Immune Globulin Products

Generic Name: Immune Globulin Replacement Therapy (IVIG) IV/SQ/IM

Therapeutic Class or Brand Name: Asceniv®, Bivigam®, Carimune® NF, Cutaquig®, Cuvitru®, Flebogamma® DIF, GamaSTAN® S/D, Gammagard®, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Hizentra®, HyQvia®, Octagam®, Panzyga®, Privigen®, and Xembify ®. Policy also applies to all other products not listed.

Applicable Drugs (if Therapeutic Class): N/A

GPI Code: 1910002010, 1910002020, 1910002030, 1999000235, 1910002080, 1910002057, 1910002000, 1910002060, 1910002064

Preferred: N/A

Non-preferred: N/A

Date of Origin: 2/1/2013

Date Last Reviewed / Revised: 8/19/2020

FDA Approved Indication(s)

Brand Name	ROA*	PI*	ITP*	CIDP*	KS*	MMN*	CLL*	VPPX*
Asceniv®	IV	X						
Bivigam®	IV	X						
Carimune NF®	IV	X	X					
Cutaquig®	SC	X						
Cuvitru®	SC	X						
Flebogamma DIF®	IV	X	X (10% only)					
GamaSTAN S/D	IM							X
Gammagard Liquid®	IV, SC	X				X (IV only)		
Gammagard S/D®	IV	X	X		X		X	
Gammaked®	IV, SC	X	X (IV only)	X (IV only)				
Gammaplex	IV	X	X					
Gamunex-C®	IV, SC	X	X (IV only)	X (IV only)				
Hizentra®	SC	X		X				
HyQvia®	SC	X						
Octagam®	IV	X (5% only)	X (10% only)					
Panzyga®	IV	X	X					
Privigen®	IV	X	X	X				
Xembify®	SC	X						

**ROA: route of administration; PI: primary humoral immunodeficiency; ITP: idiopathic thrombocytopenic purpura; CIDP: chronic inflammatory demyelinating polyneuropathy; KS: Kawasaki syndrome; MMN: multifocal motor neuropathy; CLL: B-cell chronic lymphocytic leukemia; VPPX: viral prophylaxis (for hepatitis A, measles, varicella, rubella)*

Off-Labeled Indications Include: Acquired hypogammaglobulinemia secondary to malignancy; Antibody-mediated rejection (AMR) in cardiac transplantation (treatment); Clostridioides (formerly Clostridium) difficile infection (severe, refractory, and recurrent); Dermatomyositis/polymyositis (refractory); Guillain-Barré syndrome; Hematopoietic cell transplantation with hypogammaglobulinemia (prevention of bacterial infection); HIV-associated thrombocytopenia; Lambert-Eaton myasthenic syndrome; Myasthenia gravis (acute exacerbation)

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criterion I-II are met):

I. Documented diagnosis of one of the following conditions A through G **AND** must meet criteria listed under applicable diagnosis:

A. Immunodeficiency (primary OR acquired) as defined in ONE of the following:

1. Primary Immunodeficiencies
   a) Agammaglobulinemia (X-linked, congenital)
   b) Common variable immunodeficiency (CVID)
   c) Hyper-IgM syndrome
   d) Specific antibody deficiency
      i. Normal IgG levels
      ii. Inadequate antibody response to polysaccharide vaccines (e.g. pneumococcal)
      iii. Recurrent bacterial infections within the past 12 months
   e) Selective immunodeficiency (e.g. selective IgA, IgM, or IgG subclass)
      i. Total or subclass (IgA, IgG, IgM) immune globulin level below normal
      ii. Inadequate antibody response to protein and/or polysaccharide vaccines (e.g. tetanus, pneumococcal)
      iii. Recurrent bacterial infections within the past 12 months
   f) Ataxia-telangiectasia
   g) Severe combined Immunodeficiency (SCID): adenosine deaminase (ADA), JAK3, X-SCID, RAG1/2, DiGeorge syndrome, Wiskott-Aldrich syndrome, Zeta-associated protein 70 (ZAP-70) deficiency
2. Prophylaxis for Human Immunodeficiency Virus (HIV) Infected Children (off-label)
   a) Hypogammaglobulinemia evidenced by serum IgG < 400 mg/dL
   b) Age < 13 years old
   c) Prescribed to prevent serious bacterial infections in a child with human immunodeficiency virus (HIV)

d) Prescribed by or in consultation with an infectious disease specialist

e) Dose does not exceed 400 mg/kg every 2 to 4 weeks OR dose is supported by practice guidelines

3. B-Cell Chronic Lymphocytic Leukemia Infection Prophylaxis

a) Diagnosis of B-Cell CLL

b) Prescribed to prevent bacterial infections

c) Member must meet one of the following

i. Hypogammaglobulinemia

ii. Recurrent bacterial infections

d) Prescribed by or in consultation with hematologist, oncologist, or immunologist

4. Multiple Myeloma Infections Prophylaxis (off-label)

a) Diagnosis of multiple myeloma with stable disease

b) Hypogammaglobulinemia

c) Prescribed to prevent bacterial infections

d) Prescribed by or in consultation with hematologist, oncologist, or immunologist

5. Post-Hematopoietic Cell Transplant Infection Prophylaxis (off-label)

a) Prescribed to prevent bacterial infection in allogenic hematopoietic stem cell transplant (HSCT) recipients

b) Severe hypogammaglobulinemia with serum IgG < 400 mg/dL

c) Dose does not exceed 500 mg/kg weekly

B. Immune-mediated hematologic disorder as defined in ONE of the following:

1. Autoimmune Hemolytic Anemia (off-label)

a) Inadequate response to alternative therapies (i.e. steroids, immunosuppressive agents, plasmapheresis, rituximab, and/or splenectomy)

b) Dose does not exceed 1 gram/kg daily for up to 7 days

2. Fetal/Neonatal Alloimmune Thrombocytopenia (FAIT) (off-label)

a) Diagnosis of fetal/neonatal alloimmune thrombocytopenia

b) Dose does not exceed 2 gram/kg weekly

3. Idiopathic Thrombocytopenia (ITP)

a) Diagnosis of acute or chronic ITP

i. Acute ITP

(a) Rapid increase in platelet count is necessary – active bleeding or prior to invasive procedure (i.e. surgery, epidural anesthesia, etc.)

ii. Chronic ITP

(a) Low platelet count as defined by ONE of the following:

(i) Children: < 30,000 cells/mm^3

(ii) Adults: < 20,000 cells/mm^3

(iii) Adults with signs or symptoms of bleeding: < 30,000 cells/mm^3

b) ITP in pregnancy and at least ONE of the following is met:

i. Platelet counts < 10,000 cells/mm^3 in the third trimester, despite a trial of systemic corticosteroids unless contraindicated or not tolerated.

ii. Platelet counts < 30,000 cells/mm^3 that are associated with bleeding before vaginal delivery or Cesarean section (C-section).

