Neighborhood Health Plan OF RHODE ISLAND™
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Immune Globulins (immunoglobulin) NON-HEMATOLOGY and NON-ONCOLOGY POLICY: Asceniv; Alyglo; Bivigam; Flebogamma; Gamunex-C; Gammagard Liquid; Gammagard S/D; Gammaked; Gammaplex; Octagam; Privigen; Panzyga

(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

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. Quantity Limit (max daily dose) [Pharmacy Benefit]:

Drug	Vial size in IgG grams	# of vials	
		One time only LOAD	per 28 days MAINTENANCE
Asceniv	5	18	18
Alyglo	5,10,20	1	1
Bivigam*	5	1	1
	10	23	23
Flebogamma 10% DIF	5, 10, 20	1	1
	20	11	11
	2.5, 5, 10	1	1

Flebogamma 5% DIF	20	11	11
Gamunex-C	1, 2.5, 5, 10, 20	1	1
	40	6	6
Gammagard Liquid	1, 2.5, 5, 10, 20	1	1
	30	8	8
Gammagard S/D*	5	1	1
	10	23	23
Gammaked	1, 2.5, 5, 10	1	1
	20	11	11
Gammaplex (5% and 10%)	2.5, 5, 10	1	1
	20	11	11
Octagam 10%	2, 5, 10	1	1
	20	11	11
Octagam 5%	1, 2.5, 5, 10	1	1
	25	9	9
Privigen	5, 10, 20	1	1
	40	6	6
Panzyga	1, 2.5, 5, 10, 20	1	1
	30	8	8

**Discontinued by the manufacturer*

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

Indication	Billable Units	Per # days *(unless otherwise specified)*
PID and Supportive Care after Rethymic transplant	180	21
IgG Subclass Deficiency	90	14
CIDP	Load: 460	5
	Maintenance: 230	21
FAIT	230	7
Kawasaki's Disease	460	2 doses only
Multifocal Motor Neuropathy	460	28
HIV (Pediatric Patients only)	46	14
Guillain-Barre	460	5 *(for two courses only)*
Myasthenia Gravis	460	28
Auto-immune blistering diseases	460	28
Bone Marrow or Stem Cell Transplant	Load:120	7(for 90 days)

	Maintenance:120	
Dermatomyositis/Polymyositis	460	28
Complications of transplanted solid organ *(kidney, liver, lung, heart and pancreas transplants)*	460	28
Stiff Person	460	28
Toxic shock syndrome	460	5 *(for one cycle only)*
NAIT	20	2 doses only
Management of Immune Checkpoint Inhibitor Related Toxicity	460	5 *(for one cycle only)*

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 or Panzyga the patient must have a failure or intolerance to the following preferred formulations: Gammaked/Gamunex-C, Gammagard liquid, 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***]

- Patient has an IgG level < 200 mg/dL **OR**
- Patient meets <u>both</u> of the following:
  - Patient has a history of multiple hard to treat infections as indicated by at least **<u>one</u>** 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**

- Patient 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]

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

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) †

- Patient's disease course is progressive or relapsing and remitting for 2 months or longer; **AND**
- Patient 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**
- Patient 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) ‡

- Patient's disease is severe (i.e., patient requires assistance to ambulate); **AND**
- Onset of symptoms are recent (i.e., less than 1 month); **AND**
- Patient has abnormal or absent deep tendon reflexes in upper or lower limbs; **AND**
- Patient 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 †

- Patient has progressive multi-focal weakness (without sensory symptoms); **AND**
- Complete or partial conduction block or abnormal temporal dispersion conduction must be present in at least 2 motor nerves with accompanying normal sensory nerve conduction study across the same nerve that demonstrated the conduction block; **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 ‡

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

Myasthenia Gravis ‡

- Patient has a positive serologic test for anti-acetylcholine receptor (AchR) antibodies; **AND**
- Patient has an acute exacerbation resulting in impending myasthenic crisis (i.e., respiratory compromise, acute respiratory failure, and/or bulbar compromise); **AND**
- Patient is failing on conventional immunosuppressant therapy alone (e.g., corticosteroids, azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.); **AND**
- Patient 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%) **/Polymyositis ‡**

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

Note: Initial authorization is valid for 3 months

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 ‡

- Patient has anti-glutamic acid decarboxylase (GAD) antibodies; **AND**
- Patient has failed at least 2 of the following treatments: benzodiazepines, baclofen, gabapentin, valproate, tiagabine, or levetiracetam; **AND**
- Patient 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**
- Patient's BMT was allogeneic; **AND**
- Patient 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) ‡

- Patient 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 ‡

- Patient 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**
- Patient has severe disease that is extensive and debilitating; **AND**
- Diagnosis has been confirmed by biopsy; **AND**
- Patient 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**
- Patient 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 patients with congenital athymia after surgical implantation of Rethymic; **OR**
- Used as re-initiation of treatment 2 months after stopping immunoglobulin replacement therapy in pediatric patients who have an IgG trough level lower than normal range for age

Management of Immune-Checkpoint-Inhibitor Related Toxicity ‡

- Patient has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, cemiplimab, ipilimumab, dostarlimab, tremelimumab, retifanlimab etc.); **AND**
- Patient 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**: <50 mcg/mL **Osmolarity**: 240 to 370 mOsm/kg	

		IgA-deficient with IgA antibodies	**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 10%(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	

– 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

- Patient 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**
- Patient is at a decreased risk of infection as a result of Continued treatment is necessary to decrease the risk of infection

Chronic Inflammatory Demyelinating Polyneuropathy

- Renewals will be authorized for patients 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 patients 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**
- Patient continues to be at an increased risk of infection necessitating continued therapy

Myasthenia Gravis

- May not be renewed.

Dermatomyositis/Polymyositis

- Patient 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

- Patient continues to be at an increased risk of infection necessitating continued therapy as evidenced by an IgG level < 400 mg/dL
- 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:
    - Patient is no longer on immunosuppression (at least 10% of CD3+ T cells are naïve in phenotype); **AND**
    - Patient is at least 9 months post-treatment; **AND**
    - Patient's phytohemagglutinin (PHA) response within normal limits; **OR**
- Renewals for use as re-initiation of treatment after stopping immunoglobulin replacement therapy for patients 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/m^2 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
Carimune NF❖	CSL Behring AG	J1566	500 mg	6	44206-0417-XX
				12	44206-0418-XX
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	Baxalta	J1569 or 90283	500 mg	1, 2.5, 5, 10, 20, 30	00944-2700-XX
Gammagard S/D Less IGA ❖	Baxalta	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%	Bio Products Laboratory	J1557 or 90283	500 mg	5, 10, 20	64208-8234-XX
Gammaplex 10%				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
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.

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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.