UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Immune Globulin – Intravenous Utilization Management Medical Policy

- Alyglo™ (immune globulin intravenous solution-stwk – GC Biopharma)
- Asceniv™ (immune globulin intravenous solution-sira – ADMA Biologics)
- Bivigam® (immune globulin intravenous solution – AMDA Biologics)
- Flebogamma® DIF (immune globulin intravenous solution – Grifols)
- Gammagard® Liquid (immune globulin solution – Baxalta [Takeda])
- Gammagard Liquid ERC® (immune globulin solution – Baxalta [Takeda])
- Gammagard® S/D < 1 mcg/mL in 5% solution (immune globulin intravenous solution – Baxalta [Takeda])
- Gammaked™ (immune globulin solution caprylate/chromatography purified – Kedrion)
- Gammaplex® (immune globulin intravenous solution – Bio Products Laboratory/Kedrion)
- Gamunex®-C (immune globulin solution caprylate/chromatography purified – Grifols)
- Octagam® (immune globulin intravenous solution – Octapharma/Pfizer)
- Panzyga® (immune globulin intravenous solution-ifas – Octapharma/Pfizer)
- Privigen® (immune globulin intravenous solution – CSL Behring)
- Qivigy® (immune globulin intravenous solution-kthm – Kedrion)
- Yimmugo® (immune globulin intravenous solution-dira – Biotest (Grifols)

REVIEW DATE: 11/19/2025

OVERVIEW

Immune globulin intravenous (IVIG) products are concentrated human immunoglobulins, primarily immunoglobulin G (IgG).

All of these products (except Octagam 10%) are FDA-approved for replacement therapy in patients with **primary immune deficiencies** due to defects in humoral immunity. The following indications are FDA approved:

- **B-cell chronic lymphocytic leukemia (CLL)**, for prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent infections.[6,18,21]
- **Chronic inflammatory demyelinating polyneuropathy (CIDP)**, to improve neuromuscular disability and impairment and for maintenance therapy to prevent relapse.[5,7,9,12,15,67]
- **Dermatomyositis (or polymyositis)**. Octagam 10% is indicated for the treatment of dermatomyositis in adults.[11] Patients with dermatomyositis treated with Octagam were under treatment with corticosteroids and/or maximally two immune-suppressants OR patients had previous failure or intolerance with a corticosteroid and at least one additional immunosuppressive drug.[33]
- **Idiopathic (immune) thrombocytopenic purpura (ITP)**, acute and chronic, when a rapid rise in platelet count is needed to prevent and/or control bleeding or to allow a patient with ITP to undergo surgery.[2,6-9,11,12,15,23-25]
- **Kawasaki disease** in pediatric patients for the prevention of coronary artery aneurysm.[6,26] The American Heart Association and the American Academy of Pediatrics recommend initial therapy with 2 g of IVIG per kg as a single intravenous (IV) dose given over 10 to 12 hours.[26] The dose can be repeated if needed.

- **Multifocal motor neuropathy** in adults as maintenance therapy to improve muscle strength and disability.[5]
- **Primary humoral immune deficiency (PID)**, for replacement therapy, including but not limited to the humoral immune defect in the following conditions: common variable immunodeficiency, X-linked agammaglobulinemia [congenital agammaglobulinemia], Wiskott-Aldrich Syndrome, and severe combined immunodeficiencies.[1-3,5-10,12,15,16,25,53,80,84,85] Gammagard Liquid 10%, Gammaked, Gamunex-C, and Gammagard Liquid ERC may be administered via IV or subcutaneous infusion for primary immunodeficiency.[5,7,9,84] IVIG is also indicated for measles prophylaxis in individuals with PID who have been exposed to measles or who are at high risk of measles exposure.[3,7-10,12,13,17,25,45,80,84,85]

IVIG is prepared from pooled plasma collected from a large number of human donors.[1-3,5-12,15,16,25] The donors in a typical pool of plasma have a wide range of antibodies against infectious agents. These products have IgG subclasses similar to that found in normal humans. Asceniv contains not only antibodies which satisfy the requirement to treat patients with PID, it also has elevated levels of respiratory syncytial virus (RSV) antibodies.[19]

IVIG also is used for many off-label indications. Much of the evidence for clinical effectiveness of IVIG is anecdotal (i.e., case reports, open series, or cohort studies). Some conditions have been studied in controlled trials. Usually, IVIG is indicated only if standard approaches have failed, become intolerable, or are contraindicated.

- **Antibody-mediated rejection (ABMR) in transplantation:** Current strategies for treatment of antibody-mediated rejection include plasmapheresis, IVIG, and T-cell or B-cell-depleting agents.[75] Although there are no controlled trials regarding the most appropriate treatments, the benefits of immune globulin have been well described and has been used as the standard-of-care (along with plasmapheresis) in multiple studies.[18,76] Clinical practice guidelines (2009 Kidney Disease: Improving Global Outcomes) recommends a combination of corticosteroids, plasmapheresis, IVIG, anti-CD20 antibody, and lymphocyte-depleting antibody for antibody-mediated rejection.[76,77] As in desensitization therapy, much of the information for IVIG use is in patients with kidney transplants, but the same principles apply to transplantation of other organs and tissues. Immune globulin has been used in lung transplant patients to treat ABMR[20,44,78] and a scientific statement from the American Heart Association states that primary therapy for ABMR in patients with heart transplants may include IVIG, plasmapheresis, high-dose corticosteroids, and anti-lymphocyte antibodies.[36]
- **Autoimmune mucocutaneous blistering diseases (pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid [cicatricial pemphigoid], and epidermolysis bullosa acquisita):** Conventional therapy (a systemic corticosteroid and an immunosuppressive agent) is started at the same time or before IVIG. Many case reports and uncontrolled case series suggest benefit of IVIG in patients with recalcitrant disease or in those with contraindications to conventional therapy.[28-30] International expert recommendations for the management of pemphigus note that first-line treatment includes corticosteroids and anti-CD20 monoclonal antibodies. First-line corticosteroid-sparing agents include azathioprine and mycophenolate mofetil, and other corticosteroid-sparing agents including IVIG.[2]
- **Aquaporin-4 Immunoglobulin Antibodies (AQP4-IgG)-positive Neuromyelitis Optica Spectrum Disorder (NMOSD):** NMOSD is an inflammatory disorder of the central nervous system characterized by severe, immune-mediated demyelination and axonal damage.[32] The range of NMOSD has expanded to include patients with aquaporin-4 (AQP4) antibody positivity who have single or recurrent attacks of optic neuritis, myelitis, or brainstem syndromes. Antibodies against AQP4 are present in the majority of NMOSD patients.[52] The loss of AQP4 expression leads to loss of nervous system cells and neuron damage. Products recommended for long-term

management of the condition include rituximab, azathioprine, mycophenolate, and therapeutic antibodies, such as Soliris® (eculizumab intravenous infusion), Ultomiris® (ravulizumab-cwvz intravenous infusion), Uplizna® (inebilizumab-cdon intravenous infusion), and Enspryng® (satralizumab-mwge subcutaneous injection). IVIG is recommended in children or in case of contraindications to other long-term therapies.[52]

