Effective Date: April 13, 2017

Subject: Immune Globulin

Authorization:

Prior authorization is required for all immune globulin provided to members enrolled in commercial (HMO, PPO, and POS) products.

- Authorization, including reauthorization of on-going treatment, is limited to maximum of 6 months when relevant criteria are met.

Policy and Coverage Criteria:

Harvard Pilgrim Health Care (HPHC) covers intravenous and subcutaneous immune globulin that is medically necessary and proven effective for treatment of specific conditions listed in the policy.

- Use of immune globulin must be clinically appropriate and supported by evidence-based literature; dosage, frequency, site of administration, and duration of therapy must be reasonable and appropriate based on condition and severity, alternative available treatments, and previous response to intravenous immune globulin therapy.
- HPHC covers the following drugs when criteria within the policy are met:
    - Bivigam (IV)
    - Carimune NF (IV
    - Flebogamma DIF
    - Gammagard Liquid
    - Gammagard S/D
    - Gammaked (IV, SC)
    - Gammaplex (IV)
    - Octagam (IV)
    - Privigen (IV)
    - Vivaglobin (IV)
    - Gamunex – C (IV, SC)
    - Hizentra
    - HyQvia

HPHC does not authorize any use of immune globulin (IVIG or scIG) considered investigational or unproven, and/or is not supported by evidence-based literature.

Treatment with immune globulin is authorized when all General Eligibility Criteria and relevant Condition-Specific Criteria (below) are met:

1. Medical record documentation confirms the member has been definitively diagnosed (by an appropriate specialist) with a Covered Condition; AND
2. The diagnosis is confirmed by evidence-based diagnostic criteria (supported by peer-reviewed, published literature) and supportive testing, and clearly documented in clinical notes; AND
3. Use (including requested frequency and dosage) of immunoglobulin is supported by evidence-based literature; AND
4. The member is closely followed by the prescribing specialist, and treatment response has clearly defined endpoints to measure effectiveness.

Ongoing treatment with immune globulin is authorized when ALL the following criteria are met:

1. Documentation confirms the member has a chronic medical condition that requires maintenance therapy, and has achieved a sustained beneficial response to immunoglobulin treatment, including significant improvement in defined clinical endpoints; AND
2. The member is closely followed by the prescribing specialist, and, when clinically appropriate, dose and frequency of immunoglobulin treatment have been titrated to the minimum dose/frequency required to maintain the desired clinical effect; AND
3. Treatment has not exceeded any applicable condition-specific treatment duration listed below; AND
4. Clinical documentation includes a detailed description of the proposed frequency and duration of future immunoglobulin treatment.

Condition-Specific Criteria

Hematologic/Oncologic Conditions and Transplants

Condition	Authorization Criteria	Dosage Recommendation
Acquired Factor VIII Inhibitors Associated with Autoimmune Disease and/or Malignancy)	Authorized for refractory cases of non-hemophilic members when steroids and cyclophosphamide have failed to reduce the inhibitor. **NOTE: IVIG is not authorized in place of Desmopressin (DDAVP) or clotting factor concentrates for active bleeding.**	Dosing recommendation: 2 gm/kg IV divided over 2-5 days. • Repeat dosing may be required depending on effect.
Acquired Pure Red Cell Aplasia in the Setting of Parvovirus and Immunocompromise (e.g., HIV)	Authorized when documentation confirms diagnosis, and IVIG is ordered in conjunction with treatment of the immunodeficiency.	Dosing recommendation: 1-2 gm/kg IV divided over 2-5 days. • Generally single treatment course, with repeat course in cases of relapse.
Autoimmune Hemolytic Anemia due to Warm Agglutinins	Authorized when documentation confirms refractory disease in a member who has not responded after steroid treatment and/or splenectomy.	Dosing recommendation 1gm/kg IV per day for 5 days. • May require retreatment.
Acquired von Willebrand Syndrome Associated with Autoimmune Disease and Monoclonal Gammopathy	Authorized when documentation confirms ALL the following: 1. Refractory disease; AND 2. Treatment failure or contraindication to Desmopressin (DDAVP), and von Willebrand Factor-containing concentrates.	Dosing recommendation: 1gm/kg IV per day for 2 days. • Repeat dosing depending on effect.
Autoimmune Neutropenia ➢ Most cases do not	Authorized when documentation confirms diagnosis, and history of clinical infections felt	Dosing recommendation: 1-3 gm/kg IV divided over 2-5

