytomegalovirus infections, varicella-zoster virus infection, and recurrent bacterial infection 20) after bone marrow transplantation (BMT) in patients 20 years of age or older in the first 100 days after transplantation 1, 5.

It is not indicated in BMT patients younger than 20 years of age, nor is it recommended for autologous transplants, because the benefit in these cases is slight 1.

Human immunodeficiency virus (HIV) infection, pediatric (treatment) ¾IGIV is indicated for use in HIV-infected children to reduce the risk of serious bacterial infections 1, 5 ; however, there is no evidence to suggest that IGIV confers incremental benefit to antiretroviral therapy and prophylactic antibiotics administered according to current standards of practice 51.

In children with advanced HIV disease who are receiving zidovudine, IGIV decreases the risk of serious bacterial infections 5.

However, this benefit is apparent only in children who are not receiving co-trimoxazole as prophylaxis 5 and for children with a CD4 count of greater than 200 to 400 56.

[Dermatomyositis (treatment)] *¾IGIV is used as a second-line agent in the treatment of dermatomyositis 2, 10.

Corticosteroids are the first-line agents in the treatment of dermatomyositis 2, 56.

Dermatomyositis is a clinically distinct myopathy characterized by rash and a complement-mediated microangiopathy that results in the destruction of muscle fibers 10.

In some patients the condition becomes resistant and causes severe physical disabilities 10.

High-dose IGIV is a safe and effective treatment for refractory dermatomyositis 10, 11.

However, because dermatomyositis responds to corticosteroids, IGIV therapy should be reserved for corticosteroid-resistant patients or patients in whom corticosteroids are contraindicated 2, 56.

[Guillain-Barre syndrome (treatment)] *¾IGIV is used in the treatment of Guillain-Barre syndrome (GBS) 2, 12, 13, 14, 54.

IGIV is the treatment of choice for adult patients with GBS, provided that they are so severely affected that they at least require aid to walk, that the disorder is diagnosed during the first 2 weeks of the illness, and that there are no contraindications to IGIV 15.

[Hyperimmunoglobulinemia E syndrome (treatment)] *¾IGIV is used in the treatment of hyperimmunoglobulinemia E syndrome 2, 17.

Hyperimmunoglobulinemia E syndrome is an inflammatory skin disease characterized by severe eczema, recurrent staphyloccocal infections of the skin and sinopulmonary tract, cold subcutaneous abscesses, and high serum immunoglobulin E (IgE) levels 17.

IGIV is effective in the treatment of severe eczema in patients with hyperimmunoglobulinemia E syndrome and atopic dermatitis 17.

IGIV also decreases enhanced IgE production both in vivo and in vitro17.

[Lambert-Eaton myasthenic syndrome (treatment)] *¾IGIV is used in the treatment of Lambert-Eaton myasthenic syndrome 18.

The Lambert-Eaton myasthenic syndrome is a rare autoantibody-mediated disorder of neuromuscular transmission in which a reduction in the calcium-dependent release of acetylcholine from motor nerve terminals causes fatigable muscle weakness 18.

Calcium-channel antibodies may be implicated in the reduction of functional calcium channels that underlies the disorder, and antibodies to P/Q-type calcium channels can be detected in the serum of 85 to 95% of patients 18.

About 60% of patients with Lambert-Eaton myasthenic syndrome also have small cell lung cancer 18.

Specific tumor therapy often is followed by clinical improvement, probably because tumor calcium-channel determinants are provoking the autoantibody response 18.

[Multifocal motor neuropathy (treatment)] *¾IGIV is indicated as a second-line agent in the treatment of multifocal motor neuropathy (MMN) 60, 61, 62, 63, 64, 65, 66, 67, 68, 69.

MMN is immune-mediated and treatable. It produces weakness that is typically distal and asymmetric, involves the arms early in the course of disease, and progresses slowly. Electrophysiologic abnormalities often include evidence of demyelination, especially focal conduction block, selectively on motor axons. High titers of serum immunoglobulin M (IgM) binding to GM1 ganglioside, alone or in a membrane environment, occur in 80 to 90% of patients with MMN. Treatments of MMN that commonly produce increased strength include IGIV and cyclophosphamide. Patients with MMN who had poor responses to other treatment regimens may show significant improvement after treatment with IGIV 60, 61, 62, 63, 64, 65, 66, 67, 68, 69.

[Multiple sclerosis, relapsing-remitting (treatment)] *¾IGIV is used as a second-line agent in the treatment of relapsing-remitting multiple sclerosis 23.

Multiple sclerosis is the most common demyelinating disorder of the central nervous system and is characterized by repeated episodes of neurological dysfunction with variable remission 23.

Monthly IGIV treatment is an effective and well-tolerated treatment for patients with relapsing-remitting multiple sclerosis 23.

[Neonates, high-risk, preterm, low-birth-weight, infections in (prophylaxis and treatment adjunct)] *¾IGIV is used for the prophylaxis of, and as a treatment adjunct in, infections in some high-risk, preterm, low-birth-weight neonates 19.

Studies published before 1990 suggested that prophylactic IGIV reduced nosocomial infections in low-birth-weight infants 19.

However, these studies enrolled small numbers of patients; employed varied designs, preparations, and doses; and included diverse study populations 19.

