Pharmacy Policy

Immune Globulin

Policy Number: 9.110
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Product Applicability	☐ **All Plan[+] Products**
Well Sense Health Plan	**Boston Medical Center HealthNet Plan**
☐ New Hampshire Medicaid	☐ MassHealth - MCO ☐ MassHealth - ACO ☒ Qualified Health Plans/ConnectorCare/Employer Choice Direct ☐ Senior Care Options

Note: Disclaimer and audit information is located at the end of this document.

Prior Authorization Policy

Products Affected:

- **Hyqvia SC**
- **Xembify SC**

Available through Medical Benefit Only (MBO)

- **Asceniv IV**
- **Bivigam IV**
- **Cutaquig SC**
- **Cuvitru SQ**
- **Flebogamma DIF IV**
- **Gamastan IM**
- **Gammagard IV and SC**
- **Gammagard S/D IV Less IgA IV**
- **Gammaked IV**
- **Gammaplex IV**
- **Gamunex-C IV**
- **Hizentra SC**
- **Octagam IV**
- **Panzyga IV**
- **Privigen IV**

[+] *Plan* refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.

Recommended Authorization Criteria

Coverage of intravenous immune globulin (IVIG) & subcutaneous immune globulin (SCIG) products is recommended in patients who meet one of the following criteria.

(NOTE: Criteria for intramuscular immune globulin [Gamastan] is listed separately at the end of this policy.)

Primary Immunodeficiencies (PID). 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 criteria (i and ii):

i. IVIG/SCIG is prescribed by or in consultation with an allergist/immunologist, immunologist, otolaryngologist (ear nose and throat [ENT] physician), pulmonologist, or an infectious diseases physician who treats patients with primary immune deficiencies; AND

ii. The 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) The 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 (SCID), 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

b) The patient has a diagnosis of common variable immunodeficiency (CVID), unspecified hypogammaglobulinemia, or other immunodeficiencies with significant hypogammaglobulinemia and meets the following (1 and either 2 or 3):

(1) The 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) The patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigens); OR

(3) The patient has recurrent infections; OR

c) The patient has an IgG subclass deficiency or a diagnosis of selective antibody deficiency (SAD) and meets the following criteria (1 and 2):

(1) The patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigens); AND

(2) The patient has recurrent infections.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year if the patient has been diagnosed with a primary immunodeficiency and is continuing to receive benefit from the product (e.g., increased IgG levels, preventing or controlling infections).

1. B-Cell Chronic Lymphocytic Leukemia (CLL) for Prevention of Bacterial 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 ALL of the following criteria (i or ii, and iii):

i. The patient has an immunoglobulin G (IgG) level < 500 mg/dL (5.0 g/L); OR

ii. The patient has a history of recurrent bacterial infections; AND

iii. IVIG/SCIG is prescribed by or in consultation with an oncologist, hematologist, or infectious diseases physician.

B) Patients Currently Receiving IVIG: Approve for 6 months if the patient is maintaining an IgG trough (pre-dose) level of about 500 mg/dL and up to 700 mg/dL to prevent bacterial infections.

2. 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 the following (i and ii):

i. IVIG/SCIG is prescribed by or in consultation with a neurologist; AND

ii. Electrodiagnostic studies support the diagnosis of CIDP.

B) Patients Currently Receiving IVIG: Approve for 1 year of therapy if the patient has a clinically significant improvement in neurologic symptoms (for example, improvement in disability; nerve conduction study results improved or stabilized; physical examination show improvement in neurological symptoms, strength, and sensation) as determined by the prescriber (a neurologist or in consultation with a neurologist). The patient may not have a full response after the initial 3 months, but there should be some response.

4. Idiopathic (Immune) Thrombocytopenic Purpura (ITP) or Immune Thrombocytopenia (IT), Acute and Chronic. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy: Various approval durations apply.

i. Adults and adolescents (> 17 years of age) with ITP**/**IT. Approve for ONE of the following (a, b, or c):

a) *Acute* bleeding in a patient who is newly diagnosed or requiring therapy for the first time OR in patients with persistent or chronic ITP. Approve IVIG for 1 month if the patient meets the following criteria (1, 2, and 3):

(1) IVIG/SCIG is prescribed by or in consultation with a hematologist; AND

(2) One of the following applies:

