GAMMA GLOBULINS

Included Products: Asceniv, Bivigam, Cutaquig, Cuvitru, Flebogamma, GamaStan S/D, Gammagard, Gammaked, Gammaplex, Gamunex-C, Hizentra, HyQvia, Octagam, Panzyga, Privigen, Xembify

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Nonformulary for outpatient benefit. PA required on medical benefit.

All Diagnoses

Initial Criteria: All Diagnoses		If yes	If no
1.	Is the request for Asceniv or Panzyga?	Continue to #2.	Continue to diagnosis.
2.	Has the member failed all other IVIG products?	Continue to diagnosis.	Do not approve.

Allogenic Bone Marrow Transplant

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a hematologist, oncologist, transplant specialist, or infectious disease specialist for the prevention of bacterial infections?	Continue to #2	Do not approve.
2.	Does the member have severe hypogammaglobulinemia with IgG levels less than 400 mg/dL after receiving an allogenic bone marrow transplant?	Continue to #3.	Do not approve.
3.	Approve as follows: a. Within 100 days of transplant: 500mg/kg/week for adults and adolescents, and 400mg/kg/month for children until 100 days post transplant. b. After 100 days of transplant: 500mg/kg every 3-4 weeks for 3 months.		

Renewal Criteria		If yes	If no
1.	Has there been clinical response to treatment such as a reduction in recurrent infections, or a statement of medical necessity to continue to maintain IgG levels above 400mg/dL?	Continue to #2.	Do not approve.
2.	Approve for 3 months.		

Autoimmune Hemolytic Anemia, Warm Type

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a hematologist?	Continue to #2.	Do not approve.
2.	Does the member have a diagnosis of autoimmune hemolytic anemia warm type, characterized by a predominance of IgG antibodies?	Continue to #3.	Do not approve.
3.	Has the member failed corticosteroids for at least 3 weeks?	Continue to #4.	Do not approve.
4.	Has the member failed a second line therapy from the following: a. Splenectomy b. Immunomodulators (azathioprine, danazol, cyclosporine, cyclophosphamide, or mycophenolate) c. Rituxan	Continue to #5.	Do not approve.
5.	Approve for 3 months.		
Renewal Criteria		If yes	If no
1.	Has the member had response to treatment, such as resolution of anemia?	Continue to #2.	Do not approve.
2.	Has the member failed to produce a sustained response to therapy?	Continue to #3.	Do not approve.
3.	Approve for 12 months.		

Autoimmune Mucocutaneous Blistering Diseases

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a dermatologist?	Continue to #2.	Do not approve.
2.	Does the member have one of the following diagnoses confirmed by biopsy and pathology? a. Pemphigus vulgaris b. Pemphigus foliaceous c. Bullous pemphigoid d. Mucous membrane pemphigoid e. Epidermolysis bullous acquisita	Continue to #3.	Do not approve.
3.	Has the member tried and failed or have a contraindication to systemic corticosteroids?	Continue to #4.	Do not approve.
4.	Has the member failed one of the following immunosuppressants? a. Azathioprine b. Cyclophosphamide c. Cyclosporine d. Methotrexate e. Mycophenolate	Continue to #7.	Continue to #5.
5.	Does the member have rapidly progressive disease in which a clinical response cannot be achieved quickly enough using conventional agents?	Continue to #6.	Do not approve.
6.	Does the provider have a treatment plan to use IVIG only until conventional agents take effect?	Continue to #8.	Do not approve.
7.	Is the IVIG therapy intended for short term therapy only (up to 3 months)?	Continue to #8.	Do not approve.
8.	Approve for 3 months.		

