**Primary Immunodeficiency Diseases**

Polygam 
® is indicated in the treatment of primary immunodeficiency diseases, such as: congenital agammaglobulinemia, common variable immunodeficiency, Wiskott-Aldrich syndrome, and severe combined immunodeficiency (SCID). This indication is supported by a trial of 17 patients with primary immunodeficiency who received a total of 241 infusions. Polygam 
® is especially useful when high levels or rapid elevations of circulating IgG levels or when intravenous immunoglobulins are contraindicated (e.g., small muscle mass).

**Indications and Usage**

Polygam 
® is not indicated in patients with selective IgA deficiencies where the IgA deficiency is the only abnormality of concern (see WARNINGS section).

**Precautions**

Some viruses, such as parvovirus B19 or hepatitis A, are particularly difficult to remove or inactivate at this time. Parvovirus B19 most noticeably affects pregnant women, or immunocompromised individuals, and infection can include fever, malaise, and rash. Hepatitis A virus is contracted primarily by ingestion of undercooked shellfish, lettuce, and imported foods. Hepatitis A virus can sometimes be transmitted through sexual contact. Betas, betanodavirus (VSV), a model virus for lipid-enveloped RNA viruses, and hepatitis C virus, were used as model viruses for lipid-enveloped and non-enveloped viruses, respectively. These reductions are achieved through a combination of virus chemistry, partitioning, and/or inactivation during cold ethanol fractionation and the solvent/detergent chromatography.

The manufacturing process includes an inorganic solvent/detergent mixture, 10 mg/mL surfactant, and polyethylene glycol (PEG) 4000 (the Polygam 
® detergent manufacturing process provides a significant viral reduction in vitro. In this study, the plaque-purified 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 30 days, whereas 10 patients in the Polygam 
® placebo group had bacterial infections within 30 days of receiving the first dose of IGIV. Slowing or stopping the infusion usually allows the symptoms to disappear promptly. Of these 10 patients, 7 had bacterial infections; 2 had viral infections; and 1 had an upper respiratory tract infection. All patients in the Polygam 
® trial received concurrent antibiotic therapy and none experienced hyperimmunoglobulinemia type reaction (urticaria, hypotension, hypotermia, and/or generalized asymmetry). Several studies have documented the efficacy of intravenous gammaglobulin in reducing the incidence of coronary artery disease, particularly from Kawasaki syndrome.

**CONTRAINDICATIONS**

Patients may experience severe hypersensitivity reactions or anaphylaxis in the setting of detectable IgG levels following infusion of Polygam 
®. The occurrence of severe hypersensitivity or anaphylaxis under such conditions should prompt cessation of the infusion of Polygam 
® and may suggest kidney damage (or other abnormalities) to their physician. In addition, patients may experience general systemic reactions such as fever, chills, hypotension, urticaria, dyspnea, cocaine, nausea, vomiting, seizures, syncope, and angioedema. Systemic reactions are a remote possibility. Safety should be available for treatment of any acute anaphylactic reaction (see WARNINGS).

**WARNINGS**

**WARNING**

**Immune Globulin Intravenous (Human)** (Polygam 
®) products have been reported to be associated with the occurrence of thrombocytopenia, hemolytic anemia, sepsis, nephritis, and death. Patients predicated to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetics with GFR greater than 65, volume depletion, septic, sepsis, septicemia, 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 may suggest kidney damage (or other abnormalities) to their physician. In addition, patients may experience general systemic reactions such as fever, chills, hypotension, urticaria, dyspnea, cocaine, nausea, vomiting, seizures, syncope, and angioedema. Systemic reactions are a remote possibility. Safety should be available for treatment of any acute anaphylactic reaction (see WARNINGS).

**Primary Immunodeficiency Diseases**

Twenty-one adverse reactions occurred in 341 infusions (6%), when using Polygam 
® (3.7%). Of these reactions, 20 were associated with either an abnormality of concern (see INDICATIONS and USAGE and WARNINGS sections).

**WILLINGNESS**

**Immune Globulin Intravenous (Human)** (Polygam 
®) products have been reported to be associated with the occurrence of thrombocytopenia, hemolytic anemia, sepsis, nephritis, and death. Patients predicated to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetics with GFR greater than 65, volume depletion, septic, sepsis, septicemia, 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 may suggest kidney damage (or other abnormalities) to their physician. In addition, patients may experience general systemic reactions such as fever, chills, hypotension, urticaria, dyspnea, cocaine, nausea, vomiting, seizures, syncope, and angioedema. Systemic reactions are a remote possibility. Safety should be available for treatment of any acute anaphylactic reaction (see WARNINGS).

