Neighborhood Health Plan OF RHODE ISLAND™
910 Douglas Pike, Smithfield, RI 02917 : 1-800-963-1001 : nhpri.org

Immune Globulins (immunoglobulin) NON-HEMATOLOGY and NON-ONCOLOGY POLICY: Asceniv; Alyglo; Bivigam; Flebogamma; Gamunex-C; Gammagard Liquid ERC; Gammagard S/D; Gammaked; Gammaplex; Octagam; Privigen; Panzyga; Qivigy®; Yimmugo®

(Intravenous)

Effective Date: 01/01/2020
Review Date: 10/02/2019, 1/3/2019, 1/15/2020, 8/3/2020, 6/10/2021, 5/5/2022, 3/2/2023, 12/21/2023, 01/10/2024, 9/04/2024, 07/02/2025, 07/21/2026

Scope: Medicaid*, Commercial, Medicare

***(Medication only available on the Medical Benefit)**

For oncology or hematology indications please refer to NHPRI Immune Globulin (IG) (IVIG, SCIG, IMIG) Policy

I. Length of Authorization

- Initial and renewal authorization periods vary by specific covered indication.
- Unless otherwise specified, the initial authorization will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Max Units (per dose and over time) [Medical Benefit]:

Indication	Billable Units for J1553 and J1577	Billable Units for all other codes	Per # days *(unless otherwise specified)*
PID and Supportive Care after Rethymic transplant	900	180	21
IgG Subclass Deficiency	450	90	14
CIDP	Load: 2300	Load: 460	5
	Maintenance: 1150	Maintenance: 230	21
FAIT	1150	230	7

Kawasaki's Disease	2300	460	2 doses only
Multifocal Motor Neuropathy	2300	460	28
HIV (Pediatric Patients only)	250	46	14
Guillain-Barré	2300	460	5 *(for two courses only)*
Myasthenia Gravis	2300	460	28
Auto-immune blistering diseases	2300	460	28
Dermatomyositis	2300	460	28
Polymyositis	2300	460	28
Complications of transplanted solid organ or bone marrow transplant	2300	460	28
Stiff Person Syndrome	2300	460	28
Toxic Shock Syndrome	2300	460	5 *(for one cycle only)*
NAIT	100	20	2 doses only
Management of Immune Checkpoint Inhibitor-Related Toxicities	2300	460	5 *(for one cycle only)*
Management of CAR T-Cell-Related Toxicities	2300 *(AIDP type)*	460 *(AIDP type)*	5 *(for two courses only)*
	600 *(all other types)*	120 *(all other types)*	28

III. Initial Approval Criteria

Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Coverage is provided for the following conditions:

- Baseline values for BUN and serum creatinine are obtained within 30 days of request; **AND**
- If requesting non preferred intravenous immune globulin formulations, such as Asceniv, Alyglo, Bivigam, Gammagard S/D, Gammaplex, Privigen, Qivigy, Yimmugo or Panzyga the member must have a failure or intolerance to the following preferred formulations: Gammaked/Gamunex-C, Gammagard liquid ERC, Flebogamma/Flebogamma DIF, or Octagam [for MMP members that are currently on treatment (within the past 365 days) with Asceniv, Bivigam, Gammagard S/D, Gammaplex, Privigen or Panzyga, they can remain on treatment]

Primary immunodeficiency (PID)/†

Such as: Wiskott - Aldrich syndrome, x-linked agammaglobulinemia, common variable immunodeficiency, transient hypogammaglobulinemia of infancy, IgG subclass deficiency with or without IgA deficiency, antibody deficiency

with near normal immunoglobulin levels and combined deficiencies (severe combined immunodeficiencies, ataxia-telangiectasia, x-linked lymphoproliferative syndrome) [***list not all inclusive***]

- Member has an IgG level < 200 mg/dL **OR**
- Member meets both of the following:
  - Member has a history of multiple hard to treat infections as indicated by at least **one** of the following:
    - Four or more ear infections within 1 year
    - Two or more serious sinus infections within 1 year
    - Two or more months of antibiotics with little effect
    - Two or more pneumonias within 1 year
    - Recurrent, deep skin or organ abscesses
    - Persistent thrush in mouth or fungal infections on the skin
    - Need for intravenous antibiotics to clear infections
    - Two or more deep-seated infections including septicemia
    - Family history of PID; **AND**
  - Member has a deficiency in producing antibodies in response to vaccination; **AND**
    - Titers were drawn before challenging with vaccination; **AND**
    - Titers were drawn between 4 and 8 weeks of vaccination

IgG Subclass Deficiency ‡ [68,96-98]

- Member has an IgG level < 400 mg/dL; **AND**
- Member has a history of recurrent infections; **AND**
- Member is receiving prophylactic antibiotic therapy

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) †

- Member's disease course is progressive or relapsing and remitting for 2 months or longer; **AND**
- Member has abnormal or absent deep tendon reflexes in upper or lower limbs; **AND**
- Electrodiagnostic testing indicating demyelination:
  - Partial motor conduction block in at least two motor nerves or in 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve; **OR**
  - Distal CMAP duration increase in at least 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve; **OR**
  - Abnormal temporal dispersion conduction must be present in at least 2 motor nerves; **OR**
  - Reduced conduction velocity in at least 2 motor nerves; **OR**
  - Prolonged distal motor latency in at least 2 motor nerves; **OR**

- Absent F wave in at least two motor nerves plus one other demyelination criterion listed here in at least 1 other nerve; **OR**
- Prolonged F wave latency in at least 2 motor nerves; **AND**

- Member is refractory or intolerant to corticosteroids (e.g., prednisolone, prednisone, etc.) given in therapeutic doses over at least three months; **AND**
- Baseline in strength/weakness has been documented using an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.)

Note: Initial authorization is valid for 3 months

Guillain-Barre Syndrome (Acute inflammatory polyneuropathy) ‡

- Member's disease is severe (i.e., member requires assistance to ambulate); **AND**
- Onset of symptoms are recent (i.e., less than 1 month); **AND**
- Member has abnormal or absent deep tendon reflexes in upper or lower limbs; **AND**
- Member diagnosis is confirmed using a cerebrospinal fluid analysis; **AND**
- Approval will be granted for a maximum of 2 courses of therapy within 6 weeks of onset

Note: Authorization is valid for 2 months only and cannot be renewed

Multifocal Motor Neuropathy †

- Member has progressive, focal, asymmetric limb weakness (without sensory symptoms) for greater than 1 month; **AND**
- Complete or partial conduction block or abnormal temporal dispersion conduction in at least 2 motor nerves ; **AND**
- Member has normal sensory nerve conduction on all nerves tested**; AND**
- Baseline in strength/weakness has been documented using an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.)

Note: Initial authorization is valid for 3 months

HIV Infected Children: Bacterial control or prevention ‡

- Member <13 years of age; **AND**
- Member has an IgG level <400 mg/dL

Myasthenia Gravis ‡

- Member has a positive serologic test for anti-acetylcholine receptor (AchR) antibodies; **AND**

- Member has an acute exacerbation resulting in impending myasthenic crisis (i.e., respiratory compromise, acute respiratory failure, and/or bulbar compromise); **AND**
- Member is failing on conventional immunosuppressant therapy alone (e.g., corticosteroids, azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.); **AND**
- Member will be on combination therapy with corticosteroids or other immunosuppressant (e.g., azathioprine, mycophenolate, cyclosporine, methotrexate, tacrolimus, cyclophosphamide, etc.)

