Pharmacy Drug Policy

SUBJECT: Intravenous Immune Globulin (IVIG) & Sub-Cutaneous Immune Globulin (SCIG) Therapy Drug Policy
POLICY NUMBER: PHARMACY-26
EFFECTIVE DATE: 11/2005

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Intravenous immune globulin (IVIG) therapy is used to provide antibodies to patients who are susceptible to diseases for which there is no immunization available. IVIG is a potent immunomodulating agent that consists of concentrated human immunoglobulin, prepared from pooled plasma collected from human donors. Immunologic reactions can be modified, often dramatically by the intravenous administration of a large amount of immune globulin (400 to 2000mg per kilogram of body weight over a period of two to five days). IVIG is also used to treat certain immunodeficiencies. In January 2006, the FDA approved the first immune globulin designed for subcutaneous administration.

This policy only addresses non-specified pooled preparations of intravenous immune globulin, including:
Gammagard S/D (Takeda)
Gammagard Liquid (Takeda)
Gammagard Liquid ERC (Takeda)
Gamunex-C (Grifols Therapeutics)
Gammaplex (Bio Products)
Bivigam (ADMA Biologics)
Flebogamma DIF (Instituto Grifols)
Octagam (Octapharma)
Privigen (CSL Behring)
Panzyga (Pfizer)
Asceniv (ADMA Biologics)
Alyglo (GC Biopharma Corp)
Yimmugo (Biotest)
Qivigy (Kedrion)

As well as non-specified subcutaneous immune globulins:
Cutaquig (Octapharm)
Cuvitru (Takeda)
Hizentra (CSL Behring AG)
HyQvia (Takeda),
Gammaked (Kedrion Biopharma)
Gamunex-C (Grifols Therapeutics)
Gammagard Liquid (Takeda)
Gammagard Liquid ERC (Takeda)
Xembify (Grifols Therapeutics)

This policy DOES NOT address other immunoglobulin preparations that at are specifically used for passive immunization (such as GamaSTAN) to prevent or attenuate infection with specific viral diseases such as respiratory syncytial virus, cytomegalovirus, or hepatitis A/B, or specifically used to treat infant botulism (such as BabyBig).

IVIG is a polar molecule with a small volume of distribution of 0.042 L/kg, long half-life between 24 and 28 days, and a lack of accumulation in peripheral lipophilic material (48% distributed intravascularly). Due to the properties of the drug, **ideal body weight** will be used for approved dosing calculations. Please see policy guidelines for ideal body weight calculations.

POLICY:

I. The Health Plan has determined that Asceniv, Alyglo, and Qivigy are not medically necessary due to the availability of lower costing options that are likely to produce equal therapeutic results.
    a. **This applies to all lines of business EXCEPT Medicare Part B**
II. Based upon our criteria and review of the peer-reviewed literature IVIG therapy has been medically proven effective and therefore may be considered **medically appropriate** for the following conditions when the appropriate criteria are met.

INDICATIONS	CRITERIA
Primary humoral immunodeficiencies: • Agammaglobulinemia (IgG <200 mg/dL or infants with BTK gene or absence of B lymphocytes) • Hypoglobulinemia, • Common variable immunodeficiency, • Wiskot-Aldrich Syndrome, • X-Linked immunodeficiency, • Severe combined immunodeficiency, • Selective IgG subclassdeficiency, • Selective IgM immunodeficiency • Immunodeficiency with near/normal IgM (absent IgG, IgA) or known as Hyper IgM Syndrome	Member will be covered for a documented diagnosis (as listed to the left) if: 1) There is supporting lab evidence (either a or b): I. Total IgG level <400mg/dl or infants with BTK gene or absence of B lymphocytes **OR** II. Normal IgG level and documentation of a lack of ability to produce and antibody response to a protein (e.g., tetanus) or polysaccharide antigen** (e.g., Pneumococcal polysaccharide or H. Influenza type B.) i. **Serum antibody titres to pneumococcus should be measured prior to immunization and 3-6 weeks after immunization with polyvalent pneumococcal polysaccharide vaccine (e.g., Pneumovax); at least 14 polysaccharide antigens should be tested. ii. Polysaccharide nonresponsiveness is defined as less than a 4-fold rise in antibody titer and lack of protective antibody titer (specific IgG antibody titer less than 1.3 mcg/ml) in greater than 30 percent of antigens tested (more than 50 percent in children ages 2 to 5 years).