- The patient has tried a systemic corticosteroid (e.g., prednisone) for ITP/IT; OR
- There is an urgent need to increase the platelet count quickly AND IVIG/SCIG will be started with a systemic corticosteroid; OR
- A corticosteroid is contraindicated according to the prescriber; AND

(3) The platelet count is < 30 x 10^9/L or 30,000/µL. OR

b) To increase platelet counts before surgical procedures (e.g., splenectomy) or dental procedures, approve IVIG/SCIG for 1 month if the patient meets the following criteria (1 and 2):

(1) IVIG/SCIG is prescribed by or in consultation with a hematologist; AND

(2) The platelet count is < 50 x 10^9/L or 50,000/µL OR if the patient is undergoing major surgery (e.g., central nervous system or cardiac surgery) and the platelet count is < 75 x 10^9/L or 75,000/µL. OR

c) The patient has *persistent* (3 to 12 months duration) or *chronic* (≥ 12 months duration) ITP/IT. Approve for 1 year if the patient meets the following criteria (1, 2, and 3):

(1) IVIG/SCIG is prescribed by or in consultation with a hematologist; AND

(2) One of the following applies:

- The patient has tried a systemic corticosteroid (e.g., prednisone) for ITP/IT; OR
- There is an urgent need to increase the platelet count quickly AND IVIG/SCIG will be started with a systemic corticosteroid; OR
- A corticosteroid is contraindicated according to the prescriber; AND

(3) IVIG/SCIG is required to prevent bleeding.

ii. Children and adolescents (≤ 17 years of age) with ITP/IT. Approve for one of the following (a, b, c, or d):

a) Acute bleeding in a patient who is newly diagnosed or requiring therapy for the first time OR in patients with persistent or chronic ITP. Approve for 1 month if the patient meets the following criteria (1 and 2):

(1) IVIG/SCIG is prescribed by or in consultation with a hematologist; AND

(2) There is significant acute mucous membrane bleeding or other noncutaneous bleeding; OR

b) The patient has *persistent* (3 to 12 months) or *chronic* (≥ 12 months) ITP/IT. Approve for 1 year if the patient meets the following criteria (1 and 2):
(1) IVIG/SCIG is prescribed by or in consultation with a hematologist; AND
(2) IVIG/SCIG is required to prevent bleeding; OR

c) Inaccessibility (such as travel, distance from hospital), activity level of the patient, or noncompliance is a concern with the prescriber. Approve for 1 year if the patient meets the following criteria (1 and 2):
(1) IVIG/SCIG is prescribed by or in consultation with a hematologist; AND
(2) Child/adolescent is at risk of bleeding; OR

d) To increase the platelet count before major surgery such as splenectomy, or before other surgery, dental extraction(s), or other procedures likely to cause blood loss. Approve for 1 month if IVIG/SCIG is prescribed by or in consultation with a hematologist.

iii. Pregnant patient with ITP/IT. Approve for one of the following (a or b):

a) Before normal vaginal delivery, cesarean section, or spinal or epidural anesthesia. Approve for 2 weeks if IVIG/SCIG is prescribed by or in consultation with a hematologist; OR

b) Pregnant patient in any trimester. Approve for 3 months if IVIG/SCIG is prescribed by or in consultation with a hematologist. (This does not include before normal vaginal delivery, cesarean section, or spinal or epidural anesthesia.)

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year in children, adolescents, and adults with persistent or chronic ITP/IT, if the patient responded with increased platelet count and/or absence of significant bleeding and the patient requires additional therapy with IVIG/SCIG to prevent bleeding, according to the prescriber.

Use the Initial Therapy criteria above in A) for patients who require additional therapy for one of the following: 1) acute bleeding, 2) to increase platelet counts before surgical or dental procedures, or 3) pregnant patients.

See Appendix A for more information on IVIG/SCIG use in ITP.

5. Kawasaki Disease. Approve a single dose if the patient meets the following criteria (A and B):

A) IVIG/SCIG is prescribed by or in consultation with a pediatric cardiologist or a pediatric infectious diseases physician; AND

B) The patient has persistent or recrudescent (recurring) fever or signs of inflammation at least 36 hours after completing the initial IVIG/SCIG infusion(s).

Note: These criteria assume that the first dose was given in a hospital within 7 to 10 days of onset.

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

A) Initial Therapy: Approve for 6 months if prescribed by or in consultation with a neurologist.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year if the patient has improvement in neurologic symptoms as determined by the prescriber (a neurologist or in consultation with a neurologist). IVIG should be discontinued in patients who do not respond after the first 6 months of therapy. Approve for 1 year in patients who are responding (that is, maintaining optimal function) according to the prescriber.