Condition	Authorization Criteria	Dosage Recommendation
require treatment.	to be related to neutropenia.	days.
Immune thrombocytopenia (ITP) **IVIG is not authorized in place of corticosteroids, or for chronic treatment for ITP.**	**Adults:** Authorized when documentation confirms ANY the following: ▪ Platelet count ≤ 30,000 in situations where corticosteroids have failed or are contraindicated; OR ▪ Bleeding complications related to thrombocytopenia; OR ▪ Member in preparation for splenectomy or other surgical procedures (platelet count goal is generally >50,000). **In pregnancy either corticosteroids or IVIG can be used initially. For ITP associated with Hepatitis C virus, antiviral medications should be initiated and if further treatment for the thrombocytopenia is needed, IVIG can be used without a steroid trial.** **Children and Adolescents:** Authorized when documentation confirms the need for treatment (guided by symptoms, not by platelet count). ▪ For symptomatic members, either corticosteroids or IVIG may be used.	**Adults:** Recommended dosage is 1 gm/kg IV initially, with repeat dose up to 2 mg/kg IV if needed. **Children and Adolescents:** Suggested IVIG dose is 0.8-1 mg/kg as a single dose.
Neonatal Alloimmune Thrombocytopenia	Authorized when documentation confirms IVIG to be utilized for ANY of the following: ▪ As adjunctive therapy for a neonate when platelet transfusions have been ineffective; OR ▪ Pregnant women who has previously given birth to an affected child.	**For neonates**: 400 mg/kg/day IV for 3-4 days, or 1 gm/kg IV for 1-3 days. **For pregnant women:** Weekly infusion of 1 gm/kg IV.
Neonatal Autoimmune Thrombocytopenia	Authorized when documentation confirms neonate has ANY of the following: ▪ Platelet count < 30,000; OR ▪ Bleeding complications related to thrombocytopenia.	
Post-Transfusion Purpura	Authorized when documentation confirms member has ANY of the following:	Dosing recommendation: 2gm/kg IV divided over 2-5

Condition	Authorization Criteria	Dosage Recommendation
	▪ Platelet count < 30,000; OR ▪ Bleeding complications related to thrombocytopenia.	days (generally single treatment).
Solid Organ Transplant Recipients	**Pre-Transplant:** Authorized when documentation confirms need to reduce anti-HLA antibodies in member at high risk of antibody-mediated rejection (e.g., highly sensitized patients, patients receiving an ABO incompatible organ). **Post Transplant:** Authorized when documentation confirms ANY of the following: ▪ Member with antibody-mediated rejection; OR ▪ Members with hypogammaglobulinemia post transplant (see Secondary Hypogammaglobulinemia below); OR ▪ CMV pneumonitis (IVIG used in conjunction with an anti-viral); OR ▪ Prophylaxis of CMV in high risk members in conjunction with an anti-viral. (Generally, treatment is indicated for 100 days post transplant.)	Dosing recommendation: 2 gm/kg IV monthly, or 100mg/kg IV when used after plasmapheresis session.
Stem Cell/Bone Marrow Transplant Recipients	Authorized post transplant when documentation confirms ANY of the following: ▪ Member has hypogammaglobulinemia (see Secondary Hypogammaglobulinemia below); OR ▪ Diagnosis of CMV pneumonitis (IVIG used in conjunction with an anti-viral); OR ▪ For prophylaxis of CMV in high risk member (IVIG used in conjunction with an anti-viral). (Generally, treatment is indicated for 100 days post transplant.) ▪ For prevention of GVHD in allogenic transplants (treatment generally for 100 days post transplant).	