	iii. Further evidence of infection, including sinus and lung imaging, complete blood counts, C-reactive protein measurement, and erythrocyte sedimentation rate determination, may be required to support the need for IVIG supplementation. iv. For persons with normal total IgG levels and severe polysaccharide nonresponsiveness, IVIG should be discontinued and the medical necessity of IVIG should be reevaluated 1 year after initiating therapy and every two years thereafter by reassessing immune response to protein and polysaccharide antigens. Immune response should be reevaluated at least 5 months after discontinuation of IVIG. IVIG should also be discontinued at that time if the number and/or severity of infections have not been reduced, as not all persons with polysaccharide nonresponsiveness benefit from IVIG. **AND** 2) There is documentation of an infection history meeting one of the following criteria: I. Two or more bacterial infections per year due to persistent and significant reduction in total IgG or IgG subclasses **OR** II. Unexplained recurrent or persistent severe bacterial infections despite antibiotic therapy **OR** III. Infections that fail to respond adequately to conservative measures, including prophylactic antibiotics **OR** **IV.** If total IgG level is <200mg/dl or infants have BTK gene or absence of B lymphocytes, then documentation of an infection history will not be required. **AND** 3) There is documentation of appropriate management of other conditions predisposing to recurrent sinopulmonary infections (e.g., asthma, allergic rhinitis) 4) Initial IVIG dose is 300-600 mg/kg every 4 weeks, titrated to patient response.
<u>Acquired/Secondary Humoral immunodeficiencies with recurrent infection and hypogammaglobinulemia</u> • Chronic Lymphocytic Leukemia (CLL), • Acute Myelogenous Leukemia (AML), • Chronic Myelogenous Leukemia (CML), • Hypogammaglobulinemic bone marrow transplant patients	IVIG will be covered when used to prevent recurrent bacterial infections when: 1) Member must have IgG level less than 600mg/dL; **AND** 2) One severe bacterial infection within preceding 6 months, or 2 or more bacterial infections in 1 year. 3) For CLL, AML, CML – initial IVIG dose is 400 mg/kg every 4 weeks.
Multiple Myeloma	1) For use in members with “Plateau Phase” of disease (> 3 months since diagnosis) **AND** 2) Member must have IgG< 600mg/dL **AND** 3) 2 or more significant infections in last year or a single life-threatening infection **OR** 4) Member has poor IgG response to the pneumococcal vaccine 5) Initial IVIG dose is 200-400 mg/kg every 4 to 6 weeks.
Immune Thrombocytopenia/Idiopathic Thrombocytopenia Purpura (ITP)	1) Must meet <u>one</u> of the following (a or b) with documentation of platelet count within previous 30 days: a. Must meet <u>both</u> of the following (i and ii) i. Must meet <u>one</u> of the following (1 or 2): 1. Platelet count <30 x 10^9/ L **OR**