- **Cytomegalovirus (CMV) pneumonitis or pneumonia in patients with cancer or transplant-related infection:** For CMV pneumonia, therapy generally consists of antivirals (e.g., ganciclovir, foscarnet). The National Comprehensive Cancer Network (NCCN) guidelines on prevention and treatment of cancer-related infections (version 1.2025 – June 20, 2025) lists IVIG as an adjunctive therapy for CMV pneumonitis.[31]
- **Desensitization therapy prior to and immediately after transplantation:** Most of the information on use of IVIG for desensitization is in patients with kidney transplantation but many of the same principles apply to transplantation of other organs and tissues.[34,35] Current protocols include using low-dose IVIG with plasma exchange or high-dose IVIG with or without B-cell depletions with rituximab.[18]
- **Guillain Barré syndrome (GBS):** The American Academy of Neurology recommends IVIG in patients who require aid to walk within 2 or 4 weeks from the onset of neuropathic symptoms.[37] The European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of GBS (2023) recommends IVIG or plasma exchange in patients for up to 4 weeks after onset of weakness.[38] For patients who are > 4 weeks of onset and are still deteriorating, other diagnoses should be considered. The guidelines additionally note that observational data indicates that a repeated course of IVIG can be effective in case of treatment-related fluctuation.
- **Hematologic neoplasm-associated hypogammaglobulinemia or hypogammaglobulinemia after B-cell targeted therapies (secondary immunodeficiency):** Clinical guidelines for immunoglobulin use by the National Health Service-England note secondary antibody deficiency can be hypogammaglobinemia associated with therapeutic monoclonals targeted at B-cells and plasma cells, non-Hodgkin's lymphoma, CLL, multiple myeloma, or other relevant B-cell malignancies.[27] NCCN guidelines regarding management of chimeric antigen receptor (CAR)-T cell-related toxicities (version 2.2026 – November 11, 2025) recommends that after anti-CD19 CAR-T cell therapy, IVIG replacement should be considered for patients with serum IgG levels < 400 to 600 mg/dL and serious or recurrent infections.[73] NCCN drug compendia also notes IVIG should be administered during therapy with inotuzumab ozogamicin, blinatumomab, or tisagenlecluecel until B-cell recovery.[86] European guidelines note that IgG replacement in the first 3 months after CAR-T therapy is considered routine for children due to immunological maturity.[81]
- **Hematopoietic cell transplantation (HCT) to prevent infections:** HCT is defined as transplantation of any blood- or marrow-derived hematopoietic stem cells, regardless of transplant type (i.e., allogeneic or autologous) or cell source (i.e., bone marrow, peripheral blood, or umbilical cord blood). With regard to IVIG, guidelines recommend IVIG for prevention or preemptive treatment of specific infections in HCT recipients.[39] In adult or adolescent HCT recipients (allogeneic or autologous), IVIG is used to prevent infections in those with severe hypogammaglobulinemia (i.e., serum IgG < 400 mg/dL) during the first 100 days after HCT. In pediatric patients, IVIG is indicated in those with an allogeneic HCT if hypogammaglobulinemia is severe during the first 100 days after HCT. For prevention of infections beyond 100 days post-HCT (allogeneic or autologous), IVIG is recommended in recipients with severe hypogammaglobulinemia (i.e., serum IgG < 400 mg/dL). Guidelines from the American Society for Blood and Marrow Transplantation make recommendations for IVIG dosing in HCT recipients to prevent infectious complications.[39] During the first 100 days after HCT, the dose in adults and adolescents is 0.5 g/kg per week. The IVIG dose should be individualized to maintain trough (pre-dose) serum IgG > 400 to 500 mg/dL. The dose in allogeneic pediatric HCT patients is 0.4 g/kg per month, adjusted to keep IgG > 400 mg/dL. Higher and more frequent dosing may be necessary

in patients for prevention of early disease after HCT because the half-life of IVIG is reduced to between 1 to 10 days in this population. Dosing for > 100 days post-HCT is 0.5 g/kg given every 3 to 4 weeks. The dose is not adjusted using serum IgG level in patients with multiple myeloma or malignant macroglobulinemia. NCCN guidelines on HCT (version 3.2025 – September 24, 2025) states there may be subsets of patients where prophylactic immune globulin replacement may be considered, such as recipients of an umbilical cord blood transplant, in patients undergoing transplantation for inherited or acquired disorders associated with B-cell deficiency, and in patients with chronic graft versus host disease with recurrent sinopulmonary infections.[82]

- **Human immunodeficiency virus (HIV)- or Hepatitis C-associated thrombocytopenia:** Secondary ITP can occur in patients with HIV infection.[23,24] It can also occur in patients with Hepatitis C. The American Society of Hematology (ASH) guidelines for ITP recommend initial treatment with corticosteroids, IVIG, or Rh0(D) immune globulin for patients with secondary ITP due to HIV. ASH also recommends IVIG for secondary ITP associated with Hepatitis C.[23,24]
- **HIV-infected infants and children to prevent recurrent infections:** IVIG is recommended to prevent serious bacterial infections in HIV-infected children who have hypogammaglobulinemia (IgG < 400 mg/dL).[40] Clinicians providing care for adolescents are advised to use the US Department of Health and Human Services Adult and Adolescent HIV-guideline for the care of post-pubertal adolescents (sexual maturity rating [SMR] four and five) and to use the pediatric guideline for guidance on the care of adolescents at SMR 3 or lower.[40]
- **Immune-Mediated Necrotizing Myopathy:** Muscle weakness is the predominant clinical feature and sometimes severely affects the lower limbs.[56] Pharyngeal muscles may also be affected and dysphagia is common. Serum creatine kinase (CK) is also high. The CK value can widely vary but is often well above 1,000 IU/L.[62] Myositis-specific antibodies are often detected (e.g., anti-HMGCR antibodies, anti-SRP antibodies). Muscle imaging and biopsy can also be useful to confirm the diagnosis. International consensus guidelines recommend IVIG as a second-line agent for anti-HMGCR to avoid long-term disability.[63] For patients with anti-HMGCR monotherapy with IVIG has also been used.[62]
- **Immunotherapy-related toxicities associated with checkpoint inhibitor therapy:** NCCN guidelines for the management of immunotherapy-related toxicities (version 2.2024 – October 25, 2024) recommends IVIG for the management of suspected myocarditis/pericarditis/large vessel vasculitis, severe pneumonitis after 48 hours of methylprednisolone therapy, severe myasthenia gravis, encephalitis, moderate or severe GBS, demyelinating disease, myositis, bullous dermatitis, and Stevens-Johnson syndrome/toxic epidermal necrolysis.[73] The American Society of Clinical Oncology also has practice guidelines on the management of immune-related adverse events in patients treated with checkpoint inhibitor therapy.[74] These practice guidelines note that corticosteroids may be administered for toxicities and refractory or severe cases may require other immunosuppressive therapies or IVIG.
- **Lambert-Eaton Myasthenic Syndrome:** Limited, but moderate- to high-quality evidence from randomized controlled trials have shown that 3,4-diaminopyridine or IVIG was associated with improved muscle strength score and compounded muscle action potential amplitudes. IVIG may be used as an alternative in patients who do not respond or do not tolerate other therapies.[18]
- **Multiple myeloma:** Patients with multiple myeloma are often functionally hypogammaglobulinemic with total immunoglobulin production being elevated, but the repertoire of antibody production restricted.[31] The NCCN guidelines on multiple myeloma (version 3.2026 – November 3, 2025) recommends immune globulin replacement with CAR-T cell and bispecific antibody therapies, based on clinical context.[42] NCCN also notes replacement can be considered for IgG < 400 mg/dL and recurrent life-threatening infections, making sure to consider the portion of IgG that is clonal. NCCN guidelines on CAR-T cell therapy toxicities notes that immune globulin replacement during CAR-T cell therapy in patients with multiple myeloma is not guided by the presence of infections.[73]