Other Uses with Supportive Evidence

7. Antibody-Mediated Rejection (AMBR) in Solid Organ Transplant (e.g., Kidney, Heart, Lung, Liver). Approve for 6 months if prescribed by or in consultation with a physician affiliated with a transplant center.

8. 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 criteria (i and ii):
- **i.** IVIG/SCIG is prescribed by or in consultation with a dermatologist; AND
- **ii.** The patient meets ONE of the following criteria (a, b, or c):
  - **a)** The patient has tried a systemic corticosteroid OR a corticosteroid is contraindicated according to the prescriber AND the patient has tried an immunosuppressive agent (e.g., azathioprine, cyclophosphamide, dapsone, methotrexate [MTX], cyclosporine, mycophenolate mofetil, tacrolimus) OR an immunosuppressive agent is contraindicated according to the prescriber; OR
  - **b)** The 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.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year if the patient has responded (previous lesions are healing and there are fewer new lesions) according to the prescriber.

Conventional therapy (a systemic corticosteroid and an immunosuppressive agent) is started at the same time or before IVIG/SCIG. Many case reports and uncontrolled case series suggest benefit of IVIG/SCIG in patients with recalcitrant disease or in those with contraindications to conventional therapy.[28-30]

9. Cytomegalovirus (CMV) Interstitial Pneumonia in Patients 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.

For CMV pneumonia, therapy consists of ganciclovir IV injection (or foscarnet IV injection if CMV is ganciclovir-resistant) and IVIG/SCIG in combination.[31] The NCCN guidelines on prevention and treatment of cancer-related infections (version 1.2019) show IVIG/SCIG may be added to ganciclovir or foscarnet for treatment of CMV pneumonia.[31]

10. 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 criteria (i, ii, and iii):
- **i.** IVIG/SCIG is prescribed by or in consultation with a neurologist or a rheumatologist; AND
- **ii.** The patient has tried a systemic corticosteroid OR a corticosteroid is contraindicated according to the prescriber; AND
- **iii.** The patient has tried an immunosuppressive agent (e.g., azathioprine, MTX, cyclosporine, cyclophosphamide, mycophenolate mofetil) OR an immunosuppressive agent is contraindicated according to the prescriber.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year if the patient has responded (such as improved muscle strength, improved neuromuscular symptoms, improved functional ability) according to the prescriber.

IVIG/SCIG may be used in patients with dermatomyositis with severe active illness for whom other interventions have been unsuccessful or intolerable.[32,33]

IVIG/SCIG may be considered amongst the treatment options for patients with polymyositis not responding to first line immunosuppressive treatment.[32] In uncontrolled series, IVIG/SCIG has been effective in polymyositis.

11. **Desensitization Therapy Prior to and Immediately after Solid Organ (Kidney, Heart, Lung, Liver, Intestinal) Transplantation.** Approve for the duration noted if the patient meets ONE of the following (A or B):
    - **A)** Initial Therapy: Approve for 4 months if prescribed by or in consultation with a physician affiliated with a transplant center.
    - **B)** Patients Currently Receiving IVIG/SCIG: Approve for 1 year if given before transplantation OR approve for one dose if given post-transplantation.

    Patients with preexisting anti-human leukocyte antigen (HLA) antibodies (sensitized patients) are more likely to have a positive cross match with possible donors and have a lower likelihood of receiving a solid organ transplant with longer wait times. Most of the information on use of IVIG/SCIG 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/SCIG with plasma exchange or high-dose IVIG/SCIG with or without B-cell depletions with Rituxan® (rituximab injection for IV infusion).[18]

12. **Guillain Barré Syndrome (GBS).** 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 [divided doses given over 2 to 5 days]) if the patient meets BOTH of the following criteria (i and ii):
        - **i.** IVIG/SCIG is prescribed by or in consultation with a neurologist or a specialist with experience in diagnosing and treating patients with GBS; AND
        - **ii.** The patient meets one of the following criteria (a or b):
            - **a)** IVIG/SCIG is initiated within 2 weeks and no longer than 4 weeks of onset of neuropathic symptoms (weakness, inability to stand or walk without assistance, respiratory or bulbar weakness); OR
            - **b)** The patient has had a relapse (treatment related fluctuation), but had an initial response to IVIG.
    - **B)** Patients Currently Receiving IVIG/SCIG: Approve for 1 month (this is to provide a second course [divided doses given over 2 to 5 days]) about 3 weeks after the first course