Note: Authorization is valid for 1 course (1 month) only and cannot be renewed

Dermatomyositis† (**Φ** for Octagam 10%)

- Member has severe active disease; **AND**
- Member has proximal weakness in all upper and/or lower limbs; AND
- Member has one or more of the following:
    - Muscle biopsy proven dermatomyositis
    - Dermatomyositis with classic skin manifestations (i.e., heliotrope rash or Gottron's papules); **OR**
- Member has clinically amyopathic dermatomyositis (CADM; historically termed "dermatomyositis sine myositis"); **AND**
- Member has failed a trial of corticosteroids (i.e., prednisone); **AND**
- Member has failed a trial of an immunosuppressant (e.g., methotrexate, azathioprine, etc.); **AND**
- Member will be on combination therapy with corticosteroids or other immunosppressants; **AND**
- Member has a documented baseline physical exam and muscular strength/function

Note: Initial authorization is valid for 3 months

Polymyositis

- Member has severe active disease; **AND**
- Member has proximal weakness in all upper and/or lower limbs; **AND**
- Diagnosis has been confirmed by muscle biopsy; **AND**
- Member has failed a trial of corticosteroids (i.e., prednisone); **AND**
- Member has failed a trial of an immunosuppressant (e.g., methotrexate, azathioprine, etc.); **AND**
- Member will be on combination therapy with corticosteroids or other immunosuppressants; **AND**
- Member has a documented baseline physical exam and muscular strength/function

Complications of Transplanted Solid Organ (kidney, liver, lung, heart, pancreas) and Bone Marrow Transplant ‡

Coverage is provided for one or more of the following (list not all-inclusive):

- Suppression of panel reactive anti-human leukocyte antigen (HLA) antibodies prior to transplantation
- Treatment of antibody-mediated rejection of solid organ transplantation
- Prevention or treatment of viral infections (e.g., cytomegalovirus, Parvo B-19 virus, Polyoma BK virus, etc.)

Stiff-Person Syndrome ‡

- Member has anti-glutamic acid decarboxylase (GAD) antibodies; **AND**
- Member has failed at least 2 of the following treatments: benzodiazepines, baclofen, gabapentin, valproate, tiagabine, or levetiracetam; **AND**
- Member has a documented baseline on physical exam

Allogeneic Bone Marrow or Stem Cell Transplant ‡

- Used for prevention of acute Graft-Versus-Host-Disease (aGVHD) or infection; **AND**
- Member's bone marrow (BMT) or hematopoietic stem cell (HSCT) was allogeneic; **AND**
- Member has an IgG level < 400 mg/dL

Note: Initial authorization is valid for 3 months

Kawasaki's disease (Pediatric) †

Note: Authorization is valid for 1 course (1 month) only and cannot be renewed

Fetal alloimmune thrombocytopenia (FAIT) ‡

- Member has a history of one or more of the following:
  - Previous FAIT pregnancy
  - Family history of the disease
  - Screening reveals platelet alloantibodies

Note: Authorization is valid through the delivery date only and cannot be renewed

Neonatal Alloimmune Thrombocytopenia ‡

Note: Authorization is valid for 1 course (1 month) only and cannot be renewed

Auto-immune Mucocutaneous Blistering Diseases ‡

- Member has been diagnosed with one of the following:

- Pemphigus vulgaris
- Pemphigus foliaceus
- Bullous Pemphigoid
- Mucous Membrane Pemphigoid (a.k.a. Cicatricial Pemphigoid)
- Epidermolysis bullosa aquisita
- Pemphigus gestationis (Herpes gestationis)
- Linear IgA dermatosis; **AND**

- Member has severe disease that is extensive and debilitating; **AND**
- Diagnosis has been confirmed by biopsy; **AND**
- Member has progressive disease; **AND**
- Disease is refractory to a trial of conventional therapy with corticosteroids and concurrent immunosuppressive treatment (e.g., azathioprine, cyclophosphamide, mycophenolate mofetil, etc.); **AND**
- Member has a documented baseline on physical exam

Toxic Shock Syndrome ‡

Note: Authorization is valid for 1 course (1 month) only and cannot be renewed

Supportive Care after Rethymic transplant ‡ [95]

- Used as immunoglobulin replacement therapy in pediatric members with congenital athymia after surgical implantation of Rethymic; **OR**
- Used as re-initiation of treatment 2 months after stopping immunoglobulin replacement therapy in pediatric members who have an IgG trough level lower than normal range for age

Management of Immune-Checkpoint-Inhibitor Related Toxicity ‡

- Member has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, cemiplimab, ipilimumab, dostarlimab, tremelimumab, retifanlimab etc.); **AND**
- Member has one of the following toxicities related to their immunotherapy:
  - Severe (G3) or life-threatening (G4) bullous dermatitis as an adjunct to rituximab
  - Stevens-Johnson syndrome (SJS)
  - Toxic epidermal necrolysis (TEN)
  - Severe (G3-4) myasthenia gravis
  - Demyelinating disease (optic neuritis, transverse myelitis, acute demyelinating encephalomyelitis)

- Myocarditis as further intervention if no improvement within 24-48 hours of starting high-dose methylprednisolone
- Moderate (G2) or severe (G3-4) Guillain-Barré Syndrome or severe (G3-4) peripheral neuropathy used in combination with high-dose methylprednisolone
- Moderate (G2) pneumonitis if no improvement after 48-72 hours of corticosteroids
- Severe (G3-4) pneumonitis if no improvement after 48 hours of methylprednisolone
- Encephalitis used in combination with high-dose methylprednisolone for severe or progressing symptoms
- Moderate, severe, or life-threatening steroid-refractory myositis (proximal muscle weakness, neck flexor weakness, with or without myalgias) for significant dysphagia, life-threatening situations, or cases refractory to corticosteroids

† FDA Approved Indication(s), ‡ Compendia/Literature Supported Indication(s)

For Reference Use Only

Brand Name/ Formulation	FDA Indication	Contraindications	Product Specs	Comments
Asceniv 10%	PID (≥12yo)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	• **IgA**: ≤200 mcg/mL • **Osmolality**: 370 to 510 mOsm/kg • **Stabilizer**: Glycine	Other stabilizer used is Polysorbate 80
Alyglo 10%	PID (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	• **IgA**: ≤100 mcg/mL • **Osmolality**: N/A **Stabilizer**: Glycine	
Bivigam❖ 10% (liquid)	PID (peds ≥6)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	• **IgA**: ≤200 mcg/mL • **Osmolality**: 370 to510 mOsm/kg • **Stabilizer**: glycine	
Flebogamma 5% (liquid)	PID (peds ≥2)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: <50 mcg/mL **Osmolarity**: 240 to 370 mOsm/kg **Stabilizer**: sorbitol	
Flebogamma 10% (liquid)	PID (peds ≥2) ITP (peds ≥2)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: <32 mcg/mL **Osmolarity**: 240 to 370 mOsm/L **Stabilizer**: sorbitol	
Gammagard ERC10%(liquid)	PID (peds ≥2) MMN (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: 37 mcg/mL **Osmolality**: 240 to 300 mOsm/kg **Stabilizer**: glycine	May be used SC (see policy for criteria
Gammagard S/D 5% ❖ (lyophilized)	PID ITP CLL Kawasaki *(adults/peds for all indx)*	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: <2.2 mcg/mL (5% solution) **Osmolality**: 636 mOsm/L (5% soln) **Stabilizer**: glycine	Contains some sugar (20mg/mL when prepared)