- **Multiple sclerosis, acute severe exacerbation or relapses:** Medication options for relapse management include high dose corticosteroids, intramuscular adrenocorticotrophic hormone, plasmapheresis, and IVIG. IVIG is sometimes used to treat relapses that do not respond to corticosteroids.[43] During pregnancy, relapses severe enough to require treatment can be safely managed with a short-term course of corticosteroids after the first trimester. Methylprednisolone is the preferred agent because it is metabolized before crossing the placenta.[43]
- **Myasthenia gravis:** Recommendations from an international consensus guidance statement for management of adult or juvenile myasthenia gravis include the use of IVIG in some patients.[65] Symptomatic and immunosuppressive treatment of myasthenia gravis includes pyridostigmine as initial therapy in most patients. Corticosteroids or immunosuppressive therapies are used in all patients with myasthenia gravis who have not met treatment goals after an adequate trial of pyridostigmine. A nonsteroidal immunosuppressive agent (e.g., azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus) should be used alone when corticosteroids are contraindicated or refused. In patients with refractory myasthenia gravis, chronic IVIG and chronic plasma exchange (PLEX), cyclophosphamide, or rituximab may be used. PLEX and IVIG are recommended as short-term treatments in patients with myasthenia gravis with life-threatening effects such as respiratory insufficiency or dysphagia, to prepare for surgery in patients with significant bulbar dysfunction, when rapid response is needed, when other treatments are not adequate, and before starting corticosteroids if necessary to prevent or minimize exacerbations. IVIG can be considered as maintenance therapy in patients with refractory myasthenia gravis or in patients with relative contraindications to immunosuppressive agents. Refractory myasthenia gravis is defined as the post intervention status of unchanged or worse after corticosteroids and at least two other immunosuppressive agents used in adequate doses for an adequate duration, with persistent symptoms or side effects that limit functioning as defined by the patient or physician. The international consensus guidance statement for myasthenia gravis[65] recommends an initial dose of 2 g/kg given in divided doses over 2 to 5 days. For maintenance therapy, the recommended dose is 0.4 to 1 g/kg given every 4 weeks; an attempt to decrease frequency can be made over time. If additional treatment is required, the dose should be adjusted based on the response.
- **Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD):** International MOGAD Panel proposed criteria reports the central nervous system demyelinating features of this condition include optic neuritis (most common feature), acute disseminated encephalomyelitis (with or without optic neuritis), transverse myelitis, and other less common presentations.[69] Serological evidence of myelin oligodendrocyte glycoprotein (MOG)-IgG is also seen. MOGAD can present as an acute attack and relapses of attacks; a diagnosis of multiple sclerosis should be excluded. Disease flares in MOGAD are generally treated with high dose corticosteroids.[70] A typical dose used for IVIG is 0.4 g/kg/day for 5 days. Maintenance therapy is generally offered in patients who have had two or more attacked; however, exceptions are noted in cases to prevent further disability.[70] For maintenance infusions, a loading dose of 0.4 g/kg/day for 5 days can be given, followed by treatment every 4 weeks with a dose of 0.4 g/kg to 2 g/kg.
- **Passive immunization for measles (post-exposure prophylaxis):** When administered within 6 days of exposure, immune globulin (IG) can prevent or modify measles in patients who are nonimmune.[13] IG therapy is not indicated in persons who have received one dose of measles-containing vaccine at ≥ 12 months, unless the patient is severely immunocompromised. The Advisory Committee on Immunization Practices (ACIP) recommends the use of IG therapy for post-exposure prophylaxis of measles in the following patients who are at risk for severe disease and complication from measles: infants < 12 months of age, pregnant women without evidence of measles immunity, and severely immunocompromised persons.[13] For infants < 12 months of age, intramuscular IG is used; infants 6 through 11 months of age can receive measles, mumps, and rubella vaccine instead of IG if given within 72 hours of exposure. IVIG is used for pregnant women and severely immunocompromised patients. ACIP recommends 400 mg/kg as an IV

infusion.[13] The American College of Obstetricians and Gynecologists Practice Advisory on pregnant patients during a measles outbreak (2024, last updated May 2025) recommends pregnant patients with suspected measles exposure, but without immunity (or those who cannot readily show evidence of immunity), should receive IVIG 400 mg/kg within 6 days of exposure.[4] It additionally states that infants born to pregnant patients with suspected or confirmed measles should be given postexposure prophylaxis with IVIG, as the mother with measles can be infectious for up to days after the rash appears.

- **Post-exposure prophylaxis for varicella OR treatment or post-exposure prophylaxis for tetanus:** Children infected with HIV who lack evidence of immunity to varicella or who have severe immune suppression should receive VariZIG® (human varicella-zoster immune globulin for intramuscular administration)®.[40,41] An alternative to varicella-zoster immune globulin for passive immunization is oral valacyclovir or acyclovir beginning 7 days after exposure, and if this is not available, IVIG administered once within 10 days after exposure.[41] VariZIG is indicated for post-exposure prophylaxis in high risk individuals.[47] The dose is 400 mg/kg given once.[40,41,46] Per the Centers for Disease Control and Prevention, if tetanus immune globulin is not available, clinicians can use immune globulin at a dose of 200 to 400 mg/kg.[48]
- **Parvovirus B19 infection and pure red blood cell aplasia, immunologic subtype:** In immunosuppressed patients lacking neutralizing antibodies, IVIG has been useful for the treatment of persistent B19 infection.[49] The guidelines from the American Society of Transplantation Infectious Diseases Community of Practice state that IVIG is frequently used for the treatment of solid organ transplant recipients with symptomatic parvovirus B19 infection.[66] A Canadian expert panel of hematologists recommend prednisone followed by cyclophosphamide or cyclosporine as first-line therapy for immunologic type pure red blood cell aplasia.[22] The panel considers IVIG a reasonable second-line option for this serious condition. Recent reviews note that 200 to 400 mg/kg/day for 5 to 10 days is considered the recommended treatment course.[79]
- **Stiff-Person Syndrome (Moersch-Woltman Syndrome):** Per the European Federation of Neurological Societies, IVIG should be reserved for patients who have no symptomatic relief after the use of diazepam and/or baclofen and have severe disability in carrying out daily activities.[83]
- **Thrombocytopenia, feto-neonatal alloimmune:** Antenatal therapy with IVIG administered to the mother is effective in increasing fetal platelet counts in neonatal alloimmune thrombocytopenia.[50,51] First-line therapy for newborns with fetal/neonatal alloimmune thrombocytopenia is antigen-negative compatible platelets; IVIG is adjunctive therapy.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of IVIG products. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with IVIG products as well as the monitoring required for adverse events and long-term efficacy, some approvals require IVIG products to be prescribed by or in consultation with a physician who specializes in the condition being treated.

If the prescriber is switching between IVIG products and a case has already been approved by a clinician, a new approval may be entered without another clinical review. The new approval should only be extended for the remaining doses and duration which were granted on the original review. The indication (or diagnosis code) and dosing need to be the same as the original review. If the indication or dosing is different, a new clinical review would need to be completed. If the client is using the *Immune Globulin* –

Intravenous Medical Step Management Policy in tandem with this Utilization Management policy, the new approval may be entered without another clinical review for a preferred product only.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of immune globulin intravenous products is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Primary Immunodeficiencies. Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets BOTH of the following (i and ii):

i. Patient meets ONE of the following (a, b, or c):

Note: An exception can be made for the impaired antibody response if, according to the prescriber, the delay caused by pre-vaccination and post-vaccination antibody measurement would be deleterious to the patient's health.

a) Patient has a diagnosis of congenital agammaglobulinemia, X-linked agammaglobulinemia, other agammaglobulinemia due to the absence of B-cells, Wiskott-Aldrich syndrome, ataxia telangiectasia, DiGeorge syndrome, severe combined immunodeficiency, Hyper-Immunoglobulin M (IgM) syndromes, an IgG level lower than 250 mg/dL, or a primary immune deficiency which has been confirmed by genetic or molecular testing; OR

Note: Molecular testing is a type of genetic testing.

b) Patient has a diagnosis of common variable immunodeficiency, unspecified hypogammaglobulinemia, or other immunodeficiencies with significant hypogammaglobulinemia and meets BOTH of the following [(1) and (2)]:

(1) Patient's pretreatment IgG level is below the normal range (age-adjusted and according to the normal reference range for the reporting laboratory); AND

(2) Patient meets ONE of the following (a or b):

a) Patient has an impaired antibody response (i.e., failure to product antibodies to specific antigens); OR

b) Patient has recurrent infections; OR

c) Patient has an IgG subclass deficiency, selective antibody deficiency (SAD), or another confirmed primary immunodeficiency and meets the following criteria [(1) and (2)]:

(1) Patient has an impaired antibody response (i.e., failure to product antibodies to specific antigens); AND

(2) Patient has recurrent infections; AND

ii. The medication is prescribed by or in consultation with one of the following physician specialists: an allergist, immunologist, otolaryngologist (ear nose and throat [ENT] physician), pulmonologist, or infectious diseases physician who treats patients with primary immune deficiencies; OR

B) Patient is Currently Receiving Immune Globulin. Approve if the patient has been diagnosed with a primary immunodeficiency and according to the prescriber, is continuing to receive benefit from the product.

Note: Examples of continued benefit with the product includes increased IgG levels or prevention and/or controlling of infections.

Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):

A) An initial loading dose of 1 g/kg given intravenously one time; OR

B) 0.2 g/kg to 0.8 g/kg given intravenously once every 3 to 4 weeks; OR
C) The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber; OR
D) Patients with primary immune deficiency and exposure to measles (previous exposure or risk of future measles exposure), the minimum dose has been determined by the prescriber.