(NOTE: For pregnant patients see "Immune Thrombocytopenia/Idiopathic Thrombocytopenia Purpura (ITP)—Pregnancy" section)	2. Platelet count <50 x 10^9/L with significant bleeding symptoms (e.g., mucous membrane bleeding), high bleeding risk (e.g., hypertension, peptic ulcer disease, anticoagulant therapy, vigorous lifestyle) **AND** ii. Must meet one of the following (1, 2 or 3): 1. History of corticosteroid failure (defined as platelet count < 30 x 10^9/L, or platelet count ≥ 30 x 10^9/L but with bleeding symptoms), or contraindication, or intolerance to corticosteroids, **OR** 2. IVIG will be used in combination with corticosteroids **OR** 3. Must have severe thrombocytopenia, defined as platelet <20 x 10^9/ L, considered to be at risk for intracerebral hemorrhage **OR** b. Platelet count < 100x 10^9/L and requires increase in platelet count prior to invasive major surgical procedures (e.g., splenectomy) 2) The usual dose for IVIG is 1,000-2,000 mg/kg (can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days). For pediatric patients, IVIG may be given as a single dose of 800-1,000mg/kg. 3) Treatment will be authorized for 6 months at a time and require documentation of clinical benefit (e.g., increase in platelets from baseline, decrease in bleeding symptoms).
Immune Thrombocytopenia/Idiopathic Thrombocytopenia Purpura (ITP)—**Pregnancy**	1) Authorization will be granted to pregnant patients with ITP for the duration of the pregnancy. 2) IVIG dose is 1,000 mg/kg/day for 1 to 2 days
Allogeneic Bone Marrow Transplant	1) Therapy continues for 100 days after transplant. 2) Requests for treatment 100 days or greater post-transplant require IgG less than 400mg/dL or CMV, EBV or RSV infection. 3) IVIG dose is 500mg/kg administered on day 7 and day 2 before transplant, and then once weekly. 4) Note: IVIG is not considered medically necessary in autologous bone marrow transplants as these recipients do not benefit form IVIG treatment.
Myasthenia Gravis	IVIG will be covered when used for Myasthenia Gravis for: 1) Myasthenic crisis/acute exacerbation: a) Must be defined by one or more of the following signs/symptoms: dyspnea, severe dysphagia (with weak cough/difficulty clearing secretions), signs of respiratory muscle weakness (hypophonia, pausing during speech to take a breath, poor respiratory effort, increased respiratory rate with shallow breaths, use of accessory muscles of respiration, paradoxical abdominal breathing), intubation, or mechanical ventilation b) Treatment will be authorized on a per episode basis for a duration of 1 month at a time. c) Note: For management of myasthenic crises, IVIG is administered over 2 to 5 days. 2) Refractory Myasthenia Gravis: a) Must have serious side effects or drug failure with corticosteroids and at least 1 other immunosuppressive

	agent (i.e., azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus, cyclophosphamide). b) Initial treatment will be authorized for 6 months. Recertification will be authorized for 12 months at a time. 3) Pre-operative management (e.g., prior to thymectomy or other surgery): a) Short term therapy is considered medically necessary for a 1-month approval 4) "Bridge" therapy to slower acting immunosuppressive therapy: a) Short term therapy is considered medically necessary in 6 month increments to allow adequate time for immunosuppressive therapy to take full effect. 5) Immune globulin therapy will not be authorized in in combination with Neonatal Fc Receptor (FcRn) Antagonists (Vyvgart, Vyvgart Hytrulo, Rystiggo) when being used to treat chronic myasthenia gravis, as this combination has not been studied. When immune globulin is used in the setting of myasthenia crisis, use in combination with a FcRn antagonist is permitted.
Kawasaki Disease	Only used for treatment during the 1st ten days of diagnosis. IVIG is not effective if more than ten days after onset of symptoms. Diagnosis must be established; there is no specific lab test; diagnosis is established by meeting the following criteria: 1) Fever present for at least 5 days; **AND** 2) Four of the following 5 conditions are met: 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 3) IVIG dose is 2,000 mg/kg, as a single infusion over 8-12 hours (single dose has been demonstrated to be more effective than 400 mg/kg/day for 5 days).
Prevention of bacterial infection in HIV infected children	For use in pediatric HIV infected members who meet **ANY** of the following criteria: 1) Member is less than 13 years of age 2) Serum IgG concentration less than 250mg/dL. 3) Recurrent serious bacterial infections defined as 2 or more infections such as bacteremia, meningitis, or pneumonia in a one-year period. 4) Failure to form antibodies to common antigens such as measles, pneumococcal, and/or Haemophilus influzenzae type B vaccine. 5) Living in areas where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella live virus vaccine. 6) Exposure to measles (one dose only) 7) Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy. 8) IVIG dose is 400 mg/kg every 4 weeks.
Multifocal Motor Neuropathy	1) IVIG is covered first line.

