intravenous immune globulin (IVIG)

Medicare Part B Drug Policy

- Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category).
- Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.
- Blue Shield of California (BSC) follows Medicare statutes, regulations, National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), and policy articles for determining coverage for Part B drug requests when applicable.
- BSC Medicare Part B Drug Policies will be used when coverage criteria are not fully established or there is an absence of any applicable Medicare statutes, regulations, NCDs or LCDs.

Drug Details

USP Category: IMMUNOLOGICAL AGENTS

Mechanism of Action: Immune globulin is a sterile, nonpyrogenic solution of globulins containing many antibodies normally present in adult human blood.

HCPCS:

J0850:Injection, cytomegalovirus immune globulin intravenous (human), per vial
J1459:Injection, immune globulin (privigen), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1554:Injection, immune globulin (asceniv), 500 mg
J1556:Injection, immune globulin (bivigam), 500 mg
J1557:Injection, immune globulin, (gammaplex), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1561:Injection, immune globulin, (gamunex-c/gammaked), non-lyophilized (e.g., liquid), 500 mg
J1566:Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg
J1568:Injection, immune globulin, (octagam), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1569:Injection, immune globulin, (gammagard liquid), non-lyophilized, (e.g., liquid), 500 mg
J1572:Injection, immune globulin, (flebogamma/flebogamma dif), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1576:Injection, immune globulin (panzyga), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1599:Injection, immune globulin, intravenous, non-lyophilized (e.g., liquid), not otherwise specified, 500 mg
J3490:Unclassified drugs

How Supplied:

IVIG usual concentration: 5% = 5 gm/100ml, 10%= 10 gm/100ml, 20%, 20 gm/100ml
Alyglo 10%: 5, 10, 20 gm (single-use vial)
Asceniv™ (10%): 5 gm (single-use vial)
Bivigam® (10%): 5, 10 gm (single-use vial)
Cytogam®: 2500 mg/50 mL vials (single-use vial)
Flebogamma DIF® (5%): 0.5, 2.5, 5, 10, 20 gm (single-use vial)
Flebogamma DIF® (10%): 5, 10, 20 gm (single-use vial)
Gammagard® liquid (10%): 1, 2.5, 5, 10, 20, 30 gm (single-use bottle)
Gammagard S/D® (5%): 5, 10 gm (single-use bottle)
Gamunex-C® (10%): 1, 2.5, 5, 10, 20, 40 gm (single-use bottle)

Gammaked® (10%): 1, 2.5, 5, 10 ,20 gm (single-use bottle)
Gammaplex® (10%): 5, 10, 20 gm (single-use bottle)
Gammaplex® (5%): 5, 10, 20 gm (single-use bottle)
Octagam® (5%): 1, 2.5, 5, 10, 25 gm (single-use bottle)
Octagam® (10%): 2, 5, 10, 20 gm
Panzyga® (10%): 1, 2.5, 5, 10, 20, 30 gm (single-use bottle)
Privigen® (10%): 5, 10, 20, 40 gm (single-use vial)

Condition(s) listed in policy (see coverage criteria for details)

- Acute or Chronic Inflammatory Demyelinating Neuropathy (CIDP) and variants
- Autoimmune Mucocutaneous Blistering Diseases (AMBDs)
- Autoimmune Retinopathy
- Bone Marrow/Stem Cell Transplant
- Chimeric Antigen Receptor T-Cell (CAR-T) Therapy Induced Hypogammaglobulinemia
- Chronic lymphocytic leukemia (CLL) associated hypogammaglobulinemia
- Guillain-Barre Syndrome
- Hemolytic Anemia - Autoimmune
- Human Immunodeficiency Virus (HIV)-Symptomatic
- Hypogammaglobulinemia Associated with Anti-CD20 Monoclonal Antibodies
- Idiopathic Thrombocytopenic Purpura (ITP)- Chronic, Refractory
- Idiopathic Thrombocytopenic Purpura (ITP) in Pregnancy
- Idiopathic Thrombocytopenic Purpura (ITP)-Acute
- Immunodeficiency disorders
- Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy
- Kawasaki Disease
- Multiple Myeloma
- Myasthenia Gravis
- Organ Transplants
- Polymyositis and Dermatomyositis
- Primary Immune Deficiency Disorder (PIDD)- Home setting only
- Primary Immunodeficiency Disorders
- Relapsing-Remitting Multiple Sclerosis (RRMS)

Any request for a condition not listed in policy must meet the definition of a medically accepted indication. Section 1861(t)(2)(B) of the Act defines "medically-accepted indication," as any use of a prescription drug or biological product which is approved under the Federal Food, Drug, and Cosmetic Act, or the use of which is supported by one or more citations included (or approved for inclusion) in one or more of the CMS approved compendia.