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2. B-Cell Chronic Lymphocytic Leukemia for Prevention of Infections. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 4 months if the patient meets BOTH of the following (i and ii):
i. Patient meets ONE of the following (a or b):
a) Patient has an immunoglobulin G (IgG) level < 600 mg/dL (6.0 g/L); OR
b) Patient has a history of recurrent infections; AND
ii. The medication is prescribed by or in consultation with an oncologist, hematologist, or infectious diseases physician; OR
B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has a positive response to therapy according to the prescriber.
Note: Examples of a positive response to therapy include maintaining an increased IgG trough level or a decrease in the number of infections.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 0.2 g/kg to 0.8 g/kg given intravenously every 3 to 4 weeks; OR
B) The dose and interval have been adjusted to maintain a trough (pre-dose) IgG level of greater than 500 mg/dL.

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3. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 3 months if the patient meets BOTH of the following (i and ii):
i. Electrodiagnostic studies support the diagnosis of CIDP; AND
ii. The medication is prescribed by or in consultation with a neurologist; OR
B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has a clinically significant improvement in neurologic symptoms, as determined by the prescriber.
Note: Examples of improvement in neurologic symptoms include improvement in disability; nerve conduction study results improved or stabilized; physical examination show improvement in neurological symptoms, strength (e.g., grip strength), and sensation.

Dosing. Approve ONE of the following dosing regimens (A, B, or C):
A) An initial loading dose of 2 g/kg given intravenously in divided doses over 2 to 5 consecutive days; OR
B) A maintenance dose of 1 g/kg given intravenously in divided doses over 1 to 4 consecutive days given every 3 weeks; OR
C) The dose and interval are adjusted according to clinical response with a maximum dose per treatment course of 2 g/kg.

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4. Dermatomyositis or Polymyositis. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
i. Prior to starting any therapy for this condition, the patient meets ONE of the following (a or b):

a) Patient has or had an elevated creatine kinase (CK) level, according to the prescriber; OR
b) Other measures support the diagnosis, according to the prescriber, including, but not limited to, skin manifestations, autoantibody testing, muscle biopsy results, electromyographic (EMG) findings; AND

ii. Patient has tried a systemic corticosteroid OR a corticosteroid is contraindicated according to the prescriber; AND

iii. Patient has tried an immunosuppressive agent OR an immunosuppressive agent is contraindicated according to the prescriber; AND
Note: Examples of immunosuppressive agents include azathioprine, methotrexate, cyclosporine, cyclophosphamide, and mycophenolate mofetil.

iv. The medication is prescribed by or in consultation with a neurologist or a rheumatologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has responded to therapy according to the prescriber.
Note: Examples of a response to therapy includes improved muscle strength, improved neuromuscular symptoms, and improved functional ability.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) 2 g/kg given intravenously in divided doses over 2 to 5 consecutive days every 4 weeks; OR
B) 2 g/kg given intravenously in divided doses over 2 to 5 consecutive days every 2 to 3 weeks.

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5. Immune Thrombocytopenia (ITP). Approve for the duration noted if the patient meets ONE of the following (A, B, C, D, or E):
Note: The diagnosis of ITP encompasses previous nomenclature, such as idiopathic thrombocytopenia, idiopathic thrombocytopenic purpura, immune thrombocytopenic purpura.

A) Initial Therapy – Adult ≥ 18 Years of Age: Approve for 3 months if the patient meets BOTH of the following (i and ii):

i. Patient meets ONE of the following (a, b, or c):
a) Patient has tried a systemic corticosteroid (e.g., prednisone); OR
b) There is an urgent need to increase the platelet count quickly; OR
c) A systemic corticosteroid is contraindicated according to the prescriber; AND

ii. The medication is prescribed by or in consultation with a hematologist; OR

B) Initial Therapy – Patient is < 18 Years of Age. Approve for 3 months if prescribed by or in consultation with a hematologist; OR

C) Initial Therapy – To Increase Platelet Count Before Surgical or Dental Procedures. Approve for 1 month if prescribed by or in consultation with a hematologist; OR

D) Initial Therapy – Pregnant Patient. Approve for 6 months if prescribed by or in consultation with a hematologist; OR

E) Patient is Currently Receiving Immune Globulin OR Requires Retreatment with Immune Globulin. Approve for 1 year if the patient is responding to therapy OR if the patient has previously responded to therapy, according to the prescriber.
Note: Examples of responding to therapy include increased platelet counts, absence of significant bleeding, or preventing hemorrhage/ensuring an adequate platelet count in order for delivery in pregnant patients.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) Up to 1 g/kg on 2 consecutive days OR up to 0.4 g/kg on 5 consecutive days (up to a total of 2 g per kg per treatment course); OR
B) The dose and interval between doses have been adjusted according to the platelet count and/or to prevent significant bleeding as determined by the prescriber.

6. Kawasaki Disease. Approve for 3 months if prescribed by or in consultation with a pediatric cardiologist or a pediatric infectious diseases physician.

Dosing. Approve up to 2 g/kg given intravenously as a single dose or over multiple consecutive days. The dose may be repeated if needed.

7. Multifocal Motor Neuropathy. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):
- **i.** The diagnosis is supported by weakness without sensory abnormalities, upper motor neuron signs, or marked bulbar involvement and meets ONE of the following (a, b, or c):
  - **a)** The diagnosis is supported by nerve conduction studies that demonstrate motor conduction block or probable motor conduction block; OR
  - **b)** The prescriber has determined the patient has multifocal motor neuropathy without conduction block; OR
  - **c)** The diagnosis is supported by a motor nerve biopsy or by a magnetic resonance imaging (MRI) neurography; AND
- **ii.** The medication is prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has improvement in neurologic symptoms as determined by the prescriber.
Note: Examples of improvement in neurologic symptoms include improvement in disability, grip strength improvement (measured with dynamometer), physical examination show improvement in neurological symptoms and strength.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) Therapy is initiated with 2 g/kg given intravenously in divided doses over 2 to 5 consecutive days; OR

B) ONE of the following maintenance dosing regimens is used (i, ii, or iii):
- **i.** 0.5 g/kg to 2.4 g/kg given intravenously every month; OR
- **ii.** 1 g/kg given intravenously every 2 to 4 weeks; OR
- **iii.** 2 g/kg given intravenously every 1 to 2 months.

Other Uses with Supportive Evidence

8. Antibody-Mediated Rejection in Transplantation. Approve for 1 year if prescribed by or in consultation with a physician affiliated with a transplant center.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) Up to 2 g/kg as an intravenous infusion (as a single dose or divided in smaller doses [e.g., 400 mg per kg daily for 5 days]); OR

B) The dosage is based on a transplant center's protocol.

9. Autoimmune Mucocutaneous Blistering Diseases (Pemphigus Vulgaris, Pemphigus Foliaceus, Bullous Pemphigoid, Mucous Membrane Pemphigoid [Cicatricial Pemphigoid], and

Epidermolysis Bullosa Acquisita). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):
- **i.** Patient meets ONE of the following (a, b, or c):
  - **a)** Patient meets BOTH of the following [(1) and (2)]:
    - **(1)** Patient has tried a systemic corticosteroid OR a corticosteroid is contraindicated according to the prescriber; AND
    - **(2)** Patient has tried an immunosuppressive agent OR an immunosuppressive agent is contraindicated according to the prescriber; OR
      Note: Examples of immunosuppressive agents include azathioprine, cyclophosphamide, dapsone, methotrexate, cyclosporine, mycophenolate mofetil, and tacrolimus.
  - **b)** Patient has rapid, debilitating, progressive disease that cannot be controlled with a systemic corticosteroid and an immunosuppressive agent; OR
  - **c)** The disease is so serious that there is inadequate time for therapy with a systemic corticosteroid and an immunosuppressive agent to have a rapid enough effect; AND
- **ii.** The medication is prescribed by or in consultation with a dermatologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has responded to therapy according to the prescriber.
Note: Examples of response to therapy can include healing of previous lesions or fewer new lesions.

Dosing. Approve ONE of the following dosing regimens (A, B, or C):

A) 2 g/kg per cycle given intravenously every 3 to 4 weeks. This dose is divided over 2, 3, or 5 consecutive days; OR

B) In patient with aggressive ocular disease, such as ocular cicatricial pemphigoid, 2 g/kg given intravenously may be given every 2 weeks in divided doses over 2, 3, or 5 consecutive days; OR

C) The frequency is gradually being slowly decreased as the lesions resolve and heal.

