**DESCRIPTION**

GAMMAGARD S/D immune globulin intravenous (human) [IGIV], IgA less than 1 μg/mL in a 5% solution (IgA < 1 μg/mL), is GAMMAGARD S/D, selected to have an IgA concentration of less than 1 μg/mL of IgA in a 5% solution. GAMMAGARD S/D, Immune Globulin Intravenous (Human) [IGIV] is a solvent/detergent treated, sterile, freeze-dried preparation of highly purified immunoglobulin G (IgG) derived from large pools of human plasma. The product is manufactured by the Cohn-Oncley cold ethanol fractionation process followed by ultrafiltration and ion exchange chromatography. Source material for fractionation may be obtained from another U.S. licensed manufacturer. The manufacturing process includes treatment with an organic solvent/detergent mixture, composed of tri-n-butyl phosphate, octoxynol 9 and polysorbate 80. The GAMMAGARD S/D manufacturing process provides a significant viral reduction in vitro studies. Studies have demonstrated virus clearance during GAMMAGARD S/D manufacturing using infectious human immunodeficiency virus, Types 1 and 2 (IIV-1, IIV-2); bovine viral diarrhea virus (BVDV), a model virus for hepatitis C virus; sindbis virus (SIN), a model virus for lipid-enveloped viruses; pseudorabies virus (PRV), a model virus for lipid-enveloped DNA viruses such as herpes; vesicular stomatitis virus (VSV), a model virus for lipid-enveloped RNA viruses; hepatitis A virus (HAV) and encephalomyocarditis virus (EMC), a model virus for non-lipid-enveloped RNA viruses; and porcine parovirus (PPV), a model virus for non-lipid-enveloped DNA viruses. These reductions are achieved through a combination of process chemistry, partitioning and/or inactivation during cold ethanol fractionation and the solvent/detergent treatment.³

**INDICATIONS AND USAGE**

GAMMAGARD S/D is not indicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern (see WARNINGS).

Primary Immunodeficiency Diseases

GAMMAGARD S/D is indicated for the treatment of primary immunodeficient states, such as: congenital agammaglobulinemia, common variable immunodeficiency, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.³¹This indication was supported by a clinical trial of 17 patients with primary immunodeficiency who received a total of 341 infusions. GAMMAGARD S/D is especially useful when high levels or rapid elevation of circulating IgG are desired or when intramuscular injections are contraindicated (e.g., small muscle mass).

B-cell Chronic Lymphocytic Leukemia (CLL)

GAMMAGARD S/D is indicated for prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell Chronic Lymphocytic Leukemia (CLL). In a study of 81 patients, 41 of whom were treated with GAMMAGARD, Immune Globulin Intravenous (Human), bacterial infections were significantly reduced in the treatment group.³³ In this study, the placebo group had approximately twice as many bacterial infections as the IGIV group. The median time to first bacterial infection for the IGIV group was greater than 365 days. By contrast, the time to first bacterial infection in the placebo group was 192 days. The number of viral and fungal infections, which were for the most part minor, was not statistically different between the two groups.

Idiopathic Thrombocytopenic Purpura (ITP)

When a rapid rise in platelet count is needed to prevent and/or to control bleeding in a patient with Idiopathic Thrombocytopenic Purpura, the administration of GAMMAGARD S/D, should be considered. The efficacy of GAMMAGARD has been demonstrated in a clinical study involving 16 patients. Of these 16 patients, 13 had chronic ITP (11 adults, 2 children), and 3 patients had acute ITP (one adult, 2 children). All 16 patients (100%) demonstrated a clinically significant rise in platelet count to a level greater than 40,000/mm³ following the administration of GAMMAGARD. Ten of the 16 patients (62.5%) exhibited a significant rise greater than 80,000 platelets/mm³. Of these 10 patients, 7 had chronic ITP (5 adults, 2 children), and 3 patients had acute ITP (one adult, 2 children). The rise in platelet count to greater than 40,000/mm³ occurred after a single 1 g/kg infusion of GAMMAGARD in 8 patients with chronic ITP (6 adults, 2 children), and in 2 patients with acute ITP (one adult, one child). A similar response was observed after two 1 g/kg infusions in 3 adult patients with chronic ITP; and one child with acute ITP. The remaining 2 adult patients with chronic ITP received more than two 1 g/kg infusions before achieving a platelet count greater than 40,000/mm³. The rise in platelet count was generally rapid, occurring within 5 days. However, this rise was transient and not considered curative. Platelet count rises lasted 2 to 3 weeks, with a range of 12 days to 6 months. It should be noted that childhood ITP may resolve spontaneously without treatment.