4. Parvovirus B19 Infection and Severe Anemia (off-label)

a) Diagnosis of anemia secondary to chronic parvovirus B19 infection

b) Severe anemia defined as Hgb < 10 or Hct < 30.

C. Neuromuscular disorder as defined in ONE of the following:

1. Inflammatory Demyelinating Polyneuropathy (IDP)

a) Diagnosis of acute or chronic IDP [CIDP]

i. Acute IDP/Guillain-Barré Syndrome (GBS) and ONE of the following is met:

(a) Deteriorating pulmonary function tests (PFTs).

(b) Rapid deterioration with symptoms for < 2 weeks.

(c) Rapidly deteriorating ability to ambulate.

(d) Inability to walk independently for 10 meters (30 feet)

ii. Chronic IDP and ALL of criteria are met:

(a) Significant functional disability.

(b) Documentation of slowing of nerve conduction velocity on electromyography (EMG) or nerve conduction study (NCS)

(c) Documentation of elevated spinal fluid protein on lumbar puncture OR nerve biopsy confirming the diagnosis

b) Prescribed by or in consultation with a neurologist

2. Dermatomyositis and Polymyositis (off-label)

a) Diagnosis of dermatomyositis or polymyositis.

b) Failure of a course of systemic corticosteroid unless contraindicated or clinically significant adverse effects are experienced.

3. Myasthenia Gravis (MG)/Lambert Eaton Myasthenia Syndrome (LEMS) (off-label)
   a) Diagnosis of myasthenia gravis (MG) or Lambert Eaton Myasthenia Syndrome (LEMS).
   b) Member meets one of the following
      i. Acute crisis (i.e. respiratory failure, swallowing difficulties, inability to ambulate).
      ii. Failure of one of the following (pyridostigmine, azathioprine, cyclosporine, or systemic corticosteroid) unless contraindicated or experienced clinically significant adverse effects.
4. Multifocal Motor Neuropathy (MMN)
   a) Documented diagnosis of multifocal motor neuropathy.
   b) Dose does not exceed 2.4 gram/kg monthly.
5. Paraneoplastic Neurological Syndrome (off-label)
   a) Diagnosis of Opsoclonus-myoclonus ataxia syndrome [OMS] in pediatric neuroblastoma patients with significant functional impairment.
      i. Failure of an adequate course (at least 3 to 7 days) of systemic corticosteroids unless contraindicated or experienced clinically significant adverse effects.
   b) Diagnosis of Stiff-Person Syndrome
      i. Failure of one of the following (diazepam, baclofen, clonazepam, valproic acid, clonidine) unless contraindicated or experienced clinically significant adverse effects.
6. Pemphigoid-refractory Immunobullous Disease (off-label)
   a) Diagnosis of one of the following:
      i. Bullous Pemphigoid.
      ii. Mucous Membrane Pemphigoid.
      iii. Pemphigus Foliaceus.
      iv. Pemphigus Vulgaris.
   b) Failure of an adequate course of systemic corticosteroid OR immunosuppressant (azathioprine, mycophenolate, cyclophosphamide) unless contraindicated or experienced clinically significant adverse effects
7. Systemic Lupus Erythematosus (SLE) (off-label)
   a) Diagnosis of severe active systemic lupus erythematous.

b) Failure of an adequate course of systemic corticosteroid OR immunosuppressant (azathioprine, mycophenolate, cyclophosphamide) unless contraindicated or experienced clinically significant adverse effects.

D. Solid Organ Transplant (off-label)

1. Prescribed for the prevention or treatment of antibody-mediated rejection
   a) Prevention: Prior to solid organ transplant and in the perioperative period, for patients at high risk for AMR, including highly sensitized patients, and those receiving an ABO-incompatible organ.
   b) Treatment: Following solid organ transplant and confirmed antibody-mediated rejection by either biopsy or presence of panel reactive antibodies (PRAs).

E. Kawasaki Syndrome

1. Diagnosis of Kawasaki Syndrome.
2. Therapy is initiated within first 10 days of diagnosis.
3. Prescribed concurrently with aspirin therapy unless contraindicated or experienced clinically significant adverse effects.

F. Pediatric Intractable Epilepsy (off-label)

1. In candidates for surgical resection OR when other interventions (i.e. anticonvulsant medications, systemic corticosteroids, etc.) are ineffective or not tolerated

G. Viral Prophylaxis for Hepatitis A, Measles, Varicella, Rubella Viruses

1. Request is for intramuscular formulation (GammaSTAN S/D)
2. Request is for one of the following indications
   a) Hepatitis A
      i. Meets ONE of the following:
         (a) Exposure in the past 2 weeks AND does not have clinical manifestation of hepatitis A
         (b) At high risk for exposure – travel to areas where Hepatitis A is common
      ii. Hepatitis A vaccine is contraindicated or unavailable
   b) Measles
      i. Exposure within the past 6 days.
      ii. Has not had receiving measles vaccine.
      iii. Has not previously had measles.
      iv. Measles vaccines is contraindicated or unavailable.
   c) Varicella
      i. Lacks immunity to varicella

ii. Varicella-Zoster Immune Globulin is unavailable

iii. Varicella vaccine is contraindicated or unavailable

d) Rubella

i. Pregnant women

ii. Exposure to rubella

II. Prescribed by or in consultation with a specialist (hematologist, oncologist, neurologist, or immunologist)

EXCLUSION CRITERIA

Hypersensitivity to immune globulin or any component of the formulation; IgA deficiency (with anti-IgA antibodies and history of hypersensitivity [excluding Gammagard® S/D]);hyperprolinemia (Hizentra®, Privigen®); severe thrombocytopenia or coagulation disorders where IM injections are contraindicated (GamaSTAN® S/D); hypersensitivity to corn (Octagam 5%®); hereditary intolerance to fructose (Gammaplex 5%®); infants/neonates for whom sucrose or fructose tolerance has not been established (Gammaplex 5%®); hypersensitivity to hyaluronidase, human albumin, or any component of the hyaluronidase formulation (HyQvia®).