Gammaked 10% (liquid)	PID (peds ≥2) ITP (peds/adults) CIDP (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: 46 mcg/mL **Osmolality**: 258 mOsm/kg **Stabilizer**: glycine	May be used SC (see policy for criteria
Gammaplex 5% (liquid)	PID (peds ≥2) cITP (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies Fructose intolerance	**IgA**: <10 mcg/mL **Osmolality**: 460 to 500 mOsm/kg **Stabilizer**: glycine	Other stabilizer used is Polysorbate 80
Gammaplex 10% (liquid)	PID (adults) cITP (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: <20 mcg/mL **Osmolality**: 280 mOsm/kg **Stabilizer**: glycine	Other stabilizer used is Polysorbate 80
Gamunex-C (liquid)	PID (peds ≥2) ITP (peds/adults) CIDP (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: 46 mcg/mL **Osmolality**: 258 mOsm/kg **Stabilizer**: glycine	May be used SC (see policy for criteria
Octagam 5% (liquid)	PID (peds≥6)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies Corn allergy	**IgA**: ≤100 mcg/mL **Osmolality**: 310 to 380 mOsm/kg **Stabilizer**: maltose	
Octagam 10% (liquid)	ITP (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: 106 mcg/mL **Osmolality**: 310 to 390 mOsm/kg **Stabilizer**: maltose	
Privigen (liquid)	PID cITP (ped ≥15) CIDP (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies Hyperprolinemia	**IgA**: ≤25 mcg/mL **Osmolality**: 320 mOsm/kg **Stabilizer**: L-proline	
Panzyga	PID (peds ≥2) cITP (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: ≤100 mcg/mL **Osmolality**: 0 mOsm/kg **Stabilizer**: Glycine	
Qivigy 10%	PID (adults)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: ≤50 mcg/mL **Osmolality**: ≥240 mOsm/kg **Stabilizer**: glycine	Does not contain carbohydrate stabilizers (e.g., sucrose, maltose) or preservatives
Yimmugo	PID (peds ≥2)	History of anaphylaxis to IgG IgA-deficient with IgA antibodies	**IgA**: ≤300 mcg/mL **Osmolality**: 280 to 380 mOsm/kg **Stabilizer**: glycine	Does not contain carbohydrate stabilizers (e.g., sucrose, maltose) or preservatives

- All intravenous immunoglobulins are derived from human plasma.
- Products with higher IgA content pose a greater risk for anaphylactic reactions, especially in patients with IgA deficiencies.
- All products may predispose patients to nephrotoxicity especially those with sugar-based or proline-based stabilizers. To lower risks, lower concentration products and infusions rates should be used as well as using products with osmolality/osmolarity that is near physiologic range (around 300 mOsm/kg or mOsm/L).
- Premedications (e.g., acetaminophen, antihistamine, etc.) are recommended to reduce the risk of infusion related reactions.

Adapted from: Professional Resource, Comparison of IVIG Products. Pharmacist's Letter/Prescriber's Letter. December 2016.
❖*Discontinued by the manufacturer*

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

Note: unless otherwise specified, renewal authorizations are provided for 1 year

- Member continues to meet criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include : acute kidney injury, thrombosis, hemolysis, hypersensitivity, pulmonary adverse reactions/transfusion related acute lung injury(TRALI), volume overload, etc.; **AND**
- BUN and serum creatinine have been obtained within the last 6 months and the concentration and rate of infusion have been adjusted; accordingly, **AND**

Primary Immunodeficiency (PID)

- Disease response as evidenced by one or more of the following:
  - Decrease in the frequency of infection
  - Decrease in the severity of infection

IgG Subclass Deficiency

- Disease response as evidenced by one or more of the following:
  - Decrease in the frequency of infection
  - Decrease in the severity of infection; **AND**
- Continued treatment is necessary to decrease the risk of infection

Chronic Inflammatory Demyelinating Polyneuropathy

- Renewals will be authorized for members that have demonstrated a clinical response to therapy based on an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.)

Multifocal Motor Neuropathy

- Renewals will be authorized for members that have demonstrated a clinical response to therapy based on an objective clinical measuring tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin, etc.)

HIV Infected Children: Bacterial Control or Prevention

- Disease response as evidenced by one or more of the following:
  - Decrease in the frequency of infection

- Decrease in the severity of infection; **AND**

- Member continues to be at an increased risk of infection necessitating continued therapy as evidenced by an IgG level < 400 mg/dL

Myasthenia Gravis

- May not be renewed.

Dermatomyositis or Polymyositis

- Member had an improvement from baseline on physical exam and/or muscular strength and function

Note: Renewal authorizations are provided for 6 months

Complications of Transplanted Solid Organ (kidney, liver, lung, heart, pancreas) and Bone Marrow Transplant

- Disease response as evidenced by one or more of the following:
  - Decrease in the frequency of infection
  - Decrease in the severity of infection; **AND**
- Continued treatment is necessary to decrease the risk of infection

Stiff Person Syndrome

- Documented improvement from baseline on physical exam

Allogeneic Bone Marrow or Stem Cell Transplant

- Member continues to be at an increased risk of infection necessitating continued therapy as evidenced by an IgG level < 400 mg/dL

Note: Renewal authorizations are provided for 3 months

Auto-Immune Mucocutaneous Blistering Diseases

- Documented improvement from baseline on physical exam

Note: Renewal authorizations are provided for 6 months

Management of Immune Checkpoint Inhibitor related Toxicity ‡

- May not be renewed.

Supportive Care after Rethymic transplant ‡ [95]

- Renewals for use as initial immunoglobulin replacement therapy will be authorized until all of the following criteria are met:
    - Member is no longer on immunosuppression (at least 10% of CD3+ T cells are naïve in phenotype); **AND**
    - Member is at least 9 months post-treatment; **AND**
    - Member's phytohemagglutinin (PHA) response within normal limits; **OR**
- Renewals for use as re-initiation of treatment after stopping immunoglobulin replacement therapy for members with an IgG trough level lower than normal range will be continued for 1 year before being retested using the above guidelines

Dosing Recommendations:

- Patient's dose should be reduced to the lowest necessary to maintain benefit for their condition. Patients who are stable, or who have reached the maximum therapeutic response, should have a trial of dose reduction (e.g., 25-50% reduction in dose every 3 months).
- Patients who have tolerated dose reduction and continue to show sustained improvement (i.e. remission) should have a trial of treatment discontinuation, with the following exceptions:
    - PID would be excluded from a trial of discontinuation
    - HIV-infected children should show satisfactory control of the underlying disease [e.g., undetectable viral load, CD4 counts elevated above 200 or >15% (ages 9 months – 5 years) on antiretroviral therapy, etc.]
    - Solid organ transplant, CLL, SLL, ALLand MM patients should not be at an increased risk of infection

V. Dosage/Administration

Dosing should be calculated using adjusted body weight if one or more of the following criteria are met:

- Patient's body mass index (BMI) is 30 kg/m² or more; **OR**
- Patient's actual body weight is 20% higher than his or her ideal body weight (IBW)

Use the following dosing formulas to calculate the adjusted body weight (round dose to nearest 5 gram increment in adult patients):

Dosing formulas

BMI = 703 x (weight in pounds/height in inches^2)
IBW (kg) for males = 50 + [2.3 (height in inches – 60)]
IBW (kg) for females = 45.5 + [2.3 x (height in inches – 60)]
Adjusted body weight = IBW + 0.5 (actual body weight – IBW)

This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.