Special Instructions and Pertinent Information

Provider must submit documentation (such as office chart notes, lab results or other clinical information) to ensure the member has met all medical necessity requirements.

Coverage Criteria

The following condition(s) require Prior Authorization/Preservice:

Acute or Chronic Inflammatory Demyelinating Neuropathy (CIDP) and variants

Meets medical necessity if all the following are met:

Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:

Initial:

Up to 2 g/kg given intravenously by IV over up to a 5-day period

Maintenance:

Up to 2 g/kg given intravenously as often as every 2 weeks. For requests more frequent than every 2 weeks, total dose given over a two week period should not exceed 2 g/kg.

Coverage Period:

Initial:

Up to 5 days depending on dose

Maintenance:

Cover yearly as long as patient continues to respond to treatment e.g. control of symptoms (e.g., weakness, sensory loss, imbalance, pain), and/or improvement or maintenance of functional ability.

ICD-10:

G61.81, G61.82

Autoimmune Mucocutaneous Blistering Diseases (AMBDs)

Meets medical necessity if all the following are met:

1. Diagnosis of ONE of the following:
   a. pemphigus foliaceus
   b. pemphigus vulgaris
   c. bullous pemphigoid
   d. cicatricial pemphigoid
   e. epidermolysis bullosa acquisita
2. Diagnosis is confirmed by lesional tissue biopsy or serology
3. Inadequate response to an immunosuppressant and a systemic corticosteroid, or contraindication or intolerance to immunosuppressants and systemic corticosteroids

Covered Doses:

Up to 2 g/kg given intravenously over 3-5 days once monthly

Coverage Period:

Initial:

Up to 6 months

First Reauthorization:

Cover for another 12 months if patient has had clinical response (i.e., a reduction in lesions and/or ability to reduce concomitant steroids or immunosuppressants.)

Subsequent authorizations:
Cover yearly based on continued response

ICD-10:
L10.0, L10.2, L12.0, L12.1, L13.8

Autoimmune Retinopathy
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 2 g/kg given intravenously as a single dose, OR up to 400 mg/kg given intravenously once daily for 4 consecutive days

Coverage Period:
Initial: Up to 3 months
Reauthorization: another 3 months only if there is improvement on therapy

Bone Marrow/Stem Cell Transplant
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 500 mg/kg/week given intravenously. Increased doses or frequency are covered, as needed to maintain serum IgG levels > 400 mg/dL.

Coverage Period:
6 months based upon response to therapy

CPT:
38240

ICD-10:
Z94.81, Z94.84

Chimeric Antigen Receptor T-Cell (CAR-T) Therapy Induced Hypogammaglobulinemia
Meets medical necessity if all the following are met:
1. Diagnosis of CAR-T induced hypogammaglobulinemia
2. Prescribed by an oncologist or immunologist

Covered Doses:
Given intravenously. Dose is highly variable

Coverage Period:
Yearly based upon continued response to treatment

ICD-10:
D80.1

Chronic lymphocytic leukemia (CLL) associated hypogammaglobulinemia
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 400 mg/kg given intravenously as often as every 3 weeks, or up to 500 g/kg given intravenously every 4 weeks

Coverage Period:
yearly

ICD-10:
C91.10, C91.11, C91.12

Guillain-Barre Syndrome
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 400 mg/kg given intravenously daily for 5 days

Coverage Period:
5 days

ICD-10:
G61.0, G65.0

Hemolytic Anemia - Autoimmune
Meets medical necessity if all the following are met:
1. Diagnosis of warm-type autoimmune hemolytic anemia
2. Patient has experienced an inadequate response to high dose steroids

Covered Doses:
Up to 1 g/kg given intravenously per day for up to 7 days

Coverage Period:
Initial: Up to 7 days
Reauthorization: The efficacy and safety of retreatment with IVIG has not been established.