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10. Aquaporin-4 Immunoglobulin Antibodies (AQP4-IgG)-Positive Neuromyelitis Optica Spectrum Disorder (NMOSD). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient has the presence of at least one core clinical feature of NMOSD, according to the prescriber; AND
  Note: Examples of core clinical features of NMOSD include optic neuritis, acute myelitis, acute brainstem syndrome.
- **ii.** The diagnosis was confirmed by a positive blood serum test for AQP4-IgG; AND
  Note: Detection in cerebral spinal fluid would also satisfy this requirement.
- **iii.** Patient is using the requested medication for attack prevention AND meets ONE of the following (a or b):
  - **a)** Patient is < 18 years of age; OR
  - **b)** According to the prescriber, the patient has tried or has a contraindication to one other therapy for this condition; AND
    Note: Examples of other therapies for this condition include azathioprine, mycophenolate mofetil, rituximab, Enspryng (satralizumab subcutaneous injection), Soliris (eculizumab intravenous injection), Ultomiris (ravulizumab intravenous injection), Uplizna (inebilizumab intravenous injection).
- **iv.** The medication is prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has responded to therapy, according to the prescriber.
Note: Examples of a response to therapy includes reduction in relapse rate, reduction in symptoms, slowing in the progression of symptoms.

Dosing. Approve up to 2 g/kg per month administered intravenously (as a single dose or divided in smaller doses [e.g., 400 mg per kg daily for 5 days]).

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11. Cytomegalovirus Pneumonitis or Pneumonia in a Patient with Cancer or Transplant-Related Infection. Approve for 2 months if prescribed by or in consultation with an oncologist, hematologist, or an infectious diseases physician.

Dosing. Approve 400 mg/kg given intravenously every other day for 3 to 5 doses.

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12. Desensitization Therapy Prior to and Immediately after Transplantation. Approve for 1 year if prescribed by or in consultation with a physician affiliated with a transplant center.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) Up to 2 g/kg per month administered intravenously (as a single dose or divided in smaller doses [e.g., 400 mg per kg daily for 5 days]); OR
B) The dosage is based on a transplant center's protocol.

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13. Guillain Barré Syndrome. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 1 month (this is to provide one course of therapy) if the patient meets BOTH of the following (i and ii):
  i. Patient meets ONE of the following (a or b):
    a) The medication is initiated within 2 weeks and no longer than 4 weeks after onset of neuropathic symptoms; OR
    Note: Examples of neuropathic symptoms include weakness, inability to stand or walk without assistance, and respiratory or bulbar weakness.
    b) Patient has had a relapse (treatment-related fluctuation), but had an initial response to IVIG; AND
  ii. The medication is prescribed by or in consultation with a neurologist or a specialist with experience in diagnosing and treating patients with Guillain Barré syndrome; OR
B) Patient is Currently Receiving Immune Globulin. Approve for 1 month.

Dosing. Approve 2 g/kg administered intravenously in divided doses over 2 to 5 days.

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14. Hematologic Neoplasm-Associated Hypogammaglobulinemia or Hypogammaglobulinemia or treatment after B-cell Targeted Therapies (Secondary Immunodeficiency [SID]). Approve for 6 months if the patient meets ONE of the following (A or B):
Note: Some examples of B-cell targeted therapy are chimeric antigen receptor (CAR)-T cell therapy (e.g., Kymriah [tisagenlecleucel intravenous infusion], Abecma [idecabtagene vicleucel intravenous infusion], Breyanzi [lisocabtagene maraleucel intravenous infusion], Tecartus [brexucabtagene autoleucel intravenous infusion], Yescarta [axicabtagene ciloleucel intravenous infusion]), a rituximab

product, Besponsa (inotuzumab ozogamicin intravenous infusion), Blincyto (blinatumomab intravenous infusion).
Note: Refer to B-Cell Chronic Lymphocytic Leukemia (CLL) for Prevention of Infections and Multiple Myeloma for diagnosis-specific criteria.

A) Initial Therapy. Approve if the patient meets ONE of the following (i or ii):
- **i.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient has an immunoglobulin G (IgG) level of < 600 mg/dL (6.0 g/L) [excluding paraprotein]; AND
  - **b)** Patient has recurrent or severe infections or there is a high risk of infection according to the prescriber; AND
  - **c)** The medication is being prescribed by or in consultation with an oncologist, hematologist, infectious disease physician, or immunologist; OR
- **ii.** Patient meets BOTH of the following (a and b):
  - **a)** Patient is < 18 years of age; AND
  - **b)** Patient will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy or other B-Cell targeted therapy; OR
    Note: Examples of CAR-T cell therapy includes: Abecma (idecabtagene vicleucel intravenous infusion), Carvykti (ciltacabtagene autoleucel intravenous infusion).
    Note: Examples of other B-Cell targeted therapy includes: Besponsa (inotuzumab ozogamicin intravenous infusion), Blincyto (blinatumomab intravenous infusion).

B) Patient is Currently Receiving Immune Globulin. Approve if the patient is having a positive response to therapy according to the prescriber.
Note: Examples of a positive response to therapy include maintaining an increased IgG trough level or a decrease in the number of infections.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) 0.2 g/kg to 0.8 g/kg given intravenously once every 3 to 4 weeks; OR

B) The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber.

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15. Hematopoietic Cell Transplantation (HCT) to Prevent Infection. Approve for the duration noted if the patient meets ONE of the following (A, B, or C):

A) Initial Therapy. Approve for 3 months if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient has had a HCT within the previous year; AND
- **ii.** Patient has an immunoglobulin G (IgG) level < 600 mg/dL (6.0 g/L) OR the patient has multiple myeloma or malignant macroglobulinemia; AND
- **iii.** According to the prescriber, the patient has a significant risk of having frequent and/or severe infections; AND
- **iv.** The medication is prescribed by or in consultation with a hematologist, oncologist, or infectious diseases physician; OR

B) Initial Therapy. Approve for 3 months if the patient meets ONE of the following (i, ii, or iii):
- **i.** Patient is a recipient of an umbilical cord blood transplant; OR
- **ii.** Patient is undergoing transplantation for inherited or acquired disorders associated with B-cell deficiency; OR
- **iii.** Patient with chronic graft versus host disease with recurrent sinopulmonary infections; OR

C) Patient is Currently Receiving Immune Globulin. Approve for 6 months if the patient is having a positive response to therapy according to the prescriber.
Note: Examples of a positive response to therapy include maintaining an increased IgG trough level, controlling the number of infections, or a decrease in the number of infections.

Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):
A) During the first 100 days after HCT, the patient meets ONE of the following (i or ii):
  i. Adults and adolescents: 0.5 g/kg per week given intravenously and the dose is adjusted to maintain trough (pre-dose) serum IgG greater than 400 mg/dL; OR
  ii. Pediatric patient with allogeneic HCT: 0.4 g/kg per month given intravenously and the dose is adjusted to keep IgG greater than 400 mg/dL; OR
B) Greater than 100 days post-HCT, the dose is 0.5 g/kg given intravenously every 3 to 4 weeks, and the dose is adjusted to keep IgG greater than 400 mg/dL; OR
C) 0.2 g/kg to 0.8 g/kg given intravenously every 3 to 4 weeks; OR
D) The dosage is based on a transplant center's protocol.

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16. Human Immunodeficiency Virus (HIV)- or Hepatitis C-Associated Thrombocytopenia. Approve for 1 month if the patient meets BOTH of the following (A and B):
A) Patient is receiving antiviral therapy; AND
B) The medication is prescribed by or in consultation with an infectious diseases specialist, a physician who specializes in the treatment of HIV infection, a gastroenterologist, hepatologist, or a liver transplant physician.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) Up to 2 g/kg given intravenously in divided doses over 2 to 5 days; OR
B) Up to 1 g/kg one time given intravenously up to once weekly.