    The American Academy of Neurology (AAN) recommends IVIG/SCIG in patients who require aid to walk within 2 or 4 weeks from the onset of neuropathic symptoms.[37]

    The effect of IVIG/SCIG in GBS has only been investigated in randomized controlled trials in patients who are unable to walk at nadir (i.e., severely affected patients), not in mildly affected patients who are able to walk unaided at nadir.[38] IVIG/SCIG is not indicated or proven to be effective in mildly affected GBS patients.[32,38]

13. **Hematologic Neoplasm-Associated Hypogammaglobulinemia or Hypogammaglobulinemia after B-cell Targeted Therapies (Secondary Immunodeficiency [SID]).** Approve for the duration noted if the patient meets ONE of the following (A or B):

    (*See B-Cell Chronic Lymphocytic Leukemia [CLL] for Prevention of Bacterial Infections and Multiple Myeloma for these diagnosis-specific criteria) (Some examples of B-cell targeted therapy are chimeric antigen receptor [CAR]-T cell therapy [e.g., Kymriah], a rituximab product, Besponsa [inotuzumab ozogamicin].)*

    - **A)** Initial Therapy: Approve for 6 months if the patient meets ALL of the following criteria (i, ii *and* iii):
        - **i.** The patient has an immunoglobulin G (IgG) level of < 500 mg/dL (excluding paraprotein); AND
        - **ii.** The patient has recurrent or severe bacterial infections or there is a high risk of infection, according to the prescriber; AND
        - **iii.** IVIG/SCIG is being prescribed by or in consultation with an oncologist, hematologist, infectious disease physician, or immunologist.
    - **B)** Patients Currently Receiving IVIG/SCIG: Approve for 6 months if the patient is maintaining an IgG level of over 400 mg/dL and having a positive response to therapy (e.g., decrease in infections), according to the prescriber.

14. **Hematopoietic Cell Transplantation (HCT) to Prevent Bacterial Infection.** 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 ALL of the following criteria (i, ii, iii, and iv):
        - **i.** IVIG/SCIG is prescribed by or in consultation with a hematologist, oncologist or infectious diseases physician; AND
        - **ii.** The patient has had a HCT within the previous year; AND
        - **iii.** The patient has an immunoglobulin G (IgG) level < 500 mg/dL OR the patient has multiple myeloma or malignant macroglobulinemia; AND
        - **iv.** According to the prescriber the patient has a significant risk of having frequent and/or severe bacterial infections.
    - **B)** Patients Currently Receiving IVIG/SCIG: Approve for 6 months if the patient requires IVIG/SCIG to maintain trough IgG levels greater than 400 to 500 mg/dL AND who according to the prescriber has significant risk of having frequent and/or severe bacterial infections.

15. **Human Immunodeficiency Virus (HIV)-Associated Thrombocytopenia.** Approve for 1 month if the patient meets the following criteria (A and B):
    - **A)** IVIG/SCIG is prescribed by or in consultation with an infectious diseases specialist or a physician who specializes in the treatment of HIV infection; AND
    - **B)** The patient meets ONE of the following criteria (i or ii):
        - **i.** The patient is receiving combination antiretroviral therapy (cART) for their HIV infection; OR
        - **ii.** The patient has clinically significant bleeding complications according to the prescriber.

    Secondary ITP can occur in patients with HIV infection.[24] Effective viral suppression using antiretroviral therapy improves HIV-associated cytopenias, including thrombocytopenia. Treatment of secondary ITP (HIV-associated) with short-term corticosteroid therapy increases the platelet count in a similar manner as in non-HIV infected persons and does not appear to be associated with adverse effects. IVIG/SCIG and Rh_0(D) immune globulin (IV or intramuscular [IM] injection) [Rhophylac®/WinRho® SDF] have been reported to increase the platelet count. Splenectomy is an effective option for patients who fail to respond to corticosteroid or IVIG/SCIG therapy.

    Rh_0(D) immune globulin is FDA-approved in non-splenectomized, Rh_0(D) positive patients for the treatment of childhood acute or chronic ITP, chronic ITP in adults, and ITP secondary to HIV infection (adults and children).[41] The safety and efficacy of Rh_0(D) immune globulin have not been evaluated in patients who are splenectomized or in patients who are Rh_0(D) negative. The American Society of Hematology (ASH) guidelines for immune thrombocytopenia recommend initial treatment with corticosteroids, IVIG/SCIG, or Rh_0(D) immune globulin for patients with secondary ITP due to HIV (no preference for initial therapy is expressed).[24] In symptomatic patients who fail one of these therapies, splenectomy is recommended. No platelet count cut-offs are addressed in this patient population.