The National Institute of Child Health and Human Development (NICHHD) Neonatal Research Network therefore performed a prospective, multicenter, randomized trial to test the hypothesis that the intravenous administration of immune globulin to infants with birth weights between 501 and 1500 grams would reduce the incidence of nosocomial infections 19.

In this trial, the repeated prophylactic administration of IGIV failed to reduce the incidence of nosocomial infections significantly in premature infants weighing 501 to 1500 grams at birth 19.

Furthermore, there were no significant differences in morbidity, mortality, or the duration of hospitalization between infants given IGIV and infants given no infusion or an infusion and placebo 19.

[Parvovirus B19 infection, chronic (treatment)] *¾IGIV is used in the treatment of chronic parvovirus B19 infection and severe anemia associated with bone marrow suppression 22, 42, 50, 54, 58.

Parvovirus B19 can cause aplastic anemia in sickle cell anemia and in immunodeficiency patients 22, 54.

High-dose IGIV can cure parvovirus B19 infection with reversal of anemia 22, 54.

[Polyneuropathies, chronic inflammatory demyelinating (treatment)] *¾IGIV should be considered first-line treatment for chronic inflammatory demyelinating polyneuropathies 2, 16.

IGIV is used either alone or following therapeutic plasma exchange to prolong its effect 2.

IGIV is considered easier to use than repeated therapeutic plasma exchange and to have fewer complications than long-term glucocorticoid therapy 2.

* Not included in Canadian product labeling.

Pharmacology/Pharmacokinetics

Note: Although immune globulin intravenous (IGIV) preparations vary slightly, they are generally thought to be therapeutically equivalent and are therefore usually selected on the basis of cost and convenience 24, 52.

There are minor immunoglobulin A (IgA) and immunoglobulin G (IgG) subclass differences 24, 52.

Antibody titers also may vary from lot to lot and among different IGIV preparations 24, 52.

IGIV preparations with low IgA content should be used to minimize reactions in patients with hypogammaglobulinemia and concurrent IgA deficiency or when anti-IgA antibodies are present in a recipient (see Side/Adverse Effects) 24, 52.

Physicochemical characteristics:

Source¾IGIV preparations consist of concentrated immunoglobulins (Ig), principally IgG, with a subclass distribution that largely reflects that of IgG in normal human serum 1, 25, 26.

Pooled serum is collected from large numbers of donors, ranging from 1000 to more than 50,000, depending on the manufacturer 1.

All U.S. IGIV manufacturers use Cohn-Oncley ethanol fractionation (fraction II) as an initial step in the preparation of immunoglobulin 1.

Subsequent steps differ among preparations and include ion exchange chromatography, ultrafiltration, enzymatic digestion, manipulation of the pH and salt concentration, and organic solvent-detergent partitioning 1.

These procedures remove protein and other contaminants, minimize the concentration of IgG aggregates, and deactivate viral contaminants such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) 1.

Donor serum samples are screened for antibodies to HIV, HCV, hepatitis B surface antigen, and elevated levels of alanine aminotransferase (ALT [SGPT]) 1.

As a consequence of the 1994 HCV outbreak, the Food and Drug Administration (FDA) requires additional testing to detect HCV RNA by polymerase chain reaction (PCR) in all immunoglobulin preparations, including IGIV [1, 27, 28].

Although the presence of HCV RNA in IGIV preparations may not necessarily correlate with infectivity, these measures should help prevent future transmission of HCV by IGIV preparations [27].

Mechanism of action/Effect:

The mechanisms by which IGIV exerts a therapeutic effect in many disease states are unknown, but they are probably various immunomodulatory actions operating alone or in combination [1, 2, 25, 29, 30].

Blockade of the Fc receptor on macrophages on the reticuloendothelial system in patients with immune cytopenia (e.g., idiopathic thrombocytopenic purpura [ITP]), appears to account for the major immediate effects of IGIV [29].

The more long-term effects of IGIV can be attributed to the immunomodulatory effects of IGIV on T cells and macrophages, particularly cytokine synthesis, and B-cell immune function and its regulatory action on the membrane-damaging components of the complement system [29].

In contrast, the effects of IGIV in Kawasaki disease and perhaps other diseases may be caused by the presence of specific antibodies in the IGIV that are capable of neutralizing bacterial or even viral toxins that can have profound effects on the host's immune and inflammatory systems [29].

Undoubtedly no single mechanism accounts for all of the immune modulating effects of IGIV in these inflammatory/autoimmune processes [29].

Distribution:

After an intravenous infusion of IGIV 2 grams per kg of body weight, the patient's serum IgG level increases fivefold and then declines by 50% in 72 hours before returning, in 21 to 28 days, to the pretreatment level [2].

The marked initial decrease reflects extravascular redistribution [2].

The IgG in the infusion easily enters the cerebrospinal fluid (CSF) [2].

During the first 48 hours of the infusion, when the serum IgG level is high, the concentration of IgG in the CSF increases as much as twofold, but it returns to normal within a week [2].

Biotransformation:

During their circulating life span, IgG antibodies repeatedly exit and enter the vascular compartment [30].

Most antibodies never encounter their specific target antigen and are eventually removed from the circulation and degraded at an unknown site [30].

The rate of IGIV degradation is determined by the Fc region and by the IGIV concentration, so that degradation is accelerated in hypergammaglobulinemia and reduced in hypogammaglobulinemia 30.

Half-life:

The half-life of most IGIV preparations is 18 to 32 days, similar to that of native IgG 31.