Chronic B-Cell Lymphocytic Leukemia with Hypogammaglobulinemia

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a hematologist, oncologist, or infectious disease specialist?	Continue to #2.	Do not approve.
2.	Does the member have chronic B-cell lymphocytic leukemia with hypogammaglobulinemia (IgG level	Continue to #3.	Do not approve.

	less than 600mg/dL) at baseline?		
3.	Does the member have either of the following? a. Evidence of specific antibody deficiency b. History of a serious bacterial infection that required IV antibiotic therapy or hospitalization	Continue to #4.	Do not approve.
4.	Approve for 3 months.		
Renewal Criteria		If yes	If no
1.	Is there chart note documentation of regular monitoring of IgG trough levels, blood cell counts, and serum chemistry, with improvement from baseline?	Continue to #2.	Do not approve.
2.	Has the member experienced a reduction in the number and/or severity of difficult to treat infections?	Continue to #3.	Do not approve.
3.	Approve for 12 months.		

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) / Multifocal Motor Neuropathy (MMN)

Initial Criteria: All Diagnoses		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a neurologist?	Continue to #2.	Do not approve.
2.	Has the condition persisted for longer than 2 months?	Continue to #3.	Do not approve.
3.	Is there documentation of a baseline strength and weakness using an objective clinical measuring tool, such as Inflammatory Neuropathy Cause and Treatment Score (INCAT), Medical Research Council (MRC), 6-minute timed walking test, Rankin, or Modified Rankin?	Continue to #4.	Do not approve.
4.	Has the diagnosis been made on the basis of electrophysiologic findings that support the diagnosis and rule out other possible conditions that may not respond to IVIG treatment?	Continue to #5.	Do not approve.
5.	Is the diagnosis multifocal motor neuropathy?	Continue to #7.	Continue to #6.

6.	Has the member failed one of the following, or have contraindications to both of the following to treat chronic inflammatory demyelinating polyradiculoneuropathy? a. Corticosteroids b. Plasmapheresis	Continue to #7.	Do not approve.
7.	Approve for 3 months.		
Renewal Criteria		If yes	If no
1.	Has the member displayed an improvement from baseline strength and weakness using an objective clinical measuring tool?	Continue to #2.	Do not approve.
2.	Approve for 6 months.		

Disseminated Encephalomyelitis, Acute

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a neurologist?	Continue to #2	Do not approve.
2.	Is the member under the age of 18?	Continue to #3.	Do not approve.
3.	Has the member tried and failed or have contraindication to intravenous corticosteroids?	Continue to #4.	Do not approve.
4.	Approve for 3 months.		

Fetal and Neonatal Alloimmune Thrombocytopenia

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a hematologist, immunologist, obstetrician or neonatologist?	Continue to #2.	Do not approve.
2.	Is the member a neonate with neonatal alloimmune thrombocytopenia?	Continue to #5.	Continue to #3.
3.	Is the member a pregnant woman who has experienced a previous pregnancy affected by fetal alloimmune thrombocytopenia?	Continue to #7.	Continue to #4.

4.	Has a cordocentesis revealing fetal platelets less than 20 x 10^9/L been performed?	Continue to #7.	Do not approve.
5.	Is the neonate severely thrombocytopenic with a platelet count less than 30 x 10^9/L and/or symptomatic?	Continue to #6.	Do not approve.
6.	Has the neonate failed, have a contraindication to, or is intolerant to platelet transfusions?	Continue to #7.	Do not approve.
7.	Approve for 3 months or for the duration of pregnancy.		

Guillain-Barre Syndrome

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a neurologist?	Continue to #2.	Do not approve.
2.	Has the disorder been diagnosed during the first 2 weeks of the illness, and IVIG is to be initiated within 4 weeks of onset?	Continue to #3.	Do not approve.
3.	Does the member have severe disease with significant weakness such as inability to stand or walk without aid, respiratory or bulbar weakness, or Miller-Fisher syndrome (MFS)?	Continue to #4.	Do not approve.
4.	Is IVIG to be used along with plasmapheresis?	Do not approve.	Continue to #5.
5.	Approve for 1 month.		

