DR.002.C Intravenous Immune Globulin (IVIG)

Health Partners Plans

Title: Intravenous Immune Globulin (IVIG)
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PRODUCT VARIATIONS

This policy applies to all Health Partners Plans (HPP) product lines unless noted below.

POLICY STATEMENT

Health Partners Plans (HPP) considers Intravenous Immune Globulin (IVIG) medically necessary when used to treat its approved FDA labeled indications AND all of the prior authorization criteria listed in the policy is met.

FDA APPROVED INDICATIONS

- Atgam®
- Bivigam®
- Carimune NF®
- Flebogamma®
- Gammagard Liquid®
- Gammagard S/D®
- Gammaked®
- Gammaplex®
- Gamunex-C®
- Octagam®
- Privigen®
- Thymoglobulin®

FDA APPROVED INDICATIONS (may vary by product):

- Atgam® is an equine thymocyte immune globulin injection indicated for the treatment of renal transplant rejection and aplastic anemia (moderate to severe) in patients unsuitable for bone marrow transplantation.
- Bivigam® is a human immune globulin injection indicated for the treatment of primary inherited immunodeficiency (PID).
- Carimune NF® is a human immune globulin injection indicated for the maintenance treatment of patients with PID, for acute Immune Thrombocytopenic Purpura (ITP), or for chronic ITP requiring a rapid rise in platelet count such as prior to surgery, or excessive bleeding.

- Flebogamma® is a human immune globulin injection indicated for replacement therapy in PID and chronic Primary Immune Thrombocytopenia (ITP).
- Gammagard Liquid® (IV or SC) is a human immune globulin injection indicated for the treatment of PID and Multifocal Motor Neuropathy.
- Gammagard S/D® is a human immune globulin indicated for the treatment of PID, prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell Chronic Lymphocytic Leukemia (CLL), to increase platelet count and for the prevention and/or control of bleeding in adult Chronic Idiopathic Thrombocytopenic Purpura (ITP), prevention of coronary artery aneurysms associated with Kawasaki Syndrome in some pediatric patients.
- Gammaked® (IV or SC) is a human immune globulin indicated for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) to improve neuromuscular disability and impairment and for maintenance therapy to prevent relapse, for PID, and for ITP to raise platelet counts to prevent bleeding or to allow a patient with ITP to undergo surgery.
- Gammaplex® is a human immune globulin indicated for the treatment of PID, ITP.
- Gamunex-C® (IV or SC) is a human immune globulin injection indicated for the treatment of PID, ITP (do not administer SC), CIDP.
- Octagam® is a human immune globulin injection indicated for the treatment of PID and chronic ITP.
- Privigen® is a human immune globulin indicated for the treatment of PID, Chronic ITP, and CIDP (not studied beyond six months).
- Thymoglobulin® is a rabbit immune globulin indicated for the prophylaxis and treatment of acute rejection in patients receiving a kidney transplant in conjunction with concomitant immunosuppression.

OFF-LABELED USE

Authorization for off-labeled use of medication will be evaluated on an individual basis. Review of an off-labeled request by the Medical Staff will be predicated on the appropriateness of treatment and full consideration of medical necessity. For off-label use, Medical Directors will review scientific literature and local practice patterns. Medical Directors will review all of the provided documentation to assure that:

1) The diagnosis of the disorder is reasonably certain and based on a thorough history and examination and appropriate laboratory testing (such as electromyography (EMG), spinal fluid tests, serum tests, and biopsy findings).

2) Previous treatment failures are documented (when applicable).

3) The requested dose and interval of administration are consistent with recommendations in peer-reviewed literature and professional guidelines for the requested indication.

4) Once treatment is initiated, there is an adequate documentation of improvement for continued treatment to be medically necessary. An objective, quantitative assessment to monitor the progress is required, when applicable.

5) Depending on the diagnosis and clinical circumstances, an attempt is made to decrease/wean the dosage when improvement has occurred. An attempt to stop the IVIG infusion when clinically appropriate for the diagnosis is made if improvement is sustained with dosage reduction. If improvement does not occur with

IVIG, continued infusion may not be considered medically necessary (this does not apply to persons with primary immune deficiency diseases).