Human Immunodeficiency Virus (HIV)-Symptomatic
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 400 mg/kg given intravenously as often as every 4 weeks

Coverage Period:
yearly

ICD-10:
B20

Hypogammaglobulinemia Associated with Anti-CD20 Monoclonal Antibodies
Meets medical necessity if all the following are met:
1. History of hypogammaglobulinemia or recurrent bacterial infections
2. Patient has received treatment with an anti-CD20 monoclonal antibody (e.g., rituximab, Arzerra, Gazyva)

Covered Doses:
Up to 400 mg/kg given intravenously as often as every 3 weeks, or up to 500 mg/kg given intravenously every 4 weeks

Coverage Period:
1 year

ICD-10:
D80.1

Idiopathic Thrombocytopenic Purpura (ITP)- Chronic, Refractory
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 2 g/kg IV dose per month

Coverage Period:
Up to 12 doses over 12 months

ICD-10:
D69.3

Idiopathic Thrombocytopenic Purpura (ITP) in Pregnancy
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 2 g/kg given intravenously over 3-5 days once monthly

Coverage Period:
Length of pregnancy

ICD-10:
D69.3

Idiopathic Thrombocytopenic Purpura (ITP)-Acute

Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 2 g/kg given intravenously over 2-5 days

Coverage Period:
Up to 5 days (5 doses total)

ICD-10:
D69.3

Immunodeficiency disorders
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
200-800 mg/kg given intravenously no more often than every 3-4 weeks, and not to exceed 2 doses per month

Coverage Period:
Yearly based upon continued response to treatment

ICD-10:
D80.0, D80.1, D80.2-D80.7, D81.0-D81.2, D81.5-D81.7, D81.82, D81.89, D81.9, D82.0, D82.1, D82.4, D83.0, D83.1, D83.2, D83.8, D83.9, G11.3

Immunotherapy-Related Toxicities Secondary to Immune-Checkpoint Inhibitor Therapy
Meets medical necessity if all the following are met:
1. Being treated with an immune-checkpoint inhibitor
2. Treatment of ONE of the following immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy:
   a. Severe pneumonitis refractory to methylprednisolone
   b. Severe myasthenia gravis
   c. Moderate or severe Guillain-Barré Syndrome or severe peripheral neuropathy in combination with pulse-dose methylprednisolone
   d. Encephalitis in combination with pulse-dose methylprednisolone
   e. Transverse myelitis
   f. Severe bullous dermatitis
   g. Stevens-Johnson syndrome or toxic epidermal necrolysis
   h. Severe myocarditis, pericarditis, arrhythmias, impaired ventricular function, or conduction abnormalities refractory to pulse-dose methylprednisolone
   j. Moderate or severe myalgias or myositis refractory to corticosteroids

Covered Doses:

Up to 2 gm/kg total dose

Coverage Period:
Once per treatment course

ICD-10:
J70.2, J70.4, G70.00, G70.01, G61.0, G61.1, G61.81, G61.82, G61.89, G61.9, G03.8, G03.9, G04.81, G04.89, G04.90-G04.91, G56.80-G56.83, G56.90-G56.93, G57.80-G57.83, G57.90-G57.93, G90.09, I44.0, I44.1-I44.3, I44.30, I44.39, I47.0, I45.0, I45.10, I45.19, I45.2-I45.6, I45.81, I45.89, I45.9, I49.9, L13.8, L13.9, L51.1, L51.2, M06.4, M60.80, M60.811, M60.812, M60.819, M60.821, M60.822, M60.829, M60.831, M60.832, M60.839, M60.841, M60.842, M60.849, M60.851, M60.852, M60.859, M60.861, M60.862, M60.869, M60.871, M60.872, M60.879, M60.88, M60.89, M60.9, M79.1

Kawasaki Disease
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Up to 2 g/kg given intravenously as a single dose OR up to 400 mg/kg given intravenously once daily for 4 consecutive days

Coverage Period:
Initial:

- If giving as a single dose, authorize for 2 doses (one initial and one for possible retreatment)
- If giving as a multiple dose regimen, authorize for 8 doses (4 initial and 4 for possible retreatment). Check dose to make sure only authorizing for 400 mg/kg once daily.

Reauthorization beyond the first retreatment: Subsequent retreatments after the first retreatment have not been evaluated for efficacy or safety.