HIV, Pediatric

Initial Criteria		If yes	If no
1.	Is the immune globulin being prescribed by or supervised by an immunologist or an infectious diseases provider?	Continue to #2.	Do not approve.
2.	Is the member less than 13 years old and infected with HIV?	Continue to #3.	Do not approve.
3.	Is the member on highly active antiretroviral therapy (HAART)?	Continue to #4.	Do not approve.
4.	Is the CD4+ count greater than 200/mm3?	Continue to #5.	Do not approve.

5.	Does the member meet one of the following criteria? a. Hypogammaglobulinemia defined as serum IgG concentration less than 400 mg/dL. b. Recurrent serious bacterial infections, defined as two or more infections such as bacteremia, meningitis, or pneumonia in a 1-year period. c. Failure to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine. d. 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. e. HIV-infected children who are exposed to measles (single dose indicated). f. HIV-infected children with chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy.	Continue to #6.	Do not approve.
6.	Approve up to 12 months.		
Renewal Criteria		If yes	If no
1.	Has the member demonstrated a clinical response to therapy, such as reduction of recurrent infections?	Continue to #2.	Do not approve.
2.	Approve for 12 months.		

Idiopathic Inflammatory Myopathies (Dermatomyositis and Polymyositis)

Initial Criteria: All Diagnoses		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a neurologist or rheumatologist?	Continue to #2.	Do not approve.
2.	Does the member have a diagnosis of an	Continue to #3.	Do not approve.

	idiopathic inflammatory myopathy confirmed by biopsy (muscle or skin) or by the presence of a pathognomonic skin rashes (heliotrope rash, Gottron's papules, and/or Gottron's sign)?		
3.	Does the member have severe active illness with muscle weakness?	Continue to #4.	Do not approve.
4.	Has the member failed or have a contraindication to corticosteroids?	Continue to #5.	Do not approve.
5.	Has the member failed immunosuppressants, such as methotrexate, azathioprine, mycophenolate mofetil, cyclosporine, or cyclophosphamide?	Continue to #6.	Do not approve.
6.	Approve for 3 months.		
Renewal Criteria		If yes	If no
1.	Has the member had a response to treatment, with improvement in functioning and/or in CPK?	Continue to #2.	Do not approve.
2.	Approve for 12 months.		

Immune Thrombocytopenic Purpura (ITP)

Initial Criteria: All ITP Diagnoses		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a hematologist?	Continue to specific diagnosis.	Do not approve.
	Adult ITP		
1.	Does the member have persistent or chronic ITP for longer than 6 months?	Continue to #3.	Continue to #2.
2.	Does the member require acute treatment under one of the following conditions? a. Platelet count less than 20 x 10^9/L, considered to be at risk for bleeding b. Platelet count less than 30 x 10^9/L with acute bleeding c. Member is preparing to undergo surgery, such as a splenectomy, with platelet count less than 75 x 10^9/L.	Continue to #4.	Do not approve.
3.	Are the platelet counts persistently at or below 20 x 10^9/L?	Continue to #4.	Do not approve.
4.	Has the member failed corticosteroids?	Continue to #6.	Continue to #5.