16. **Human Immunodeficiency Virus (HIV)-Infected Infants and Children to Prevent Recurrent Bacterial 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 the following criteria (i, ii, iii and iv):
        - **i.** IVIG/SCIG is prescribed by or in consultation with an infectious diseases specialist or an immunologist; AND
        - **ii.** The patient is < 13 years of age; AND
        - **iii.** The patient is receiving combination antiretroviral therapy (cART); AND
        - **iv.** The patient has ONE of the following (a, b, or c):

a) Hypogammaglobulinemia (i.e., IgG < 400 mg/dL); 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 bacterial infections (e.g., bacteremia, meningitis, pneumonia) despite administration of combination antiretroviral therapy (cART) and appropriate antimicrobial prophylaxis.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year if the frequency and/or severity of infections have decreased according to the prescriber.

17. 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), Opdivo (nivolumab), Yervoy (ipilimumab), Tecentriq (atezolizumab), Bavencio (avelumab), Imfinzi (durvalumab).

A) Initial Therapy: Approve for 1 month if the patient meets the following criteria (i or ii):
i. The patient has tried a systemic corticosteroid (e.g., prednisone, methylprednisolone) and has not adequately responded to therapy OR IVIG/SCIG is being started with a systemic corticosteroid; OR
ii. A corticosteroid is contraindicated, per the prescriber.

B) Patients Currently Receiving IVIG/SCIG: 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.

18. 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 [divided doses given over 2 to 5 days]) if the patient meets the following criteria (i, ii and iii):
i. IVIG/SCIG is prescribed by or in consultation with a neurologist; AND
ii. The patient is having refractory weakness after symptomatic treatment of LEMS with an amifampridine product (e.g., Firdapse, Ruzurgi), guanidine, or pyridostigmine; AND
iii. The patient meets ONE of the following (a or b):
a) The patient has paraneoplastic LEMS; OR
b) The 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.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year if the patient has a response (for example, improved muscle strength, other clinical response) or continued effectiveness, according to the prescriber.

IVIG/SCIG may be used as an alternative in patients who do not respond or do not tolerate other therapies for LEMS.[18]

19. 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 the following criteria (i, and ii):
i. The patient has severe recurrent bacterial infections according to the prescriber; AND
ii. IVIG/SCIG is prescribed by or in consultation with a hematologist, oncologist, or infectious diseases specialist.
B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year.

20. **Multiple Sclerosis (MS), Acute Severe Exacerbation or Relapses.** Approve for 1 month (this is to provide one course of therapy [either a single dose or in divided doses given over 1 to 5 days]) if the patient meets BOTH of the following criteria (A and B):
    A) IVIG/SCIG is prescribed by or in consultation with, a neurologist or a physician who specializes in the treatment of MS; AND
    B) The patient meets ONE of the following criteria (i or ii):
        i. The 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.

21. **Multiple Sclerosis (MS), Post-Partum to Prevent Relapses.** 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 the following criteria (i and ii):
        i. IVIG/SCIG is prescribed by or in consultation with, a neurologist or a physician who specializes in the treatment of MS; AND
        ii. The patient is not currently receiving disease modifying therapy (DMT) for MS to prevent relapses.
        - Note: Disease modifying therapy can include: Avonex® [interferon beta-1a injection, IM], Plegridy® [peginterferon beta-1a SC injection], Rebif® [interferon beta-1a injection, SC], Betaseron®/Extavia® [interferon beta-1b injection], Copaxone®/Glatopa™ [glatiramer acetate injection, SC], Gilenya® [fingolimod capsules], Lemtrada™ (alemtuzumab injection for IV use), Aubagio® [teriflunomide tablets], Mavenclad® [cladribine tablets], Mayzent® [siponimoid tablets], Tecfidera® [dimethyl fumarate capsules], Tysabri® [natalizumab injection], Novantrone® [mitoxantrone injection]).