OTHER CRITERIA

- N/A

QUANTITY / DAYS SUPPLY RESTRICTIONS

- When prior authorization is approved, immune globulins may be authorized for the dose as stated in product package insert although dosage is highly variable:

Medication	Indication	Dosing Regimen (Prescribing Information)
Asceniv®	PI	300 to 800 mg/kg IV every 3 to 4 weeks
Bivigam®	PI	300 to 800 mg/kg IV every 3 to 4 weeks
Carimune NF®	ITP	0.4 gram/kg IV daily consecutively on day 2 to 5
	PI	0.4 to 0.8 gram/kg IV every 3 to 4 weeks
Cutaquig®	PI	Switching from immunoglobulin IV: $\frac{\text{IGIV dose (grams)} \times 1.40}{\text{No. of weeks between doses}}$ = Initial weekly dose
Cuvitru®	PI	IV to SC: initial weekly dose= $\frac{\text{IGIV/HYQVIA dose (grams)} \times 1.30}{\text{No. of weeks between doses}}$
Flebogamma 5%	PI	300 to 600 mg/kg IV every 3 to 4 weeks
Flebogamma 10%®	PI	300 to 600 mg/kg IV every 3 to 4 weeks
	ITP	1 gram/kg IV daily for 2 consecutive days

GamaSTAN S/D®	Hepatitis A	Recent exposure: 0.1 mL/kg High risk for exposure: < 1 month: 0.1 mL/kg; 1 to 2 months: 0.2 mL/kg; >2 months: Repeat dose of 0.2 mL/kg every 2 months
	Measles	0.25 mL/kg IM once
	Rubella	0.55 mL/kg IM once
	Varicella	0.6 to 1.2 mL/kg IM once
Gammagard® Liquid	MMN	0.5 to 2.4 gram/kg IV monthly
	PI	Intravenous: 300 to 600 mg/kg every 3 to 4 weeks Subcutaneous: weekly dose= $\frac{\text{IGIV dose (grams)} \times 1.37}{\text{No. of weeks between doses}}$
Gammagard S/D®	CLL	400 mg/kg IV every 3 to 4 weeks
	ITP	1 gram/kg IV, maximum 3 doses on alternate days
	KS	1 gram/kg once or 400 mg/kg daily for 4 consecutive days
	PI	300 to 600 mg/kg every 3 to 4 weeks
Gammaked®	CIDP	Loading dose: 2 gram/kg IV in divided doses over 2 to 4 consecutive days Maintenance dose: 1 gram/kg IV every 3 weeks
	ITP	1 gram/kg IV daily on 2 consecutive days OR 0.4 gram/kg IV daily on 5 consecutive days
	PI	Intravenous: 300 to 600 mg/kg every 3 to 4 weeks Subcutaneous: Weekly dose= $\frac{\text{IGIV dose (grams)} \times 1.37}{\text{No. of weeks between doses}}$
Gammaplex®	ITP	1 gram/kg IV daily for 2 consecutive days
	PI	300 to 800 mg/kg IV every 3 to 4 weeks
Gamunex-C®	CIDP	2 gram/kg IV given in divided doses over 2 to 4 consecutive days
	ITP	1 gram/kg daily on 2 consecutive days OR 0.4 gram/kg IV daily on 5 consecutive days
	PI	Intravenous: 300 to o600 mg/kg every 3 to 4 weeks Subcutaneous: Weekly dose= $\frac{\text{IGIV dose (grams)} \times 1.37}{\text{No. of weeks between doses}}$
Hizentra®	CIDP	0.2 to 0.4 gram/kg SC weekly
	PI	IV to SC: Weekly dose= $\frac{\text{IGIV dose (grams)} \times 1.37}{\text{No. of weeks between doses}}$ Administer at regular interval from daily up to every 2 weeks
HyQvia®	PI	IG therapy naïve or switching from SC: 300 to 600 mg/kg every 3 to 4 weeks Switching from IGIV: same dose and frequency
Octagam 5%®	PI	300 to 600 mg/kg every 3 to 4 weeks
Octagam 10%®	ITP	1 gram/kg IV daily for 2 consecutive days
Panzyga®	PI	300 to 600 mg/kg IV every 3 to 4 weeks

	ITP	1 gram/kg IV daily for 2 consecutive days
Privigen®	CIDP	Loading dose: 2 gram/kg IV in divided doses over 2 to 5 consecutive days Maintenance dose: 1 gram/kg IV every 3 weeks
	ITP	1 gram/kg IV for 2 consecutive days
	PI	200 to 800 mg/kg IV every 3 to 4 weeks
Xembify®	PI	IV to SC: Weekly dose= $\frac{\text{IGIV dose (grams)} \times 1.37}{\text{No. of weeks between doses}}$ OR previous SC weekly dose administered in regular intervals from daily up to every week

APPROVAL LENGTH

- **Authorization:** See table below
- **Re-Authorization:** Must submit an updated letter of medical necessity or progress notes showing the criteria for the applicable indication are met and that the medication is effective (i.e. disease stability, decrease in infections, improvement of functional impairment, etc.)