5.	Are corticosteroids contraindicated, or does the provider make a statement that a rapid increase in platelets is required?	Continue to #6.	Do not approve.
6.	Approve for 3 months.		
	Pediatric ITP		
1.	Does the member have persistent (3-12 months) or chronic (greater than 12 months) ITP?	Continue to #3.	Continue to #2.
2.	Does the member present with significant acute mucous membrane bleeding or other noncutaneous bleeding?	Continue to #4.	Do not approve.
3.	Does the member have significant ongoing bleeding?	Continue to #4.	Do not approve.
4.	Has the member failed corticosteroids?	Continue to #6.	Continue to #5.
5.	Are corticosteroids contraindicated, or does the provider make a statement that a rapid increase in platelets is required?	Continue to #6	Do not approve.
6.	Approve for 3 months.		
	ITP in pregnancy		
1.	Is the member a pregnant woman with ITP?	Continue to #2.	Do not approve.
2.	Does the member require treatment based on one of the following conditions? a. Previously delivered an infant with autoimmune thrombocytopenia. b. Platelet count of less than 10 x 109/L during the third trimester c. Platelet count of less than 30 x 109/L associated with bleeding d. Platelet count of less than 75 x 109/L at time of delivery, to achieve minimum platelet counts recommended to undergo the procedures e. Past history of splenectomy.	Continue to #3.	Do not approve.
3.	Has the member failed corticosteroids?	Continue to #5.	Continue to #4.
4.	Are corticosteroids contraindicated, or does the provider make a statement that a rapid increase in platelets is required?	Continue to #5.	Do not approve.
5.	Approve for appropriate duration for pregnancy term.		
Renewal Criteria		If yes	If no
1.	Has the member experienced a reduction of bleeding episodes and/or increased quality of	Continue to #2.	Do not approve.

	life?		
2.	Is there documentation of medical necessity to continue in order to prevent bleeding episodes?	Continue to #3.	Do not approve.
3.	Approve 12 months.		

Kawasaki Disease, Mucocutaneous Lymph Node Syndrome (MCLS)

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a pediatric cardiologist or a pediatric infectious diseases physician?	Continue to #2.	Do not approve.
2.	Has the diagnosis been confirmed by the presence of fever for at least 5 days with four of the following clinical signs: a. Mucous membrane changes such as a red tongue and dry fissured lips; b. Swelling of the hands and feet; c. Enlarged lymph nodes in the neck; d. Diffuse red rash covering most of the body; e. Redness of the eyes.	Continue to #3.	Do not approve.
3.	Is the treatment being initiated within 10 days of onset of fever?	Continue to #4.	Do not approve.
4.	Is the treatment being administered with aspirin, or if contraindicated with an alternative antiplatelet agent?	Continue to #5.	Do not approve.
5.	Approve for 1 month.		

Kidney Transplant

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a transplant specialist?	Continue to #2.	Do not approve.
2.	Is IVIG being used for the prevention of acute humoral rejection in renal transplant?	Continue to #3.	Continue to #4.

3.	Is the member at high risk of antibody mediated rejection?	Continue to #5.	Do not approve.
4.	Has the member experienced an antibody mediated rejection?	Continue to #5.	Do not approve.
5.	Approve for 1 month.		

Myasthenia Gravis

Initial Criteria		If yes	If no
1.	Is immune globulin being prescribed by or supervised by a neurologist?	Continue to #2.	Do not approve.
2.	Does the member have acute decompensated myasthenic crisis with respiratory failure or impending respiratory failure with severe bulbar symptoms?	Continue to #8.	Continue to #3.
3.	Does the member require stabilization of myasthenia gravis before surgery, such as for thymectomy?	Continue to #8	Continue to #4.
4.	Is IVIG being used in a treatment plan including a specific supported immunosuppressive therapy, and is intended to bridge until the immunosuppressant takes effect?	Continue to #5.	Continue to #6.
5.	Is there documentation of trial and failure of or contraindication to corticosteroids?	Continue to #9.	Do not approve.
6.	Is IVIG being used for maintenance?	Continue to #7.	Do not approve.
7.	Is there a contraindication to ALL of the following immunosuppressants? a. Corticosteroids b. Azathioprine c. Cyclosporine d. Mycophenolate mofetil e. Methotrexate f. Tacrolimus g. Cyclophosphamide	Continue to #9.	Do not approve.
8.	Is there a contraindication to plasmapheresis, such as poor venous access?	Continue to #9	Do not approve.
9.	Approve for 3 months.		
Renewal Criteria		**If yes**	**If no**
1.	Is the request for renewal of maintenance	Continue to #2.	Evaluate on

	therapy?		initial criteria.
2.	Has the member demonstrated a response in reduction of number of myasthenic crises or improvement in function?	Continue to #3.	Do not approve.
3.	Approve for 6 months.		