ICD-10:
M30.3

Multiple Myeloma
Meets medical necessity if all the following are met:

1. Greater than or equal to 2 significant infections within the last year or a single life-threatening infection

Covered Doses:
Up to 500 mg/kg given intravenously every month

Coverage Period:
Yearly

ICD-10:

C90.00, C90.01, C90.02

Myasthenia Gravis

Meets medical necessity if all the following are met:

1. Diagnosis of myasthenia gravis
2. Prescribed by a neurologist
3. Patient has experienced an inadequate response or has an intolerance or contraindication to at least one of the following: a corticosteroid, mycophenolate, azathioprine, cyclosporine, or cyclophosphamide

Covered Doses:
Up to 2 g/kg given intravenously per month

Coverage Period:
Initial: 3 months
Reauthorization: Yearly based upon continued response to treatment

ICD-10:
G70.00, G70.01

Organ Transplants

Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Dose is highly variable

Coverage Period:
Up to 16 weeks per treatment course

ICD-10:
Z94.0, Z94.1, Z94.4

Polymyositis and Dermatomyositis

Meets medical necessity if all the following are met:

1. Inadequate response to treatment with high dose corticosteroids (equivalent to prednisone 40-60 mg/d or highest tolerated dose)
2. Inadequate response, intolerable side effect, or contraindication to an immunosuppressant (i.e., azathioprine, methotrexate, tacrolimus, cyclosporin A, mycophenolate, cyclophosphamide)

Covered Doses:
Up to 2 gm/kg total given intravenously each month

Coverage Period:
Yearly based upon continued response to treatment

ICD-10:
M33.19, M33.29, M33.99, M36.0

Primary Immune Deficiency Disorder (PIDD)- Home setting only

Meets medical necessity if all the following are met:

Requirements listed within the Medicare Benefit Policy Manual, Chapter 15, section 50.6: Coverage of Intravenous Immune Globulin for Treatment of Primary Immune Deficiency Diseases in the Home

Covered Doses:

200-800 mg/kg given intravenously no more often than every 3-4 weeks, and not to exceed 2 doses per month

Coverage Period:

Yearly based upon continued response to treatment

ICD-10:

G11.3, D80.0, D80.2, D80.3, D80.4, D80.5, D80.6, D80.7, D81.0, D81.1, D81.2, D81.5, D81.6, D81.7, D81.82, D81.89, D81.9, D82.0, D82.1, D82.4, D83.0, D83.1, D83.2, D83.8, or D83.9 if only an unspecified diagnosis is necessary

Primary Immunodeficiency Disorders

Meets medical necessity if all the following are met:

1. Diagnosis of ONE of the following primary immunodeficiency disorders
   a. Common variable hypogammaglobulinemia
   b. Congenital agammaglobulinemia (e.g., X-linked agammaglobulinemia, BTK deficiency)
   c. Ectodermodysplasia with immunodeficiency (IKBKG: Inhibitor of kB kinase g chain, NEMO (nuclear factor kB essential modulator) deficiency, IKBA/IKBKB GOF mutation)
   d. Variable immunodeficiency with hyper-IgM (e.g., AID deficiency, UNG deficiency, INO90 deficiency, MSH6 deficiency)
   e. WHIM: Warts, hypogammaglobulinemia, immunodeficiency, myelokathexis
   f. Severe combined immunodeficiency (SCID)
   g. Wiskott-Aldrich Syndrome
   h. Combined immunodeficiency (CID) [e.g., IL21 deficiency, Wiskott-Aldrich Syndrome, WIP deficiency, Arp2/3-mediated filament branching defect, RIDDLE (Radiosensitivity, Immune Deficiency, Dysmorphic features, Learning difficulties) syndrome, ICF (immunodeficiency with centromeric instability and facial anomalies), FILS syndrome, Ligase I deficiency, MYSM1 deficiency, Roifman syndrome, Tricho-Hepato-Enteric Syndrome (THES), Wiedemann-Steiner syndrome]
   i. Di George's syndrome
   j. Hyper IgE syndrome (e.g., IL6 receptor deficiency)
   k. AIPS-Caspase 8
   l. CD70 deficiency, CD20 deficiency, SAP deficiency (XLP1), X-linked magnesium EBV and neoplasia (XMEN)
   m. P14/LAMTOR2 deficiency
   n. PLAID (PLCγ2 associated antibody deficiency and immune dysregulation)
   o. GOOD syndrome