The half-life of IGIV in neonates is similar to that in adults 31.

There is, however, considerable individual variability, which reflects several factors including the immunoglobulin level before infusion, the peak immunoglobulin level after infusion, the presence of infection or burns, the reliability in determining immunoglobulin levels, and other factors 31.

Precautions to Consider

Pregnancy/Reproduction

Pregnancy¾Studies have not been done in humans 32, 33.

However, intact immune globulins cross the placenta from maternal circulation increasingly after 30 weeks of gestation 33.

IGIV should be administered to pregnant women only if clearly needed 3, 4, 7, 8, 34.

In cases of maternal idiopathic thrombocytopenic purpura (ITP) where immune globulin intravenous (IGIV) was administered to the mother prior to delivery, the platelet response and clinical effect were similar in the mother and neonate 33.

Studies have not been done in animals 4, 8, 32, 33.

FDA Pregnancy Category C 7, 32, 33.

Breast-feeding

It is not known whether IGIV is distributed into breast milk. However, problems in humans have not been documented.

Pediatrics

Appropriate studies on the relationship of age to the effects of IGIV have not been performed in the pediatric population 33.

However, administration of high doses of IGIV to children with ITP did not cause any pediatrics-specific problems 33.

Geriatrics

Appropriate studies on the relationship of age to the effects of IGIV have not been performed in the geriatric population. However, no geriatrics-specific problems have been documented to date.

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)¾not necessarily inclusive (>> = major clinical significance):
>> Live virus vaccines

(live virus vaccines given parenterally can have diminished immunogenicity when given shortly before or during a period of several months after receipt of IGIV; high doses of IGIV have been demonstrated to inhibit the response to measles vaccine for a prolonged period; the duration of inhibition varies directly with the dose of IGIV administered; inhibition of immune response to rubella, while of shorter duration, also has been demonstrated; the appropriate suggested interval between IGIV administration and measles vaccination is 8 to 11 months, depending on the dose of IGIV administered 41)
(if IGIV must be given within 14 days after the administration of measles or measles-containing vaccines, these vaccines should be administered again after the recommended interval unless serologic testing indicates immunity, i.e., adequate serum antibodies were produced 41)
(the effect of administration of IGIV on the antibody response to varicella vaccine is not known; because of potential inhibition of the response, however, varicella vaccine should not be administered for at least 5 months after receipt of an IGIV preparation; in addition, IGIV preparations, if possible, should not be administered for 3 weeks after vaccination; if IGIV is given in this interval, the vaccinee either should be revaccinated 5 months later or tested for varicella immunity at that time and revaccinated if seronegative 41)
(administration of IGIV does not interfere with the antibody response to oral polio vaccine [OPV] given as a booster dose to young adults who already had received primary immunization or to yellow fever vaccination; these vaccines can be administered simultaneously with IGIV, such as to travelers whose departure is imminent 41)
(in contrast to live virus vaccines, administration of IGIV preparations has not been demonstrated to cause significant inhibition of the immune responses to inactivated vaccines and toxoids 41)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)¾ not necessarily inclusive (>> = major clinical significance).
Except under special circumstances, this medication should not be used when the following medical problems exist

>> Anaphylactic reaction to IGIV

>> Immunoglobulin A (IgA) deficiencies, selective, in patients who have known antibody to IgA

(the use of IGIV preparations should be avoided in patients with known IgA deficiency, in whom anaphylaxis is more common, and in the presence of renal failure, which may be exacerbated 14,

35 ; however, if a decision is made to administer IGIV, preparations that contain only small amounts of IgA are recommended 2.

The first infusion should be administered in the hospital under medical supervision 35)

Risk-benefit should be considered when the following medical problems exist

>> Cardiac function impairment in seriously ill patients

(these patients may be at increased risk for vasomotor or cardiac complications, such as elevated blood pressure and cardiac failure 42)

Diabetes mellitus

(IGIV preparations may cause a temporary increase in serum glucose in patients with diabetes 35)

>> Renal failure, acute

(it has been reported that patients experienced acute renal failure after receiving IGIV, particularly patients with compromised renal function; preliminary evidence suggests that IGIV preparations containing sucrose may present a greater risk for this complication [see General Dosing Information] 32, 49)

Sensitivity to immune globulins

(patients allergic to other immune globulins, either intramuscular or intravenous, may be allergic to IGIV also 42)

Sensitivity to maltose or sucrose

(these ingredients may be present in some IGIV products 32, 33, 35, 36)

Patient monitoring

The following may be especially important in patient monitoring (other tests may be warranted in some patients, depending on condition; >> = major clinical significance):
Blood urea nitrogen (BUN) and

Creatinine, serum and

Urine output

(determination recommended prior to initiation of therapy, particularly in patients judged to have a potential increased risk for developing acute renal failure, and again at appropriate intervals 49)

Side/Adverse Effects

Note: Immune globulin intravenous (IGIV) is a pooled plasma product, collected from large numbers of donors 1.

Although potential blood donors are screened for antibodies to hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV), the risks of viral transmission cannot be ruled out 59.

The reported incidence of adverse effects associated with the administration of IGIV ranges from 1 to 15%, but usually is less than 5% 42.

Most of these reactions are mild and self-limited 42.

Severe reactions occur very infrequently and usually do not contraindicate further IGIV therapy 24, 35, 42.