Primary Immunodeficiencies

Initial Criteria		If yes	If no
1.	Is the immune globulin being prescribed by or supervised by an allergist, immunologist, otolaryngologist or an infectious diseases provider?	Continue to #2.	Do not approve.
2.	Has the member been diagnosed with selective IgG subclass deficiency with deficiency of 1 or more IgG subclasses (e.g. IgG1, IgG2, IgG3, or IgG4) > 2 standard deviations (SD) below age-specific mean, assessed on 2 separate occasions during infection free period?	Continue to #9.	Continue to #3.
3.	Has the member been diagnosed with specific antibody deficiency (SAD) AND normal levels of immunoglobulin and normal levels of IgG subclasses?	Continue to #9.	Continue to #4.
4.	Has the member been diagnosed with CVID or unspecified hypogammaglobulinemia?	Continue to #5.	Continue to #6.
5.	Does the member have at least one of the following? a. Reduced total serum IgG level b. Reduced IgG1 and IgG3 subclass levels c. Reduced IgG1 alone d. Markedly impaired antibody response to protein (e.g., tetanus, diphtheria) antigen OR a polysaccharide antigen (pneumococcus)	Continue to #9.	Do not approve.
6.	Does the member have hypogammaglobulinemia, X-linked agammaglobulinemia (Bruton's agammaglobulinemia, congenital agammaglobulinemia), severe combined immunodeficiency (SCID), Wiskott-Aldrich syndrome, Hyper-IgM syndromes (X-linked or	Continue to #7.	Do not approve and check other diagnoses.

	autosomal recessive), or another humoral immunodeficiency?		
7.	Does the member have agammaglobulinemia with ONE of the following? a. Total IgG < 200 mg/dL (at baseline prior to immune globulin therapy), OR b. Patients with an abnormal Bruton tyrosine kinase (BTK) gene/absence of BTK protein, OR c. Absence of B lymphocytes	Continue to #10	Continue to #8.
8.	Does the member have hypogammaglobulinemia with a total IgG < 600mg/dL (at baseline prior to immune globulin therapy)?	Continue to #9.	Do not approve.
9.	Has the member had poor antibody response to vaccines (and/or absent isohaemagglutinins); i.e. absence of protective levels despite vaccination)?	Continue to #10.	Do not approve.
10.	Does the member have evidence of recurrent, persistent, severe, difficult-to-treat infections (e.g. recurring otitis media, bronchiectasis, recurrent infections requiring IV antibiotics, etc.) despite aggressive management and treatment with antibiotics?	Continue to #11.	Do not approve.
11.	Approve for 12 months.		
Renewal Criteria		If yes	If no
1.	Is there chart note documentation of regular monitoring of IgG trough levels, blood cell counts, and serum chemistry, with improvement from baseline?	Continue to #2.	Do not approve.
2.	Has the member experienced a reduction in the number and/or severity of difficult to treat infections?	Continue to #3.	Do not approve.
3.	Approve for 12 months.		

REFERENCES

- Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective
- NCCN Prevention and Treatment of Cancer-Related Infections
- Evidence-based focused review of the treatment of idiopathic warm immune hemolytic anemia in adults

- The diagnosis and management of primary autoimmune haemolytic anaemia
- National Coverage Determination (NCD) for Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases (250.3)
- Guidelines for the management of pemphigus vulgaris
- Guidelines for the management of bullous pemphigoid
- NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Guidelines
- Evidence-based guideline: Intravenous immunoglobulin in the treatment of neuromuscular disorders
- 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups
- The American Society of Hematology 2019 evidence-based practice guideline for immune thrombocytopenia
- AHA Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease
- International consensus guidance for management of myasthenia gravis
- Practice parameter for the diagnosis and management of primary immunodeficiency
- Update on the use of immunoglobulin in human disease: A review of evidence