Off-Labeled use includes the following (not an all-inclusive list):

- Auto-immune mucocutaneous blistering diseases
- Dermatomyositis
- Fetal/neonatal alloimmune thrombocytopenia (FAIT)
- Guillain-Barre syndrome (GBS)
- Lambert-Eaton myasthenic syndrome
- Multifocal motor neuropathy
- Myasthenia gravis
- Parvovirus B19-induced pure red cell aplasia (PRCA)
- Polymyositis
- Prophylaxis of bacterial and viral infection in pediatric human immunodeficiency virus (HIV) infection.
- Prophylaxis of bacterial and viral infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
- Relapsing-Remitting Multiple Sclerosis (not primary or secondary progressive)
- Stiff-person syndrome
- Toxic Shock Syndrome

The use of IVIG or Subcutaneous Immune Globulin (SCIG) is considered experimental, investigational, or unproven for ANY other use including the following list (this may not be all-inclusive):

- Hashimoto encephalopathy
- Inclusion body myositis (IBM)
- Lyme neuropathy
- Neonatal sepsis
- Pediatric acute-onset neuropsychiatric syndrome (PANS) and Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS), Primary progressive multiple sclerosis (MS) and secondary progressive MS, acute MS exacerbations, or clinically isolated syndrome, recurrent pregnancy loss

PRIOR AUTHORIZATION CRITERIA

INITIAL CRITERIA

1) Have baseline values for BUN and serum creatinine been obtained within 30 days of request?
   If YES, go to 2. If NO, refer to Medical Director.

2) Is the prescriber a specialist (Allergy, Immunology, Hematology, Cardiology, Oncology, or Neurology)?
   If YES, go to 3. If NO, refer to Medical Director.

3) Does the patient have Primary Immunodeficiency (PID) / Wiskott-Aldrich syndrome (such as: x-linked agammaglobulinemia, common variable immunodeficiency, transient hypogammaglobulinemia of infancy, IgG subclass deficiency with or without IgA deficiency, antibody deficiency with near normal immunoglobulin levels, severe combined immunodeficiencies, ataxia-telangiactasia, x-linked lymphoproliferative syndrome)? *If YES, go to 4. If NO, go to 9.*

    a. Does the patient have Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (e.g., X-linked or autosomal recessive agammaglobulinemia) and one of the following: confirmed by genetic or molecular testing, OR pretreatment IgG level < 200 mg/dL, OR Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation? *If YES, approve 3 months. If NO, go to 3b.*

    b. Does the patient have Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency) AND diagnosis confirmed by genetic or molecular testing (if applicable), AND History of recurrent bacterial infections (e.g., pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), AND Impaired antibody response to pneumococcal polysaccharide vaccine? *If YES, approve for 3 months. if No, go to 3c.*

    c. Does the patient have Common variable immunodeficiency (CVID) AND is 4 years or older AND Other causes of immune deficiency have been excluded (e.g., drug induced, genetic disorders, infectious diseases such as HIV, malignancy) AND Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age AND History of recurrent bacterial infections AND Impaired antibody response to pneumococcal polysaccharide vaccine? *If YES, approve for 3 months. If NO, go to 3d.*

    d. Does the patient have Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency AND a history of recurrent bacterial infections AND one of the following: Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age, OR Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels, OR Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels, OR IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels OR Specific antibody deficiency: normal IgG, IgA and IgM levels? *If YES, approve for 3 months, if NO go to 4.*

4) Is the patient's IgG level < 500 mg/dL with a history of recurrent bacterial infections AND Impaired antibody response to pneumococcal polysaccharide vaccine, AND IgG < 500 mg/dL or ≥ 2 SD below the mean for age? *If YES, approve for 3 months. If NO, go to 5.*

5) Does the patient have a history of recurrent, severe, difficult to treat infections (such as recurrent otitis media, bronchtiectasis, and recurrent infections requiring intravenous antibiotics, multiple antibiotic hypersensitivities, chronic or recurrent sinusitis? *If YES, go to 6. If NO, refer to Medical Director.*

6) Does a patient have a deficiency in producing antibodies in response to vaccination? *If YES, go to 7. If NO, refer to Medical Director.*

7) Were titers drawn before challenging with vaccination? *If YES, go to 8. If NO, refer to Medical Director.*

8) Were titers drawn between 4 and 8 weeks of vaccination? *If YES, approve for 3 months. If NO, refer to Medical Director.*

9) Does the patient have a diagnosis of acute Immune thrombocytopenia/Idiopathic thrombocytopenia purpura (ITP)? *If YES, go to 10. If NO, go to 13.*

10) Is the prescriber trying to manage acute bleeding due to severe thrombocytopenia (platelet count less than 30 x 109/L)? *If YES, approve for 1 month [not eligible for renewal]. If NO, go to 11.*

