Pharmacy Drug Policy & Procedure

Policy Name:	Immune Globulin Products	Policy #:	1815P

Purpose of the Policy

The purpose of this policy is to establish the criteria for coverage of Immune Globulin products (Atgam, Bivigam, Carimune NF, Cutaquig, Cuvitru, Glebogamma DIF, Gamastan S/D, Gammagard, Gammaked, Gammaplex, Gamunex, Gamunex-C, Hizentra, Hyqvia, Nabi-HB, Octagam, Privigen, and Xembify).

Statement of the Policy

Health Alliance Medical Plans will approve the use of Atgam, Bivigam, Carimune NF, Cutaquig, Glebogamma DIF, Gamastan S/D, Gammagard, Gammaked, Gammaplex, Gamunex, Gamunex-C, Nabi-HB, Octagam or Privigen under the Specialty Medical benefit or Cuvitru, Hizentra, Hyqvia, or Xembify under the Specialty Pharmacy benefit when the following criteria have been met.

Criteria

IVIG contains at least 90 percent IgG, with distribution of IgG subclasses corresponding to normal serum as well as trace amounts of IgA and IgM. IVIG is used when an immediate increase or higher level of circulating immunoglobulin are required to correct a deficiency state or modify an ongoing immunologic reaction, or when intramuscular injections of immunoglobulin are contraindicated.

1. Coverage Criteria for Immunodeficiency Disorders

1.1 Common Variable Immunodeficiency (CVID), Hypogammaglobulinemia (excluding IgA deficiency), or X-linked immunodeficiency
- Documented serum IgG level below the lower limits of normal of the laboratory's reported value

1.2 Immunosuppression related to B-cell chronic lymphocytic leukemia (CLL)
- Documentation to support hypogammaglobulinemia or recurrent bacterial infections

1.3 Immunosuppression related to multiple myeloma
- Documentation to support diagnosis of multiple myeloma and hypogammaglobulinemia or recurrent infections

1.4 Selective IgG subclass deficiencies
- Documented serum immune globulin (Ex IgG, IgM, etc) level below the lower limits of normal of the laboratory's reported value
- Documented history of recurrent infections causing extended antibiotic use

2. Coverage Criteria for Infection related conditions

2.1 HIV
- Children: diagnosis of HIV in children who either have been exposed to measles or who live in a high-prevalence measles area, HIV-related immune thrombocytopenic purpura
- Adults: diagnosis of HIV-ITP who have severe bleeding

2.2 Chronic enteroviral meningoencephalitis

2.3 Staphylococcal or streptococcal toxic shock syndrome

3. Coverage Criteria for transplant related conditions

3.1 Cytomegalovirus (CMV) viremia in solid organ transplants or cancer

3.2 Bone marrow transplantation
- Confirmed allogeneic bone marrow transplant within the last 100 days
- Documented hypogammaglobulinemia with intent to prevent GVHD or infection

3.3 Prevention or treatment of acute humoral rejection in renal transplants

4. Coverage Criteria for blood related conditions

4.1 Autoimmune hemolytic anemia with hemoglobin < 7 or hepatomegaly

4.2 Hemolytic disease of newborn (Erythroblastosis Fetalis)

4.3 Idiopathic thrombocytopenic purpura (ITP)

- Diagnosis of ITP in patients with bleeding complications, unsafe platelet counts, or requiring invasive interventions

4.4 Post-transfusion purpura

4.5 Rasmussen syndrome

- Diagnosis of Rasmussen syndrome with persistent disease symptoms despite surgical treatment (or not a candidate for surgery)

4.6 Thrombocytopenia secondary to chronic condition

- Thrombocytopenia related to hepatitis C infection, HIV or pregnancy
- Documentation of unsafe platelet level

5. Coverage Criteria for nervous system related conditions

5.1 Acute disseminated encephalomyelitis

- Documented trial and failure of intravenous corticosteroids

5.2 Guillain-Barre syndrome

- Diagnosis of Guillain-Barre Syndrome with severe disease requiring aid to walk
- Prescribed by or in consultation with a neurologist (nervous system doctor)

5.3 Chronic inflammatory demyelinating polyneuropathy (CIDP)

- Diagnosis of chronic inflammatory demyelinating polyneuropathy as confirmed by progressive or relapsing motor or sensory impairment of more than one limb for more than 2 months
- Prescribed by or in consultation with a neurologist (nervous system doctor)