Immunologic Conditions

Condition	Authorization Criteria	Dosage Recommendation

Condition	Authorization Criteria	Dosage Recommendation
Autosomal Recessive Agammaglobulinemia	Authorized when documentation confirms ALL the following: 1. IgG and IgA and IgM levels more than 2 standard deviations below mean for age on at least two occasions when the member was clinically well; 2. Recurrent bacterial infections attributed to low IgG (e.g., sinopulmonary infections, otitis) or serious bacterial infections (e.g., bacteremia, meningitis, osteomyelitis) in the first 5 years of life. Reauthorization requests must include evidence that treatment has been effective (e.g., fewer and/or less severe clinical infections).	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or equivalent scIG weekly.
Common Variable Immunodeficiency (CVID)	Authorized when documentation confirms ALL the following: 1. IgG level more than 2 standard deviations below mean for age on at least two occasions when the member is clinically well; 2. Recurrent bacterial infections (e.g., sinopulmonary infections, otitis) attributed to low IgG, or serious bacterial infections (e.g., bacteremia, meningitis, osteomyelitis). **NOTE: For members undergoing treatment expected to cause immunosuppression (i.e., for malignancy or inflammatory arthritis), prophylactic IVIG may authorized without evidence of prior clinical infections.**	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or equivalent scIG weekly.
Defects of NF-Kappa-B Regulation- NEMO Mutation	Authorized when documentation confirms ANY of the following: ▪ IgG levels less than 200-300 in an asymptomatic patient with an elevated risk of severe infection; ▪ Poor specific antibody response in a patient with normal IgG; ▪ IgG level more than 2 standard deviations below mean for age on at	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or equivalent scIG weekly.

Condition	Authorization Criteria	Dosage Recommendation
	least two occasions when the member is clinically well, **and** recurrent bacterial/viral infections (e.g., sinopulmonary infections, otitis), serious bacterial infections (e.g., bacteremia, meningitis, osteomyelitis), or atypical mycobacterium infections. **NOTE: For members with a history of serious or recurrent infections, requests for reauthorization must include evidence that treatment has been effective in reducing the number or severity of clinical infections.**	
Hyperimmunoglobulin M Syndrome - CD40 and CD40L Deficiency	Authorized when documentation (including flow cytometry testing) confirms diagnosis and ALL the following: 1. IgG level more than 2 standard deviations below mean for age on at least two occasions when the member was clinically well; 2. Recurrent bacterial infections attributed to low IgG (e.g., sinopulmonary infections, otitis), or serious bacterial infections (e.g., bacteremia, meningitis, osteomyelitis), or opportunistic infections.	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or equivalent scIG weekly.
IgG Subclass Deficiency	Authorized when documentation confirms member with normal total IgG meets ALL the following: 1. IgG subclass level(s) more than 2 standard deviations below mean for age on at least two occasions when the member is clinically well; 2. Poor immunologic response to the pneumococcal polysaccharide vaccine, in a member over the age of two years; 3. History of recurrent bacterial infections attributed to low IgG subclass (e.g., sinopulmonary infections, otitis) or serious bacterial infections (e.g., bacteremia, meningitis, osteomyelitis).	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or equivalent scIG weekly, then titrated to clinical response.

Condition	Authorization Criteria	Dosage Recommendation
	Requests for re-authorization should include evidence that: ▪ Treatment has been effective in reducing the number or severity of clinical infections; AND/OR ▪ Other appropriate measures (e.g., prophylactic antibiotic therapy, correction of septal deviation or other mechanical contributions to infection) have been considered or are contraindicated.	
Selective Antibody Deficiency with Normal Immunoglobulin	Authorized when documentation confirms member with normal total IgG and IgG subclasses meets ALL the following: 1. Poor immunologic response to pneumococcal polysaccharide vaccine, in a member over the age of two years; 2. History of recurrent bacterial infections attributable to IgG dysfunction (e.g., sinopulmonary infections, otitis) or serious bacterial infections (e.g., bacteremia, meningitis, osteomyelitis); 3. Prophylactic antibiotic therapy and/or correction of mechanical contributions to infection (e.g.,septal deviation, ongoing sinus rinses) have been considered. Requests for re-authorization should include evidence that: ▪ Treatment has been effective in reducing the number or severity of clinical infections; AND/OR ▪ Other appropriate measures (e.g., prophylactic antibiotic therapy, correction of septal deviation or other mechanical contributions to infection) have been considered or are contraindicated. **For members who have been treated with IVIG for 2 or more years, documentation must include evidence that a trial period off IVIG was considered (and ruled out), is contraindicated, or resulted in**	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks, or equivalent scIG weekly, titrated to clinical response.