**Primary Immunodeficiency Diseases**

Twenty-one adverse reactions occurred in 341 infusions (6%), when using Polygam 
® (3.7%). Of these reactions, 20 were associated with either an abnormality of concern (see INDICATIONS and USAGE and WARNINGS sections). In a cross-over study comparing Polygam 
® and Polygam 
® (3.7% solution) conducted in a small number (n=10) of primary immunodeficient patients, no anaphylactic or unexpected adverse reactions were observed in the Polygam 
® group. The adverse reactions observed were equivalent between the two products and those normally observed following infusions of standard IGIV products. In addition, most reports were not specific enough to allow the symptoms to disappear promptly. Immediate anaphylactic and hypotensive reactions are a remote possibility. Safety should be available for treatment of any acute anaphylactic reaction (see WARNINGS).

**ADVERSE REACTIONS**

**types of rare renal adverse reactions that have been seen following IGIV therapy include**

- acute renal failure
- acute tubular necrosis
- proximal tubular proteinuria
- systemic edema

In general, adverse reports associated with Immune Globulin Intravenous (Human), Polygam 
® in patients with either congenital or acquired immunodeficiencies are similar in kind and frequency. Various minor reactions, such as mild or moderate hypertension, headache, fatigue, chills, nausea, vomiting, headaches, fever, respiratory, urticaria, flushing, slight elevations of blood pressure, nausea and vomiting may occasionally occur. "Slight elevations of blood pressure and respiratory rates may not habitually usually allow the symptoms to disappear promptly. Immediate anaphylactic and hypotensive reactions are a remote possibility. Safety should be available for treatment of any acute anaphylactic reaction (see WARNINGS).
8-cell Chronic Lymphocytic Leukemia (CLL)  
In the study of patients with 8-cell Chronic Lymphocytic Leukemia, the incidence of adverse reactions associated with Polygam® infusion was approximately 1-3% while that which associated with plasmal (normal saline) infusions was 6.6%.

Idiopathic Thrombocytopenic Purpura (ITP)  
During the clinical study of Polygam® for the treatment of Idiopathic Thrombocytopenic Purpura, the number of adverse reactions reported was blood clots which occurred in 12 of 18 patients (68%). Of these 12 patients, 11 had chronic ITP (2 children), and 2 had chronic small ITP. All antithrombin and analyses followed the symptoms and were used in thrombocytopenia for those patients requiring additional IVIG therapy. The remaining 6 patients did not report any side effects and did not require treatment.

Kawasaki Syndrome  
In a study of 280 patients (9) with Kawasaki syndrome, no hyperactivity type reactions (urticaria, bronchospasm or generalized anaphylaxis) were reported in patients receiving either a single 1 g/kg dose of Polygam® or 400 mg/kg of Polygam®. For the 280 patients described above, no adverse reactions were reported in 72/75 (96.3%) patients and 1 patient associated with 1/75 (1.3%) infusions. Of the 25 patients who received a single 1 g/kg dose, 4 patients experienced adverse reaction for an incidence of 16%, of the 54 patients who received 400 mg/kg for 4 days, 1 experienced a single adverse reaction for an incidence of 11.1%.

DOSAGE AND ADMINISTRATION  
Primary Immunodeficiency Diseases  
For patients with primary immunodeficiencies, monthly doses of at least 100 mg/kg are recommended. Initially, patients may receive 200-400 mg/kg. 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. A total dose per month is to be determined by monitoring clinical response. The minimum serum concentration of IgG necessary for protection has not been established.

8-cell Chronic Lymphocytic Leukemia (CLL)  
For patients with 8-cell recurrent infectious diseases but at 8-cell Chronic Lymphocytic Leukemia, a dose of 400 mg/kg every 3 to 4 weeks is recommended.

Polygam® for the treatment of 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 3 separate doses may be given to achieve an optimal response if it is required.

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 3 separate doses may be given to achieve an optimal response if it is required.

Reconstitution: Use Aseptic Technique  
When reconstitution is performed aseptically outside of a sterile laminar air flow hood, administration should be given as soon as possible, but not more than 2 hours after reconstitution.

When reconstitution is performed aseptically outside of a sterile laminar air flow hood, the reconstituted Polygam® product must be refrigerated in the unopened container or returned to the refrigerator if the solution is taken out of the refrigerator.

Infectious disease treatment in patients with hypogammaglobulinemia and/or recurrent bacterial infections due to Idiopathic Thrombocytopenic Purpura (ITP)  
Intravenous Immune Globulin reduces bacterial infections.  

S/D is to be stored at a temperature not to exceed 25°C (77°F).

Parenteral drug products should be inspected visually for particulate matter and discoloration before administration. The reconstituted material should be at room temperature during administration.

Storage  
Polygam® S/D is to be stored at a temperature not to exceed 25°C (77°F). Freezing should be avoided to prevent the diluent bottle from breaking.

REFERENCES  
3. Polygam is a registered trademark of the American National Red Cross.

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Revied August 2002  R1210