Policy Title:	Immune Globulins (immunoglobulin) (Intravenous and Subcutaneous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	10/02/2019, 12/19/2019		
Revision Date:	10/02/2019, 12/19/2019		

Purpose: To support safe, effective and appropriate use of Immune Globulins (immunoglobulin).

Scope: Medicaid*, Exchange, Medicare-Medicaid Plan (MMP)

*(Medication only available on the Medical Benefit)

Policy Statement:

Immune Globulins (immunoglobulin) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Immune Globulins (immunoglobulin) will be reviewed prospectively via the prior authorization process based on criteria below.

Initial Criteria:

- Baseline values for BUN and serum creatinine obtained within 30 days of request; AND
- If requesting subcutaneous immune globulin formulations, such as Cuvitru, Hizentra or Hyqvia, the patient must have failure or intolerance to Gammaked/Gamunex-C or Gammagard liquid; AND
- If requesting intravenous immune globulin formulations, such as Bivigam, Gammagard S/D, Gammaplex, Privigen or Panzyga the patient must have a failure or intolerance to Gammaked/Gamunex-C, Gammagard liquid, Flebogamma/Flebogamma DIF, or Octagam

Primary immunodeficiency (PID)/Wiskott - Aldrich syndrome

Such as: 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

- Patient's IgG level is < 200 mg/dL OR both of the following

- Patient 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 or deep skin abscesses
  - Need for intravenous antibiotics to clear infections
  - Two or more deep-seated infections including septicemia; AND
- The 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

Immune thrombocytopenia/Idiopathic thrombocytopenia purpura (ITP)

For acute disease state:

- To manage acute bleeding due to severe thrombocytopenia (platelet counts less than 30 X 10^9 /L); OR
- To increase platelet counts prior to invasive surgical procedures such as splenectomy. (Platelets less than 100 X 10^9 /L); OR
- Patient has severe thrombocytopenia (platelet counts less than 20 X 10^9 /L) and is considered to be at risk for intracerebral hemorrhage

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

Chronic Immune Thrombocytopenia (CIT):

- The patient is at increased risk for bleeding as indicated by a platelet count less than 30 X 10^9 /L; AND
- History of failure, contraindication, or intolerance to corticosteroids; AND
- Duration of illness > 6 months; AND
- Patient age ≥ 2 years

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
- Cerebrospinal fluid analysis indicates the following:
  - CSF white cell count of <10 cells/mm^3 ; AND
  - CSF protein is elevated; 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 rounds 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 age does not exceed 13 years of age; AND
- Patient's IgG level is less than 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/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
- Must be used as part of combination therapy with other agents; 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, and Polyoma BK virus)

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's IgG level is less than 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's disease is progressive; 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

Acquired Immune Deficiency secondary to Acute Lymphoblastic Leukemia (ALL)

- Used for prevention of infection; AND
- Patient age is less than 18 years old; AND
- Patient's IgG level is less than 400 mg/dL

Acquired Immune Deficiency secondary to Chronic lymphocytic leukemia or Multiple Myeloma

- Patient's IgG level is < 200 mg/dL OR both of the following
- Patient 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 or deep skin abscesses
  - Need for intravenous antibiotics to clear infections

- Two or more deep-seated infections including septicemia; AND
- The 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

Note: other secondary immunodeficiencies resulting in hypogammaglobulinemia and/or B-cell aplasia will be evaluated on a case-by-case basis

Toxic Shock Syndrome

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

Management of Immune-Checkpoint-Inhibitor Related Toxicity

- Patient has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, etc.); AND
- Patient has one of the following toxicities related to their immunotherapy:
  - Myasthenia gravis refractory to high-dose corticosteroids
  - Severe transverse myelitis
  - Moderate or severe Guillain-Barre Syndrome or peripheral neuropathy toxicity used in combination with pulse-dose methylprednisolone
  - Severe pneumonitis refractory to methylprednisolone after 48 hours of therapy
  - Encephalitis used in combination with pulse-dose methylprednisolone

Continuation of Therapy Criteria:

- Patient continues to meet initial criteria; AND
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: acute kidney injury, thrombosis, hemolysis, hypersensitivity, pulmonary adverse reactions, 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

Patient meets the disease-specific criteria identified below:

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

Chronic Immune Thrombocytopenia/ITP

- Disease response as indicated by the achievement and maintenance of a platelet count of at least 50 X 10^9 /L as necessary to reduce the risk for bleeding

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

Dermatomyositis/Polymyositis

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

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
- Patient continues to be at an increased risk of infection necessitating continued therapy

Stiff Person Syndrome

- Documented improvement from baseline on physical exam

Allogeneic Bone Marrow or Stem Cell Transplant

- Patient's IgG trough is less than 400 mg/dL

Note: Renewal authorizations are provided for 3 months

Auto-Immune Mucocutaneous Blistering Diseases

- Documented improvement from baseline on physical exam

Acquired Immune Deficiency secondary to Chronic Lymphocytic Leukemia or Multiple Myeloma

- 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

Acquired Immune Deficiency secondary to Acute Lymphoblastic Leukemia (ALL)

- 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

Coverage durations:

- Initial coverage: 6 months, unless otherwise indicated
  1 month only & cannot be renewed: for ITP(acute), Myasthenia Gravis, Kawasaki's Disease, Neonatal Alloimmune Thrombocytopenia, Toxic Shock, Management of Immune Checkpoint Inhibitor related Toxicity
  2 months & cannot be renewed: Guillain-Barre
  3 months: CIDP, Multifocal Motor Neuropathy, Dermatomyositis/Polymyositis, Bone Marrow or Stem Cell Transplant
  Through the delivery date only & cannot be renewed: FAIT

- Continuation of therapy coverage: 6 months, unless otherwise indicated
  3 months for Bone Marrow or Stem Cell Transplant

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable.***

Dosage/Administration:

Indication	Dose
PID	200 to 800 mg/kg every 21 to 28 days
CIPD	2 g/kg divided over 2-5 days initially, then 1 g/kg administered in 1-2 infusions every 21 days
ITP	2 g/kg divided over 5 days or 1 g/kg once daily for 2 consecutive days in a 28-day cycle
FAIT	1 g/kg/week until delivery
Kawasaki's Disease (Pediatric Patients)	1 g/kg to 2 g/kg x 1 course
Multifocal Motor Neuropathy	Up to 2 g/kg divided over 5 days in a 28-day cycle

Acquired immune deficiency: CLL, MM and ALL	400 mg/kg every 3 to 4 weeks
Pediatric HIV	400 mg/kg every 2 to 4 weeks
Guillain-Barre	2 g/kg divided over 5 days x 1 course
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	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
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.	

Maximum Units (per dose and over time):

Indication	Billable units	Per # days (unless otherwise specified)
PID	184	21
CIPD	Load: 460	4
	Maintenance: 230	21
ITP	460	28
FAIT	200	7
Kawasaki's Disease (Pediatric Patients)	232	One dose only
Multifocal Motor Neuropathy	460	28
Acquired immune deficiency: CLL, MM and ALL	92	21
Pediatric HIV	47	28
Guillain-Barre	460	5 (for one cycle only)
Myasthenia Gravis	460	28
Auto-immune blistering diseases	460	28
Dermatomyositis/Polymyositis	460	28

Complications of transplanted solid organ: (kidney, liver, lung, heart, pancreas) transplant	460	28
Stiff Person	460	28
Toxic shock syndrome	460	5 (for one cycle only)
Management of Immune Checkpoint Inhibitor Related Toxicity	460	5 (for one cycle only)
NAIT	16	2 doses only

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J1556	Injection, immune globulin (Bivigam), 500 mg
J1566	Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg
J1572	Injection, immune globulin, (Flebogamma/Flebogamma Dif), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard liquid), nonlyophilized, (e.g., liquid), 500 mg
J1561	Injection, immune globulin, (Gamunex/Gamunex-C/Gammaked), nonlyophilized (e.g., liquid), 500 mg
J1557	Injection, immune globulin, (Gammaplex), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1568	Injection, immune globulin, (Octagam), intravenous, nonlyophilized (e.g., liquid), 500 mg

J1459	Injection, immune globulin (Privigen), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1599	Injection, immune globulin, intravenous, nonlyophilized (e.g., liquid), not otherwise specified, 500 mg
J1555	Injection, immune globulin (Cuvitru), 100 mg
J1559	Injection, immune globulin (Hizentra), 100 mg
J1575	Injection, immune globulin/hyaluronidase, 100 mg immuneglobulin

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