	2) Must have documentation of baseline score on an objective scale to assess clinical response (e.g., Rankin, Modified Rankin, Medical Research Council (MRC)). 3) IVIG dose is 500 - 2,400 mg/kg per month (typically, dose infused over 2 to 5 days-i.e., can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days). 4) Initial approval will be for 6 months; Recertification requests will be authorized for 2 years at a time and requires documentation of clinical improvement from baseline on the objective scale used for the initial request (e.g., Rankin, Modified Rankin, Medical Research Council (MRC), Inflammatory Neuropathy Cause and Treatment (INCAT)). 5) Requested dosing should be based on patient's ideal body weight and should remain within recommended guidelines stated above. a. If titration of the original dose is required, there must be documentation of titration to the minimum dose and frequency needed to maintain sustained clinical effect.
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	1) Member must have symmetric or focal neurologic deficits with slowly progressive or relapsing course over 2 months or longer with neurophysiological abnormalities 2) Must have documentation of baseline score on an objective scale to assess clinical response (e.g., Rankin, Modified Rankin, Medical Research Council (MRC), Inflammatory Rasch-built Overall Disability Scale (I-RODS), Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale). 3) IVIG dose is 2,000 mg/kg per month (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days) 4) Initial approval will be for 3 months. Recertification requests will be authorized for 2 years at a time and requires documentation of clinical improvement from baseline on an objective scale used for the initial request (e.g., Rankin, Modified Rankin, Medical Research Council (MRC), Inflammatory Rasch-built Overall Disability Scale (I-RODS), Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale). 5) Requested dosing should be based on patient's ideal body weight and should remain within recommended guidelines stated above. a. If titration of the original dose is required, there must be documentation of titration to the minimum dose and frequency needed to maintain sustained clinical effect. 6) Immune globulin therapy will not be authorized in combination with Vyvgart Hytrulo for maintenance use. Allowances may be made for brief overlap in the setting of acute immune globulin use or transitioning between treatments. 7) Note: IVIG is recommended under accepted guidelines as an alternative to plasma exchange in children and adults, or when there is difficulty with venous access for plasmapheresis.

Refractory dermatomyositis, Polymyositis	1) Diagnosis established by biopsy, EMG abnormalities, and/or increased CPK levels. 2) Member has failed a trial or is intolerant of 1st and 2nd line therapies a. Corticosteroids are 1st line therapy b. Immunosuppressants are 2nd line therapy (ex: methotrexate, azathioprine, cyclophosphamide) 3) IVIG dose is 2,000 mg/kg per month (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days). 4) Initial approval will be for 6 months. If further IVIG therapy is required, documentation of efficacy of the initial 6 months of therapy must be submitted. Subsequent approvals will be for 2 years.

III. Based upon our criteria and review of the peer-reviewed literature, IVIG has been medically proven effective and is considered **medically appropriate** for the following off label indications when other treatments or interventions have been unsuccessful or are contraindicated:

INDICATION	CRITERIA
Guillain-Barre Syndrome	1) Severe Guillain-Barre Syndrome defined as having significant weakness such as inability to walk or stand without aid, respiratory weakness, or bulbar weakness; or Miller-Fisher Syndrome; **AND** 2) The disorder has been diagnosed in the 1st two weeks of the illness; **AND** 3) IVIG is initiated within 1 month of onset of symptoms. 4) IVIG dose is 2,000 mg/kg per month (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days).
Neonates predisposed to Group B strep infections	1) Member must have total IgG less than 400mg/dL; **AND** 2) Member must have low birth weight of less than 1500 mg: **OR** 3) Member must be in setting with high baseline infection rate or morbidity.
Autoimmune hemolytic anemia or acquired Factor VIII or Factor IX inhibitors	1) Member must have warm-type autoimmune hemolytic anemia 2) Member does not respond to, is intolerant of, or contraindicated to corticosteroids or splenectomy.
Fetal or natal alloimmune thrombocytopenia (FAIT) also known as Neonatal alloimmune thrombocytopenia (NAIT)	1) Documented Diagnosis of FAIT. 2) IVIG dose is 1,000 mg/kg per week until delivery
HIV-associated thrombocytopenia	<u>Adults:</u> 1) Significant bleeding in Thrombocytopenic members or platelet count less than 20,000u/mm^3; **AND** 2) Failure of RhIG in Rh-positive patients 3) IVIG dose for adults is 400 mg/kg every 2 to 4 weeks. <u>Pediatric (infants and children <13 years of age)</u> 1) IgG level is <400mg/dL; **AND** 2) Two or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent; **OR**