Kawasaki Syndrome

GAMMAGARD S/D, is indicated for the prevention of coronary artery aneurysms associated with Kawasaki syndrome. The percentage incidence of coronary artery aneurysm in patients with Kawasaki syndrome receiving GAMMAGARD either at a single dose of 1 g/kg (n=22) or at a dose of 400 mg/kg for four consecutive days (n=22), beginning within seven days of onset of fever, was 3/44 (6.8%). This was significantly different (p=0.008) from a comparable group of patients that received aspirin only in previous trials and of whom 42/185 (22.7%) experienced coronary artery aneurysms.³¹ ³² All patients in the GAMMAGARD trial received concomitant aspirin therapy and none experienced hypersensitivity-type reactions (urticaria, bronchospasm or generalized anaphylaxis).³³ Several studies have documented the efficacy of intravenous gamaglobulin in reducing the incidence of coronary artery abnormalities resulting from Kawasaki syndrome.³⁴ ³⁵ ³⁶ ³⁷

CONTRAINDICATIONS

GAMMAGARD S/D is contraindicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern (see INDICATIONS AND USAGE and WARNINGS). Patients may experience severe hypersensitivity reactions or anaphylaxis in the setting of detectable IgA levels following infusion of GAMMAGARD S/D. The occurrence of severe hypersensitivity reactions or anaphylaxis under such conditions should prompt consideration of an alternative therapy.

---

**Table 1**

<table>
<thead>
<tr>
<th>Process Step Evaluated</th>
<th>Lipid-Envelope Viruses</th>
<th>Non-Lipid-Envelope Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1: Processing of Cryo-Poor Plasma to Fraction I+II+III Precipitate</td>
<td>BVD</td>
<td>HIV-1</td>
</tr>
<tr>
<td>0.6*</td>
<td>5.7</td>
<td>1.0*</td>
</tr>
<tr>
<td>Step 2: Processing of Resuspended Suspension A Precipitate to Suspension B Filter Press Filterate</td>
<td>1.3</td>
<td>4.9</td>
</tr>
<tr>
<td>Step 3: Processing of Suspension B Filter Press to Suspension B Cuno 70 Filterate</td>
<td>0.7*</td>
<td>4.0</td>
</tr>
<tr>
<td>Cumulative Reduction of Virus (log10)</td>
<td>8.6</td>
<td>18.3</td>
</tr>
</tbody>
</table>

* These values are not included in the computation of the cumulative reduction of virus since the virus clearance is within the variability limit of the assay (x<1.0).

NA: Not Applicable. Solvent/detergent treatment does not affect non-lipid-enveloped viruses.

NT: Not Tested.
Immune Globulin Intravenous (Human) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentration available and the minimum rate of infusion practicable. While these reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IGIV products, those containing sucrose as a stabilizer accounted for a disproportionate share of the total number.

See PRECAUTIONS and DOSAGE AND ADMINISTRATION sections for important information intended to reduce the risk of acute renal failure.

GAMMAGARD S/D does not contain sucrose.

### WARNINGS

**Warning**

Immune Globulin Intravenous (Human) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentration available and the minimum rate of infusion practicable. While these reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IGIV products, those containing sucrose as a stabilizer accounted for a disproportionate share of the total number.

See PRECAUTIONS and DOSAGE AND ADMINISTRATION sections for important information intended to reduce the risk of acute renal failure.

GAMMAGARD S/D, Immune Globulin Intravenous (Human) is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. (See DESCRIPTION). Despite these measures, such products can still potentially transmit disease. Because this product is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses and theoretically, the Creutzfeldt-Jakob disease (CJD) agent. All infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Baxter Healthcare Corporation at 1-800-423-2862 (in the U.S.). The physician should discuss the risks and benefits of this product with the patient.