Indication	Approval Duration
Immunodeficiency	
Primary immunodeficiencies	12 months
Prophylaxis for HIV infected children	12 months
B-cell CLL infection prophylaxis	12 months
Multiple myeloma infection prophylaxis	12 months
Post-HSCT infection prophylaxis	12 months
Immune mediated hematologic disorders	
Autoimmune hemolytic anemia	6 months
Fetal/neonatal alloimmune thrombocytopenia	Weekly dose until delivery
Idiopathic thrombocytopenia (ITP) • Acute/chronic • Pregnancy	 6 months Monthly dose until delivery
Parvovirus B19 infection and severe anemia	6 months
Neuromuscular disorder	
Inflammatory demyelinating polyneuropathy (IDP) • Acute/GBS • Chronic	 3 months 6 months
Dermatomyositis and polymyositis	3 months
Myasthenia gravis/Lambert-Eaton myasthenic syndrome (LEMS)	6 months
Multifocal motor neuropathy (MMN)	6 months
Paraneoplastic neurologic syndrome • Opsoclonus-myoclonus ataxia • Stiff-Person Syndrome	 One dose (up to a 2-week window) Monthly dose for 3 months
Pemphigoid-refractory immunobullous disease	Monthly dose x 6 months
Systematic lupus erythematosus (SLE)	Monthly dose x 6 months

Solid Organ Transplant	
Prevention	3 months: up to 4 doses pre-transplant, then weekly dose for 4 weeks post-transplant (Not to exceed 8 total doses)
Treatment	One dose per rejection episode (up to a 2-week window)
Kawasaki Syndrome	One-time approval for up to a 2-week window
Pediatric intractable epilepsy	Monthly dose for 6 months
Viral prophylaxis	
Hepatitis A	6 months
Measles, Varicella, Rubella	One-time approval

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HISTORICAL TRACKING OF CHANGES MADE TO POLICY

Date	Notes/Changes
8/19/2020	**Policy was retired in 2016, and is now reactivated in 2020** 1. **Changed** "Immunodeficiency (primary or acquired) as defined in ONE of the following 1 OR 2" **to "**Immunodeficiency (primary OR acquired) as defined in ONE of the following" **under Prior Authorization Criteria.** 2. **Changed** "Hypogammaglobulinemic neonates, with a low birth weight (less than 1500g) or in a setting with high baseline infection rate or morbidity" **to** "Hypogammaglobulinemic neonates, with a low birth rate (< 1500 g) or in a setting with high baseline infection rate or morbidity" **under Prior Authorization Criteria.** 3. **Changed** "A diagnosis of dysgammaglobulinemia, primary or due to multiple myeloma in patients with stable disease…" **to** "Diagnosis of dysgammaglobulinemia, primary or due to multiple myeloma (MM) in patients with stable disease…" **under Prior Authorization Criteria.** 4. **Changed** "Hematologic disorders (immune-mediated), not responding to alternative therapies, or at high risk of bleeding, AND ONE of the following criteria 1 through 8 is met" **to** "Hematologic disorders (immune-mediated), not responding to alternative therapies, or at high risk of bleeding, AND ONE of the following criteria is met" **under I.B. under Prior Authorization Criteria.** 5. **Changed** "Chronic ITP when the platelet count is dangerously low as defined by ONE of the flowing platelet counts listed in a through c: a. Less than 30,000 cells/mm3 in children, b. Less than 20,000 cells/mm3 in adults, c. Less than 30,000 cells/mm3 in adults with signs or symptoms of bleeding" **to** "Chronic ITP when the platelet count is dangerously low as defined by ONE of the following: a. Children: < 30,000 cells/mm3, b. Adults: < 20,000 cells/mm3, c. Adults with signs or symptoms of bleeding: < 30,000 cells/mm^3 **under Prior Authorization Criteria.** 6. **Changed** "ITP in pregnancy and at least ONE of the following a or b is met: a. Platelet counts are less than 10,000/mm3 in the third trimester, despite an adequate course of corticosteroids, unless use of steroids are contraindicated, or not tolerated, b. Platelet counts are less than 30,000/mm3 associated with bleeding before vaginal delivery or C-section" **to** "ITP in pregnancy and at least ONE of the following is met: a. Platelet counts < 10,000 cells/mm^3 in the third trimester, despite an adequate course of corticosteroids, unless use of steroids are contraindicated, or not tolerated, b. Platelet counts < 30,000 cells/mm^3 that are associated with bleeding before vaginal delivery or Cesarean section (C-section)" **under Prior Authorization Criteria.**

	7. **Changed** "Neuromuscular disorders, when significant functional impairment is present, and ONE of the following criteria 1 through 12 is met" **to** "Neuromuscular disorders, when significant functional impairment is present, and ONE of the following criteria are met" **under Prior Authorization Criteria.** 8. **Changed** "Acute inflammatory demyelinating polyneuropathy, including Guillain-Barré syndrome (GBS) and ONE of the following criteria a through d is met: a. Deteriorating pulmonary function tests, b. Rapid deterioration with symptoms for less than 2 weeks, c. Rapidly deteriorating ability to ambulate, d. Inability to walk for 10 meters" **to** "Acute inflammatory demyelinating polyneuropathy, including Guillain-Barré Syndrome (GBS) AND ONE of the following criteria is met: a. Deteriorating pulmonary function tests (PFTs), b. Rapid deterioration with symptoms for < 2 weeks, c. Rapidly deteriorating ability to ambulate, d. Inability to walk independently for 10 meters" **under Prior Authorization Criteria.** 9. **Changed** "Chronic inflammatory demyelinating polyneuropathy (CIDP) and ALL of criteria a through c are met: a. Significant functional disability, b. Documentation of slowing of nerve conduction velocity on EMG/NCS, c. Documentation of elevated spinal fluid protein on lumbar puncture OR a nerve biopsy confirming the diagnosis" **to** "Chronic inflammatory demyelinating polyneuropathy (CIDP) and ALL of criteria are met: a. Significant functional disability, b. Documentation of slowing of nerve conduction velocity on electromyography (EMG) or nerve conduction study (NCS), c. Documentation of elevated spinal fluid protein on lumbar puncture OR nerve biopsy confirming the diagnosis" **under Prior Authorization Criteria.** 10. **Changed** "Adult dermatomyositis (DM), with documented EMG abnormalities and/or increased CPK levels, with associated severe disability when steroid therapy is ineffective or not tolerated" **to** "Adult dermatomyositis (DM) with documented EMG abnormalities and/or increased creatine phosphokinase (CPK) levels, with associated severe disability when steroid therapy is ineffective or not tolerated" **under Prior Authorization Criteria.** 11. **Changed** "Juvenile dermatomyositis (JDM), with muscle weakness and associated severe disability, and documentation that at least ONE of criteria a through c is met" **to** "Juvenile dermatomyositis (JDM) with muscle weakness and associated severe disability, and documentation that at least ONE of the criteria is met" **under Prior Authorization Criteria.** 12. **Changed** "Systemic lupus erythematosus for severe active disease…" **to** "Systemic lupus erythematosus (SLE) for severe active disease…" **under Prior Authorization Criteria.** 13. **Changed** "Transplant (solid organ), antibody-mediated rejection and ONE of the following criteria 1 or 2 is met: 1. Prevention of antibody (Ab)-mediated rejection: Prior to solid organ transplant and in the peri-operative period, for patients at high risk for Ab-mediated rejection, including highly sensitized patients, and those receiving an ABO-incompatible organ. 2. Treatment of antibody-mediated rejection (i.e. vascular rejection, humoral rejection): following solid organ transplant and confirmed by either biopsy or presence of panel reactive antibodies (PRAs)" **to** "Solid organ transplant