Adverse effects tend to be associated with rapid infusion rates in patients with concurrent acute infections, in previously untreated patients, or when significant time between infusions has transpired (more than 6-week intervals) 24.

Immediate minor reactions can be avoided or diminished by reducing either the rate or the volume of infusion 24, 35, 42.

A few investigators have given high concentrations (9% and 12% solutions) infused rapidly over a period of 20 to 40 minutes 24.

This rapid rate can be tolerated by some patients; however, this should not be performed except by experts equipped to manage adverse reactions 24.

Therapy with IGIV increases serum viscosity 2.

In patients with high normal serum viscosity in conditions such as cryoglobulinemia, hypercholesterolemia, or hypergammaglobulinemia, viscosity increases even further 2.

Serum viscosity greater than 2.5 centipoise (normal 1.2 to 1.8 centipoise) increases the risk for thromboembolic events, which probably accounts for rare cases of stroke or pulmonary embolism after IGIV therapy 2.

Therapy with IGIV also can induce a hyperviscosity syndrome in children with HIV infection who have high pretreatment levels of serum immunoglobulins 2.

Reversible cerebral vasospasm has occurred in a patient treated with IGIV 2.

In patients with a history of migraine headache, IGIV therapy may trigger a migraine attack, which sometimes can be prevented by propranolol prophylaxis 2.

The incidence of aseptic meningitis is also high in these patients 2.

Therapy with IGIV was associated with stroke in a young woman with a history of migraine 2.

Aseptic meningitis develops in as many as 10% of patients treated with IGIV and is unrelated to the commercial source of the IGIV product, the infusion rate, or the underlying disease 2.

Prophylaxis with intravenous corticosteroids often is ineffective 2.

The symptoms respond to strong analgesia and subside in 24 to 48 hours 2.

Additional diagnostic testing rarely is necessary 2.

Acute renal tubular necrosis, usually reversible, occurs rarely following IGIV therapy in patients who have pre-existing kidney disease and volume depletion, especially elderly, diabetic, or poorly hydrated patients 2.

This complication has been associated with a high concentration of sucrose in some IGIV preparations 2.

Osmotic tubular nephrosis, caused by intravenous solutions containing a concentration of hypertonic sucrose similar to that in IGIV preparations, is also a rare reaction; diluting the IGIV preparation and slowing the rate of infusion minimize the risk for this event 2.

After IGIV therapy, the erythrocyte sedimentation rate increases sixfold or more, probably as a result of enhanced rouleaux formation and reduced surface area caused by the infused gammaglobulin 2.

The increase can persist for 2 to 3 weeks and should not be considered a sign of developing vasculitis 2.

Since IGIV preparations were first introduced in 1981, the Food and Drug Administration (FDA) has received over 114 adverse effect reports of renal dysfunction and/or acute renal failure associated with the administration of these products 49.

Although acute renal failure was successfully managed in the majority of cases, deaths were reported in 17 patients 49.

Many of the patients who died had serious underlying conditions 49.

Preliminary evidence suggests that IGIV preparations containing sucrose may present a greater risk for this complication (see General Dosing Information) 49.

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)¾not necessarily inclusive:
Those indicating need for medical attention

Incidence more frequent

Dyspnea troubled breathing); tachycardia fast or pounding heartbeat); 42

Incidence less frequent

Burning sensation in head; cyanosis bluish coloring of lips or nail beds); faintness or lightheadedness; fatigue unusual tiredness or weakness); wheezing
Incidence rare

Anaphylactic reaction difficulty in breathing or swallowing); hives); itching, especially of feet or hands); reddening of skin, especially around ears); swelling of eyes, face, or inside of nose); unusual tiredness or weakness, sudden and severe); 2, 14, 24, 42

Note: A severe anaphylactic reaction may occur in patients who have a serious deficiency of immunoglobulin A (IgA) associated with anti-IgE or anti-IgG antibodies against IgA, which react with the IgA in the IGIV preparation 2, 31, 37.

The reaction is rare and occurs primarily in patients with common variable immunodeficiency 1, 2.

The use of IGIV preparations should be avoided in patients with known IgA deficiency, in whom anaphylaxis is more common, and in the presence of renal failure, which may be exacerbated 14.

However, if a decision is made to administer IGIV, preparations that contain only small amounts of IgA are recommended for treating patients with low serum IgA levels 2, 54.

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Arthralgia 24 (joint pain); backache or pain; headache 24, 33; malaise 14 (general feeling of discomfort or illness); myalgia 24 (muscle pain); nausea 14, 24, 31; vomiting 3, 14, 37, 42
Incidence less frequent

Chest or hip pain 31; leg cramps; redness, rash, or pain at injection site; urticaria (hives)

Patient Consultation

As an aid to patient consultation, refer to Advice for the Patient, Immune Globulin Intravenous (Human) (Systemic) .
In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):
Before using this medication

>> Conditions affecting use, especially:

Sensitivity to intramuscular or intravenous immune globulins
Other medications, especially live virus vaccines
Other medical problems, especially acute renal failure, anaphylactic reaction to IGIV, cardiac function impairment in seriously ill patients, or selective IgA deficiencies
Proper use of this medication

Waiting at least 2 to 3 weeks after receiving live virus vaccines before receiving IGIV, depending on the vaccine received

Waiting at least 5 to 11 months after receiving IGIV before receiving live virus vaccines, depending on the vaccine to be received

>> Proper dosing
Side/adverse effects

Signs of potential side effects, especially dyspnea, tachycardia, burning sensation in head, cyanosis, faintness or lightheadedness, fatigue, wheezing, and anaphylactic reaction

General Dosing Information

Anaphylactic reactions may occur in patients with a history of prior systemic allergic reactions or seizures following administration of human immunoglobulin preparations 2.