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17. Human Immunodeficiency Virus (HIV), to Prevent Recurrent Infections. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
  i. Patient is < 18 years of age; AND
  ii. Patient is receiving combination antiretroviral therapy; AND
  iii. Patient has ONE of the following (a, b, or c):
    a) Hypogammaglobulinemia (i.e., IgG < 400 mg/dL [4.0 g/L]); OR
    b) Functional antibody deficiency is demonstrated by poor specific antibody titers (that is, the patient does not develop specific antibody responses against protein and polysaccharide antigens); OR
    c) Functional antibody deficiency is demonstrated by the patient having recurrent (two or more per year), serious infections (e.g., bacteremia, meningitis, pneumonia) despite administration of combination antiretroviral therapy and appropriate antimicrobial prophylaxis; AND
  iv. The medication is prescribed by or in consultation with an infectious diseases specialist or an immunologist; OR
B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the frequency and/or severity of infections have decreased according to the prescriber.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) The dose is 0.4 g/kg given by intravenous infusion every 2 to 4 weeks; OR
B) The dose and interval are adjusted according to clinical effectiveness.
Note: Examples of adjusting according to clinical effectiveness may include the need to increase the dose or frequency based on frequency or severity of infections, hospitalizations, days of school or work missed, failure to thrive.

18. Immune-Mediated Necrotizing Myopathy. Approve for the duration noted if the patient meets ONE of the following (A or B):
Note: Also known as necrotizing autoimmune myopathy.

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):
- **i.** Patient has muscle weakness; AND
- **ii.** Patient has or had an elevated creatine kinase (CK) level above 1,000 IU/L; AND
- **iii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has myositis-associated autoantibodies; OR
    Note: Examples of myositis-associated autoantibodies include anti-SRP autoantibodies, anti-HMGCR autoantibodies.
  - **b)** Patient has an electromyography, muscle magnetic resonance imaging, or muscle biopsy which, according to the prescriber, supports the given diagnosis; AND
- **iv.** Patient meets ONE of the following (a, b, c, or d):
  - **a)** Patient has tried a systemic corticosteroid; OR
  - **b)** Corticosteroids are contraindicated, according to the prescriber; OR
  - **c)** Patient has tried one of rituximab, methotrexate, mycophenolate, or tacrolimus; OR
  - **d)** Patient has anti-HMGCR autoantibodies; AND
- **v.** The medication is prescribed by or in consultation with a neurologist or rheumatologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has responded to therapy, according to the prescriber.
Note: Examples of a response to therapy includes improved muscle strength, improved functional ability, and CK decrease.

Dosing. Approve up to 2 g/kg per month administered intravenously (as a single dose or divided in smaller doses [e.g., 400 mg per kg daily for 5 days]).

19. Immunotherapy-Related Toxicities Associated with Checkpoint Inhibitor Therapy. Approve for the duration noted if the patient meets ONE of the following (A or B):
Note: Examples of checkpoint inhibitors are Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Yervoy (ipilimumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion), Bavencio (avelumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), Libtayo (cemiplimab intravenous infusion), Jemperli (dostarlimab intravenous infusion).

A) Initial Therapy. Approve for 1 month if the patient meets ONE of the following (i, ii, or iii):
- **i.** Patient has tried a systemic corticosteroid and has not adequately responded to therapy; OR
  Note: Examples of systemic corticosteroids include prednisone, methylprednisolone.
- **ii.** The medication is being started with a systemic corticosteroid; OR
- **iii.** A corticosteroid is contraindicated per the prescriber; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 6 months if the patient is having a positive response to therapy, as determined by the prescriber, and the prescriber has determined extended therapy is required.

Dosing. Approve ONE of the following dosing regimens (A, B, or C):

A) Up to 0.4 g/kg given intravenously daily for 5 days; OR

B) Up to 2 g/kg given intravenously over 2 to 5 days; OR

C) The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber.

20. Lambert-Eaton Myasthenic Syndrome (LEMS). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 month (to allow for one course of therapy) if the patient meets ALL of the following (i, ii, and iii):

i. Patient is having refractory weakness after symptomatic treatment of LEMS with an amifampridine product (e.g., Firdapse, Ruzurgi), guanidine, or pyridostigmine; AND

ii. Patient meets ONE of the following (a or b):

a) Patient has paraneoplastic LEMS; OR

b) Patient has non-paraneoplastic LEMS AND has tried a systemic corticosteroid (e.g., prednisone) or another immunosuppressive agent (e.g., azathioprine), or has a contraindication to corticosteroids and/or immunosuppressive agents, according to the prescriber; AND

iii. The medication is prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has a response or continued effectiveness, according to the prescriber.

Note: Examples of a response to therapy include improved muscle strength or other clinical response.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) Up to 2 g/kg given intravenously in divided doses over 2 to 5 consecutive days; OR

B) Maintenance therapy every 4 weeks with up to 2 g/kg with the dose being adjusted based on clinical symptoms.

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21. Multiple Myeloma. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):

i. Patient meets ONE of the following (a or b):

a) Patient has or is at risk of severe, recurrent infections according to the prescriber; OR

b) Patient will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy, bispecific antibody therapy, or other B-Cell targeted therapy; AND

Note: Examples of CAR-T cell therapy includes: Abecma (idecabtagene vicleucel intravenous infusion), Carvykti (ciltacabtagene autoleucel intravenous infusion).

Note: Examples of bispecific antibody therapy or other B-Cell targeted therapy includes: Elrexfio (elranatamab-bcmm subcutaneous injection), Tecvayli (teclistamab-cqyv subcutaneous injection), Talvey (talquetamab-tgvs subcutaneous injection).

ii. The medication is prescribed by or in consultation with a hematologist, oncologist, or infectious diseases specialist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year.

Dosing. Approve 0.2 g/kg to 0.8 g/kg given intravenously every 3 to 4 weeks.

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22. Multiple Sclerosis (MS), Acute Severe Exacerbation or Relapses. Approve for 1 month (this is to provide one course of therapy) if the patient meets ALL of the following (A, B, and C):

A) Patient meets ONE of the following (i or ii):

i. Patient has either not responded to OR has had a significant adverse reaction with systemic corticosteroids (e.g., methylprednisolone sodium succinate injection) OR plasma exchange; OR
Note: A trial of Acthar H.P. gel (repository corticotropin injection; adrenocorticotropic hormone, ACTH) would also count toward meeting this requirement.
ii. A systemic corticosteroid is contraindicated, according to the prescriber; AND

B) Patient meets ONE of the following (i or ii):
i. Patient is already on maintenance therapy for MS or will be starting maintenance therapy for MS; OR
Note: Maintenance therapy does NOT include IVIG. Examples of maintenance therapy for MS would include: Avonex (interferon beta-1a subcutaneous injection), Plegridy (peginterferon beta-1a subcutaneous injection), Rebif (interferon beta-1a subcutaneous injection), Betaseron (interferon beta-1b subcutaneous injection)/Extavia (interferon beta-1b subcutaneous injection), Copaxone (glatiramer subcutaneous injection)/Glatopa (glatiramer subcutaneous injection), Gilenya (fingolimod capsule), Lemtrada (alemtuzumab intravenous infusion), Aubagio (teriflunomide tablet), Mavenclad (cladribine tablet), Mayzent (siponimod tablet), Tecfidera (dimethyl fumarate capsule), Vumerity (diroximel fumarate capsule), Zeposia (ozanimod capsule), Tysabri (natalizumab intravenous infusion), Novantrone (mitoxantrone intravenous infusion), Bafiertam (monomethyl fumarate capsule), Kesimpta (ofatumumab subcutaneous injection), Ocrevus (ocrelizumab intravenous infusion), Ponvory (penesimod tablet).
ii. Patient is pregnant or post-partum and the prescriber has determined maintenance therapy is not clinically appropriate; AND

C) The medication is prescribed by or in consultation with a neurologist or a physician who specializes in the treatment of MS.

Dosing. Approve ONE of the following dosing regimens (A or B):
A) A single 1 g/kg given intravenously; OR
B) 0.4 g/kg per day IV infusion for 5 consecutive days.