	antibody-mediated rejection (AMR) AND ONE of the following criteria is met: 1. Prevention of AMR: Prior to solid organ transplant and in the perioperative period, for patients at high risk for AMR, including highly sensitized patients, and those receiving an ABO-incompatible organ, 2. Treatment of AMR (i.e. vascular rejection, humoral rejection) following solid organ transplant and confirmed by either biopsy or presence of panel reactive antibodies (PRAs)" **under Prior Authorization Criteria.** 14. **Changed** "Other Miscellaneous conditions and ONE of the following criteria 1 or 2 is met: 1. Kawasaki syndrome, during the first ten days of diagnosis…" **to** "Other Miscellaneous Conditions and ONE of the following criteria is met: Kawasaki Syndrome during the first 10 days of diagnosis…" **under Prior Authorization Criteria.**
2/19/2016	1. **Changed** "Preferred: Flebogamma®) 5% DIF and Gamunex®-C. Policy also applies to all other products not listed (all products are considered non-preferred)" **to** "Bivigam®, Carimune® NF, Flebogamma® DIF, Gammagard®, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Hlzentra®, HyQvia®, Octagam®, and Privigen®. Policy also applies to all other products not listed." **Under Applicable Drugs.** 2. **Added** "1999000235" **to list following GPI Code.** 3. **Changed** "2. Multiple myeloma in patients with stable disease…" **to** "2. A diagnosis of dysgammaglobulinemia, primary or due to multiple myeloma in patients with stable disease…" **under I.A. under Prior Authorization Criteria.** 4. **Changed** "4. Idiopathic thrombocytopenic purpura (acute; ITP), when a rapid increase in platelet count is necessary, such as in an acute bleeding episode or prior to surgery" **to** "4. Acute idiopathic thrombocytopenia purpura (ITP; immune thrombocytopenia) when a rapid increase in platelet count is necessary, such as in an acute bleeding episode or prior to an invasive procedure (i.e. surgery, epidural anesthesia, etc.)" **under I.B. under Prior Authorization Criteria.** 5. **Changed** "5. ITP (chronic), when the platelet count…" **to** "5. Chronic ITP when the platelet count…" **under I.B. under Prior Authorization Criteria.** 6. **Changed** "3. Dermatomyositis, with documented EMG abnormalities and/or increased CPK levels, with associated severe disability when steroid therapy is ineffective or not tolerated" **to** "3. Adult dermatomyositis (DM), with documented EMG abnormalities and/or increased CPK levels, with associated severe disability when steroid therapy is ineffective or not tolerated; 4. Juvenile dermatomyositis (JDM), with muscle weakness and associated severe disability, and documentation that at least ONE of criteria a through c is met; a. Evidence of myositis, shown by abnormality of muscle biopsy, MRI, or EMG; b. Increased muscle enzyme levels (i.e. CPK, AST, LDH, aldolase); c. Cutaneous changes (i.e. heliotrope dermatitis, Gottron's papules) when an immunosuppressant is ineffective or not tolerated (i.e. oral corticosteroids, methotrexate, etc.)" **under I.C. under Prior Authorization Criteria.** 7. **Changed** "2. Treatment of antibody-mediated rejection (a.k.a. vascular rejection, humoral rejection): following solid organ transplant and confirmed by either biopsy or presence of panel reactive antibodies (PRAs), if used in combination with plasmapheresis" **to** "2. Treatment of antibody-mediated rejection (i.e. vascular rejection, humoral rejection): following solid organ transplant and confirmed by either biopsy or presence of panel reactive antibodies (PRAs)" **under I.D. under Prior Authorization Criteria.**