	3) Child has received 2 doses of measles vaccine and lives in a region with a high prevalence of measles; **OR** 4) Member has HIV associated thrombocytopenia despite antiretroviral therapy: **OR** 5) Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy, **OR** 6) T4 cell count is greater than or equal to 200mm^3. 7) IVIG dose for pediatric patients is 400 mg/kg every 4 weeks.
Parvovirus B19 infection red cell aplasia	1) Member must have severe, refractory anemia with documented Parvovirus B19 viremia. 2) IVIG dose is 400 mg/kg/day for 5 to 10 days
Acquired Factor VIII inhibitor	1) Member must have sufficient trials with conventional therapy. Such treatment options include, but not limited to immunosuppressive therapy with corticosteroids, cyclosporine, or azathioprine. A sufficient course is usually 6 to 12 weeks.
Organ Transplant	1) Prior to solid organ transplant, when patient is at high risk for antibody-mediated rejection, including highly sensitized patients, and those receiving an ABO incompatible organ; **OR** 2) Following solid organ transplant 3) IVIG dose is 2,000 mg/kg per month (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days), typically for up to 4 cycles.
Post-Transfusion purpura (PTP)	1) Member must have platelets < 10,000/mm 2) Recommended IVIG dose is 500mg/kg/day for two consecutive days.
Hemolytic disease of newborn	1) Member must not be responding to phototherapy to decrease the need for exchange transfusion. 2) Therapy should be given to patients with severe hemolysis. 3) IVIG dose is 500-1,000mg/kg, as a single dose in the first few hours of life.
<u>Autoimmune Mucocutaneous Blistering Diseases</u>: Bullous Pemphigoid, Cicatrical Pemphigoid Epidermolysis Bulossa Acquista Mucous Membrane Pemphigoid Pemphigus Vulgaris Pemphigus Foliaceus	1) Diagnosis is proven by biopsy, **AND** 2) Condition is rapidly progressing, extensive or debilitating, **AND** 3) Member has had a failure or intolerance to conventional agents such as corticosteroids and immunosuppressants. 4) IVIG may be used in members with rapidly progressive disease in whom a clinical response could not be affected quickly enough using conventional agents. In such situations, IVIG therapy would be given along with conventional treatment, and the IVIG would only be used until conventional therapy could take effect. 5) IVIG dose is typically 2,000 mg/kg (dose is infused over 2 to 5 days. Examples of dosing include 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days), however, for a diagnosis of Cicatrical pemphigoid the IVIG dose is 2 to 3 g/kg total dose over 3 days every 2 to 6 weeks. 6) IVIG therapy must be used for short-term therapy and not as maintenance therapy. Regular use of repeated courses of IVIG for a continuous cycle of exacerbation and remission constitutes maintenance therapy.
Moersch-Woltman (Stiff-man) Syndrome	1) Presence of Anti-GAD antibody; and 2) Benzodiazepines and/or baclofen, phenytoin, clonidine, tizanidine, have failed.