Indication	Dose
PID and Supportive Care after Rethymic transplant	200 to 800 mg/kg every 21 to 28 days
CIDP	2 g/kg divided over 2-5 days initially, then 1 g/kg administered in 1-2 infusions every 21 days
FAIT	1 g/kg/week until delivery
Kawasaki's Disease	1 g/kg to 2 g/kg x 1 dose, may be repeated once if needed
Multifocal Motor Neuropathy	Up to 2 g/kg divided over 5 days in a 28-day cycle
Pediatric HIV	400 mg/kg every 2 to 4 weeks
Guillain-Barre	2 g/kg divided over 5 days x 1 course. May be repeated once within 6 weeks of onset if needed
Myasthenia Gravis	1-2 g/kg divided as either 0.5 g/kg daily x 2 days or 0.4 g/kg daily x 5 days x 1 course
Auto-immune blistering diseases	Up to 2 g/kg divided over 5 days in a 28-day cycle
Dermatomyositis/Polymyositis	2 g/kg divided over 2 to 5 days in a 28-day cycle
Bone Marrow or Stem Cell Transplant	500 mg/kg once weekly x 90 days, then 500 mg/kg every 3 to 4 weeks
Complications of transplanted solid organ: (kidney, liver, lung, heart, pancreas) transplant	2 g/kg divided over 5 days in a 28-day cycle
Stiff Person Syndrome	2 g/kg divided over 5 days in a 28-day cycle
Toxic Shock Syndrome	2 g/kg divided over 5 days x 1 course

Indication	Dose
Neonatal Alloimmune Thrombocytopenia	1 g/kg x 1 dose, may be repeated once if needed
Management of Immune Checkpoint Inhibitor Related Toxicity	2 g/kg divided over 5 days x 1 course
**Dosing for IVIG is highly variable depending on numerous patient specific factors, indication(s), and the specific product selected. For specific dosing regimens refer to current prescribing literature.*	

VI. Billing Code/Availability Information

HCPCS code & NDC:

Drug	Manufacturer	J-Code or CPT Code	1 Billable Unit Equivalent	IgG (grams) per SDV	NDC
Asceniv	ADMA Biologics	J1554 or 90283	500mg	5	N/A
Bivigam❖	Biotest Pharmaceuticals	J1556 or 90283	500 mg	5	59730-6502-XX
				10	59730-6503-XX
Alyglo	GC Biopharma	J1552	N/A	5, 10, 20	61476-0104-XX
			500 mg		
Flebogamma 10% DIF	Instituto Grifols, S.A.	J1572 or 90283	500 mg	5, 10, 20	61953-0005-XX
Flebogamma 5% DIF				2.5, 5, 10, 20	61953-0004-XX
Gamunex-C	Grifols Therapeutics	J1561	500 mg	1, 2.5, 5, 10, 20, 40	13533-0800-XX
Gammagard Liquid ERC	Takeda	J1569 or 90283	500 mg	1, 2.5, 5, 10, 20, 30	00944-2705-XX
Gammagard S/D Less IGA ❖	Takeda	J1566 or 90283	500 mg	5	00944-2656-XX
				10	00944-2658-XX
Gammaked	Grifols Therapeutics	J1561	500 mg	1, 2.5, 5, 10, 20	76125-0900-XX
Gammaplex 5%			500 mg	5, 10, 20	64208-8234-XX

Gammaplex 10%	Bio Products Laboratory	J1557 or 90283		5, 10, 20	64208-8235-XX
Octagam 10%	Octapharma USA Inc	J1568 or 90283	500 mg	2, 5, 10, 20	68982-0850-XX
Octagam 5%				1, 2.5, 5, 10, 25	68982-0840-XX
Privigen	CSL Behring LLC	J1459 or 90283	500 mg	5	44206-0436-XX
				10	44206-0437-XX
				20	44206-0438-XX
				40	44206-0439-XX
Panzyga	Octapharma USA Inc	J1576 or 90283	500mg	1, 2.5, 5, 10, 20, 30	68982-0820-XX
Qivigy 10%	Kedrion S.p.A.	J1577 *(Effective 07/01/2026)*	100 mg	5, 10	76179-0010-XX
Yimmugo	Biotest AG	J1553	100 mg	5, 10, 20	83372-0605-XX
Injection, immune globulin, intravenous, non-lyophilized (e.g., liquid), not otherwise specified	N/A	J1599	500 mg	N/A	N/A

❖*Discontinued by the manufacturer*

VII. Summary of Evidence

Asceniv:

Asceniv is a 10% liquid intravenous immune globulin (IGIV) used for the treatment of primary humoral immunodeficiency (PI) in adults and adolescents aged 12 to 17 years. Clinical efficacy was established in a multicenter, prospective, open-label study in PI patients, measuring trough IgG levels and the rate of serious bacterial infections (SBIs) as the primary outcome. The study demonstrated a mean of 0.02 SBIs per subject per year, meeting the efficacy threshold of <1 SBI/year. Asceniv showed consistent trough IgG

levels with dosing every 3 to 4 weeks. Safety monitoring included assessments for thrombotic events, renal dysfunction, and hypersensitivity reactions. The most common adverse events (≥5%) were headache, sinusitis, viral gastroenteritis, and upper respiratory infections.

Alyglo:
Alyglo is a 10% liquid intravenous immune globulin (IGIV) approved for the treatment of primary humoral immunodeficiency (PI) in adults. Efficacy was evaluated in a prospective, open-label clinical trial assessing infection rates and maintenance of adequate serum IgG levels. Dosing was individualized every 21 or 28 days based on patient response. The study demonstrated low rates of serious bacterial infections and maintained serum IgG levels above protective thresholds. Alyglo is sucrose-free and includes safety precautions for patients at risk of thrombosis or renal dysfunction. Common adverse events (≥5%) included headache, nausea, fatigue, muscle aches, and infusion site pain.

Bivigam:
Bivigam is a 10% liquid intravenous immune globulin (IGIV) indicated for adults and pediatric patients ≥2 years old with primary humoral immunodeficiency (PI). Efficacy was established through studies evaluating infection rates and IgG trough levels. The product was administered every 3 to 4 weeks and demonstrated a mean SBI rate below 1 per year. Pharmacokinetic data supported adequate serum IgG maintenance with individualized dosing. Common adverse reactions (≥5%) were headache, fatigue, infusion site reactions, nausea, and sinusitis. Bivigam is sucrose-free and includes monitoring for renal function and thrombotic risks.

Flebogamma 10% DIF:
Flebogamma 10% DIF is a 10% intravenous immune globulin (IGIV) used for primary immunodeficiency (PI) and chronic primary immune thrombocytopenia (ITP) in patients 2 years and older. Clinical trials demonstrated reduced infection rates and increased platelet counts in ITP, using standardized trough IgG targets and monitoring of adverse events. Efficacy in PI was established by maintaining IgG levels and minimizing infections. In ITP, platelet counts increased following 1 g/kg dosing for two consecutive days. Flebogamma is sucrose-free but contains sorbitol and is contraindicated in hereditary fructose intolerance. The most frequent adverse events (≥5%) were headache, pyrexia, back pain, and hypotension.

Gamunex-C:
Gamunex-C is a 10% immune globulin solution indicated for intravenous (IV) or subcutaneous (SC) administration. For IV use, it is approved to treat primary humoral immunodeficiency (PI) in patients aged 2 years and older, idiopathic thrombocytopenic purpura (ITP) in adults, and chronic inflammatory demyelinating polyneuropathy (CIDP) in adults. In PI, a clinical trial showed a serious bacterial infection (SBI) rate of 0.043 per patient-year, demonstrating efficacy in infection prevention. In ITP, platelet counts rose significantly following a 2 g/kg total dose over 2–5 days. In CIDP, a double-blind, placebo-controlled ICE trial showed improved INCAT disability scores in patients treated with Gamunex-C. Common adverse events (≥5%) include headache, fever, nausea, chills, and fatigue. Gamunex-C is stabilized with glycine and is sucrose-free, with boxed warnings for thrombosis, renal dysfunction, and hemolysis.