	8. **Removed** "II. Non-preferred products require a documented trial and failure of or contraindication to a preferred product" **from Prior Authorization Criteria.** 9. **Added** http://www.bivigam.com/clientuploads/pdfs/Prescribing_Information.pdf", http://labeling.sclbehring.com/PI/US/Carimune%20NF/EN/Carimune%20NF-Prescribing-Information.pdf", http://www.grifolsusa.com/documents/10192/89551/flebo5-ft-us-en/2224ef9e-34e5-4808-afde-d470dba5825d", "http://www.grifolsusa.com/documents/10192/63615/flebo10-ft-us-en/f477695f-32d7-4d2b-bdb6-85f49d8eab67", "http://www.baxalta.com/assets/documents/gamliquid_PI.pdf", "http://www.baxalta.com/assets/documents/GGSD_PI.pdf", "http://www.gammaked.com/filebin/pdf/2013-09-gammaked.pdf", "http://www.gammaplex.com/pdf/GMX_US_PI_VSUS6PI_Final.pdf", "http://www.labeling.cslbehring.com/PI/US/Hizentra/EN/Hizentra-Prescribing-Information.pdf", "http://www.octagamus.net/B.840.013.USA_420x340_05.pdf", "http://www.octagamus.net/octagam_10_pi_112015.PDF", **and "**http://labeling.cslbehring.com/PI/US/Privigen/EN/Privigen-Prescribing-Information.pdf" **under References.**
3/23/2015	1. **Added** "1910002020" to **GPI Code.** 2. **Changed** "A. Immunodeficiency (primary or acquired) with a diagnosis of ONE of the following 1, 2, OR 3 and a documented baseline serum IgG level: 1. Primary humoral immunodeficiency diseases (PID) (as defined in Appendix) OR HIV infected children (< 13 years of age) with hypogammaglobulinemia; 2. Hematologic malignancy-related hypogammaglobulinemia from ONE of the following conditions a, b, OR c: a Post-allogeneic bone marrow transplant (BMT); b. B-cell medicated cancer...; c. Multiple myeloma; 3. Hypogammaglobulinemic neonates..." **to** "A. Immunodeficiency (primary or acquired) as defined in ONE of the following 1 OR 2: 1. A diagnosis of ONE of the following a through d AND documented hypogammaglobulinemia (a low baseline serum IgG level): a. Primary humoral immunodeficiency diseases (PID) (as defined in Appendix); b. HIV infected children (< 13 years of age) with hypogammaglobulinemia; c. Hematologic malignancy-related hypogammaglobulinemia from ONE of the following conditions I or ii: i. Post-allogeneic bone marrow transplant (BMT); ii. B-cell mediated cancer...; d. Hypogammaglobulinemic neonates...; 2. Multiple myeloma in patients with stable disease and high risk of recurrent infections despite prophylactic antibiotic therapy, patients with poor IgG response to the pneumococcal vaccine, or patients who have low normal IgG levels during acute sepsis episodes" **under Prior Authorization Criteria.** 3. **Changed** "B. Hematologic disorders...and ONE of the following criteria 1 through 8 are met: 1. Acquired Factor VIII inhibitor when conventional therapy is ineffective or not tolerated (i.e.....; 2. Autoimmune hemolytic anemia (AIHA) not responding to alternative therapies (i.e. steroids, immunosuppressive agents, plasmapheresis, rituximab and/or splenectomy);...5. ITP (chronic), when the platelet count is dangerously low (i.e. platelet count less than 30,000 cells/mm3 in children, and less than 20,000 cells/mm3 in adults); 6. ITP in pregnancy and at least ONE of the following criteria a or b are met: a. Platelet counts less than 10,000 cells/mm3 in the third trimester...; b. Platelet counts less than 30,000

	cells/mm3 associated with bleeding before vaginal delivery or C-section" **to** "B. Hematologic disorders…AND ONE of the following criteria 1 through 8 is met: 1. Acquired Factor VIII inhibitor when conventional therapy is ineffective or not tolerated (i.e.…; 2. Autoimmune hemolytic anemia (AIHA) not responding to alternative therapies (i.e. steroids, immunosuppressive agents, plasmapheresis, rituximab, and/or splenectomy)…; 5. ITP(chronic), when the platelet count is dangerously low as defined by ONE of the following platelet counts listed in a through c: a. Less than 30,000 cells/mm3 in adults with signs or symptoms of bleeding; 6. ITP in pregnancy and at least ONE of the following a or b is met: a. Platelet counts are less than 10,000/mm3 in the third trimester…; b. Platelet counts are less than 30,000/mm3 associated with bleeding…" **under Prior Authorization Criteria.** 4. **Changed** "C. Neuromuscular disorders…and ONE of the following criteria 1 through 11 are met: 1. Acute inflammatory demyelinating polyneuropathy…and ONE of criteria a, b, c, OR d below are met:2. Chronic inflammatory demyelinating polyneuropathy (CIDP)…4. Lambert-Eaton myasthenic syndrome (LEMS) when other treatment options are ineffective or not tolerated. (i.e.…10. Stiff-Person Syndrome when treatment with other agents is ineffective or not tolerated (i.e.…" **to** "C. Neuromuscular disorders…and ONE of the following criteria 1 through 11 is met: 1. Acute inflammatory demyelinating polyneuropathy…and ONE of the following criteria a through d is met:…2. Chronic inflammatory demyelinating polyneuropathy (CIDP)…4. Lambert-Eaton myasthenic syndrome (LEMS) when other treatment options are ineffective or not tolerated (i.e.…10. Stiff-Person Syndrome when treatment with other agents is ineffective or not tolerated (i.e.…" **under Prior Authorization Criteria.** 5. **Changed** "D. Transplant (solid organ), antibody-mediated rejection and ONE of the following criteria 1 or 2 are met: …" **to** "D. Transplant (solid organ), antibody-mediated rejection and ONE of the following criteria 1 or 2 is met: …" **under Prior Authorization Criteria.** 6. **Changed** "E. Other Miscellaneous conditions and ONE of the following criteria 1 or 2 are met: …2. Pediatric intractable epilepsy in candidates for surgical resection or when other interventions are ineffective or not tolerated. Examples of other interventions include, but are not limited to, anticonvulsant medications, ketogenic diets, and steroids" **to** "E. Other Miscellaneous conditions and ONE of the following criteria 1 or 2 is met: …2. Pediatric intractable epilepsy in candidates for surgical resection or when other interventions (i.e. anticonvulsant medications, ketogenic diets, steroids, etc.) are ineffective or not tolerated" **under Prior Authorization Criteria.** 7. **Changed** "Non-preferred products require a documented trial and failure of or contraindication to a preferred product (Flebogamma® 5% DIF and Gamunex®-C)" **to** "Non-preferred products require a documented trial and failure of or contraindication to a preferred product" **under Prior Authorization Criteria.** 8. **Changed** "When prior authorization is approved, immune globulins may be authorized for the period defined in the table in the Approval Length section up to 1200 billing units per claim (600 gm)" **to** "When prior authorization is approved, immune globulins may be authorized for the frequency and duration defined in the table in the Approved Length section" **under Quantity/Days Supply Restrictions.** 9. **Changed** "…Must submit an updated letter of medical necessity or progress notes showing the criteria for the applicable indication is met" **to** "…Must submit