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23. Myasthenia Gravis. Approve for the duration noted if the patient meets ONE of the following (A, B, C, or D):

A) Initial Therapy for Short-Term (Acute) Use. Approve for 5 days (to allow for one course of therapy) if the patient meets BOTH of the following (i and ii):
i. Patient meets ONE of the following conditions (a, b, c, or d):
a) Patient has an exacerbation of myasthenia gravis; OR
b) Patient requires stabilization of myasthenia gravis before surgery; OR
c) Patient has been started on an immunosuppressive drug and is waiting for full effect; OR
Note: Examples of immunosuppressive drugs include azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil, methotrexate, or tacrolimus.
d) Patient is starting therapy with a corticosteroid and IVIG is being given to prevent or minimize exacerbations; AND
ii. The medication is prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Immune Globulin Short-Term (Acute) Use. Approve for 5 days (to allow for one course of therapy); OR

C) Initial Therapy for Maintenance. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient has refractory myasthenia gravis; AND
ii. Patient has tried pyridostigmine; AND

iii. Patient has tried immunosuppressive therapy with at least one of the following agents: azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil, methotrexate, tacrolimus AND has had an inadequate response; AND
iv. The medication is prescribed by or in consultation with a neurologist; OR

D) Patient is Currently Receiving Immune Globulin for Maintenance Therapy. Approve for 1 year if the patient is responding according to the prescriber.
Note: Examples of responding to therapy include improvement in weakness (bulbar, limb, or respiratory), improvement with ocular symptoms.

Dosing. Approve ONE of the following dosing regimens (A, B, or C):
A) Short-term use: 2 g/kg given intravenously in divided doses over 2 to 5 consecutive days; OR
B) Maintenance therapy: 0.4 g/kg to 1 g/kg given intravenously every 4 weeks; OR
C) The dose and interval between doses have been adjusted based on clinical response as determined by the prescriber.

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24. Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient has a clinical demyelinating event, according to the prescriber; AND
Note: Examples of a clinical demyelinating event includes, but is not limited to, optic neuritis, acute disseminated encephalomyelitis, traverse myelitis.
ii. The diagnosis was confirmed by a positive blood serum test which was positive for myelin oligodendrocyte glycoprotein (MOG)-Immune globulin G (IgG); AND
Note: Detection in cerebral spinal fluid would also satisfy this requirement.
iii. Patient meets ONE of the following (a or b):
a) Patient is using the requested medication for the treatment of acute attacks AND meets ONE of the following [(1) or (2)]:
(1) Patient has tried a systemic corticosteroid; OR
(2) Corticosteroids are contraindicated, according to the prescriber; OR
b) Patient is using the requested medication for attack prevention AND meets ONE of the following [(1) or (2)]:
(1) Patient has tried an immunosuppressant; OR
(2) Immunosuppressants are contraindicated, according to the prescriber; AND
iv. The medication is prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has responded to therapy, according to the prescriber.
Note: Examples of a response to therapy includes a reduction in relapse rate, slowing of disability, slowing in the progression of symptoms.

Dosing. Approve up to 2 g/kg per month administered intravenously (as a single dose or divided in smaller doses [e.g., 400 mg per kg daily for 5 days]).

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25. Passive Immunization for Measles (Post-Exposure Prophylaxis). Approve for 1 day (to allow for a single dose) if the patient meets ONE of the following (A, B, or C):
Note: For patients with primary immune deficiency (PID), see criteria for PID.

A) Patient is pregnant and meets BOTH of the following (i and ii):
i. Patient has been exposed to measles; AND

ii. Patient cannot readily show they have evidence of immunity against measles (e.g., the patient does not have a history of the disease or age-appropriate vaccination); OR

B) Infants born to pregnant patients with suspected or confirmed measles; OR

C) Patient meets BOTH of the following (i and ii):

i. Patient is immunocompromised; AND

ii. Patient has been exposed to measles.

Dosing. Approve the following dosing regimen: 0.4 g/kg intravenously administered one time.

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26. Post-Exposure Prophylaxis for Varicella OR Treatment or Post-Exposure Prophylaxis for Tetanus. Approve for 1 day (to allow for a single dose) if the patient meets ONE of the following (A or B):

A) For Varicella post-exposure, Varicella immune globulin is not available or cannot be administered; OR

B) For Tetanus treatment or post-exposure, Tetanus Immune globulin is not available.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) 0.4 g/kg given intravenously one time; OR

B) 0.2 to 0.4 g/kg given intravenously one time.

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27. Parvovirus B19 Infection. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 2 months if the patient meets BOTH of the following (i and ii):

i. Patient has an immunodeficiency condition; AND
Note: Examples of an immunodeficiency condition include patients with HIV infection, solid organ transplants (e.g., renal, liver), chemotherapy for hematologic malignancy.

ii. The medication is prescribed by or in consultation with an infectious diseases specialist, immunologist, hematologist, or transplant specialist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 6 months.

Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):

A) 2 g/kg given intravenously over a period of 2 to 5 consecutive days; OR

B) 0.4 g/kg to 0.5 g/kg given intravenously daily for 5 days; OR

C) 0.4 g/kg given intravenously once every 4 weeks; OR

D) 0.2 g/kg to 0.4 g/kg given intravenously daily for 5 to 10 days.

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28. Pure Red Blood Cell Aplasia (PRCA), Immunologic Subtype. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 1 month if the patient meets ALL of the following (i, ii, and iii):

i. Patient has tried a systemic corticosteroid (e.g., prednisone); AND

ii. Patient has tried either cyclophosphamide OR cyclosporine; AND

iii. The medication is prescribed by or in consultation with an infectious diseases specialist, immunologist, hematologist, or transplant specialist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 month if the patient has responded with an increase in hemoglobin and reticulocytosis according to the prescriber.

Dosing. Approve 0.5 g/kg given intravenously for 4 weeks.

29. Stiff-Person Syndrome (Moersch-Woltman Syndrome). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 3 months if the patient meets BOTH of the following (i and ii):

i. Patient meets ONE of the following (a or b):

a) Patient has tried a benzodiazepine (e.g., diazepam) OR baclofen; OR

b) Patient has contraindications to both a benzodiazepine AND baclofen according to the prescriber; AND

ii. The medication is prescribed by or in consultation with a neurologist; OR

B) Patient is Currently Receiving Immune Globulin. Approve for 1 year if the patient has responded to therapy according to the prescriber.

Note: Examples of response to therapy includes reduced stiffness or frequency of spasms, ability to walk unassisted.

Dosing. Approve ONE of the following dosing regimens (A or B):

A) 2 g/kg given intravenously over a period of 2 to 5 consecutive days every month; OR

B) For maintenance therapy, the dose is adjusted to provide the minimum effective dosage of IVIG. Maximum dose is 2 g/kg given intravenously.

30. Thrombocytopenia, Feto-neonatal Alloimmune. Approve for 6 months if the pregnant mother or newborn patient is prescribed the medication by or in consultation with a hematologist or an obstetrician.

Dosing. Approve ONE of the following dosing regimens (A, B, C, or D):

A) For the mother: 1 g/kg given intravenously every week; OR

B) For the mother: 2 g/kg given intravenously every week; OR

C) For the mother: 1 g/kg given intravenously twice weekly; OR

D) For the newborn: 1 g/kg to 2 g/kg given intravenously dosed per the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of immune globulin intravenous is not recommended in the following situations:

1. **Adrenoleukodystrophy.** Evidence does not support IVIG use.[18]

2. **Alzheimer's Disease (AD).** In one multicenter, double-blind, Phase III, placebo-controlled trial, 390 patients with mild to moderate AD were randomized to therapy with IVIG 400 mg/kg or 200 mg/kg, or to placebo given every 2 weeks for 18 months.[61] There was no statistically significant difference in the rate of cognitive decline when compared with placebo. Also, there was not a statistically significant change in functional ability when compared to placebo.

3. **Amyotrophic Lateral Sclerosis.** There is insufficient evidence to recommend IVIG.[18]

4. **Asthma.** Global Initiative for Asthma (GINA) guidelines for asthma management and prevention do not include recommendations for use of IVIG.[54]

5. **Atopic Dermatitis.** Limited data exist to determine the utility of IVIG in the management of atopic dermatitis.[55]

6. **Autism.** Evidence does not support IVIG use.[18] Well controlled, double-blind trials are needed.

7. **Complex Regional Pain Syndrome (Reflex Sympathetic Dystrophy).** There is insufficient evidence to recommend IVIG. In one single center study a single dose of 0.5 g/kg of IVIG produced a decrease in pain intensity by 50% or more compared to placebo in 3 of 12 patients.[57] In a randomized, placebo-controlled, multicenter trial, low-dose immunoglobulin treatment for 6 weeks was not effective in relieving pain in patients with moderate-to-severe complex regional pain syndrome.[58] Well-controlled large-scale trials are needed.