Gammagard S/D:
Gammagard S/D is an IGIV product treated with solvent detergent and available in 5% or 10% concentrations. It is indicated for PI in adults and children ≥2 years, prevention of bacterial infections in B-cell CLL, treatment of chronic ITP in adults, and prevention of coronary artery aneurysms in pediatric Kawasaki syndrome. Efficacy for PI and CLL was shown via infection reduction and serum IgG maintenance. For ITP, platelet response was achieved with 1 g/kg up to three times. For Kawasaki syndrome, efficacy was demonstrated with a single 1 g/kg dose or 400 mg/kg for four days along with aspirin. Gammagard S/D is sucrose-free and adverse effects (≥5%) include headache, nausea, fatigue, chills, fever, and back pain. Risks include thrombosis, renal failure, hemolysis, and aseptic meningitis.

Gammaplex 10%:
Gammaplex 10% is a liquid intravenous immune globulin (IGIV) used for the treatment of primary humoral immunodeficiency (PI) in adults and pediatric patients 2 years and older, and chronic immune thrombocytopenic purpura (ITP) in adults. Efficacy in PI was demonstrated through maintenance of IgG trough levels and reduction in serious bacterial infections, meeting FDA criteria of <1 SBI/year. In ITP, efficacy was shown by an increase in platelet counts with 1 g/kg daily for two days. Safety data showed the most common adverse reactions (≥5%) were headache, migraine, pyrexia, infusion site reaction, fatigue, and nausea. Gammaplex contains no sucrose and is contraindicated in patients with IgA deficiency and antibodies to IgA.

Octagam 10%:
Octagam 10% is a 10% liquid IGIV preparation indicated for primary humoral immunodeficiency (PI) in adults and chronic immune thrombocytopenic purpura (ITP) in adults to rapidly increase platelet counts. The pivotal PI trial demonstrated low rates of serious bacterial infections and stable IgG levels. In ITP, a prospective, open-label study showed platelet counts increased in >70% of patients after a total 2 g/kg dose over 2–5 days. Octagam 10% is stabilized with maltose and is sucrose-free. Adverse events (≥5%) include headache, fever, nausea, chills, hypertension, and back pain.

Privigen:
Privigen is a 10% IGIV formulation approved for primary humoral immunodeficiency (PI) in patients ≥2 years and for chronic immune thrombocytopenic purpura (ITP) in adults. Efficacy for PI was established in a prospective, open-label study showing a serious bacterial infection rate of 0.08 per patient-year. In ITP, platelet counts increased in 80% of patients receiving 1 g/kg/day for two consecutive days. Privigen does not contain sucrose or preservatives and includes proline as a stabilizer. Common adverse events (≥5%) include headache, nausea, fever, chills, fatigue, and rash. It carries risks for thrombosis, renal dysfunction, and hemolysis, especially in at-risk populations.

Panzyga:
Panzyga is a 10% liquid IGIV approved for use in primary humoral immunodeficiency (PI) in patients ≥2 years, chronic immune thrombocytopenia (ITP) in adults, and chronic inflammatory demyelinating polyneuropathy (CIDP) in adults. In clinical trials, Panzyga demonstrated a low SBI rate in PI patients and sustained platelet count increases in ITP patients following two doses of 1 g/kg. For CIDP, efficacy was

shown through improvement in INCAT disability scores in a randomized trial. Panzyga is free of sucrose and stabilized without added sugars. Adverse events occurring in ≥5% include headache, nausea, fever, fatigue, and dermatitis.

Gammaked:
Gammaked is a 10% liquid immune globulin formulation for intravenous (IV) or subcutaneous (SC) administration. It is indicated for the treatment of primary humoral immunodeficiency (PI) in patients aged 2 years and older, chronic immune thrombocytopenic purpura (ITP) in adults, and chronic inflammatory demyelinating polyneuropathy (CIDP) in adults. In PI, efficacy was shown through maintenance of serum IgG and a serious bacterial infection (SBI) rate of 0.02 per patient-year. In ITP, efficacy was based on platelet count increases with a 2 g/kg total dose administered over 2–5 days. CIDP efficacy was demonstrated in a double-blind, placebo-controlled study using INCAT scores to measure functional improvements. Common adverse events (≥5%) include headache, nausea, pyrexia, chills, and fatigue. Gammaked is sucrose-free and carries boxed warnings for thrombosis and renal dysfunction.

Qivigy:
Qivigy is a 10% liquid intravenous immunoglobulin approved for the treatment of primary humoral immunodeficiency in adults. Efficacy was evaluated in a prospective, open label clinical trial of 47 adults assessing serious bacterial infections, other infections, and serum IgG concentrations. Patients received individualized doses of 266-826 mg/kg every 3 or 4 weeks for 12 months. The study reported no acute serious bacterial infections and maintained mean minimum serum IgG concentrations of approximately 994-1,140mg/dL. Qivigy is sucrose free and includes safety precautions for patients at risk of thrombosis or renal dysfunction. Common adverse events include headache, fatigue, nausea, infusion related reactions, positive direct Coombs test, sinusitis, dizziness, and diarrhea.

Yimmugo:
Yimmugo is a 10% liquid intravenous immunoglobulin approved for the treatment of primary humoral immunodeficiency in patients 2 years of age and older. Efficacy was evaluated in a prospective, open label, multicenter, multinational clinical trial of 67 patients, including children and adolescents, assessing infection rates, safety, pharmacokinetics, and maintenance of adequate serum IgG levels. Patients received individualized doses of 200-800mg/kg every 3 or 4 weeks for approximately 12 months. The study demonstrated a low rate of serious bacterial infections and maintained serum IgG concentrations with either dosing schedule. Yimmugo is sucrose free and includes safety precautions for patients at risk of thrombosis or renal dysfunction. Common adverse events include headache, upper respiratory tract infection, fatigue, nausea and increased blood pressure.

VIII. References

1. Bivigam™ [package insert]. Boca Raton, FL; Biotest Pharmaceuticals; May 2025. Accessed June 2025.
2. Flebogamma® 10% DIF [package insert]. Barcelona, Spain; Instituto Grifols, S.A.; November 2024. Accessed June 2025.
3. Flebogamma® 5% DIF [package insert]. Barcelona, Spain; Instituto Grifols, S.A.; November2024. Accessed June 2025.
4. Gammagard Liquid [package insert]. Westlake Village, CA; Baxalta US Inc.; November 2024. Accessed June 2025.
5. Gammagard S/D Less IgA [package insert]. Westlake Village, CA; Baxalta US Inc.; March 2025. Accessed June 2025.
6. Gamunex®-C [package insert]. Research Triangle, NC; Grifols Therapeutics, Inc.; April 2022. Accessed June 2025.
7. Gammaked™ [package insert]. Research Triangle, NC; Grifols Therapeutics, Inc; January 2020. Accessed June 2025.
8. Gammaplex® 5% [package insert]. Durham, NC; Bio Products Laboratory Ltd.; October 2024. Accessed June 2025 .
9. Gammaplex® 10% [package insert]. Durham, NC; Bio Products Laboratory Ltd.; October2024. Accessed June 2025.
10. Octagam® 5% [package insert]. Hoboken, NJ; Octapharma USA Inc; April 2022. Accessed June 2025.
11. Octagam® 10% [package insert]. Hoboken, NJ; Octapharma USA Inc; April 2022 . Accessed June 2025.
12. Privigen® [package insert]. Berne, Switzerland; CSL Behring LLC; May 2025. Accessed June 2025.
13. Panzyga® [package insert]. Hoboken, NJ; Octapharma USA Inc; March 2021. Accessed June 2025.
14. Asceniv™ [package insert]. Boca Raton, FL; ADMA Biologics; May 2025. Accessed June2025.
15. Skeie GO, Apostolski S, Evoli A, et al. Guidelines for the treatment of autoimmune neuromuscular transmission disorders. Eur J Neurol. 2010;17(7):893-902.
16. Van den Bergh PY, Hadden RD, Bouche P, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies [trunc]. Eur J Neurol 2010 Mar;17(3):356-63
17. Patwa HS, Chaudhry V, Katzberg H, et al. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2012 Mar 27;78(13):1009-15.
18. French CIDP Study Group. Recommendations on diagnostic strategies for chronic inflammatory demyelinating polyradiculoneuropathy. J Neurol Neurosurg Psychiatry 2008; 79: 115–118.
19. Donofrio PD, Berger A, Brannagan TH, et al. Consensus statement: The use of intravenous immunoglobulin in the treatment of neuromuscular conditions report of the AANEM ad hoc committee. Muscle Nerve. 2009;40:890-900.
20. Feasby T, Banwell B, Benstead T, et al. Guidelines on the use of intravenous immune globulin for neurologic conditions. Transfus Med Rev. 2007;21(2 suppl 1):S57-107.

