Reference number(s)
3950-A

JURISDICTION SPECIFIC MEDICARE PART B

Intravenous Immune Globulin (IVIG):

Asceniv, Bivigam, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Panzyga and Privigen

POLICY

I. COVERED USES

The indications below are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. Primary immunodeficiency
B. Idiopathic thrombocytopenic purpura (ITP)
C. Chronic inflammatory demyelinating polyneuropathy
D. Multifocal motor neuropathy
E. Kawasaki syndrome
F. B-cell chronic lymphocytic leukemia (CLL)
G. Dermatomyositis
H. Prevention of infections in patients with acquired hypogammaglobulinemia secondary to malignancy
I. Acquired thrombocytopenia
J. Antiphospholipid syndrome
K. Asthma
L. Autoimmune hemolytic anemia
M. Autoimmune neutropenia
N. Autoimmune retinopathy
O. Secondary hypogammaglobulinemia
P. Chronic graft versus host disease (GVHD)
Q. Scleromyxedema
R. Systemic capillary leak syndrome (Clarkson's disease)
S. Immune-mediated necrotizing myositis
T. Bone marrow transplant
U. Hematopoietic stem cell transplant
V. Cerebellar ataxia due to Epstein-Barr virus infection
W. Clostridium difficile colitis
X. Adjunct to Crohn's disease treatment
Y. Cytomegalovirus treatment and prophylaxis
Z. Desensitization therapy – heart transplant
AA. Diabetic amyotrophy
BB. Hopkins' syndrome
CC. Acute disseminated encephalomyelitis
DD. Prophylaxis of enteritis due to rotavirus
EE. Epilepsy
FF. Gastroenteritis
GG. Granulomatosis with polyangiitis

HH. Guillain-Barre syndrome
II. Hemolytic disease of fetus or newborn due to RhD isoimmunization, prophylaxis
JJ. Hemophagocytic syndrome
KK. Induction of Factor VIII immune tolerance
LL. Measles (Rubeola) prophylaxis
MM. Moderate and severe immune checkpoint inhibitor-related toxicities
NN. Hypogammaglobulinemia from CAR-T therapy
OO. Herpes gestationis
PP. Prevention of bacterial infections in HIV infected patients
QQ. Prevention of bacterial infections in post-surgical or ICU patients
RR. Isaacs syndrome
SS. Japanese encephalitis virus disease
TT. Severe IgA nephropathy
UU. Lambert-Eaton myasthenic syndrome
VV. Linear IgA dermatosis
WW. Lysinuric protein intolerance
XX. Prevention of bacterial infections in patients with multiple myeloma
YY. Multiple sclerosis
ZZ. Myasthenia gravis
AAA. Myocarditis
BBB. Prevention and treatment of bacterial infections in high-risk, preterm, low-birth-weight neonates
CCC. Neonatal jaundice
DDD. Otitis media
EEE. Paraneoplastic visual loss
FFF. Polyarteritis nodosa
GGG. Polymyositis
HHH. Post-transplant lymphoproliferative disorder
III. Pure red cell aplasia
JJJ. Pyoderma gangrenosum
KKK. Renal transplant rejection
LLL. Respiratory syncytial virus infection
MMM. Sepsis
NNN. Stevens-Johnson syndrome
OOO. Stiff-person syndrome
PPP. Systemic lupus erythematosus
QQQ. Systemic onset juvenile chronic arthritis
RRR. Systemic vasculitis
SSS. Tetanus treatment and prophylaxis
TTT. Fetal or neonatal thrombocytopenia
UUU. Toxic epidermal necrolysis
VVV. Toxic necrotizing fasciitis
WWW. Toxic shock syndrome
XXX. Heart transplant rejection
YYY. Desensitization of highly sensitized patients awaiting renal transplantation
ZZZ. Uveitis
AAAA. Varicella prophylaxis
BBBB. Von Willebrand disorder
CCCC. Pemphigus vulgaris
DDDD. Pemphigus foliaceus
EEEE. Bullous pemphigoid
FFFF. Mucous membrane pemphigoid (cicatricial pemphigoid)

GGGG. Epidermolysis bullosa acquisita

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. DOCUMENTATION

The following documentation must be available, upon request, for all submissions:

A. Relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures
B. Medical record must include the following information:
    1. History and physical
    2. Office/progress note(s)
    3. Test results with written interpretation
    4. Accurate weight in kilograms should be documented prior to the infusion, since the dosage is based on a mg/kg dosage
    5. Documentation of prior treatment therapies (where appropriate or referenced by this policy)
    6. Evidence of blood level results demonstrating a significant deficiency in gammaglobulin levels prior to initial treatment (where appropriate or referenced by this policy)
    7. History of recurrent and severe infections
    8. Current effectiveness of IVIG therapy
    9. Goals and/or treatment plan
C. Diagnostic testing appropriate for the condition under treatment should be documented, and this may include nerve conduction study (NCS), electromyography (EMG), cerebral spinal fluid (CSF), serum immunoprotein, or biopsy (muscle-nerve). The reason for choosing IVIG as a treatment must be well supported on review of records. Previous treatment failures with alternative agents should be documented.
D. When used for neuromuscular disorders, when there is improvement and continued treatment is necessary, then quantitative assessment to monitor progress is required. Quantitative monitoring may use any accepted measure, such as medical research council (MRC) scale and activities of daily living (ADL) measurements. Changes in these measures must be clearly documented. Subjective or experimental improvement alone is insufficient to support continued use of IVIG.
E. When used for chronic neuromuscular conditions, there should be an attempt made to wean the dosage when improvement has occurred and an attempt to discontinue IVIG infusion when improvement is sustained with dosage reduction. In addition, when improvement does not occur with IVIG, then continued infusions would not be considered reasonable and necessary.
F. When used for recurrent severe infection and documented severe deficiency or absence of IgG subclass deficiency, a serum IgG subclass trough level should be monitored at least every three months prior to the dose of intravenous immune globulin, along with clinical progress of signs and symptoms for which intravenous immune globulin therapy is required.
G. When used for clinically significant functional deficiency of humoral immunity as evidenced by documented failure to produce antibodies to specific antigens and a history of recurrent infections, the deficient antibody(ies) should be monitored at least every 3 months, prior to the dose of intravenous immune globulin, along with clinical progress of signs and symptoms for which intravenous immune globulin therapy is required.
H. When used for bone marrow/stem cell transplantation, one of the following must apply:
    1. The recipient was seropositive for cytomegalovirus (CMV) before transplantation; or