	3) IVIG dose is 2,000 mg/kg per month dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days).
Lambert-Eaton myasthenic syndrome	1) Treatment options are ineffective or not tolerated. Examples include but are not limited to, pyridostigmine bromide, azathioprine, and prednisone. 2) IVIG dose is 2,000 mg/kg (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days).
Birdshot (vitiligenous) retinochoroidopathy	1) Insufficient response to immunosuppressives (corticosteroids, cyclosporine)
Neonatal hemochromatosis, prophylaxis	1) Treatment of pregnant women who have a history of pregnancy ended in neonatal hemochromatosis 2) IVIG dose should be 1g/kg weekly from the 18th week until the end of gestation
Hyperimmunoglobulinemia E syndrome (Job Syndrome; Hyper IgE syndrome)	1) Recurrent staphylococcal abscesses and markedly elevated serum IgE with normal IgG, IgA, and IgM concentrations. 2) IVIG dose is 300-600 mg/kg, given every 3 to 4 weeks and titrated to response.
Opsoclonus-myoclonus	1) Last-resort treatment for refractory opsoclonus-myoclonus. I 2) IVIG dose is 400 – 1,000 mg/kg given monthly.
Stapylococcal Toxic Shock syndrome	1) Severe cases of toxic shock syndrome that have not responded to fluids and vasopressors. 2) IVIG dose is 2,000 mg/kg dose (infused as 400 mg/kg/day for 5 days).
Rasmussen Encephalitis	1) Trial and failure with anti-epileptic drugs and corticosteroids. 2) IVIG is not recommended for long term therapy for Rasmussen's Encephalitis as surgical treatment is the current standard of care. 3) IVIG dose is 2,000 mg/kg (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days).
Churg-Strauss Syndrome (CSS)	1) Diagnosis of severe CSS 2) Trial and failure of previous treatment options
Stevens-Johnson Syndrome	1) Medically necessary in severe cases of toxic epidermal necrolysis and Stevens-Johnson syndrome
Pediatric Intractable Epilepsy	1) For members who are candidates for surgical resection or when other interventions are ineffective or not tolerated. 2) Examples of other interventions include, but are not limited to, anticonvulsant medications, ketogenic diets, and steroids
Acute Disseminated Encephalomyelitis	1) Insufficient response to intravenous corticosteroid treatment
Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD)	1) Must have a diagnosis of MOGAD is considered when both of the following are met (a and b) a) Must have documentation or prescriber attestation of a demyelinating event (e.g., optic neurotis, myelitis, acute disseminated encephalomyelitis) **AND** b) Must have positive MOG-IgG test [Note: individuals with MOG-IgG test that is low positive, positive without reported titer, or negative but CSF positive may be considered positive for MOG-IgG test if they are AQP4-IgG seronegative and have have presence of 1 or more supporting clinical or MRI feature] **AND**

	2) Must have failure to respond to at least one therapy (e.g., corticosteroids, plasma exchange)
Systemic Lupus Erythematosus (SLE)	1) Must have severe, active systemic lupus erythematosus **AND** 2) Must have an inadequate response to at least two lines of therapy (i.e., hydroxychloroquine, glucocorticoids, anifrolumab, belimumab, non-steroidal immunosuppressant)

IV. Based upon our criteria and review of the peer-review literature IVIG and SCIG therapy for the treatment of all other indications have not been proven to be medically effective and remains **investigational**. The clinical evidence does not support the use of IVIG therapy for all indications including, but not limited to, the following:

- Acute Lymphoblastic Anemia
- Acute Renal Failure
- Adrenoleukodystrophy
- Alzheimer's disease
- Amyotrophic Lateral Sclerosis (ALS)
- Aplastic Anemia
- Asthma
- Atopic Dermatitis
- Autism
- Autoimmune autonomic neuropathy
- Autoimmune liver disease
- Behcet's Syndrome
- Chronic Fatigue Syndrome
- Cardiomyopathy
- Chronic Fatigue Syndrome
- Chronic Sinusitis
- Cystic Fibrosis
- Demyelinating Optic Neuritis
- Diabetes
- Diamond-Blackfan Anemia
- Eczema
- Fahr's Disease
- Endotoxemia
- Erythroblastosis Fetalis
- Goodpasture's Syndrome
- Hemolytic Uremic Syndrome
- Immune-related Neutropenia
- Inclusion body myositis
- Lumbosacral plexopathy
- Motor neuron syndromes
- Multiple Sclerosis
- Narcolepsy/cataplexy
- Neonatal hemolytic disease
- Nephropathy, membranous
- Nephrotic Syndrome
- Nonimmune thrombocytopenia
- Ophthalmopathy, euthyroid

- Otitis Media
- Paraproteinemic neuropathy
- Polyarteritis Nodosa
- Polyneuritis
- Post Infection Sequelae
- Post-polio syndrome
- Recent onset dilated cardiomyopathy
- Recurrent spontaneous abortion
- Reiter's syndrome
- Scleroderma
- Septic Shock
- Small Fiber Neuropathy
- Rheumatoid Arthritis
- Still's disease
- Thrombotic Thrombocytopenic purpura
- Tic Disorder
- Urticaria
- Uveitis
- Vasculitic syndromes
- Wegener's Granulomatosis

V. Subcutaneous Ig administered (only) products

Subcutaneous Ig (SC) products
Cutaquig, Cuvitru, Hizentra, HyQvia, Xembify
• In addition to the requirements for diagnosis as indicated above for IVIG products, coverage will require documentation of drug failure or serious side effects with two of the following administered subcutaneously: Gamunex-C, Gammaked, Gammagard Liquid, or Gammagard Liquid ERC. ○ This step does not apply for a diagnosis of ITP (idiopathic (immune) thrombocytopenic purpura), as there is risk of hematoma formation. ○ This applies to all lines of business EXCEPT Medicare Part B.