Very rarely, an anaphylactoid reaction may occur in patients with no prior history of severe allergic reaction to human immunoglobulin (Ig) preparations 2.

Patients previously sensitized to certain antigens, most commonly immunoglobulin A (IgA), may be at risk for immediate anaphylactoid and hypersensitivity reactions 2.

Therefore, appropriate precautions should be taken prior to immune globulin intravenous (IGIV) injection to prevent allergic or any other unwanted reactions 2.

Precautions should include review of the patient's history regarding possible sensitivity and the ready availability of 1:1000 epinephrine injection and other appropriate agents used for control of immediate allergic reactions 2, 42.

In an effort to reduce the risk of acute renal failure and based on data that currently are available, the Food and Drug Administration (FDA) recommends that the following precautions be taken when considering administration of IGIV preparations 49 :
· Patients should be adequately hydrated prior to the initiation of the infusion of IGIV 49.

· Particular caution should be exercised in the administration of IGIV preparations in patients at increased risk for developing acute renal failure 21, 49.

Such patients include, but are not limited to, those with:
¾Any degree of pre-existing renal insufficiency 21, 49.

¾Diabetes mellitus 21, 49.

¾Age greater than 65 21, 49.

¾Volume depletion 21, 49.

¾Paraproteinemia sepsis 21, 49.

¾Concomitant nephrotoxic drugs 21, 49.

¾For patients at increased risk, physicians should carefully weigh the potential benefits of administering sucrose-containing IGIV preparations against the risks of causing renal damage 49.

¾The recommended dose should not be exceeded 49.

Reduction in dose, concentration, and/or rate of administration in patients at risk of acute renal failure has been proposed in order to reduce the risk of acute renal failure 49.

Because no prospective data are presently available to identify a maximal safe dose, concentration, or rate of infusion for IGIV preparations for patients at risk for acute renal failure, the FDA recommends that, for such patients, prescribers reconstitute/dilute the product in such a manner as to produce both the minimum concentration and rate of infusion practicable 49.

For sucrose-containing IGIV preparations a maximum infusion rate of 3 mg per kg of body weight per minute should not be exceeded 49.

¾Renal function, including urine output, blood urea nitrogen (BUN), and serum creatinine, should be assessed prior to infusion of IGIV, particularly in patients judged to have a potential increased risk for developing acute renal failure, and again at appropriate intervals 49.

If renal function deteriorates, discontinuation of IGIV should be considered 49.

The dosing regimen for IGIV in patients with primary immunodeficiencies is not standardized, and treatment is tailored to the needs of the individual based on clinical response and trough immunoglobulin G (IgG) levels 1, 42.

Although trough IgG levels of greater than 500 mg/dL appear beneficial in the majority of patients, the minimum serum concentration necessary for protection has not been established 1, 42.

Monthly doses of at least 150 mg per kg of body weight (mg/kg) are recommended, and most patients receive 200 to 400 mg/kg every 3 to 4 weeks 1, 42.

However, comparative studies of dose, dosing schedules, and product selection in patients with primary immunodeficiencies have not been conducted 1.

At present there are no data to suggest that clinically significant differences exist among IGIV preparations commercially available in the U.S., and thus it is reasonable to assume that they are therapeutically interchangeable 1.

Idiopathic thrombocytopenic purpura (ITP) is a disorder in which antiplatelet autoantibodies cause the destruction of platelets, resulting in thrombocytopenia 38.

In children, ITP tends to be acute and short-lived, with only supportive management required 38.

However, in many adults the disorder is chronic and often requires medical therapy or splenectomy 38.

Treatment with high-dose IGIV causes a transient rise in the platelet count in both children and adults with ITP 20, 38.

Although there is evidence to suggest efficacy in ITP, many questions remain regarding the use of IGIV 1.

Some patients do not respond to therapy, and the treatment is not curative 1, 38.

A study comparing high-dose oral methylprednisolone with IGIV found no difference in the response of the platelet counts among the groups and concluded that these two therapies are equally effective in childhood ITP 1.

It was suggested that the choice of treatment in childhood ITP be based on consideration of cost as well as on therapy-related risks 1.

Kawasaki disease represents one of the few conditions for which efficacy of IGIV has been demonstrated in carefully designed, prospective, controlled trials 1.

When administered in conjunction with aspirin within 10 days of the onset of disease, IGIV resulted in a 65 to 78% decrease in the incidence of coronary artery abnormalities compared with treatment with aspirin alone 1.

The recommended dosage regimen is a single 2 gram/kg of body weight dose 1.

Because all studies of IGIV in Kawasaki disease involved concurrent administration of aspirin, the treatment regimen should include oral aspirin as well 1, 56.

In hypogammaglobulinemic patients with chronic lymphocytic leukemia (CLL), IGIV at the recommended dosage of 400 mg/kg of body weight every 3 to 4 weeks has been shown to reduce bacterial infections significantly 1.

However, treatment is costly and does not alter overall mortality 1.

The benefit of IGIV in the prevention of bacterial infections in human immunodeficiency virus (HIV)-infected children has been demonstrated in several trials 42.