21. Gajdos P, Tranchant C, Clair B, et al; Myasthenia Gravis Clinical Study Group. Treatment of myasthenia gravis exacerbation with intravenous immunoglobulin: a randomized double-blind clinical trial. Arch Neurol. 2005;62(11):1689-1693.
22. Elovaara I, et al. EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases. European Journal of Neurology 2008;15(9):893-908.
23. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society--first revision. J Peripher Nerv Syst. 2010 Dec;15(4):295-301. doi: 10.1111/j.1529-8027.2010.00290.x.
24. Hahn AF, Bolton CF, Pillay N, et al. Plasma exchange therapy in chronic inflammatory demyelinating polyneuropathy. A double-blind, sham controlled, cross-over study. Brain 1996;119:1055–66.
25. The National Institute of Child Health and Human Developments Intravenous Immunoglobulin Study Group. Intravenous immune globulin for the prevention of bacterial infections in children with symptomatic human immunodeficiency virus infection. N Engl J Med. 1991 Jul 11;325(2):73-80.
26. Silberry GK, Abzug MJ, Nachman, S, et al. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children: Recommendations from the National Institutes of Health, Centers for Disease Control and Prevention, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. J Pediatric Infect Dis Soc. 2013 Nov; 32 Suppl 2: i-KK4.
27. Wolfe GI, Barohn RJ, Foster BM, et al; Myasthenia Gravis-IVIG Study Group. Randomized, controlled trial of intravenous immunoglobulin in myasthenia gravis. Muscle Nerve. 2002;26(4):549-552.
28. Hughes RA, Wijdicks EF, Barohn R, et al; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2003;61(6):736-740.
29. Hughes RA, Swan AV, Raphael JC, Annane D, van Koningsveld R, van Doorn PA. Immunotherapy for Guillain-Barré syndrome: a systematic review. Brain. 2007;130(pt 9):2245-2257.
30. Bussel, JB et al. Antenatal management of alloimmune thrombocytopenia with Intravenous Immunoglobulin: A randomized trial of low dose steroid to intravenous immunoglobulin. Am J Obstet Gynecol 1996; 174 1414-23.
31. Ratko TA, Burnett DA, The Univ Hospital Consortium Expert Panel for the Off-label Use of Polyvalent Intravenously Administered Immunoglobulin Preparations, et al. Recommendations for the off-label use of intravenously administered immunoglobulin preparations. JAMA 1995; 273:1865-70.
32. Ahmed AR, Spigelman Z, Cavacine LA et al. Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. N Eng J Med 2006; 1772-9
33. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004; 114:297-316
34. Gottstein R, Cooke R. Systematic Review of intravenous immunoglobulin in haemolytic disease of the newborn. Arch Dis Child Fetal Neonatal Ed 2003; 88:F6-10

35. Orange J, Hossny E, Weiler C, et al. Use of intravenous immunoglobulin in human disease: A review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol 2006;117(4 Suppl): S525-53.
36. Amagai M, Ikeda S, Shimizu H, et al. A randomized, double-blind trial of intravenous immunoglobulin for pemphigus. J Am Acad Dermatol 2009; 60:595-602
37. Ahmed AR. Intravenous immunoglobulin therapy in the treatment of patients with pemphigus vulgaris unresponsive to conventional immunosuppressive treatment. J Am Acad Dermatol 2001; 45:679-90.
38. Hughes R, Bensa S, Willison H, Van den Bergh P, Comi G, Illa I, Nobile-Orazio E, van Doorn P, Dalakas M, Bojar M, Swan A; Inflammatory Neuropathy Cause and Treatment (INCAT) Group. Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy. Ann Neurol. 2001 Aug;50(2):195-201.
39. Zinman L, Ng E, Bril V. IV immunoglobulin in patients with myasthenia gravis: a randomized controlled trial. Neurology. 2007 Mar 13;68(11):837-41.
40. Koski CL, Baumgarten M, Magder LS, et al. Derivation and validation of diagnostic criteria for chronic inflammatory demyelinating polyneuropathy. Journal of the Neurological Sciences 2009; 277:1-8.
41. Sullivan KM, Storek J, Kopecky KJ, et al. A controlled trial of long-term administration of intravenous immunoglobulin to prevent late infection and chronic graft-vs.-host disease after marrow transplantation: clinical outcome and effect on subsequent immune recovery. Biol Blood Marrow Transplant 1996;2:44-53.
42. Alejandria MM, Lansang MA, Dans LF, Mantaring JB. Intravenous immunoglobulin for treating sepsis and septic shock. Cochrane Database Syst Rev 2002;CD001090.
43. American College of Obstetricians and Gynecologists (ACOG), Committee on Practice Bulletins -- Obstetrics. Thrombocytopenia in pregnancy. ACOG Practice Pattern No. 6. Washington, DC: ACOG; September 1999.
44. Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. MMWR 2000;49(No. RR-10):1-128.
45. Emerson GG, Herndon CN, Sreih AG. Thrombotic complications after intravenous immunoglobulin therapy in two patients. Pharmacotherapy. 2002;22:1638-1641.
46. Department of Health (London). Clinical Guidelines for Immunoglobulin Use: Update to Second Edition. August, 2011.
47. Provan, Drew, et al. "Clinical guidelines for immunoglobulin use." Department of Health Publication, London (2008).
48. Sussman J, Farrugia ME, Maddison P, et al. Myasthenia gravis: Association of British Neurologists' management guidelines. Pract Neurol 2015; 15: 199-206.
49. Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis-Executive Summary. Neurology. 2016 Jul 26; 87(4): 419-25.
50. Orange JS, Ballow M, Stiehm, et al. Use and interpretation of diagnostic vaccination in primary immunodeficiency: A working group report of the Basic and Clinical Immunology Interest Section of the American Academy of Allergy, Asthma & Immunology. J Allergy Clin Immunol Vol 130 (3).
51. Jeffrey Modell Foundation Medical Advisory Board, 2013. 10 Warning Signs of Primary Immunodeficiency. Jeffrey Modell Foundation, New York, NY.