Condition	Authorization Criteria	Dosage Recommendation
	development of recurrent infections.	
Secondary Hypogammaglobulinemia Due to: ➢ **Chemotherapeutic agents** ➢ **Chronic Lymphocytic Leukemia (CLL)** ➢ **Multiple Myeloma (MM)/Plasma Cell Leukemia (PCL)** ➢ **Solid Organ Transplant Recipient** ➢ **Allogeneic Bone Marrow Transplant Recipient**	Authorized when documentation confirms ALL the following: 1. The member's IgG level was more than 2 standard deviations below mean for age on at least two occasions when the member is clinically well ; 2. Recurrent bacterial infections attributed to low IgG (e.g., sinopulmonary infections, otitis) or serious bacterial or fungal infections (e.g., bacteremia, meningitis, osteomyelitis). **NOTE: Prophylactic IVIG is authorized <u>without documentation of recurrent bacterial infections</u> for members with secondary hypogammaglobulinemia without prior clinical infections who are undergoing therapy that causes additional immunosuppression.** Requests for reauthorization must include evidence that treatment has been effective in reducing the number or severity of clinical infections.	Dosing recommendation: 400-600 mg/kg IV every 3-4 weeks, or equivalent scIG weekly.
Severe Combined Immunodeficiency (SCID)	Authorized when documentation confirms high clinical suspicion of diagnosis (bacterial, viral, opportunistic infections), supported by laboratory findings of low T cells, low IgM, IgA and IgE.	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or equivalent scIG weekly.
Wiskott-Aldrich Syndrome (WAS)	Authorized when documentation confirms a diagnosis of WAS.	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or equivalent scIG weekly.
X-linked Agammaglobulinemia (XLA)	Authorized when documentation confirms diagnosis of XLA and ALL the following: 1. IgG and IgA and IgM levels more than 2 standard deviations below mean for age on at least two occasions when the member was clinically well equivalent; AND 2. Recurrent bacterial infections attributed	Initial dosing recommendation: 400-600 mg/kg IV every 3-4 weeks or scIG weekly.

Condition	Authorization Criteria	Dosage Recommendation
	to low IgG (e.g., sinopulmonary infections, otitis) or serious bacterial infections (e.g., bacteremia, meningitis, osteomyelitis) in the first 5 years of life.	

Neurological Conditions

Conditions	Criteria	Dosage Recommendation
Acute Inflammatory Demyelinating Polyneuropathy (AIDP)	Authorized for 2 courses of therapy (for AIDP and potential relapse).	Dosing recommendation: 2 gm/kg IV divided over 2-5 days
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) Clinical endpoints and specific neurologic exam deficits must be defined prior to treatment, and parameters must be closely monitored.	Authorized when documentation confirms ALL the following: 1. Member with typical CIDP with progressive symmetrical proximal and distal weakness, impairment of predominantly large-fiber sensory modalities, and absent or diminished deep tendon reflexes; 2. Electrodiagnostic studies demonstrate abnormalities of compound muscle action potential (CMAP), distal motor latency (DL), conduction velocity, F-wave or H-wave-reflex minimal latencies in at least 3 nerves, with demyelinating range abnormalities or partial conduction block in at least one nerve; 3. ANY of the following: ▪ Member is intolerant of, or condition is refractory to, therapeutic doses of steroids; OR ▪ Steroid sparing (in the case of chronic steroid use of 6 months or more); OR ▪ Neurologic function assessment score 3 or greater on the Rankin Scale*. Subsequent requests must include documentation confirming ALL the following: 1. Parameters have improved significantly with IVIG treatment; 2. Titration to the minimum dose and frequency to achieve sustained clinical effect have occurred. **For members with Atypical (sensory-only) CIDP** (with distal numbness and	Dosing recommendation: • Initial therapy: 2 gm/kg divided over 2-5 days, and if needed, initial maintenance therapy up to 2 gm/kg every 3-4 weeks, then adjusted to maintain clinical response (generally 0.5-1.0 gm/kg every 3-4 weeks). • Where clinically appropriate, titration to the minimum dose and frequency to achieve sustained clinical effect should be attempted since in some patients the dose can be tapered over 1-2 years and withdrawn.