GAMMAGARD S/D, Immune Globulin Intravenous (Human), should only be administered intravenously. Other routes of administration have not been evaluated.

Immediate anaphylactic and hypersensitivity reactions are a remote possibility. Epinephrine and antihistamines should be available for treatment of any acute anaphylactoid reactions.

GAMMAGARD S/D, IgA < 1 μg/mL, contains trace amounts of IgA (less than 1 μg/mL in a 5% solution). GAMMAGARD S/D is not indicated in patients with selective IgA deficiencies. The degree of IgA deficiency is the only abnormality of concern. It should be given with caution to patients with antibodies to IgA or IgA deficiencies, that are a component of an underlying primary immunodeficiency disease for which IGIV therapy is indicated. 12-14 GAMMAGARD S/D, IgA < 1 μg/mL, has a lower IgA concentration less than 1 μg/mL. GAMMAGARD S/D has an IgA concentration less than or equal to 2.2 μg/mL. IgA preparations depleted of IgA (0.4 to 2.9 μg/mL) were shown to be better tolerated by a limited number of patients who reacted to IGIV preparations with higher IgA concentrations. However, the concentration of IgA that will not provoke a reaction is not known, and therefore all IGIV preparations carry the risk of inducing an anaphylactic reaction to IgA. In such instances, a risk of anaphylaxis may exist despite the fact that GAMMAGARD S/D, IgA < 1 μg/mL, contains trace amounts of IgA.

### PRECAUTIONS

**General**

Some viruses, such as B19V (formerly known as parvovirus B19) or hepatitis A, are particularly difficult to remove or inactivate at this time. B19V most seriously affects pregnant women, or immune-compromised individuals. Symptoms of B19V infection include fever, dizziness, chills, and runny nose followed about two weeks later by a rash and joint pain. Evidence of hepatitis A may be several days to weeks of poor appetite, tiredness, and low-grade fever followed by nausea, vomiting, and abdominal pain. Dark urine and a yellowed complexion are also common symptoms. Patients should be encouraged to consult their physician if such symptoms appear.

An aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with Immune Globulin Intravenous (Human) [IGIV] therapy. Despite the reported infrequency, transmission of AMS within several days without sequelae. The syndrome usually begins within several hours to two days following IGIV treatment. It is characterized by symptoms and signs including severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, and nausea and vomiting. Cerebrospinal fluid (CSF) studies are frequently positive with pleocytosis up to several thousand cells per mm³, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dL. 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) IGIV treatment.

Periodic monitoring of renal function tests and urine output is particularly important in patients judged to have a potential increased risk for developing acute renal failure. Assure that patients are not volume depleted prior to the initiation of the infusion of IGIV Renal function, including measurement of blood urea nitrogen (BUN)/serum creatinine, should be assessed prior to the initial infusing of GAMMAGARD S/D and again at appropriate intervals thereafter. If renal function deteriorates, discontinuation of the product should be considered. For patients judged to be at risk for developing renal dysfunction, it may be prudent to reduce the rate of infusion to less than 4 mL/hour (<3.3 mg IgG/hour) for a 5% solution or at a rate of less than 2 mL/kg/hour (<3.3 mg/kg/hour) for a 10% solution. Certain components used in the packaging of this product contain natural rubber latex.

### Hemolytic Anemia

Immune Globulin Intravenous (Human) [IGIV] products can contain blood group antibodies which may act as hemolysins and induce in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, hemolysis. Hemolytic anemia may develop subsequent to IGIV therapy due to enhanced RBC sequestration (see ADVERSE REACTIONS). IGIV recipients should be monitored for clinical signs and symptoms of hemolysis (see PRECAUTIONS: Laboratory Tests).

### Transfusion-Related Acute Lung Injury (TRALI)

There have been reports of noncardiogenic pulmonary edema (Transfusion-Related Acute Lung Injury [TRALI]) in patients administered IGIV. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever and typically occurs within 1 to 6 hours after transfusion. Patients with TRALI may be managed using oxygen therapy with adequate ventilatory support.