52. Bonilla FA, Khan DA, Ballas ZK, et al. Practice Parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol 2015 Nov;136(5):1186-205.e1-78.
53. Kuitwaard K, de Gelder J, Tio-Gillen AP, et al. Pharmacokinetics of intravenous immunoglobulin and outcome in Guillain-Barré syndrome. Ann Neurol. 2009;66(5):597.
54. Shehata N, Palda VA, Meyer RM, et al: The use of immunoglobulin therapy for patients undergoing solid organ transplantation: an evidence-based practice guideline. Transfus Med Rev 2010; 24 Suppl 1:S7-S27.
55. Jordan SC, Tyan D, Stablein D, et al: Evaluation of intravenous immunoglobulin as an agent to lower allosensitization and improve transplantation in highly sensitized adult patients with end-stage renal disease: report of the NIH IG02 trial. J Am Soc Nephrol 2004; 15(12):3256-3262.
56. Yuan XP, Wang CX, Gao W, et al: Kidney transplant in highly sensitized patients after desensitization with plasmapheresis and low-dose intravenous immunoglobulin. Exp Clin Transplant 2010; 8(2):130-135.
57. Jordan SC, Quartel AW, Czer LSC, et al: Posttransplant therapy using high-dose human immunoglobulin (intravenous gamma globulin) to control acute humoral rejection in renal and cardiac allograft recipients and potential mechanism of action. Transplantation 1998; 66(6):800-805.
58. Sullivan KM, Kopecky KJ, Jocom J, et al: Immunomodulatory and antimicrobial efficacy of intravenous immunoglobulin in bone marrow transplantation. N Engl J Med 1990; 323:705-712.
59. Bhatti AB, Gazali ZA. Recent Advances and Review on Treatment of Stiff Person Syndrome in Adults and Pediatric Patients. Cureus. 2015 Dec 22;7(12):e427
60. Tanimoto K, Nakano K, Kano S, et al. Classification criteria for polymyositis and dermatomyositis. J Rheumatol. 1995 Apr;22(4):668-74.
61. Kyriakides T, Angelini C, Schaefer J, et al. EFNS guidelines on the diagnostic approach to pauci- or asymptomatic hyperCKemia. Eur J Neurol. 2010 Jun 1;17(6):767-73.
62. Feliciani C, Joly P, Jonkman MF, et al. Management of bullous pemphigoid: the European Dermatology Forum consensus in collaboration with the European Academy of Dermatology and Venereology. Br J Dermatol. 2015 Apr;172(4):867-77.
63. Hertl M, Jedlickova H, Karpati S, et al. Pemphigus. S2 Guideline for diagnosis and treatment--guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV). J Eur Acad Dermatol Venereol. 2015 Mar;29(3):405-14.
64. Harman KE, Albert S, Black MM; British Association of Dermatologists. Guidelines for the management of pemphigus vulgaris. Br J Dermatol. 2003 Nov;149(5):926-37.
65. Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: A review of evidence. J Allergy Clin Immunol. 2017 Mar;139(3S):S1-S46.
66. Dantal J. Intravenous Immunoglobulins: In-Depth Review of Excipients and Acute Kidney Injury Risk. Am J Nephrol 2013;38:275-284.
67. Rajabally YA et al. Validity of diagnostic criteria for chronic inflammatory demyelinating polyneuropathy: A multicentre European study. J Neurol Neurosurg Psychiatry 2009 Dec; 80:1364.
68. Postow, MA. Managing Immune Checkpoint-Blocking Antibody Side Effects. American Society of Clinical Oncology Education Book. 2015; 76-83.

69. Williams TJ, Benavides DR, Patrice KA. Association of Autoimmune Encephalitis with combined immune checkpoint inhibitor treatment for metastatic cancer. *JAMA Neurol* .933-928:(8)73;2016 doi:10.1001/jamaneurol.2016.1399
70. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Biol Blood Marrow Transplant. 2009;15(10):1143-1238. doi: 10.1016/j.bbmt.2009.06.019. [PubMed 19747629]
71. Willison HJ, Jacobs BS, van Doom PA. Guillain-Barré Syndrome. Lancet. 2016 Aug;388(10045):717-27. Epub 2016 Mar 2
72. Sanders DB, Wolfe GI, Benetar M, et al. International consensus guidance for management of myasthenia gravis. Neurology 2016;87:1–7
73. First Coast Service Options, Inc. Local Coverage Determination (LCD): Intravenous Immune Globulin (L34007). Centers for Medicare & Medicaid Services, Inc. Updated on 4/13/2018 with effective date 4/12/2018. Accessed August 2018.
74. Noridian Administrative Services, LLC. Local Coverage Determination (LCD): Immune Globulin Intravenous (IVIg) (L34074; L34314). Centers for Medicare & Medicaid Services, Inc. Updated on 5/25/2018 with effective date 07/1/2018. Accessed August 2018.
75. Novitas Solutions, Inc. Local Coverage Determination (LCD): Intravenous Immune Globulin (IVIG) (L35093). Centers for Medicare & Medicaid Services, Inc. Updated on 7/20/2018 with effective date 4/13/2018. Accessed August 2018.
76. Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Immune Globulins (L34771). Centers for Medicare & Medicaid Services, Inc. Updated on 12/19/2017 with effective date 1/1/2018. Accessed August 2018.
77. CGS, Administrators, LLC. Local Coverage Determination (LCD): Intravenous Immune Globulin (L35891). Centers for Medicare & Medicaid Services, Inc. Updated on 3/28/2018 with effective date 3/1/2018. Accessed August 2018.
78. Palmetto GBA. Local Coverage Determination (LCD): Intravenous Immunoglobulin (IVIG) (L34580). Centers for Medicare & Medicaid Services, Inc. Updated on 7/20/2018 with effective date 7/26/2018. Accessed August 2018.
79. National Coverage Determination (NCD) for Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases (250.3). Centers for Medicare and Medicaid Services, Inc. Updated on 12/01/2015 with effective date 10/1/2015. Accessed August 2018.
80. National Government Services, Inc. Local Coverage Article for Intravenous Immune Globulin (IVIG) - Related to LCD L33394 (A52446). Centers for Medicare & Medicaid Services, Inc. Updated on 9/22/2017 with effective date 10/7/2017. Accessed August 2018.
81. Noridian Healthcare Solutions, LLC. Local Coverage Article for Intravenous Immune Globulin (IVIG)-NCD 250.3 – Related to LCD L34314, L34074 (A54641, A54643). Centers for Medicare & Medicaid Services, Inc. Updated on 1/18/2017 with effective date 11/7/2015. Accessed August 2018.
82. Noridian Healthcare Solutions, LLC. Local Coverage Article: Coverage of Intravenous Immune Globulin for Treatment of Primary Immune Deficiency Diseases in the Home – Medicare Benefit Policy Manual, Chapter 15,

(A54660, A54662). Centers for Medicare & Medicaid Services, Inc. Updated 4/2/2018 with effective date 4/12/2018. Accessed August 2018.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
A48.3	Toxic shock syndrome
B20	Human immunodeficiency virus (HIV) disease
B25.0	Cytomegaloviral pneumonitis
B25.1	Cytomegaloviral hepatitis
B25.2	Cytomegaloviral pancreatitis
B25.8	Other cytomegaloviral diseases
B25.9	Cytomegaloviral disease, unspecified
D69.41	Evans syndrome
D80.0	Hereditary hypogammaglobulinemia
D80.1	Nonfamilial hypogammaglobulinemia
D80.3	Selective deficiency of immunoglobulin G [IgG] subclasses
D80.5	Immunodeficiency with increased immunoglobulin M [IgM]
D80.7	Transient hypogammaglobulinemia of infancy
D81.0	Severe combined immunodeficiency [SCID] with reticular dysgenesis
D81.1	Severe combined immunodeficiency [SCID] with low T- and B-cell numbers
D81.2	Severe combined immunodeficiency [SCID] with low or normal B-cell numbers
D81.6	Major histocompatibility complex class I deficiency
D81.7	Major histocompatibility complex class II deficiency
D81.89	Other combined immunodeficiencies
D81.9	Combined immunodeficiency, unspecified
D82.0	Wiskott-Aldrich syndrome
D82.1	DiGeorge's syndrome
D83.0	Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function
D83.2	Common variable immunodeficiency with autoantibodies to B- or T-cells
D83.8	Other common variable immunodeficiencies
D83.9	Common variable immunodeficiency, unspecified
D89.810	Acute graft-versus-host disease