Conditions	Criteria	Dosage Recommendation
	parasthesias, and predominantly large-fiber impairment with reduced or absent deep tendon reflexes), IVIG is authorized when documentation confirms ALL the following: 1. Electrodiagnostic studies demonstrate axonal pathology, or delayed or absent H reflexes, or prolonged/absent somatosensory potentials; and 2. Sural nerve biopsy findings are consistent with chronic myelinopathy; and 3. Member is intolerant or refractory to therapeutic doses of steroids, or for steroid sparing (in the case of chronic steroid use of ≥ 6 months), or neurologic function assessment score is ≥ 3 on the Rankin Scale*. Subsequent requests must include documentation confirming that parameters have significantly improved with IVIG.	
Guillain Barre Syndrome (GBS)	Initial requests authorized for 2 courses of therapy (for acute inflammatory demyelinating polyneuropathy and potential relapse).	
Lambert-Eaton Myasthenic Syndrome (LEMS) Clinical endpoints and specific neurologic exam deficits must be defined prior to treatment, and parameters must be closely monitored.	Authorized during or after treatment of the underlying malignancy. Subsequent requests must include documentation confirming that parameters have significantly improved with IVIG.	
Multifocal Motor Neuropathy Clinical endpoints and specific neurologic exam deficits must be defined prior to treatment, and parameters must be closely monitored.	Authorized when documentation confirm ALL the following: 1. Member with motor weakness in 2 or more nerves without sensory findings (generally arms rather than legs, and generally asymmetric and distal); 2. GM1 antibodies (present in 30-80%) and conduction block on EMG are supportive. Subsequent requests must include documentation confirming that parameters	Dosing recommendation: Initial therapy - 2 gm/kg IV divided over 2-5 days. Initial maintenance therapy up to 2 gm/kg every 3-4 weeks, then adjusted to maintain clinical response (generally 0.5-1.0 gm/kg every 3-4 weeks).

Conditions	Criteria	Dosage Recommendation
	have significantly improved with IVIG treatment.	
Multiple Sclerosis (MS) • **Relapse-remitting** Clinical endpoints and specific neurologic exam deficits must be defined prior to treatment, and parameters must be closely monitored. **NOTE: IVIG is not authorized for treatment of primary or secondary progressive MS, or progressive relapsing MS.**	Authorized when documentation confirms member with relapsing-remitting MS has exacerbation that is refractory to treatment with an appropriate trial of high dose steroids, and/or interferon ß-1a or 1b (Avonex®, Betaserone®, Rebif®) or glatiramer acetate (Copaxone®). Subsequent requests must include documentation confirming that parameters have significantly improved with IVIG.	
Myasthenia Gravis (MG) **NOTE: IVIg is not authorized for members with moderate exacerbations (steroids are usually effective), or for steroid sparing effect and chronic use.**	Authorized when documentation confirms ANY of the following: ▪ Member with severe exacerbation with respiratory failure, or impending respiratory failure with severe bulbar symptoms, and contraindication to plasmapheresis; ▪ As a treatment bridge for symptomatic members when chronic, slower acting immunotherapies (e.g., azathioprine, cyclosporine) have been added to steroid treatment; ▪ Preparation for surgery for significantly symptomatic patients. May also be authorized for members with refractory disease that has failed standard medical therapy (i.e., 4 month or longer trial of corticosteroids and immunosuppressant [e.g., azathioprine]), and persistent lack of improvement on muscle strength improvement scales. Requests are also considered on a case by case basis when diagnosis of MG is confirmed by the presence of ANY of the following: ▪ Acetylcholine receptor; OR ▪ Muscle specific tyrosine kinase antibodies;	Dosing recommendation: ➢ Single treatment, 2gm/kg IV divided over 2-5 days. ➢ For bridge therapy or refractory cases, up to 2 gm/kg every 3-8 weeks, adjusted to maintain clinical response.

Conditions	Criteria	Dosage Recommendation
	OR ▪ Electrophysiologic study showing decrement on repetitive stimulation.	
Stiff Person Syndrome (Paraneoplastic, Autoimmune, Idiopathic) Clinical endpoints and specific neurologic exam deficits must be defined prior to treatment, and parameters must be closely monitored.	Authorized when documentation confirms ALL the following: 1. Diagnosis (i.e., by supportive testing including EMG findings, anti-glutamic acid decarboxylase antibodies, or anti-amphiphysin antibodies); 2. Symptoms are refractory to benzodiazepines, baclofen, and corticosteroids. Subsequent requests must include documentation confirming that parameters have significantly improved with IVIG.	Dosing recommendation: 2gm/kg IV divided over 2-5 days. Positive treatment effects can last 6 weeks to several months.

Rankin Scale

The Rankin Scale is commonly used for measuring an individual's degree of disability or dependence in daily activities..