IGIV can delay the time to development of bacterial infections and decrease the frequency of hospitalizations in infants and children with CD4+ T-lymphocyte counts 200/mm 3 or higher, but it does not affect survival 42.

Accordingly, the Working Group on Antiretroviral Therapy of the National Pediatric HIV Resource Center has recommended IGIV every 4 weeks for children with HIV-infection, including:

· Those with hypogammaglobulinemia, i.e., serum IgG concentration less than 250 mg/dL 42.

· Those with recurrent serious bacterial infections, i.e., defined as two or more infections such as bacteremia, meningitis, or pneumonia in a 1-year period 42.

· Those who fail to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine 42.

· Those living in areas where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live 42.

IGIV is recommended for intravenous administration only 35.

The intramuscular route has not been evaluated for this medication and is not recommended 35.

For some patients, intravenous administration of IGIV is not feasible because of poor venous access, severe side effects, or rapid IgG catabolism 53.

Clinical studies demonstrated that the slow subcutaneous infusion of IGIV is a suitable alternative in these patients 53.

The IgG concentration area under the curve after subcutaneous IGIV is equivalent to that of intravenous administration; however, peak serum levels usually are not obtained for 4 days 53.

This slow release into the blood stream is advantageous when there has been prior anaphylaxis, aseptic meningitis, or rapid IgG catabolism 53.

Subcutaneous IGIV permits selective patients to continue immunoglobulin therapy in a safe and effective fashion 53.

The infusion of IGIV should be at approximately room temperature for administration 32, 35.

Diluents are product-specific. Only the specific diluent indicated by each manufacturer should be used for its particular product.

For treatment of adverse effects

Recommended treatment includes
· For reducing the incidence of adverse reactions¾Adverse reactions often can be alleviated by reducing either the rate or the volume of infusion 42.

For patients with repeated severe reactions unresponsive to these measures, hydrocortisone, 1 to 2 mg per kg of body weight, can be given intravenously 30 minutes before infusion 42.

Utilizing a different IGIV preparation or pretreatment with diphenhydramine, acetaminophen, or aspirin also may be helpful 42, 54.

For prolonged infusions in patients with a history of side effects, the premedication can be repeated after 2 hours of medication 54.

· For mild hypersensitivity reaction¾Administering antihistamines and, if necessary, corticosteroids 14, 35, 39.

In mild anaphylaxis, antihistamines or subcutaneous epinephrine may be all that is necessary if the condition is progressing slowly and is not life-threatening, regardless of the organ or system affected 39.

Under these circumstances, the risks associated with intravenous epinephrine administration outweigh the benefits 39.

· For severe hypersensitivity or anaphylactic reaction¾Administering epinephrine. Antihistamines and/or corticosteroids also may be administered as required 39.

Epinephrine is the treatment of choice for severe hypersensitivity or anaphylactic reaction 39.

If the patient's condition is not stable, epinephrine should be infused 39.

Norepinephrine may be preferable if there is no bronchospasm. For bronchospasm, epinephrine should be given with corticosteroids 39.

Other bronchodilators, such as intravenous aminophylline or albuterol by nebulization, also should be considered 39.

Parenteral Dosage Forms

Note: Bracketed uses in the Dosage Forms section refer to categories of use and/or indications that are not included in U.S. product labeling.

IMMUNE GLOBULIN INTRAVENOUS; (HUMAN) INJECTION

Usual adult and adolescent dose

Immunodeficiency, primary (treatment) ¾
Intravenous, 200 to 400 mg (4 to 8 mL) per kg of body weight once a month. If the patient"s response is felt to be inadequate or the level of IgG achieved in the circulation is felt to be insufficient, the frequency of dosing may be increased to two times a month 55.

However, the minimum level of IgG required for protection has not been determined 3, 4, 7, 8.

Idiopathic thrombocytopenic purpura (ITP) (treatment)¾
Intravenous, 400 mg per kg of body weight per day for two to five consecutive days 3, 4, 7, 8, 20.

If the patient"s response to this five-day treatment period is inadequate, an additional 400 mg per kg of body weight may be administered as a single maintenance dose, repeated intermittently as needed 3, 4, 7, 8.

Kawasaki disease (treatment adjunct)¾
Intravenous, a single dose of 2 grams per kg of body weight may be administered 35, 43.

Because all studies have involved concurrent administration of aspirin, the treatment regimen should include aspirin, 100 mg per kg of body weight each day, until fever defervesces 56 , then 3 to 5 mg per kg of body weight as a single daily dose for six to eight weeks if coronary artery abnormalities are not detected 56.

Usual pediatric dose

See Usual adult and adolescent dose .