IGIV recipients should be monitored for pulmonary adverse reactions. If TRALI is suspected, appropriate tests should be performed for the presence of anti-neutrophil antibodies in both the product and patient serum (see PRECAUTIONS: Laboratory Tests).

### Thrombotic Events

Thrombotic events have been reported in association with IGIV (see ADVERSE REACTIONS). Patients at risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, and/or known or suspected hyperviscosity, hypercoagulable disorders and prolonged periods of immobilization. The potential risks and benefits of IGIV should be weighed against those of alternative therapies for all patients for whom IGIV administration is being considered. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammapathies (see PRECAUTIONS: Laboratory Tests). Analysis of adverse event reports 12,14 has indicated that a rapid rate of infusion may be a risk factor for vascular occlusive events.

### Laboratory Tests

If signs and/or symptoms of hemolysis are present after IGIV infusion, appropriate confirmatory laboratory testing should be done (see PRECAUTIONS).

If TRALI is suspected, appropriate tests should be performed for the presence of anti-neutrophil antibodies in both the product and patient serum (see PRECAUTIONS).

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

### Information For Patients

Patients should be instructed to immediately report symptoms of decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath (which may suggest kidney damage) to their physician.

### Drug Interactions

See DOSAGE AND ADMINISTRATION.

### Pregnancy Category C

Animal reproduction studies have not been conducted with GAMMAGARD S/D, Immune Globulin Intravenous (Human). It is also not known whether GAMMAGARD S/D can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. GAMMAGARD S/D should be given to a pregnant woman only if clearly needed.

### ADVERSE REACTIONS

Increases in creatinine and blood urea nitrogen (BUN) have been observed as soon as one to two days following infusion. Progression to oliguria and anuria requiring dialysis has been observed, although some patients have improved spontaneously following cessation of treatment. 18 Types of severe renal adverse reactions that have been seen following IGIV therapy include:

- acute renal failure
- acute tubular necrosis
- proximal tubular nephropathy
- osmotic nephrosis

In general, reported adverse reactions to GAMMAGARD, in patients with either congenital or acquired immunodeficiencies are similar in kind and frequency. Various minor reactions, such as mild to moderate hypotension, headache, fatigue, chills, backache, leg cramps, lightheadedness, fever, urticaria, flushing, slight elevation of blood pressure, nausea and vomiting may occasionally occur. Slowing or stopping the infusion usually allows the symptoms to disappear promptly.

Immediate anaphylactic and hypersensitivity reactions are a remote possibility. Epinephrine and antihistamines should be available for treatment of any acute anaphylactoid reaction (see WARNINGS).

### Primary Immunodeficiency Diseases

Twenty-one adverse reactions occurred in 341 infusions (6%), when using GAMMAGARD (5% solution), in a clinical trial of 17 patients with primary immunodeficiency.16,17 Of the 17 patients, 12 (71%) were adults, and 5 (29%) were children (16 years or younger).

In a cross-over study comparing GAMMAGARD and GAMMAGARD S/D (5% solutions) conducted in a small number (n=10) of primary immunodeficient patients, no unusual or unexpected adverse reactions were observed in the GAMMAGARD S/D group. The adverse reactions experienced in the GAMMAGARD S/D group were similar in frequency and nature to those observed in the control group consisting of patients receiving GAMMAGARD.

GAMMAGARD, reconstituted to a concentration of 10%, was administered intravenously at rates varying from 2 to 11 mL/hour. Systemic reactions occurred in 23 (10.5%) of 219 infusions. This compares with an adverse reaction incidence of 6% (only systemic reactions reported) for primary immunodeficient patients previously treated with a 5% solution at infusion rates varying between 2 and 8 mL/hour, as described above (see reference 40). Local pain or irritation was experienced during 35 (16%) of 219 infusions. Application of a warm compress to the infusion site alleviated local symptoms. These local reactions tended to be associated with hand vein infusions and their incidence may be reduced by infusions via the antecubital vein.
B-cell Chronic Lymphocytic Leukemia (CLL)
In the study of patients with B-cell Chronic Lymphocytic Leukemia, the incidence of adverse reactions associated with GAMMAGARD infusions was approximately 1.3% while that associated with placebo (normal saline) infusions was 0.8%.2