APPROVAL TIME PERIODS:

Line of Business	Initial approval	Recertification
Commercial, Exchange, SafetyNet (Medicaid, Harp, CHP, Essential Plan)	2 years	2 years
Medicare	2 years	2 years

POLICY GUIDELINES:

1. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
   a. IVIG and SCIG will be covered under the medical benefit, however, select benefits may allow for coverage under the pharmacy benefit.
2. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable,

if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.

- The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
- The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
- The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
- The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
- The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
- The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug

3. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
4. The following may be used for clinical evaluation of suspected cases of immunodeficiency:
    a. Measurement of quantitative immunoglobulins (IgG, IgA, IgM); it is important to compare patient results with age-matched ranges since significant differences exist between infants, children, and adults. There are no rigid standards regarding the diagnosis of immunoglobulin deficiency although an IgG value below 600mg/dl, other than in early childhood is suggestive of antibody deficiency.
    b. IgA and IgM may be absent or present in normal amounts; and
    c. It may be appropriate to measure IgG subclasses. For subclass deficiency, a serum IgG subclass trough level should be monitored at least every three months prior to the dose of IVIG and SCIG, along with clinical progress of signs and symptoms for which intravenous immune globulin therapy is required.
5. Patient may be recommended for rapidly progressive forms of these diseases.
6. Approved dosing for IVIG and SCIG products will be based on the patient's ideal body weight (IBW) on initial and recertification requests (see exception criteria below):
    - IBW (males): 50 kg + (2.3 kg for each inch over 5 feet)
    - IBW (females): 45.5 kg + (2.3 kg for each inch over 5 feet)

7. IVIG products will not be approved for subcutaneous use unless FDA approved for that route of administration.
8. Recertification for continued use of IVIG therapy will require documentation of clinical efficacy and treatment to desired outcomes.
    a. For autoimmune disorders, including Primary Humoral Immunodeficiency and Acquired/Secondary Humoral Immunodeficiency with recurrent infections and Hypogammaglobulinemia, recertification will require documentation of:
        i. Reduction/elimination of persistent bacterial infections
        ii. Reduction/elimination of hospitalization related to infectious illness
        iii. Stable disease
        iv. Lab values showing normalized trough IgG (ideally greater than 600 mg/dL) are **not** required but can be considered when documenting treatment to desired outcome.
        v. Requested dosing should be based on patient's ideal body weight and should remain within recommended guidelines stated in policy above
            I. Exception: Primary Humoral Immunodeficiencies - may approve a higher dose, not based on IBW, when requested dose is based on the individual's clinical response
    b. For all other conditions (where recertification criteria are not otherwise specified) recertification will require documentation of:
        i. Stable disease (maintenance of desired clinical outcome)
        ii. Requested dosing should be based on patient's ideal body weight and should remain within recommended guidelines stated in policy above.
            I. Exception: hyperimmunoglobulinemia E syndrome - may approve a higher dose, not based on IBW, when requested dose is based on the individual's clinical response.
            II. If titration of the original dose is required, there must be documentation of titration to the minimum dose and frequency needed to maintain sustained clinical effect.
9. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
10. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
11. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
12. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
13. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html
14. The requested site of care may impact approval timeframe and subject to review.

RATIONALE:

There is no compelling evidence that IVIG is effective for patients with Relapsing Remitting Multiple Sclerosis. The 2002 AAN guidelines on MS concluded that studies to date have involved small numbers of patients, have lacked complete data on clinical and MRI outcomes, or have used methods that have been questioned.[29] In addition, a 2008 double blind placebo-controlled trial of 127 patients with RRMS found that IVIG treatment conferred no benefit for reducing relapses or new lesions on MRI.[24]

The FDA has approved a number of IVIG preparations for use in patients with primary immunodeficiency disorder, idiopathic (immune) thrombocytopenic purpura, chronic lymphocytic leukemia, or Kawasaki syndrome, and as prophylaxis in pediatric HIV patients and allogeneic bone marrow transplant recipients. The FDA has approved one SCIG for use in patients with primary immunodeficiency disorder.

