RATIONAL FOR INCLUSION IN PA PROGRAM

Background
Immune globulin products from human plasma were first used in 1952 to treat immune deficiency. Intravenous immunoglobulin (IVIG) contains the pooled immunoglobulin G (IgG) immunoglobulins from the plasma of approximately a thousand or more blood donors (1).

IVIG is used to treat various autoimmune, infectious, and idiopathic diseases. IVIG is an approved treatment for graft versus host disease and ITP. It is accepted for use in persons with Kawasaki disease, Guillain-Barré syndrome, and polymyositis/dermatomyositis (1).

Regulatory Status
The immune globulins addressed by this policy are FDA-approved for use in one or more of the following conditions:
- Primary immune deficiency (PID)
- Acute and Chronic Thrombocytopenic Purpura (ITP)
- Prevention of bacterial and viral infections in patients with hypogammaglobulinemia and/or recurrent bacterial and viral infections associated with B-cell Chronic Lymphocytic Leukemia (CLL)
- Prevention of coronary artery aneurysms associated with Kawasaki syndrome
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)(2-13)

Off-Label Use: (12-29)
1. Prophylaxis of bacterial and viral infections in pediatric human immunodeficiency virus (HIV) infection
2. Prophylaxis of bacterial and viral infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
3. Dermatomyositis
4. Polymyositis
5. Myasthenia gravis
6. Guillain-Barre syndrome
7. Lambert-Eaton myasthenic syndrome
8. Fetal/neonatal alloimmune thrombocytopenia
9. Parvovirus B19-induced pure red cell aplasia
10. Stiff-person syndrome

There are various types of immune-mediated encephalopathy, including anti-NMDA encephalitis, VGKG-associated limbic encephalopathies, and Hu and Ma2-mediated encephalitis. These have been seen in patients both with cancer and cancer-free of all ages, notably in young adults and children. First-line treatment, showing moderate success, includes the use of IVIGs (14-15).

Immune globulin use is associated with increased risk of thrombosis, particularly in the elderly and patients with risk factors such as cardiovascular disease, hypercoagulopathy, those on estrogen therapy, and patients with central venous catheters. Patients should be monitored carefully for signs and symptoms of thrombosis both at the time of infusion and after infusion. For those patients who will be self-administering the medication, practitioners need to instruct the patients and caregivers on how to monitor for signs and symptoms of thrombosis. Thrombosis may occur regardless of the route of administration (2-13).

IVIG products have been 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, > 65 years of age, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs.(2-13)

Other potential complications to monitor include the following (2-13):

**Immunoglobulin A deficiency:** People with this condition have the potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products that contain IgA.

**Aseptic meningitis syndrome (AMS):** Rare occurrences of AMS have been reported in association with IVIG treatment. AMS usually begins within several hours to 2 days following IVIG treatment and
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Bivigam, Carimune NF, Flebogamma, Gammagard, Gammagard S/D,
Gammaked, Gammaplex, Gamunex-C, Octagam, Privigen

is characterized by symptoms including severe headache, drowsiness, fever, photophobia, painful eye
movements, muscle rigidity, nausea, and vomiting. 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.

Bleeding complications: Bleeding complications may be encountered in patients with
thrombocytopenia or other bleeding disorders.

Severe reactions: Severe reactions, such as anaphylaxis or angioneurotic edema, have been
reported in association with IV immunoglobulins, even in patients not known to be sensitive to human
immunoglobulins or blood products.

Summary
IVIG is used to provide immediate passive immunity after suspected exposure to an organism for
which no active immunization exists or if there is inadequate time to develop active immunization, and
as replacement therapy for patients with antibody deficiencies. The passive immunity imparted by
IVIG is capable of attenuating or preventing infectious diseases or deleterious reactions from toxins,
mycoplasma, parasites, bacteria, and viruses. The IVIG products differ in the preparation method,
viral inactivation steps, stabilizing agent, osmolality, and IgA content (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of IVIG while
maintaining optimal therapeutic outcomes.

References
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