    B) Patients Currently Receiving IVIG/SCIG: Approve for a second 6 months of therapy if the patient is not taking a disease modifying therapy (DMT) for MS.
    Note: Disease modifying therapy can include: Avonex [interferon beta-1a injection, IM], Plegridy [peginterferon beta-1a SC injection], Rebif [interferon beta-1a injection, SC], Betaseron/Extavia [interferon beta-1b injection], Copaxone/Glatopa [glatiramer acetate injection, SC], Gilenya [fingolimod capsules], Lemtrada (alemtuzumab injection for IV use), Aubagio [teriflunomide tablets], Mavenclad [cladribine tablets], Mayzent [siponimoid tablets], Tecfidera [dimethyl fumarate capsules], Tysabri [natalizumab injection], Novantrone [mitoxantrone injection]).

    None of the DMTs have been approved for use in women who are nursing. IVIG/SCIG is the treatment of choice for post-partum mothers with MS who are nursing.[46]

22. **Myasthenia Gravis.** Approve for the duration noted if the patient meets ONE of the following (A or B or C):
    A) Initial Therapy for Short-Term (Acute) Use: Approve for 5 days (to allow for one course of therapy to be given in divided doses over 2 to 5 consecutive days) if the patient meets the following criteria (i and ii):
        i. IVIG/SCIG is prescribed by or in consultation with a neurologist; AND
        ii. The patient meets ONE of the following conditions (a, b, c, or d):
            a) The patient has an exacerbation of myasthenia gravis; OR
            b) The patient requires stabilization of myasthenia gravis before surgery; OR

c) The patient has been started on an immunosuppressive drug (e.g., azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil, MTX, or tacrolimus) and is waiting for full effect; OR

d) The patient is starting therapy with a corticosteroid and IVIG/SCIG is being given to prevent or minimize exacerbations.

B) Initial Therapy for Maintenance: Approve for 1 year if the patient meets ALL of the following criteria (i, ii, iii, and iv):

i. IVIG/SCIG is prescribed by or in consultation with a neurologist; AND

ii. The patient has refractory myasthenia gravis; AND

iii. The patient has tried pyridostigmine; AND

iv. The patient has tried immunosuppressive therapy with at least one of the following agents: azathioprine, cyclosporine, cyclophosphamide, mycophenolate mofetil, MTX, tacrolimus AND has had an inadequate response.

C) Patients Currently Receiving IVIG/SCIG for Maintenance Therapy: Approve for 1 year if the patient is responding according to the prescriber.

Patients who require additional short-term (acute) therapy for exacerbations or relapses are reviewed using the Initial Therapy for Short-Term Use above in A).

Note: Patients with myasthenia gravis crisis are hospitalized. Crisis is defined by respiratory failure resulting from myasthenic weakness and necessitating assisted ventilation.

23. 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 criteria (A or B):

A) The patient is pregnant and meets the following criteria (i and ii):

i. The patient has been exposed to measles and IVIG/SCIG will be given within 6 days of exposure; AND

ii. The patient does not have evidence of immunity to measles (i.e., the patient does not have a history of the disease or age-appropriate vaccination); OR

B) The patient is severely immunocompromised (e.g., patients with a bone marrow transplant, graft-versus-host disease [GVHD], acute lymphoblastic leukemia [ALL], acquired immunodeficiency syndrome [AIDS], human immunodeficiency virus [HIV]-infected patients) according to the prescriber, AND the patient has been exposed to measles and IVIG/SCIG will be given within 6 days of exposure.

Note: For patients with primary immune deficiency, see criteria for Primary Immunodeficiencies.

24. Passive Immunization for Varicella (Chickenpox) [**Post-Exposure Prophylaxis].** Approve for 1 day (to allow for a single dose) if the patient meets ONE of the following criteria (A or B):

A) The patient is human immunodeficiency virus (HIV)-infected and meets ALL of the following criteria (i, ii and iii):

i. IVIG/SCIG is prescribed by or in consultation with an infectious diseases specialist or an immunologist; AND

ii. VariZIG® (varicella zoster immune globulin [human] IM injection) is not available; AND

iii. The patient does not have evidence of immunity to varicella (i.e., patient does not have a history of the disease or age-appropriate vaccination);

OR

B) The patient is not HIV-infected and meets ALL of the following criteria (i, ii, iii, and iv):

i. IVIG/SCIG is prescribed by or in consultation with an infectious diseases specialist or immunologist; AND

ii. VariZIG (varicella zoster immune globulin [human] IM injection) is not available; AND

iii. The patient does not have evidence of immunity to varicella (i.e., patient does not have a history of the disease or age-appropriate vaccination); AND

iv. The patient meets ONE of the following criteria (a or b):

a) The patient is immune compromised; OR

b) The patient is pregnant.