Strength(s) usually available

U.S.¾500 mg protein in 10 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%) 3] [Gamimune N 5% S/D (maltose 9 to 11%) 4]

1 gram protein in 10 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%) 7] [Gamimune N 10% S/D (maltose 9 to 11%) 8]

2.5 grams protein in 50 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%) 3] [Gamimune N 5% S/D (maltose 9 to 11%) 4]

5 grams protein in 50 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%) 7] [Gamimune N 10% S/D (maltose 9 to 11%) 8]

5 grams protein in 100 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%) 3] [Gamimune N 5% S/D (maltose 9 to 11%) 4]

10 grams protein in 100 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%) 7] [Gamimune N 10% S/D (maltose 9 to 11%) 8]

10 grams protein in 200 mL solution (Rx)[Gamimune N 5% S/D (maltose 9 to 11%) 4]

20 grams protein in 200 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%) 7] [Gamimune N 10% S/D (maltose 9 to 11%) 8]

12.5 grams protein in 250 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%) 3] [Gamimune N 5% S/D (maltose 9 to 11%) 4]

Canada¾500 mg protein in 10 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%)] [Gamimune N 5% S/D (maltose 9 to 11%) 36]

1 gram protein in 10 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%)] [Gamimune N 10% S/D (maltose 9 to 11%) 36]

2.5 grams protein in 50 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%)] [Gamimune N 5% S/D (maltose 9 to 11%) 36]

5 grams protein in 50 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%)] [Gamimune N 10% S/D (maltose 9 to 11%) 36]

5 grams protein in 100 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%)] [Gamimune N 5% S/D (maltose 9 to 11%) 36]

10 grams protein in 100 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%)] [Gamimune N 10% S/D (maltose 9 to 11%) 36]

10 grams protein in 200 mL solution (Rx)[Gamimune N 5% S/D (maltose 9 to 11%) 36]

20 grams protein in 200 mL solution (Rx)[Gamimune N 10% (maltose 9 to 11%)] [Gamimune N 10% S/D (maltose 9 to 11%) 36]

12.5 grams protein in 250 mL solution (Rx)[Gamimune N 5% (maltose 9 to 11%)] [Gamimune N 5% S/D (maltose 9 to 11%) 36]

Packaging and storage:

Store at 2 to 8 °C (36 to 46 °F), unless otherwise specified by manufacturer 4, 8, 36.

Protect from freezing 4, 8, 36.

Preparation of dosage form:

The medication may be diluted only with 5% dextrose in water 36.

Stability:

A solution that has been frozen should be discarded.
The contents of any vial that has been entered should be used promptly. The solution should not be used if it is not clear and colorless. Partially used vials should be discarded.

Incompatibilities:

Incompatibilities have not been evaluated. It is recommended that IGIV be administered through a separate line, by itself, and without mixing with other intravenous fluids (with the exception of 5% dextrose in water for this particular product) or medications.

IMMUNE GLOBULIN INTRAVENOUS; HUMAN FOR INJECTION

Usual adult and adolescent dose

Immunodeficiency, primary (treatment) ¾
Intravenous, initially, 200 to 400 mg per kg of body weight once a month 55.

Idiopathic thrombocytopenic purpura (ITP) (treatment)¾

Intravenous, 400 mg per kg of body weight per day for two to five consecutive days. If the patient"s response is inadequate, 400 mg per kg of body weight may be administered as a single maintenance dose once every several weeks. In some patients, it may be necessary to increase the maintenance dose up to 800 mg or 1 gram per kg of body weight.
Bacterial infections secondary to B-cell chronic lymphocytic leukemia (CLL) (treatment adjunct) *¾
Intravenous, 400 mg per kg of body weight once every three to four weeks.
Kawasaki disease (treatment adjunct)¾
Intravenous, a single dose of 2 grams per kg of body weight may be administered 35, 43.

Because all studies have involved concurrent administration of aspirin, the treatment regimen should include aspirin, 100 mg per kg of body weight each day, until fever defervesces 56 , then 3 to 5 mg per kg of body weight as a single daily dose for six to eight weeks if coronary artery abnormalities are not detected 56.

[Dermatomyositis (treatment)] *¾
Intravenous, 1 gram per kg of body weight for two days per month for three months 10, 11, 40, 57.

[Guillain-Barre syndrome (GBS) (treatment)] *¾
Intravenous, 400 mg per kg of body weight a day for five days 12, 13, 15.

[Hyperimmunoglobulinemia E syndrome (treatment)] *¾
Intravenous, 400 mg per kg of body weight a day for five days 17.

[Lambert-Eaton myasthenic syndrome (treatment)] *¾
Intravenous, 1 gram per kg of body weight a day for two consecutive days 18.

[Multifocal motor neuropathy (MMN) (treatment)] *¾
Intravenous, 400 mg per kg of body weight a day for five days 60, 61, 62, 63, 64, 65, 66, 67, 68, 69.

[Multiple sclerosis, relapsing-remitting (treatment)] *¾
Intravenous, 200 mg per kg of body weight a month for two years 23.

[Parvovirus B19 infection, chronic (treatment)] *¾
Intravenous, 400 mg per kg of body weight per day for five days followed by twice a week for two weeks 22.

Usual pediatric dose

See Usual adult and adolescent dose .

Size(s) usually available:

U.S.¾0.5 gram with 10 mL sterile water for injection as diluent (Rx)[Gammagard S/D 0.5 g (sodium chloride 0.15 M) (glucose 20 mg per mL) (polyethylene glycol 2 mg per mL) (glycine 0.3 M) (human albumin 3 mg per mL) 45] [Venoglobulin-I (D-mannitol 20 mg per mL) (human albumin 10 mg per mL) (sodium chloride 5 mg per mL) (polyethylene glycol £ 6 mg per mL)]

1 gram with 20 mL sterile water for injection as diluent (Rx)[Gammar-P IV (human albumin 3%) (sucrose 5%) (sodium chloride 0.5%) (citric acid) (sodium carbonate) 32]

1 gram with 33 mL sodium chloride injection as diluent (Rx)[Sandoglobulin 33]