	an updated letter of medical necessity or progress notes showing the criteria for the applicable indication are met and that the medication is effective (i.e. disease stability, decrease in infections, improvement of functional impairment, etc.)" **following Re-Authorization under Approval Length.** 10. **Changed** "Platelet count 30,000 to 150,000/mm3, OR less than 30,000/ mm3 but platelets have increased from baseline accompanied by resolution of previous bleeding; x 12 months" **to** "Documented initial response and ONE of the following a through c is met: a. Platelet count is less than 20,000 cells/mm3 for an invasive procedure with high bleeding risk; x 6 months" **on line for "ITP (chronic" in column for "Reauthorization Criteria/Duration" on table under Approval Length.** 11. **Changed** "Documented" to "Documentation" **on line for "Pediatric intractable epilepsy" in column for "Reauthorization Criteria/Duration" on table under Approval Length.**
1/31/2014	1. **Adapted policy to new format.** 2. **Added GPI Codes.** 3. **Organized all of the diagnoses into the following give main categories a through E:** "A Immunodeficiency (primary or acquired) and a documented baseline serum IgG level; B. Hematologic disorders (immune-mediated), not responding to alternative therapies, or at high risk of bleeding; C. Neuromuscular disorders, when significant functional impairment is present; D. Transplant (solid organ), antibody-mediated rejection; E. Other Miscellaneous conditions" **under Prior Authorization Criteria.** 4. **Changed** "Allogeneic bone marrow transplant recipients who are at least 20 years old for up to 4 months following transplantation; HIV infected children (less than 13 years old) when the CD4 cell count is greater than 200/mm3; Hypogammaglobulinemia (acquired) associated with either chronic B-cell lymphocytic leukemia or post allogeneic bone marrow transplant and documented with laboratory findings (serum IgG); Multiple myeloma in patients with stable disease and high risk of recurrent infections despite prophylactic antibiotic therapy, patients with poor IgG response to the pneumococcal vaccine, or have low normal IgG levels during acute sepsis episodes; Primary humoral immunodeficiency diseases: A baseline IgG level is needed, along with the laboratory findings specified below prior to the initiation of immune globulin for newly diagnosed primary humoral immunodeficiency diseases such as 1 through 5 listed below" **to** "Immunodeficiency (primary or acquired) with a diagnosis of ONE of the following 1, 2, OR 3 and a documented baseline serum IgG level: 1. Primary humoral immunodeficiency diseases (PID) (as defined in Appendix) OR HIV infected children (< 13 years of age) with hypogammaglobulinemia; 2. Hematologic malignancy-related hypogammaglobulinemia from ONE of the following conditions a, b, OR c: a. Post-allogeneic bone marrow transplant (BMT); b. B-cell medicated cancer [i.e. chronic lymphocytic leukemia (CLL), B-cell lymphoma]; c. Multiple myeloma; 3. Hypogammaglobulinemic neonates, with a low birth weight (less than 1500g) or in a setting with high baseline infection rate or morbidity" **under Prior Authorization Criteria.** 5. **Changed** "Post-transfusion purpura in severely affected patients" **to** "Post-transfusion purpura (hemolytic transfusion reaction) in severely affected patients" **under Prior Authorization Criteria.**

	6. **Changed** "ITP in pregnancy, in patients who meet ONE of criteria 1 through 5 below: 1. Refractory to steroids with platelet counts less than 10,000/mm3 in the third trimester; OR 2. Platelet counts less than 30,000/mm3 associated with bleeding before vaginal delivery or C-section; OR 3. Pregnant women who have developed autoimmune thrombocytopenia during a previous pregnancy; OR 4. Pregnant women who have platelet counts less than 50,000/mm3 during the current pregnancy; OR 5. Pregnant women with a past history of splenectomy" **to** "ITP in pregnancy and at least ONE of the following criteria a or b are met: a. Platelet counts less than 10,000/mm3 in the third trimester, despite an adequate course of corticosteroids, unless steroids are contraindicated, or not tolerated; b. Platelet counts less than 30,000/mm3 associated with bleeding before vaginal delivery or C-section" **under Prior Authorization Criteria.** 7. **Changed** "Inflammatory demyelinating polyneuropathy (acute), including Guillain-Barré syndrome. IVIG can be used as an alternative to plasma exchange in patients who meet ONE of criteria 1 through 4 below" **to** "Acute inflammatory demyelinating polyneuropathy, including Guillain-Barré syndrome (GBS) and ONE of criteria a, b, c, OR d below are met" **under Prior Authorization Criteria.** 8. **Changed** "Multifocal motor neuropathy in patients with anti-GM1 antibodies and conduction block" **to** "Multifocal motor neuropathy (MMN) in patients with conduction block" **under Prior Authorization Criteria.** 9. **Changed** "Myasthenia gravis for the treatment of acute severe decompensation (i.e. respiratory failure, swallowing difficulties) or chronic decompensation, when other treatments (i.e. plasmapheresis; pyridostigmine; and immunosuppressive therapy such as azathioprine, cyclosporine, and cyclophosphamide) are ineffective or not tolerated" **to** "Myasthenia gravis for the treatment of acute crisis (i.e. respiratory failure, swallowing difficulties) OR chronic decompensation, when other treatments are ineffective or not tolerated (i.e. plasmapheresis, pyridostigmine, azathioprine, cyclosporine, and cyclophosphamide)" **under Prior Authorization Criteria.** 10. **Changed** "Refractory pemphigus foliaceus resistant to conventional treatments (i.e. immunosuppressive agents and plasmapheresis), until conventional treatment takes effect" **to** "Pemphigoid – refractory immunobullous disease (i.e. bullous pemphigoid, pemphigus foliaceus, pemphigus vulgaris) until conventional treatment takes effect (i.e. immunosuppressive agents and plasmapheresis)" **under Prior Authorization Criteria.** 11. **Added** "Paraneoplastic opsoclonus ataxia syndrome (Opsoclonus-myoclonus ataxia syndrome, OMS) in pediatric neuroblastoma patients with significant functional impairment and not responding to an adequate course of steroids (at least 3 to 7 days)" **under Prior Authorization Criteria.** 12. **Changed** "Solid organ transplant in the treatment of antibody-mediated rejection in patients who meet ONE of criteria 1 or 2 below: 1. Prior to solid organ transplant, when patient is at high risk for antibody-mediated rejection, including highly sensitized patients, and those receiving an ABO incompatible organ; OR 2. Following solid organ transplant" **to** "Transplant (solid organ), antibody-mediated rejection and ONE of the following criteria 1 or 2 are met: 1. Prevention of antibody (Ab)-mediated rejection: Prior to solid organ transplant and in the peri-operative period, for patients at high risk for Ab-mediated rejection, including highly sensitized patients, and those receiving an ABO-incompatible organ; 2. Treatment of antibody-mediated rejection (a.k.a. vascular rejection, humoral rejection): following solid organ transplant and