8. **Crohn's Disease.** There is insufficient evidence to recommend IVIG. In one single center case collection report, 19 patients with acute Crohn's disease (Crohn's Disease Activity Index [CDAI] 284.1 ± 149.8) who were resistant to steroids received IVIG daily for 7 to 10 days.[59] Four weeks after completing therapy, 14 patients were in clinical remission (CDAI < 150). Prospective, randomized, placebo-controlled trials are needed to determine if IVIG has a role in the treatment of Crohn's disease.

9. **Cystic Fibrosis.** There is insufficient evidence to recommend IVIG. In one single-center retrospective case review of 16 children with cystic fibrosis, IVIG was reportedly effective.[60] Well-designed, controlled trials are needed.[18]

10. **Diabetes Mellitus, Immunotherapy.** Evidence does not support IVIG use.[18]

11. **Fibromyalgia Syndrome.** There is insufficient evidence to recommend IVIG. In one open-label single center study, 15 patients with fibromyalgia syndrome and distal demyelinating polyneuropathy received IVIG 400 mg/kg given daily for 5 days.[64] Pain, tenderness, and strength reportedly improved. Double-blind, placebo-controlled trials are needed to determine if IVIG is effective in fibromyalgia syndrome.

12. **In Vitro Fertilization (IVF).** There is insufficient evidence to recommend IVIG administration as part of IVF outcomes.[68]

13. **Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy, and Skin Changes (POEMS) Syndrome.** Evidence does not support IVIG use.[18]

14. **Recurrent Spontaneous Pregnancy Loss (RSPL) [Including a Patient with Antiphospholipid Antibody-Positive].** The American Society for Reproductive Medicine practice committee states that several trials and meta-analyses concluded that IVIG is ineffective for primary recurrent pregnancy loss and this treatment is not recommended.[72] According to the European Society of Human Reproduction and Embryology guideline on recurrent pregnancy loss (RPL) [2022], IVIG may improve live birth rates in women with four or more unexplained RPLs.[71] The recommendation is conditional and high-quality evidence is lacking. Data is also limited in antiphospholipid syndrome in pregnancy and further study is needed on the role of IVIG.

15. **Selective Immune Globulin A (IgA) Deficiency as the Sole Immunologic Abnormality.** Evidence does not support use of IVIG.[14,18] Selective IgA deficiency is defined as a serum IgA level less than 0.07 g/L, but normal serum IgG and IgM levels in a patient greater than 4 years of age in whom other causes of hypogammaglobulinemia have been excluded.[14] Selective IgA deficiency may co-exist in some patients with poor specific IgG antibody production, with or without IgG2 subclass deficiency.[14,18] Some of these patients with a concomitant specific antibody defect might benefit from therapy with IVIG.

16. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Cytomegalovirus Pneumonitis or Pneumonia in a Patient with Cancer or Transplant-Related Infection:** Added the wording pneumonitis; the diagnosis wording was previously Cytomegalovirus Pneumonia in a Patient with Cancer or Transplant-Related Infection. **Multiple Myeloma:** The following option for approval was added in initial therapy as an alternative to infection status 1) Patient will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy OR bispecific antibody therapy. Note: Examples of CAR-T cell therapy includes: Abecma (idecabtagene vicleucel intravenous infusion), Carvykti (ciltacabtagene autoleucel intravenous infusion). Note: Examples of bispecific antibody therapy includes: Elrexfio (elranatamab-bcmm subcutaneous injection), Tecvayli (teclistamab-cqyv subcutaneous injection), Talvey (talquetamab-tgvs subcutaneous injection). **Parvovirus B19 Infection:** 0.2 g/kg to 0.4 g/kg given intravenously daily for 5 to 10 days was added as an alternative dosing regimen. **Anemia, Aplastic** was removed from Conditions Not Recommended for Approval.	10/25/2023
Selected Revision	**Alyglo was added to the policy** with the same criteria as all other immune globulin products. **Chronic Inflammatory Demyelinating Polyneuropahy (CIDP) or Polyradiculoneuropahy**: Updated dosing from an initial loading dose of 2 g/kg given intravenously in divided doses over 2 to 4 days consecutive days to 2 to 5 days consecutive days. Updated dosing from a maintenance dose of 1 g/kg given intravenously over one day or divided into two doses of 0.5 g/kg given on 2 consecutive days to a maintenance dose of 1 g/kg given intravenously in divided doses over 1 to 4 consecutive days.	02/07/2024
Selected Revision	**Immune Thrombocytopenia (ITP).** The duration of approval for initial therapy for adults and pediatric patients was changed from 1 year to 3 months. Criterion for patients requiring retreatment with immune globulin was added to the continuation criteria. Continuation criterion was also updated from "Patient has responded to therapy" to patient is responding to therapy OR the patient has previously responded to therapy. **The following was added to the Policy Statement:** If the client is using the IVIG MSM Policy in tandem with this UM policy, the new approval may be entered without another clinical review for a preferred product only.	04/10/2024
Selected Revision	**Yimmugo was added to the policy** with the same criteria as all other immune globulin products.	07/24/2024
Annual Revision	**Primary Immunodeficiencies:** Added a note that molecular testing is a type of genetic testing. **Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy:** Added grip strength as an example of an improvement at physical examination. **Aquaporin-4 Immunoglobulin Antibody (AQP4-IgG)-Positive Neuromyelitis Optica Spectrum Disorder (NMOSD); Immune-Mediated Necrotizing Myopathy; Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD):** These conditions of approval were added to the policy. **Guillain Barre Syndrome:** For criterion 'patient currently receiving immune globulin', the wording "(this is to provide a second course) about 3 weeks after the first course" was removed. **Passive Immunization for Measles (Post-Exposure Prophylaxis):** Patient does not have evidence of immunity to measles (i.e.,) was updated to Patient cannot readily show they have evidence of immunity against measles (e.g.,). **Post-Exposure Prophylaxis for Varicella:** "within 10 days of exposure" was removed.	11/06/2024

	Chronic Fatigue Syndrome was removed from Conditions Not Recommended for Approval.	
Annual Revision	**Gammagard Liquid ERC** and **Qivigy** were added to the policy with the same criteria as all other immune globulin products. **B-Cell Chronic Lymphocytic Leukemia for Prevention of Infections**: Updating dosing to an expanded dose of 0.2 g/kg to 0.8 g/kg given intravenously every 3 to 4 weeks. Removing 0.4 g/kg given intravenously every 3 to 4 weeks and 0.3 g/kg to 0.5 g/kg given intravenously once monthly. **Hematologic Neoplasm-Associated Hypogammaglobulinemia or Hypogammaglobulinemia or treatment after B-Cell Targeted Therapies (Secondary Immunodeficiency [SID])**: Added the wording "or treatment" to the indication. The following option for approval was added in initial therapy 1) Patient is < 18 years of age and will be starting, has taken, or is currently receiving chimeric antigen receptor (CAR)-T cell therapy OR other B-cell targeted therapy. Note: Examples of CAR-T cell therapy includes: Abecma (idecabtagene vicleucel intravenous infusion), Carvykti (ciltacabtagene autoleucel intravenous infusion). Note: Examples of other B-cell targeted therapy includes: Besponsa (inotuzumab ozogamicin intravenous infusion), Blincyto (blinatumomab intravenous infusion). Removed dosing option 0.4 g/kg to 0.6 g/kg given intravenously once a month (this dose is already covered by available dosing regimens). **Hematopoietic Cell Transplantation (HCT) to Prevent Infection**: The following option for approval was added in initial therapy: Patient is a recipient of an umbilical cord blood transplant; or patient is undergoing transplantation for inherited or acquired disorders associated with B-cell deficiency; or patient with chronic graft versus host disease with recurrent sinopulmonary infections. Added an option for a dosing regimen of 0.2 g/kg to 0.8 g/kg given intravenously every 3 to 4 weeks. **Multiple Myeloma**: Added the wording "or other B-Cell targeted therapy" in addition to CAR-T therapy and bispecific antibody therapy. Updated dosing from 0.4 g/kg to 0.5 g/kg given intravenously every 3 to 4 weeks to 0.2 g/kg to 0.8 g/kg given intravenously every 3 to 4 weeks. **Passive Immunization for Measles (Post-Exposure Prophylaxis)**: The following option for approval was added: "Infants born to pregnant patients with suspected or confirmed measles."	11/19/2025