Idiopathic Thrombocytopenic Purpura (ITP)
During the clinical study of GAMMAGARD for the treatment of Idiopathic Thrombocytopenic Purpura, the only adverse reaction reported was headache which occurred in 12 of 16 patients (75%). Of these 12 patients, 11 had chronic ITP (9 adults, 2 children), and one child had acute ITP. Oral antihistamines and analgesics alleviated the symptoms and were used as pretreatment for those patients requiring additional IGIV therapy. The remaining 4 patients did not report any side effects and did not require pretreatment.

Kawasaki Syndrome
In a study of patients (n=51) with Kawasaki syndrome, no hypersensitivity-type reactions (urticaria, bronchospasm or generalized anaphylaxis) were reported in patients receiving either a single 1 g/kg dose of IGIV, GAMMAGARD, or 400 mg/kg of IGIV, GAMMAGARD, for four consecutive days.13 Mild adverse reactions, including chills, flushing, cramping, headache, hypotension, nausea, rash and wheezing, were reported with both dose regimens. These adverse reactions occurred in 7/51 (13.7%) patients and in association with 7/129 (5.4%) infusions. Of the 25 patients who received a single 1 g/kg dose, 4 patients experienced adverse reactions for an incidence of 16%. Of the 26 patients who received 400 mg/kg/day for 4 days, 3 experienced a single adverse reaction for an incidence of 11.5%.3

Postmarketing:
The following is a list of adverse reactions that have been identified and reported during the post-approval use of IGIV products:

Respiratory
cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm
Cardiovascular
thromboembolism, hypotension
Neurological
seizures, tremor
Hematological
hemolysis, positive direct antiglobulin (Coombs) test
General/Body as a Whole
pyrexia, rigors
Musculoskeletal
back pain
Gastrointestinal
hepatic dysfunction, abdominal pain

Rare and Uncommon Adverse Events:
Respiratory
apnea, Acute Respiratory Distress Syndrome (ARDS), Transfusion Associated Acute Lung Injury (TRALI)
Integumentary
bullous dermatitis, epidermolysis, erythema multiforme, Stevens-Johnson syndrome
Cardiovascular
cardiac arrest, vascular collapse
Neurological
coma, loss of consciousness
Hematological
pancytopenia, leukopenia

Because postmarketing reporting of these reactions is voluntary and the at-risk populations are of uncertain size, it is not always possible to reliably estimate the frequency of the reaction or establish a causal relationship to exposure to the product. Such is also the case with literature reports authored independently3 (see PRECAUTIONS).

DOSEAGE AND ADMINISTRATION
Primary Immunodeficiency Diseases
For patients with primary immunodeficiencies, monthly doses of approximately 300-600 mg/kg infused at 3 to 4 week intervals are commonly used.40-42 As there are significant differences in the half-life of IgG among patients with primary immunodeficiency, the frequency and amount of immunoglobulin therapy may vary from patient to patient. The proper amount can be determined by monitoring clinical response. The minimum serum concentration of IgG necessary for protection varies among patients and has not been established by controlled clinical trials.

B-cell Chronic Lymphocytic Leukemia (CLL)
For patients with hypogammaglobulinemia and/or recurrent bacterial infections due to B-cell Chronic Lymphocytic Leukemia, a dose of 400 mg/kg every 3 to 4 weeks is recommended.

Kawasaki Syndrome
For patients with Kawasaki syndrome, either a single 1 g/kg dose or a dose of 400 mg/kg for four consecutive days beginning within seven days of the onset of fever, administered concomitantly with appropriate aspirin therapy (80-100 mg/kg/day in four divided doses) is recommended.44

Idiopathic Thrombocytopenic Purpura (ITP)
For patients with acute or chronic Idiopathic Thrombocytopenic Purpura, a dose of 1 g/kg is recommended. The need for additional doses can be determined by clinical response and platelet count. Up to three separate doses may be given on alternate days if required. No prospective data are presently available to identify a maximum safe dose, concentration, and rate of infusion in patients determined to be at increased risk of acute renal failure. In the absence of prospective data, the recommended doses should not be exceeded and the concentration and infusion rate selected should be the minimum level practicable. Reduction in dose, concentration, and/or rate of administration in patients at risk of acute renal failure has been proposed in the literature in order to reduce the risk of acute renal failure.43