	confirmed by either biopsy or presence of panel reactive antibodies (PRAs), if used in combination with plasmapheresis" **under Prior Authorization Criteria.** 13. **Changed** "for the period defined in the table in the Appendix section" **to** "for the period defined in the table in the Approval Length section" **under Quantity/Days Supply Restrictions.** 14. **Edited and moved Authorization/Re-authorization Table from Appendix section to Approval section.** 15. **Changed** "See table in the Appendix section" **to** "See table directly below" **under Authorization under Approval Length.** 16. **Changed** "See table in Appendix section" **to** "See table directly below" **under Re-authorization under Approval Length.** 17. **Made the following changes to the Authorization/Re-Authorization Table under Approval Length:** - **Organized all the diagnoses into the following five main categories:** Replacement Therapy – Immunodeficiency [with documented hypogammaglobulinemia (low IgG levels) or poor immune response (dysgammaglobulinemia)]; Hematologic disorders (immune-mediated); Neuroimmunology disorders; Transplant (solid organ); Other Miscellaneous disorders". - **Changed "Allogeneic bone marrow transplant:** On days 7 and 2 prior to transplant, then once weekly for up to 90 days (total therapy duration of 97 days); Reauthorization may be considered under hypogammaglobulinemia criteria; **Hypogammaglobulinemia, acquired, associated with chronic B-cell lymphocytic leukemia or post allogeneic bone marrow transplant:** One treatment per month; Documentation of clinical improvement and current IgG levels that are in the low to normal range. Consideration of up to 1 year of therapy based on clinical benefit; **Multiple myeloma:** One treatment per month; Documentation of clinical improvement and current IgG levels that are in the low to normal range" **to "Hematologic malignancy-related hypogammaglobulinemia (i.e. CLL, post-BMT):** One dose per month x 12 months; Documented current IgG levels that are in the low to normal range and evidence of clinical improvement, such as decreased occurrence of infections; x 12 months" under Replacement Therapy – Immunodeficiency [with documented hypogammaglobulinemia (low IgG levels) or poor immune response (dysgammaglobulinemia)]. - **Changed Indication name and Reauthorization Criteria for "HIV + children (< 13 years old)" from** "Documentation of clinical improvement" **to HIV+ children with hypogammaglobulinemia:** Documented current IgG levels that are in the low to normal range and evidence of clinical improvement, such as decreased occurrence of infections" Replacement Therapy – Immunodeficiency [with documented hypogammaglobulinemia (low IgG levels) or poor immune response (dysgammaglobulinemia)]. - **Changed "Fetal alloimmune thrombocytopenia (FAIT):** One treatment per week; Documented previous history of FAIT; Treatment not to exceed the duration of pregnancy" **to "Fetal (neonatal) alloimmune thrombocytopenia (FAIT):** One dose per week until the estimated date of delivery; No reauthorization" under Hematologic disorders (immune-mediated). - **Changed ITP in pregnancy:** "One treatment per month x 3 months; Platelet count (see policy criteria). Treatment is not to exceed the duration of pregnancy" **to** "One dose per month until the estimated date of delivery;

	May re-authorize under Chronic ITP" under Hematologic disorders (immune-mediated). - **Added "Paraneoplastic opsoclonus ataxia syndrome:** One dose (authorization is for up to a 2-week window); Documented functional improvement; x 6 months" under Neuroimmunology disorders. - **Changed Reauthorization Criteria for Systematic lupus erythematosus from** "Documentation of initial response to IVIG and evidence of clinical improvement" **to** "Documented improvement in muscle strength and/or decreased CPK levels" under Neuroimmunology disorders. - **Changed "solid organ transplant:** Up to 4 doses pre-transplant, then 1 dose weekly for 4 weeks post-transplant; No further authorization shall be given" **to "Transplant (solid organ): Prevention of acute rejection (pre- and peri-operative):** Up to 4 doses pre-transplant, then 1 dose weekly for 4 weeks post-transplant. (not to exceed 8 doses total; authorization is for up to a 3-month window); Further authorization may be considered under "Treatment of Ab-mediated rejection"; **Treatment of antibody (Ab)-mediated (humoral) rejection:** One dose, once per rejection episode (authorization is for up to a 2-week window); Documented improvement from previous course and confirmation of another episode of rejection; one dose". - **Changed Kawasaki syndrome form:** "One treatment given within 10 days of symptom onset" **to** "Up to two doses given within 1- days of symptom onset" under Other Miscellaneous disorders. 18. **Moved criteria for** "Primary Humoral Immunodeficiencies" **to Appendix** and labeled as "Primary Humoral Immunodeficiencies, as defined by having ONE of the following diagnostic criteria 1 through 5:" 19. **Updated references** to include Medi-Span and package inserts.