- 0: No symptoms.
- 1: No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2: Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- 3: Moderate disability. Requires some help, but able to walk unassisted.
- 4: Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- 5: Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
- 6: Deceased

Rheumatologic/Dermatologic Conditions

Condition	Criteria	Dosage Recommendation
Dermatomyositis (DM) Positive biopsy is the gold standard for diagnosis with supportive evidence by a clinical picture of proximal muscle weakness, elevated CK and myopathy by EMG, and skin rash for DM. **Documentation describing treatment history and/or**	Authorized when documentation confirms member has refractory disease that has failed to respond to ALL the following (unless contraindicated): 1. At least 4-month trial of corticosteroids; 2. Immunosuppressants (e.g., Azathioprine, Methotrexate); 3. Rituxan (rituximab) therapy. ******May be authorized after less than a four month trial of prednisone or prednisone	Dose recommendation: 2 gm/kg IV divided over 2-5 days. Initial maintenance dose of up to 2 gm/kg IV per month adjusted to maintain clinical response (generally 0.5-1.0 gm/kg every 3-4 weeks).

Condition	Criteria	Dosage Recommendation
contraindications is required.	combination therapies when documentation confirms a profound, rapidly progressive, and/or potentially life threatening muscular weakness refractory to, or intolerant of previous therapy.	
Immune Mediated-Necrotizing Myopathy (NM) Positive biopsy is the gold standard for diagnosis with supportive evidence by a clinical picture of proximal muscle weakness, elevated CK and myopathy by EMG, and skin rash for DM. **Documentation describing treatment history and/or contraindications is required.**	Authorized for members with refractory disease that has failed to respond to ALL the following (unless contraindicated): 4. At least 4 month trial of corticosteroids; 5. Immunosuppressants (e.g., Azathioprine, Methotrexate); 6. Rituxan (rituximab) therapy. **Documentation describing prior treatment, and/or contraindications is required.** May be authorized after less than a 4-month trial of prednisone or prednisone combination therapies when there is documentation of a profound, rapidly progressive, and/or potentially life threatening muscular weakness refractory or intolerant to previous therapy.	Dose recommendation: 2 gm/kg IV divided over 2-5 days. Initial maintenance dose of up to 2 gm/kg IV per month then adjusted to maintain clinical response (generally 0.5-1.0 gm/kg every 3-4 weeks).
Kawasaki disease **Acute Febrile Mucocutaneous Lymph Node Syndrome**	Authorized for acute treatment when given, in conjunction with aspirin, within ten days of the onset of symptoms.	Dosing recommendation: 2 gm/kg IV as a single dose; may repeat dose if patient is still febrile.
Bullous Pemphigoid **Cicatrical Pemphigoid** **Pemphigus Foliaceous** **Pemphigus Vulgaris** **Epidermolysis Bullosa Acquisita (EBA)**	Authorized for treatment of: ➢ Biospsy-proven disease; ➢ Refractory pemphigoid/pemphigus that has failed standard medical therapy (including corticosteroids and immunosuppressive medications such as methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide): o For members with pemphigus, standard medical therapy must have been used over at least 6 months unless contraindicated; o For members with pemphigoid, standard medical therapy must have been used over at least 9	Dosing recommendation: 2 gm/kg IV divided over 2-5 days, then monthly as a 3-6 month trial. If there is improvement (with good disease control), a trial of progressively increasing the intervals between doses should be attempted. In addition to IVIG, use of rituximab should be considered for refractory pemphigus vulgaris as well.

Condition	Criteria	Dosage Recommendation
	months for unless contraindicated. For EBA, IVIG may be authorized for initial treatment. The severity of impact on functional abilities of basic activities of daily living should guide the need for further treatment.	
Polymyositis (PM) Positive biopsy is the gold standard for diagnosis with supportive evidence by a clinical picture of proximal muscle weakness, elevated CK and myopathy by EMG, and skin rash for DM. **Documentation describing treatment history and/or contraindications is required.**	Authorized for members with refractory disease that has failed to respond to ALL the following (unless contraindicated): 7. At least 4 month trial of corticosteroids; 8. Immunosuppressants (e.g., Azathioprine, Methotrexate); 9. Rituxan (rituximab) therapy. **Documentation describing prior treatment, and/or contraindications is required.** May be authorized after less than a four month trial of prednisone or prednisone combination therapies when there is documentation of a profound, rapidly progressive, and/or potentially life threatening muscular weakness refractory or intolerant to previous therapy.	Dose recommendation: 2 gm/kg IV divided over 2-5 days. Initial maintenance dose of up to 2 gm/kg IV per month then adjusted to maintain clinical response (generally 0.5-1.0 gm/kg every 3-4 weeks).