2. ONE of the following:
   a. IgG <200 mg/dL
   b. ALL of the following:
      i. Member has a history of recurrent bacterial infections
      ii. Inability to respond to IgG antibody production after antigenic challenge against diphtheria and tetanus toxoids or pneumococcal polysaccharide vaccine
      iii. Decreased IgG concentrations (<500mg/dL or below normal as defined by testing laboratory) documented on two or more occasions OR diagnosed by an allergist or immunologist if IgG concentrations are not decreased (>500mg/d or normal as defined by the testing laboratory)

Covered Doses:
200-800 mg/kg given intravenously no more often than every 3-4 weeks, and not to exceed 2 doses per month

Coverage Period:
Yearly based upon continued response to treatment

ICD-10:
D80.0, D80.1, D80.3, D80.5, D80.6, D80.7, D81.6, D81.7, D81.89, D81.9, D82.0, D82.1, D82.3, D82.4, D83.0, D83.1, D83.2, D83.8, D83.9

Relapsing-Remitting Multiple Sclerosis (RRMS)
Meets medical necessity if all the following are met:
Requirements listed within the Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)

Covered Doses:
Not to exceed the compendia supported maximum

Coverage Period:
yearly

ICD-10:
G35

Additional Information

Summary of Evidence
The contents of this policy were created after examining the following resources:
1. The prescribing information for Asceniv, Bivigam, Cytogam, Flebogamma DIF, Gammagard liquid, Gammagard S/D, Gamunex-C, Gammaked, Gammaplex, Octagam, Panzyga, Privigen
2. CMS approved compendium in accordance with the accepted compendia ratings listed:
   a. Micromedex DrugDex - Class I, Class IIa, of Class IIb
   b. American Hospital Formulary Service-Drug Information (AHFS-DI) - supportive narrative text
   c. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium - Category 1 or 2A

d. Lexi-Drugs – "Use: Off-Label" and rated as "Evidence Level A"
e. Clinical Pharmacology - supportive narrative text

3. National Coverage Determination (NCD) 250.3: Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases
4. Local Coverage Determination (LCD) L34314: Immune Globulin Intravenous (IVIg)
5. NCCN Guidelines: B-Cell Lymphomas;
6. NCCN Guidelines:Chronic Lymphocytic Leukemia/ Small Lymphocytic Leukemia
7. NCCN Guidelines:Management of Immunotherapy-Related Toxicities
8. NCCN Guidelines:Multiple myeloma
9. NCCN Guidelines:Prevention and Treatment of Cancer-Related Infections
10. American Academy of Allergy, Asthma & Immunology: Update on the use of immunoglobulin in human disease (2017)
11. American Academy of Dermatology: Diagnosis and management of pemphigus: Recommendations of an International Panel of Experts (2020)
12. International Consensus Guidance for Management of Myasthenia Gravis (2016)
13. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (2012)
14. EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases (2008)
15. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy (2021)

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Asceniv, Bivigam, Cytogam, Flebogamma DIF, Gammagard liquid, Gammagard S/D, Gamunex-C, Gammaked, Gammaplex, Octagam, Panzyga, Privigen and the indications listed in NCD and LCD are covered in addition to the following:

- CAR-T induced hypogammaglobulinemia
- Hemolytic anemia - autoimmune
- Hypogammaglobulinemia associated with anti-CD20 monoclonal antibodies
- Immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy
- Multiple myeloma
- Myasthenia gravis
- Polymyositis and dermatomyositis

Explanation of Rationale:

- Support for FDA-approved indications can be found in the manufacturer's prescribing information.
- Support for National Coverage Determination (NCD) covered indications can be found in NCD 250.3 Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases
- Support for Local Coverage Determination (LCD) covered indications can be found in LCD L34314 Immune Globulin Intravenous (IVIg)
- **Immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy**
  - Support for using intravenous immune globulin for immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy is found in the National Comprehensive