Reconstitution: Use Aseptic Technique
When reconstitution is performed aseptically outside of a sterile laminar air flow hood, administration should begin as soon as possible, but not more than 2 hours after reconstitution. When reconstitution is performed aseptically in a sterile laminar air flow hood, the reconstituted product may be either maintained in the original glass container or pooled into VAPLEX bags and stored under constant refrigeration (2-8°C), for up to 24 hours. (The date and time of reconstitution/pooling should be recorded). If these conditions are not met, sterility of the reconstituted product cannot be maintained. Partially used vials should be discarded.

A. 5% Solution
1. Note: Reconstitute immediately before use.
2. If refrigerated, warm the Sterile Water for Injection, USP (diluent) and GAMMAGARD S/D, Immune Globulin Intravenous (Human) (dried concentrate), to room temperature.
3. Remove caps from concentrate and diluent bottles to expose central portion of rubber stoppers.
4. Cleanse stoppers with germicidal solution.
5. Remove protective covering from the spike at one end of the transfer device (Fig. 1).
6. Place the diluent bottle on a flat surface and, while holding the bottle to prevent slipping, insert the spike of the transfer device perpendicularly through the center of the bottle stopper.
7. Press down firmly so that the transfer device fits snugly against the diluent bottle (Fig. 2). Caution: Failure to use center of stopper may result in dislodging the stopper.
8. Remove the protective covering from the other end of the transfer device. Hold diluent bottle to prevent slipping.
9. Hold concentrate bottle firmly and at an angle of approximately 45 degrees. Invert the diluent bottle with the concentrate device at an angle complementary to the concentrate bottle (approximately 45 degrees) and firmly insert the transfer device into the concentrate bottle through the center of the rubber stopper (Fig. 3). Note: Invert the diluent bottle with attached transfer device rapidly into the concentrate bottle in order to avoid loss of diluent.
10. The diluent will flow into the concentrate bottle quickly. When diluent transfer is complete, remove empty diluent bottle and transfer device from concentrate bottle. Discard transfer device after single use.
11. Thoroughly wet the dried material by tilting or inverting and gently rotating the bottle (Fig. 4). Do not shake. Avoid foaming.
12. Repeat gentle rotation as long as undissolved product is observed.

B. 10% Solution
Follow steps 1-4 as previously described in A.
5. To prepare a 10% solution, reconstitute with the appropriate volume of diluent for a 5% or 10% concentration. Using aseptic technique, draw the required volume of diluent into a sterile hypodermic syringe and needle. Discard the filled syringe.
6. Using the residual diluent in the diluent vial, follow steps 5-12 as previously described in A.

<p>| Table 2 |</p>
<table>
<thead>
<tr>
<th>Required Diluent Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration</td>
</tr>
<tr>
<td>5%</td>
</tr>
<tr>
<td>10%</td>
</tr>
</tbody>
</table>

Rate of Administration
It is recommended that initially a 5% solution be infused at a rate of 0.5 mL/kg/Hr. If infusion at this rate and concentration causes the patient no distress, the administration rate may be gradually increased to a maximum rate of 4 mL/kg/Hr for patients with no history of adverse reactions to IGIV and no significant risk factors for renal dysfunction or thrombotic complications. Patients who tolerate the 5% concentration at 4 mL/kg/Hr can be infused with the 10% concentration starting at 0.5 mL/kg/Hr. If no adverse effects occur, the rate can be increased gradually up to a maximum of 6 mL/kg/Hr.
In general, it is recommended that patients beginning therapy with IGIV or switching from one IGIV product to another be started at the lower rates of infusion and should be advanced to the maximal rate only after they have tolerated several infusions at intermediate rates of infusion. It is important to individualize rates for each patient. As noted in the WARNINGS section, patients who have underlying renal disease or who are judged to be at risk of developing thrombotic events should not be infused rapidly with any IGIV product.