2.5 grams with 50 mL sterile water for injection as diluent (Rx)[Gammagard S/D (sodium chloride 0.15 M) (glucose 20 mg per mL) (polyethylene glycol 2 mg per mL) (glycine 0.3 M) (human albumin 3 mg per mL) 46] [Gammar-P IV (human albumin 3%) (sucrose 5%) (sodium chloride 0.5%) (citric acid) (sodium carbonate) 32] [Iveegam (glucose 50 mg per mL) (sodium chloride 3 mg per mL) (polyethylene glycol < 0.5 gram per dL) 43] [Venoglobulin-S (D-sorbitol 50 mg per mL) (human albumin £ 1.3 mg per mL) (polyethylene glycol £ 100 mcg per mL) (polysorbate 80 £ 100 mcg per mL) (tri- n-butyl phosphate £ 10 mcg per mL)]

2.5 grams with or without 50 mL sterile water for injection as diluent (Rx)[Polygam S/D (sodium chloride 0.15 M) (glucose 20 mg per mL) (polyethylene glycol 2 mg per mL) (glycine 0.3 M) (human albumin 3 mg per mL) 44] [Venoglobulin-I (D-mannitol 20 mg per mL) (human albumin 10 mg per mL) (sodium chloride 5 mg per mL) (polyethylene glycol £ 6 mg per mL)]

3 grams with or without 100 mL sodium chloride injection as diluent (Rx)[Sandoglobulin 33]

5 grams with 100 mL sterile water for injection as diluent (Rx)[Gammagard S/D (sodium chloride 0.15 M) (glucose 20 mg per mL) (polyethylene glycol 2 mg per mL) (glycine 0.3 M) (human albumin 3 mg per mL) 46] [Gammar-P IV (human albumin 3%) (sucrose 5%) (sodium chloride 0.5%) (citric acid) (sodium carbonate) 32] [Iveegam (glucose 50 mg per mL) (sodium chloride 3 mg per mL) (polyethylene glycol < 0.5 gram per dL) 43] [Polygam S/D (sodium chloride 0.15 M) (glucose 20 mg per mL) (polyethylene glycol 2 mg per mL) (glycine 0.3 M) (human albumin 3 mg per mL) 44] [Venoglobulin-S (D-sorbitol 50 mg per mL) (human albumin £ 1.3 mg per mL) (polyethylene glycol £ 100 mcg per mL) (polysorbate 80 £ 100 mcg per mL) (tri- n-butyl phosphate £ 10 mcg per mL)]

5 grams with or without 100 mL sterile water for injection as diluent (Rx)[Venoglobulin-I (D-mannitol 20 mg per mL) (human albumin 10 mg per mL) (sodium chloride 5 mg per mL) (polyethylene glycol £ 6 mg per mL)]

6 grams with or without 200 mL sodium chloride injection as diluent (Rx)[Sandoglobulin 33]

10 grams with 200 mL sterile water for injection as diluent (Rx)[Gammagard S/D (sodium chloride 0.15 M) (glucose 20 mg per mL) (polyethylene glycol 2 mg per mL) (glycine 0.3 M) (human albumin 3 mg per mL) 46] [Gammar-P IV (human albumin 3%) (sucrose 5%) (sodium chloride 0.5%) (citric acid) (sodium carbonate) 32] [Polygam S/D (sodium chloride 0.15 M) (glucose 20 mg per mL) (polyethylene glycol 2 mg per mL) (glycine 0.3 M) (human albumin 3 mg per mL) 44] [Venoglobulin-I (D-mannitol 20 mg per mL) (human albumin 10 mg per mL) (sodium chloride 5 mg per mL) (polyethylene glycol £ 6 mg per mL)] [Venoglobulin-S (D-sorbitol 50 mg per mL) (human albumin £ 1.3 mg per mL) (polyethylene glycol £ 100 mcg per mL) (polysorbate 80 £ 100 mcg per mL) (tri- n-butyl phosphate £ 10 mcg per mL)]

12 grams with or without 200 mL sodium chloride injection as diluent (Rx)[Sandoglobulin 47]

Canada¾5 grams with 100 mL sterile water for injection as diluent (Rx)[Iveegam (glucose 50 mg ± 5 mg per mL) (sodium chloride 3 mg ± 1 mg per mL)] 35

Packaging and storage:

Store at 2 to 8 °C (36 to 46 °F), unless otherwise specified by manufacturer 35.

Protect from freezing 35.

Preparation of dosage form:

The diluent and lyophilized product should be brought to room temperature prior to reconstitution. When the diluent is added, dissolution usually occurs within a few minutes, although in rare cases, or when the product and/or diluent are cold, dissolution may take up to 20 minutes. The reconstituted solution should not be shaken, since excessive shaking will cause foaming. Reconstituted solution should be at approximately room temperature at the time of administration 35.

Stability:

Only the specific diluent that the product"s manufacturer indicates for that particular product should be used. The solution should not be used if it is not clear and colorless to slightly straw-colored, or if there is particulate matter present. Administration should begin promptly after reconstitution, or within 2 to 3 hours, according to the individual manufacturer"s instructions. Partially used vials should be discarded 35.

Incompatibilities:

Incompatibilities have not been evaluated. It is recommended that IGIV be administered through a separate line, by itself, and without mixing with other intravenous fluids (with the exception of the product"s specified diluent) or medications 35.