5.4 IgM antimyelin-associated glycoprotein paraprotein-associated peripheral neuropathy

5.5 Lambert-Eaton myasthenic syndrome (LEMS)

- Diagnosis of Lambert-Eaton myasthenic syndrome (LEMS)
- Prescribed by or in consultation with a neurologist (nervous system doctor)
- Documented trial and failure with immunomodulator therapy (azathioprine, corticosteroids, etc)

5.6 Lennox Gastaut

- Diagnosis of Lennox Gastaut seizures
- Prescribed by or in consultation with a neurologist (nervous system doctor)
- Documented trial and failure with traditional anti-epileptics (lamotrigine, phenytoin, etc)

5.7 Moersch-Woltmann (Stiff-person) syndrome

- Diagnosis of stiff-person syndrome
- Prescribed by or in consultation with a neurologist (nervous system doctor)
- Documented trial and failure to benzodiazepines and/or baclofen, tizanidine, etc

5.8 Multifocal motor neuropathy

- Diagnosis of multifocal motor neuropathy as supported by weakness with continued progression over at least one month
- Prescribed by or in consultation with a neurologist (nervous system doctor)

5.9 Myasthenia gravis (chronic or exacerbation)

- Diagnosis of generalized myasthenia gravis
- Documentation to support exacerbation in symptoms over the last month
- Prescribed by or in consultation with a neurologist (nervous system doctor)

6. Coverage Criteria for musculoskeletal related conditions

6.1 Dermatomyositis or polymyositis

- Diagnosis of dermatomyositis or polymyositis
- Documented trial and failure to immunosuppressive therapy (azathioprine, corticosteroids, etc)

6.2 Kawasaki disease
- Acute treatment only when given in conjunction with aspirin within 10 days of symptom onset

6.3 Severe rheumatoid arthritis refractory to conventional treatments (methotrexate, etc)

7. Coverage Criteria for skin related conditions

7.1 Autoimmune bullous disease such as pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa acquisita
- Diagnosis of a supported autoimmune bullous disease that is extensive and debilitating
- Documented trial and failure of corticosteroids with immunosuppressives

8. Coverage Criteria for eye related conditions

8.1 Birdshot retinochoroidopathy

8.2 Autoimmune uveitis
- Diagnosis of refractory autoimmune uveitis
- Documented trial and failure with corticosteroids in addition to immunosuppressants

8.3 Graves' ophthalmopathy

9. Coverage Criteria for lung related conditions

9.1 Churg-Strauss syndrome
- Documented trial with corticosteroids in addition to cyclophosphamide

10. Coverage Criteria for Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) and Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection (PANDAS)
- Diagnosis of moderate-to-severe or severe-to-life-threatening PANS/PANDAS, including all of the following:
  - Presence of clinically significant obsessions, compulsions and/or tic, occupying greater than 50% of waking hours with Children's Yale-Brown Obsessive Compulsive Scale (CYBOCS), performed by a trained mental health clinician rating of ≥ 20; AND
  - Age 3 years to the beginning of puberty; AND
  - Abrupt onset of symptoms or a relapsing-remitting course of symptom severity; AND
  - Other neuropsychiatric symptoms which have an onset within 1 to 2 days of the onset of obsessions, compulsions or tics. (Examples: emotional lability, irritability, aggression, increased urinary frequency, bed-wetting, painful or disruptive movements, sleep disturbances, cognitive impairment, memory loss, deterioration in school performance, reduced food or fluid intake); AND
- Diagnosis made by a medical team of pediatric subspecialists, including but not limited to, a psychiatrist, neurologist, and infectious disease provider; AND
- Provider documentation indicates that appropriate differential diagnostic testing (e.g., imaging, blood tests, CSF studies, cardiac testing) has been performed to rule out all other more specific causes of the patient's symptoms such as autoimmune encephalitis, central nervous system vasculitis, neuropsychiatric systemic lupus erythematosus, acute disseminated encephalomyelitis, infectious encephalitis, etc.; AND
- For a diagnosis of PANDAS, documentation of a group A streptococcal (GAS) infection within one to two weeks prior to onset or exacerbation of symptoms.
- Documentation that patient is currently free of streptococcal and other infections; AND
- Active participation in cognitive behavioral therapy (e.g., exposure response prevention) AND
- One of the following:
  - Prescriber indicates the member is currently stable on a selective-serotonin reuptake inhibitor (SSRI) indicated for the treatment of pediatric OCD, OR
  - Prior treatment with SSRIs resulted in pre-mature discontinuation of SSRI therapy due to an