25. Pure Red Blood Cell Aplasia (PRCA) Secondary to Chronic (Persistent) 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 ALL of the following criteria (i, ii, and iii):

i. IVIG/SCIG is prescribed by or in consultation with an infectious diseases specialist, immunologist, hematologist, or transplant specialist; AND

ii. The patient has a chronic immunodeficiency condition (e.g., patients with HIV infection, solid organ transplants [e.g., renal, liver], chemotherapy for hematologic malignancy); AND

iii. The patient has clinically significant anemia as determined by the prescriber OR the patient is transfusion dependent.

B) Patients Currently Receiving IVIG/SCIG: Approve for 3 months in patients who responded with an increase in hemoglobin to previous IVIG/SCIG therapy but relapse when off IVIG/SCIG or in patients who respond and require maintenance therapy to prevent relapse.

26. 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 criteria (i, ii, and iii):

i. IVIG/SCIG is prescribed by or in consultation with an infectious diseases specialist, immunologist, hematologist, or transplant specialist; AND

ii. The patient has tried a systemic corticosteroid (e.g., prednisone); AND

iii. The patient has tried either cyclophosphamide OR cyclosporine.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 month if the patient has responded with an increase in hemoglobin and reticulocytosis, according to the prescriber.

27. 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 the following criteria (i and ii):

i. IVIG/SCIG is prescribed by or in consultation with a neurologist; AND

ii. The patient meets ONE of the following criteria (a or b):

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

b) The patient has contraindications to both a benzodiazepine AND baclofen according to the prescriber.

B) Patients Currently Receiving IVIG/SCIG: Approve for 1 year if the patient has responded (such as reduced stiffness or frequency of spasms, ability to walk unassisted) according to the prescriber.

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

29. Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS) / Pediatric acute onset neuropsychiatric syndrome (PANS): Approve for 6 months

a. Diagnosis of pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS) OR pediatric acute onset neuropsychiatric syndrome (PANS); **AND**

b. Medication prescribed by or in consultation with a pediatric psychiatrist or pediatric neurologist; **AND**

c. ~~For a diagnosis of PANDAS~~ Member has been evaluated for and if applicable treated for infective causes: **AND**

d. Prescriber will continue with individualized standard neuropsychiatric treatment while undergoing immune globulin treatment; **AND**

e. Member is less than 18 years of age

Coverage Criteria for Gammastan (MBO):

a. Hepatitis A exposure and the exposure was no more than 2 weeks previously; **OR**

b. Measles exposure and the exposure was no more than 6 days previously; **AND**

a. Member has not had a previous vaccination or previous measles outbreak; **OR**

b. Member is immunocompromised; **OR**

c. Varicella-zoster immune globulin (VariZig) is unavailable and member is immunosuppressed; **OR**

d. Rubella postexposure prophylaxis; **AND**

a. Member is pregnant and has been exposed to Rubella; **AND**

b. Member will not consider a therapeutic abortion

EXCLUSION CRITERIA

When immune globulin is prescribed for condition(s) in which there is insufficient clinical evidence to support its use and/ or if the request is for one for the following:

- Adrenoleukodystrophy
- Alzheimer's Disease (AD)
- Amyotrophic Lateral Sclerosis
- Anemia, Aplastic
- Asthma
- Atopic Dermatitis
- Autism
- BK Virus Associated Nephropathy (BKVAN) in Kidney Transplant Patient
- Chronic Fatigue Syndrome
- Chronic Myasthenia Gravis
- Complex Regional Pain Syndrome (Reflex Sympathetic Dystrophy)
- Crohn's Disease
- Cystic Fibrosis
- Cytomegalovirus (CMV) Disease Prophylaxis in Hematopoietic Cell Transplantation [HCT] Recipients