Cancer Network's guideline for Management of Immunotherapy-Related Toxicities. The NCCN Guideline for Management of Immunotherapy-Related Toxicities supports the use of intravenous immune globulin for immunotherapy-related toxicities secondary to immune-checkpoint inhibitor therapy: 1) as additional immunosuppression for myocarditis if no improvement within 24-48 hours of starting high-dose methylprednisolone; 2) as an adjunct to rituximab for severe (G3) or life-threatening (G4) bullous dermatitis; 3) for Stevens-Johnson syndrome, or toxic epidermal necrolysis; 4) for moderate, severe, or life-threatening corticosteroid-refractory myositis (proximal muscle weakness, neck flexor weakness, with or without myalgias) for significant dysphagia, life-threatening situations, or cases refractory to corticosteroids; 5) as treatment for severe (G3-4) myasthenia gravis; 6) as treatment for moderate (G2) or severe (G3-4) Guillain-Barré Syndrome or severe (G3-4) peripheral neuropathy in combination with high-dose methylprednisolone; 7) as treatment for encephalitis in combination with high-dose methylprednisolone if severe or progressing symptoms (strongly consider if progressing over 24 hours); 8) for demyelinating disease (optic neuritis, transverse myelitis, acute demyelinating encephalomyelitis); and 9) for moderate (G2) pneumonitis if no improvement after 48-72 hours of corticosteroids or severe (G3-4) pneumonitis if no improvement after 48 hours of methylprednisolone.

- **Hypogammaglobulinemia associated with anti-CD20 monoclonal antibodies and CAR-T therapy**
  - Support for using intravenous immune globulin for hypogammaglobulinemia associated with anti-CD20 monoclonal antibodies and CAR-T therapy is found in the National Comprehensive Cancer Network's guideline for B-cell lymphomas. The NCCN Guideline for B-cell lymphomas states patients receiving anti CD20 mAb and CAR T-cell (CD19-directed therapy) may experience hypogammaglobulinemia and that patients with recurrent infections may benefit from IVIG replacement.
  - Support for using intravenous immune globulin for CAR-T induced hypogammaglobulinemia is also found in the National Comprehensive Cancer Network's guideline for Management of Immunotherapy-Related Toxicities. The NCCN Guideline for Management of Immunotherapy-Related Toxicities supports the use of intravenous immune globulin after anti-CD19 CAR T-cell therapy as replacement for hypogammaglobulinemia in select patients (those with serum IgG levels <400-600 mg/dL and serious or recurrent infections [particularly sinopulmonary]) until serum IgG levels normalize and infections resolve.
- **Multiple myeloma**
  - Support for using intravenous immunoglobulin for multiple myeloma is found in the National Comprehensive Cancer Network's guideline for Multiple Myeloma. The NCCN Guideline for Multiple Myeloma supports the use of intravenous immune globulin for multiple myeloma patients with hypogammaglobulinemia at high risk of infections and/or during CAR-T and bi-specific antibody (BsAb) treatment.
- **Autoimmune mucocutaneous blistering diseases (AMBDs)**
  - American Academy of Dermatology support the use of intravenous immune globulin for pemphigus as a second-line corticosteroid-sparing treatment option. DrugDex supports use of intravenous immune globulin for resistant/refractory pemphigus and epidermolysis bullosa.
- **Myasthenia gravis**

- International Consensus Guidance for Management of Myasthenia Gravis supports use of chronic immune globulin therapy for refractory myasthenia gravis. DrugDex supports use of intravenous immune globulin for myasthenia gravis.

- **Dermatomyositis and polymyositis**
  - EFNS supports use of IVIG as a second-line treatment in combination with prednisone in dermatomyositis and as a treatment option in polymyositis. American Academy of Neurology recommends use of IVIG as possibly effective and may be considered for treating nonresponsive dermatomyositis. DrugDex and AHFS support use of IVIG for dermatomyositis and polymyositis. Octagam 10% is FDA-indicated for the treatment of dermatomyositis in adults.
- **Autoimmune hemolytic anemia**
  - DrugDex supports use of IVIG in warm-type antibody autoimmune hemolytic anemia unresponsive to corticosteroids.

References

1. CMS Benefit Policy Manual. Chapter 15; § 50 Drugs and Biologicals
2. Medicare Coverage Database. Available at https://www.cms.gov/Medicare-Coverage-Database/search.aspx
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Review History

Date of Last Annual Review: 2Q2024
Changes from previous policy version:

- New Part B policy

Blue Shield of California Medication Policy to Determine Medical Necessity Reviewed by P&T Committee