Off label use of IVIG for myasthenia gravis, Guillain-Barre syndrome, has evidence that was obtained from at least one properly designed randomized controlled trial. Evidence has also been obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.

The patients for whom IVIG therapy would be used would have failed all other conservative therapies or become refractory to their effects.

Treatment of fetal or neonatal alloimmune thrombocytopenia with maternal IVIG infusions is associated with an increase in the fetal platelet count. A randomized trial compared weekly IVIG with and without associated dexamethasone. Although there was no placebo-controlled arm, results were compared to the course in a prior affected sibling, since the natural history of the disease suggests that subsequent births should be similarly if not more severely affected with thrombocytopenia.

IVIG use in the treatment of acquired factor VIII inhibitors is usually given as part of a combined immunomodulatory protocol. Recent literature suggests that IVIG should be considered only as second-line immunosuppressive therapy for acquired hemophilia.
Multiple small case studies support the use of IVIG to treat pure red cell aplasia secondary to parvovirus B19 viremia. Commercial IVIG is known to contain IgG antibodies to PV B19, which can control and possibly eradicate PV B19. Profound PRCA secondary to PV B19 infection usually occurs in patients who are immunocompromised.

Guidelines from the AAP regarding Hemolytic Disease of the Newborn state that in isoimmune hemolytic disease, administration of IVIG is recommended if the total serum, bilirubin is rising despite intensive phototherapy, or the total serum bilirubin level is within 2 to 3 mg/dL of the exchange level. IVIG has been shown to reduce the need for exchange transfusions in Rh and ABO hemolytic disease.

CODES: **Number** **Description**

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).
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HCPCS:

J1554	Asceniv
J1552	Alyglo
J1556	Bivigam
J1551	Cutaquig
J1555	Cuvitru
J1572	Flebogamma
J1569	Gammagard Liquid/Gammagard Liquid ERC
J1566	Gammagard S/D (powder)
J1561	Gammaked
J1557	Gammaplex
J1561	Gamunex-C
J1559	Hizentra
J1575	Hyqvia
J1568	Octagam
J1576	Panzyga
J1459	Privigen
J1558	Xembify
J1553	Yimmugo

UPDATES:

Date	Revision
09/11/2026	Revised
08/27/2026	Revised
08/13/2026	Reviewed / P&T Committee Approval
06/01/2026	Revised
05/14/2026	Reviewed / P&T Committee Approval
04/14/2026	Revised
03/05/2026	Revised
01/23/2026	Revised
11/19/2025	Revised
10/16/2025	Revised
05/08/2025	Reviewed / P&T Committee Approval
04/28/2025	Revised
03/10/2025	Revised
03/06/2025	Revised
01/13/2025	Revised
01/01/2025	Revised
12/15/2024	Revised
11/21/2024	P&T Committee Review / Approval
06/20/2024	Revised

04/05/2024	Revised
03/11/2024	Revised
02/15/2024	Revised
11/30/2023	P&T Committee Approval
10/2023	Revised
07/2023	Revised
03/2023	Revised
12/2022	Revised
11/17/2022	P&T Committee Approval
11/2022	Revised
06/2022	Revised
01/2022	Revised
11/24/2021	P&T Committee Approval
11/2021	Revised
4/2021	Revised
2/2021	Revised
11/12/2020	P&T Committee Approval
10/2020	Revised
9/2020	Revised
3/2020	Revised
10/2019	Revised
9/2019	Revised
5/2019	Revised
2/2019	P&T Committee Approval
11/2018	Revised
8/2018	Revised
10/2017	Revised
9/14/2017	P&T Committee Approval
4/2017	Revised
9/2016	Revised
1/2016	Revised
5/2015	Revised
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3/2014	Revised
2/2014	Revised
11/2013	Revised
7/2012	Revised
3/2012	Revised
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5/2009	Revised
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9/2008	Revised
9/2007	Revised

10/2006	Created

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