- Cytomegalovirus (CMV) Infection, Preemptive Therapy for Cytomegalovirus [CMV] Infection or Treatment of Cytomegalovirus {CMV} Disease, in Allogeneic Hematopoietic Cell Transplantation (HCT) Recipients
- Cytomegalovirus (CMV) Infections, Prophylaxis or Treatment in Solid Organ Transplantation, (e.g., Heart, Kidney) for Prophylaxis
- Diabetes Mellitus, Immunotherapy
- Epilepsy, Pediatric Intractable
- Fibromyalgia Syndrome
- Graft Versus Host Disease (GVHD), Acute [Within First 100 days After Hematopoietic Cell Transplantation {HCT}]
- Graft Versus Host Disease (GVHD), chronic, Prevention in Hematopoietic Cell Transplantation [HCT] Recipient
- Heart Block, Congenital (Prevention)
- Heart Failure, Chronic
- Hematopoietic Cell Transplantation (HCT) in Allogeneic Recipients from Human Leukocyte Antigen [HLA]-Identical Sibling Donors
- Human Immunodeficiency Virus (HIV) Infection, Adults, for Prophylaxis of Infections
- Immune Globulin M (IgM) Paraproteinemic Demyelinating Neuropathy [or Other Paraproteinemic Demyelinating Neuropathies]
- In Vitro Fertilization (IVF)
- Infantile Spasms (West Syndrome)
- Marburg Variant Multiple Sclerosis (MS)
- Multiple Sclerosis (MS), Primary or Secondary Progressive, Relapsing Remitting for the Prevention of Relapses
- Nephropathy, Membranous
- Organomegaly, Endocrinopathy, Monoclonal Gammopathy, and Skin Changes (POEMS) Syndrome
- Post-Polio Syndrome
- Recurrent Spontaneous Pregnancy Loss (RSPL) [Including Antiphospholipid Antibody-Positive Women]
- Selective Immune Globulin A (IgA) Deficiency as the Sole Immunologic Abnormality
- Systemic Lupus Erythematosus (SLE)
- Systemic Sclerosis (Scleroderma)
- Thrombocytopenia, Heparin-Induced (HIT)
- Thrombotic Thrombocytopenic Purpura (TTP)/Hemolytic Uremic Syndrome (HUS)
- Urticaria, Chronic Autoimmune
- Uveitis, Noninfectious

Applicable Coding:

Code	Medication
90283	Immune Globulin (IgIV), human, for intravenous use
90284	Immune globulin (SCIG), human, for use in subcutaneous infusions, 100 mg, each

J1459	Injection, immune globulin (Privigen), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1556	Injection, immune globulin (Bivigam), 500 mg
J1557	Injection, immune globulin, (Gammaplex), intravenous, non-lyophilized (e.g., liguid), 500 mg
J1559	Injection, immune globulin (Hizentra), 100 mg
J1561	Injection, immune globulin, (Gamunex/Gamunex-C/Gammaked), intravenous, 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), intravenous, non-lyophilized, (e.g., liquid), 500 mg
J1572	Injection, immune globulin, (Flebogamma/Flebogamma DIF), intravenous, non-lyophilized (e.g., liquid),500 mg
J1599	Injection, immune globulin, intravenous, non-lyophilized (e.g. liquid), not otherwise specified, 500 mg
J1562	Injection, immune globulin(Vivaglobin), 100mg
J1575	Injection, immune globulin/kyaluronidase, (Hyqvia), 100mg immunoglobulin
J1555	Injection, immune globulin, (Cuvitru) Subcutaneous Inj 1gm/5ml
No code yet - use J1599 for unspecified	Injection, Immune Globulin (Human)-ifas IV Soln (Panzyga)
J3590	Immune globulin subcutaneous, Human – klhw 20% solution (Xembify)

Clinical Background Information and References

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Original Approval Date	Original Effective Date	Policy Owner	Approved by
12/1/2020	1/1/2021	Pharmacy Services	Pharmacy & Therapeutics (P&T) Committee

Policy Revisions History			
Review Date	**Summary of Revisions**	**Revision Effective Date**	**Approved by**
12/1/2020	9.129 IVIG SCIG Policy retired, new policy created.	1/1/2021	P&T Committee
8/12/2021	P&T Annual Review. Added back IVIG products, which are available via medical benefit only but still require PA. Added Gammastan criteria.	12/1/2021	P&T Committee
9/22/2021	Diagnoses of PANDAS/PANS added to policy in accordance with MA DOI requirements for 1/1/22	1/1/2022	P&T Committee

Next Review Date

8/2022

Other Applicable Policies

Reference to Applicable Laws and Regulations, If Any

Disclaimer Information

Medical Policies are the Plan's guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member's benefit document, and when appropriate, coordinates with the Member's health care Providers to consider the individual Member's health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan's service area who are medical experts in the particular field, and adherence to FDA and other government

agency policies. Applicable state or federal mandates, as well as the Member's benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.