intolerance, OR
  - Member has an absolute contraindication which prevents treatment with an SSRI, AND
- One of the following:
  - Symptoms did not improve following an adequate trial with corticosteroids. Adequate is defined as: Administration of an appropriate dose for the recommended duration of time, based on the severity of the disease, found on Table 2 in the Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome: Part II – Use of Immunotherapy Therapies, OR
  - Prior treatment with corticosteroids resulted in pre-mature discontinuation of corticosteroid therapy due to an intolerance, OR
  - Member has an absolute contraindication which prevents treatment with an adequate trial of corticosteroids, AND
- Documentation that provider has determined patient's IgA level; AND
  - If member is IgA-deficient (<10mg/dL), IgA-depleted IVIG should be chosen for administration to lessen the risk of anaphylactic reaction possibly caused by anti-IgA antibodies. (See this chart for IgA content of Immunoglobulin products).
- Approval time is 3 monthly doses.
- Quantity limit of 2 g/kg up to 70 g.
  - Dose may divided in up to 5 daily doses on 5 consecutive days.
- Reapproval for 3 additional months with documentation of the following:
  - Patient had a clear response following treatment with IVIG as shown by a decrease of ≥ 30% on CY-BOCS scale
  - Symptoms re-emerge over the three to six week period after IVIG administration (Frankovich 2017).
  - In provider's opinion, the benefit of treatment outweighs the burden of continued infusions.
  - Coverage for medically necessary treatment is not limited over the member's lifetime
- PANS/PANDAS Exclusions
  - This criteria does not apply to Self-Funded Groups and groups outside of Illinois that exclude coverage of IVIG for this indication.
  - Health Alliance Medical Plans will cover up to six months of PANS/PANDAS treatment with IVIG. Use beyond six months will require documentation of a new strep infection and presentation of symptoms with all the above criteria being met. Repeated doses of IVIG have not been systematically assessed for PANS. [Experts] feel the burden of monthly IVIG (beyond 3–6 monthly doses) may outweigh the benefit in many cases. (Frankovich 2017).

2. Approval Period

2.1 Initial: 12 months

2.2 Reapprovals: 12 months with documentation of beneficial response

2.3 Per 215 ILCS 5/356z.24, if member has been on therapy for at least 2 years and has beneficial response, approval will be for 12 months at a time.

CPT Codes

Atgam, Bivigam, Carimune NF, Cuvitru, Glebogamma DIF, Gamastan S/D, Gammagard, Gammaplex, Gamunex, Gamunex-C, Hizentra, Hyqvia, Nabi-HB, Octagam and Privigen

90281	Immune globulin (Ig), human, for intramuscular use
90283	Immune globulin (IgIV), human, for intravenous use
90284	Immune globulin (SCIg), human, for use in subcutaneous infusions, 100 mg, each

HCPCS Codes	
J1459	Injection, immune globulin (Privigen), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1460	Injection, gamma globulin, intramuscular, 1 cc
J1556	Injection, immune globulin (Bivigam), 500 mg
J1557	Injection, immune globulin, (Gammaplex), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1559	Injection, immune globulin (Hizentra), 100 mg
J1560	Injection, gamma globulin, intramuscular, over 10 cc
J1561	Injection, immune globulin, (Gamunex-c/Gammaked), nonlyophilized (e.g. liquid), 500 mg
J1566	Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg
J1568	Injection, immune globulin, (Octagam), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard liquid), nonlyophilized, (e.g. liquid), 500 mg
J1572	Injection, immune globulin, (Flebogamma / Flebogamma Dif), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1575	Injection, immune globulin/hyaluronidase, (Hyqvia), 100 mg immunoglobulin
J1599	Injection, immune globulin, intravenous, non-lyophilized (eg, liquid), not otherwise specified, 500 mg
J1551	Injection, immune globulin (Cutaquig), 100 mg
J1555	Injection, immune globulin (Cuvitru), 100 mg
J1558	Injection, immune globulin (Xembify), 100 mg
J1576	Injection, immune globulin (Panzyga), intravenous, non-lyophilized (e.g., liquid), 500 mg

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