ICD-10	ICD-10 Description
D89.812	Acute on chronic graft-versus-host disease
G03.8	Meningitis due to other specified causes
G03.9	Meningitis, unspecified
G04.81	Other encephalitis and encephalomyelitis
G04.89	Other myelitis
G04.90	Encephalitis and encephalomyelitis, unspecified
G04.91	Myelitis, unspecified
G25.82	Stiff-man syndrome
G56.80	Other specified mononeuropathies of unspecified upper limb
G56.81	Other specified mononeuropathies of right upper limb
G56.82	Other specified mononeuropathies of left upper limb
G56.83	Other specified mononeuropathies of bilateral upper limbs
G56.90	Unspecified mononeuropathy of unspecified upper limb
G56.91	Unspecified mononeuropathy of right upper limb
G56.92	Unspecified mononeuropathy of left upper limb
G56.93	Unspecified mononeuropathy of bilateral upper limbs
G57.80	Other specified mononeuropathies of unspecified lower limb
G57.81	Other specified mononeuropathies of right lower limb
G57.82	Other specified mononeuropathies of left lower limb
G57.83	Other specified mononeuropathies of bilateral lower limbs
G57.90	Unspecified mononeuropathy of unspecified lower limb
G57.91	Unspecified mononeuropathy of right lower limb
G57.92	Unspecified mononeuropathy of left lower limb
G57.93	Unspecified mononeuropathy of bilateral lower limbs
G61.0	Guillain-Barre syndrome
G61.1	Serum neuropathy
G61.81*	Chronic inflammatory demyelinating polyneuritis
G61.82	Multifocal motor neuropathy
G61.89	Other inflammatory polyneuropathies
G61.9	Inflammatory polyneuropathy, unspecified

ICD-10	ICD-10 Description
G62.89	Other specified polyneuropathies
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation
G90.09	Other idiopathic peripheral autonomic neuropathy
J70.2	Acute drug-induced interstitial lung disorders
J70.4	Drug-induced interstitial lung disorders, unspecified
L10.0	Pemphigus vulgaris
L10.2	Pemphigus foliaceous
L12.0	Bullous pemphigoid
L12.1	Cicatricial pemphigoid
L12.30	Acquired epidermolysis bullosa, unspecified
L12.31	Epidermolysis bullosa due to drug
L12.35	Other acquired epidermolysis bullosa
L12.5	Other acquired epidermolysis bullosa
L13.8	Other specified bullous disorders
M06.4	Inflammatory polyarthropathy
M30.3	Mucocutaneous lymph node syndrome [Kawasaki]
M33.00	Juvenile dermatomyositis, organ involvement unspecified
M33.01	Juvenile dermatomyositis with respiratory involvement
M33.02	Juvenile dermatomyositis with myopathy
M33.03	Juvenile dermatomyositis without myopathy
M33.09	Juvenile dermatomyositis with other organ involvement
M33.10	Other dermatomyositis, organ involvement unspecified
M33.11	Other dermatomyositis with respiratory involvement
M33.12	Other dermatomyositis with myopathy
M33.13	Other dermatomyositis without myopathy
M33.19	Other dermatomyositis with other organ involvement
M33.20	Polymyositis, organ involvement unspecified
M33.21	Polymyositis with respiratory involvement
M33.22	Polymyositis with myopathy

ICD-10	ICD-10 Description
M33.29	Polymyositis with other organ involvement
M33.90	Dermatopolymyositis, unspecified, organ involvement unspecified
M33.91	Dermatopolymyositis, unspecified with respiratory involvement
M33.92	Dermatopolymyositis, unspecified with myopathy
M33.93	Dermatopolymyositis, unspecified without myopathy
M33.99	Dermatopolymyositis, unspecified with other organ involvement
M36.0	Dermato(poly)myositis in neoplastic disease
O26.40	Herpes gestationis, unspecified trimester
O26.41	Herpes gestationis, first trimester
O26.42	Herpes gestationis, second trimester
O26.43	Herpes gestationis, third trimester
P61.0	Transient neonatal thrombocytopenia
T86.00	Unspecified complication of bone marrow transplant
T86.01	Bone marrow transplant rejection
T86.02	Bone marrow transplant failure
T86.03	Bone marrow transplant infection
T86.09	Other complications of bone marrow transplant
T86.10	Unspecified complication of kidney transplant
T86.11	Kidney transplant rejection
T86.12	Kidney transplant failure
T86.13	Kidney transplant infection
T86.19	Other complication of kidney transplant
T86.20	Unspecified complication of heart transplant
T86.21	Heart transplant rejection
T86.22	Heart transplant failure
T86.23	Heart transplant infection
T86.290	Cardiac allograft vasculopathy
T86.298	Other complications of heart transplant
T86.30	Unspecified complication of heart-lung transplant
T86.31	Heart-lung transplant rejection

ICD-10	ICD-10 Description
T86.32	Heart-lung transplant failure
T86.33	Heart-lung transplant infection
T86.39	Other complications of heart-lung transplant
T86.40	Unspecified complication of liver transplant
T86.41	Liver transplant rejection
T86.42	Liver transplant failure
T86.43	Liver transplant infection
T86.49	Other complications of liver transplant
T86.810	Lung transplant rejection
T86.811	Lung transplant failure
T86.812	Lung transplant infection
T86.818	Other complications of lung transplant
T86.819	Unspecified complication of lung transplant
T86.890	Other transplanted tissue rejection
T86.891	Other transplanted tissue failure
T86.892	Other transplanted tissue infection
T86.898	Other complications of other transplanted tissue
T86.899	Unspecified complication of other transplanted tissue
Z48.21	Encounter for aftercare following heart transplant
Z48.22	Encounter for aftercare following kidney transplant
Z48.23	Encounter for aftercare following liver transplant
Z48.24	Encounter for aftercare following lung transplant
Z48.280	Encounter for aftercare following heart-lung transplant
Z48.290	Encounter for aftercare following bone marrow transplant
Z94.0	Kidney transplant status
Z94.1	Heart transplant status
Z94.2	Lung transplant status
Z94.3	Heart and lungs transplant status
Z94.4	Liver transplant status
Z94.81	Bone marrow transplant status

ICD-10	ICD-10 Description
Z94.83	Pancreas transplant status
Z94.84	Stem cells transplant status

**G61.81 is not payable when associated with diabetes mellitus, dysproteinemias, renal failure, or malnutrition*

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
E	A57187, A54660, A54641	Noridian Healthcare Solutions, LLC
F	A54643, A57194, A54662	Noridian Healthcare Solutions, LLC
H, L	A56786	Novitas Solutions, Inc.
J, M	A56718	Palmetto GBA, LLC
N	A57778	First Coast Service Options, Inc.
5, 8	A57554	Wisconsin Physicians Service Insurance Corporation (WPS)
6, K	A59105	National Government Services, Inc. (NGS)
15	A56779, A57160	CGS Administrators, LLC
ALL	250.3	ALL

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corporation (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corporation (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Asceniv, Alyglo, Bivigam, Flebogamma, Gamunex-C, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Octagam, Privigen, and Panzyga were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Asceniv, Bivigam, Flebogamma, Gamunex-C, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Octagam, Privigen, and Panzyga according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.