2. After allogenic transplantation for hematologic neoplasm when the donor(s) and recipient were seronegative

I. When used for solid organ transplantation, the donor was seropositive, and the recipient was seronegative for cytomegalovirus (CMV) before transplantation

III. CRITERIA FOR APPROVAL

A. Pure Red Cell Aplasia

Authorization of 6 months may be granted for treatment of pure red cell aplasia for severe, refractory anemia associated with bone marrow suppression, with parvovirus B19 viremia.

B. Hematopoietic Stem Cell Transplantation

Authorization of 6 months may be granted for hematopoietic stem cell transplantation to prevent the risk of acute graft versus host disease, associated interstitial pneumonia (infectious or idiopathic) and infections (e.g., cytomegalovirus infections [CMV], varicella-zoster virus infection, and recurrent bacterial infection) when all of the following are met:

1. The member is 20 years of age or older.
2. IVIG will be used during the first 100 days after transplantation.
3. IVIG will not be used for autologous transplants.

C. Chronic Graft versus Host Disease (GVHD)

Authorization of 6 months may be granted for chronic graft versus host disease when all of the following criteria are met:

1. Member has laboratory proven hypogammaglobulinemia with IgG levels <400 mg/dl.
2. Member has at least one acute infection requiring hospitalization and/or parenteral antibiotics.
3. Member has a confirmed diagnosis of chronic graft versus host disease.
4. Member is at least 100 days post-transplant.

D. Systemic Lupus Erythematosus

Authorization of 6 months may be granted for treatment of severe active systemic lupus erythematosus when other interventions have been unsuccessful, have become intolerable or are contraindicated.

E. Autoimmune Retinopathy

Authorization of 6 months may be granted for treatment autoimmune retinopathy that is sight threatening and refractory to corticosteroids and immunosuppressant therapy.

F. Stiff-Man Syndrome

Authorization of 6 months may be granted for treatment of stiff-man syndrome when both of the following criteria are met:

1. Diagnosis has been confirmed by anti-glutamic acid decarboxylase (GAD antibody testing.
2. Member had an inadequate response to first-line treatment (benzodiazepines [e.g., diazepam] and/or baclofen).

G. Autoimmune Mucocutaneous Blistering Diseases

Authorization of 6 months may be granted for treatment of biopsy proven autoimmune mucocutaneous blistering diseases when all of the following criteria are met:

1. Member has one of the following diagnoses: pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid (cicatricial pemphigoid), or epidermolysis bullosa acquisita
2. At least one of the following criteria is met regarding prior treatment with conventional therapy:

a. Member has failed conventional therapy
b. Member has a contraindication to conventional therapy
c. Member has rapidly progressive disease and a clinical response could not be affected quickly enough using conventional agents, and IVIG will be given in combination with conventional treatment

3. IVIG will be used for short-term control of the member's condition and will not be used as maintenance therapy

H. Acquired thrombocytopenia, acute disseminated encephalomyelitis, Guillain-Barre syndrome, Japanese encephalitis virus disease, Kawasaki disease, measles (rubeola) prophylaxis, moderate and severe immune checkpoint inhibitor-related toxicities, tetanus treatment and prophylaxis, toxic epidermal necrolysis, toxic shock syndrome, toxic necrotizing fasciitis, Steven-Johnson syndrome, varicella prophylaxis

Authorization of 1 month may be granted for the treatment of acquired thrombocytopenia, acute disseminated encephalomyelitis, Guillain-Barre syndrome, Japanese encephalitis virus disease, Kawasaki disease, measles (rubeola) prophylaxis, moderate and severe immune checkpoint inhibitor-related toxicities, tetanus treatment and prophylaxis, toxic epidermal necrolysis, toxic shock syndrome, toxic necrotizing fasciitis, Steven-Johnson syndrome, varicella prophylaxis.

I. All Other Indications

Authorization of 6 months may be granted for treatment of all other approvable indications listed in section I of this document.

IV. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. When dose and/or frequency are different from the FDA-approved labeling, literature support for the specific schedule chosen should be available.

V. REFERENCES

1. Off-Label Use of Intravenous Immune Globulin (IVIG) (L39314) Original Version. Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39314&ver=7&bc=0. Accessed December 27, 2022.
2. Billing and Coding: Off-Label Use of Intravenous Immune Globulin (IVIG) (A59105) Version R1. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. Accessed December 27, 2022.
3. The NCCN Drugs & Biologics Compendium® © 2022 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed December 27, 2022.
4. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, CO. Available at: https://www.micromedexsolutions.com. Accessed December 27, 2022.
5. National Coverage Determination (NCD) for Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases (250.3- Version1). Accessed at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=158&ncdver=1&SearchType=Advanced&CoverageSelection=National&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&KeyWord=Immune+Globulin&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=IAAAACAAAAAAAA%3d%3d&. Accessed December 27, 2022.

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