Exclusions:

Harvard Pilgrim Health Care (HPHC) does not cover immune globulin for the following conditions:

Hematologic /Oncologic Conditions:

- Acute lymphoblastic leukemia
- Aplastic anemia
- Diamond-Blackfan anemia
- Hemophagocytic syndrome
- Nonimmune thrombocytopenia
- Red cell aplasia (except as noted above due to parvovirus in the setting of immunocompromise)
- Thrombotic thrombocytopenic purpura

Immunological Conditions

- Cellular immunodeficiencies without IgG deficiencies
- Complement deficiencies
- Selective IgA deficiency without IgG or IgG subclass deficiency, and impaired antibody response to vaccination

Infectious Conditions

- Chronic mucocutaneous candidiasis (CMCC)
- Chronic sinusitis
- Lyme disease
- Post-infectious sequelae
- Recurrent otitis media
- Rheumatic fever

Neurologic Conditions

- Alzheimer's Disease
- Amyotrophic lateral sclerosis
- Autism
- Demyelinating optic neuritis
- Epilepsy
- Multiple sclerosis: primary progressive or secondary progressive types
- Myasthenia gravis – chronic management, or in patients responsive to immunosuppressive treatment30
- Paraneoplastic syndromes including but not limited to Lambert-Eaton syndrome16
- Primary progressive, secondary progressive, or progressive relapsing Multiple Sclerosis;
- Pediatric Autoimmune Neuropsychiatric Disorder associated with Streptococcal Infection (PANDAS), Pediatric Acute-onset Neuropsychiatric Syndrome (PANS)
- Stiff-man syndrome

Rheumatological Conditions

- Behcet's syndrome
- Goodpasture's syndrome, and vasculitis associated with other connective tissue diseases
- Inclusion body myositis
- Rheumatoid arthritis
- Scleroderma
- Systemic Lupus Erythematosis
- Vasculitides other than Kawasaki's disease

Other Conditions

- Adrenoleukodystrophy
- Asthma;
- Atopic dermatitis
- Chronic fatigue syndrome
- Cystic fibrosis
- Demyelinating optic neuritis
- Diabetes mellitus
- Hemolytic uremic syndrome
- Idiopathic environmental illness
- Idiopathic lumbosacral flexopathy
- Organ transplant rejection
- Post-infectious sequelae
- Recent onset dilated cardiomyopathy
- Recurrent fetal loss
- Recurrent Spontaneous Abortion or recurrent spontaneous pregnancy loss

- Uveitis
- Other disorders not listed above
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Coding:

Codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible.

CPT® Code	Description
J0850	Injection, cytomegalovirus immune globulin intravenous (human), per vial
J1459	Injection, immune globulin (Privigen), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1557	Injection, immune globulin, (Gammaplex), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1550	Injection, immune globulin (Hizentra), 100 mg
J1561	Injection, immune globulin (GAMUNEX/Gamunex-C/Gammaked), non-lyophilized (e.g. liquid), 500 mg
J1562	Injection, immune globulin (Vivaglobin), 100 mg
J1566	Injection, immune globulin, intravenous, lyophilized (e.g. powder), not otherwise specified, 500 mg
J1568	Injection, immune globulin, (OCTAGAM) intravenous, non-lyophilized (e.g. liquid), 500 mg
J1569	Injection, immune globulin, (GAMMAGARD LIQUID), intravenous, non-lyophilized (e.g. liquid), 500 mg
J1572	Injection, immune globulin, (FLEBOGAMMA/FLEBOGAMMA Dif) intravenous, non-lyophilized (e.g. liquid), 500 mg
J1575	Injection, immune globulin/hyaluronidase, (Hyqvia), 100mg immuneglobulin (effective 4/1/16)
J1599	Injection, immune globulin, intravenous, nonlyophilized (e.g., liquid), not otherwise

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8. Goodin DS, Frohman EM, Garmany GP. Disease modifying therapies in multiple sclerosis. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology 2002; 58(2):169-78.

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Summary of Changes

Date	Revision
4/17	Updated references for reissue
4/13/16	Updated references. Listed available drugs in beginning of policy. Minor language edits.
12/9/15	Added Hyqvia code to list
2/25/15	Formatting and language changes. Remove requirement for trial period off IVIG for multiple conditions (e.g. XLA, hyper IgM, proven genetic disorders). Remove requirement for prophylactic antibiotics.

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