11) Does the patient require an increase in platelet counts prior to an invasive surgical procedure (platelet count less than 100 x 109/L)? *If YES, approve for 1 month [not eligible for renewal]. If NO, go to 12.*

12) Does the patient have severe thrombocytopenia (platelet count less than 20 x 109/L) and considered to be at risk for intracerebral hemorrhage? *If YES, approve for 1 month [not eligible for renewal]. If NO, refer to Medical Director.*

13) Is the patient not a candidate for splenectomy or has experienced relapse post-splenectomy AND failure, contraindication, or intolerance to ALL of the following: corticosteroids, thrombopoietin receptor agonists (Promacta or Nplate), rituximab (Rituxan). *If YES, go to 14. If NO, refer to Medical Director.*

14) Does the patient have a diagnosis of Chronic Immune Thrombocytopenia (CIT)? *If YES, go to 15. If NO, go to 18.*

15) Is the patient at an increased risk for bleeding as indicated by a platelet count less than 30 x 109/L? *If YES, go to 16. If NO, refer to Medical Director.*

16) Does the patient have a history of failure, contraindication, or intolerance to corticosteroids (must attach documentation including medication, dose, and dates)? *If YES, go to 17. If NO, refer to Medical Director.*

17) Has the duration of illness lasted greater than 6 months? *If YES, go to 18. If NO, refer to Medical Director.*

18) Is the patient greater than or equal to 2 years old? *If YES, approve for 3 months. If NO, refer to Medical Director.*

19) Does the patient have a diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)? *If YES, go to 20. If NO, go to 27.*

20) Is the disease course progressive or relapsing and remitting for two months or longer? *If YES, go to 21. If NO, refer to Medical Director.*

21) Does the patient have abnormal or absent deep tendon reflexes in upper and lower limbs? *If YES, go to 22. If NO, refer to Medical Director.*

22) Does electrodiagnostic testing indicate demyelination as follows: partial motor conduction block in at least two motor nerves (or in one nerve plus one other demyelination criterion in at least one other nerve), or distal CMAP duration increase in at least one nerve plus one other demyelination criterion in at least one other nerve, or abnormal temporal dispersion conduction in at least two motor nerves, or reduced conduction velocity in at least two motor nerves, or prolonged distal motor latency in at least two motor nerves, or absent F wave in at least two motor nerves plus one other demyelination criterion in at least one other nerve, or prolonged F wave latency in at least two motor nerves? *If YES, go to 23. If NO, refer to Medical Director.*

23) Does cerebrospinal fluid (CSF) analysis indicate a white cell count of less than 10 cells/mm3? *If YES, go to 24. If NO, refer to Medical Director.*

24) Is CSF protein elevated? *If YES, go to 25. If NO, refer to Medical Director.*

25) Have other causes of demyelinating neuropathy been excluded (from the European Federation of Neurological Societies and the Peripheral Nerve Society): Borrelia burgdorferi infection (Lyme disease), diphtheria, drug or toxin exposure probably to have caused the neuropathy, hereditary demyelinating neuropathy, Prominent sphincter disturbance, diagnosis of multifocal motor neuropathy, IgM monoclonal gammopathy with high titer

antibodies to myelin-associated glycoprotein, other causes for a demyelinating neuropathy including POEMS syndrome, osteosclerotic myeloma, diabetic and non-diabetic lumbosacral radiculoplexus neuropathy, PNS lymphoma and amyloidosis. *If YES, go to 26. If NO, refer to Medical Director*.

26) Is the patient refractory or intolerant to corticosteroids given in therapeutic doses over at least three months? (Must attach documentation including medication, dose, dates, and response to therapy). *If YES, go to 27. If NO, refer to Medical Director.*

27) Has baseline strength/weakness been documented using an objective clinical measuring tool (such as INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin)? *If YES, approve for 3 months. If NO, refer to Medical Director.*

28) Does the patient have a diagnosis of Guillain-Barre Syndrome (acute inflammatory polyneuropathy)? *If YES, go to 29. If NO, go to 31.*

29) Is the patient's disease severe (does the patient require assistance to ambulate)? *If YES, go to 30. If NO, refer to Medical Director.*

30) Is the onset of symptoms recent (within six weeks of onset)? *If YES, approve for 2 months [not eligible for renewal]. If NO, refer to Medical Director.*

31) Does the patient have a diagnosis of Multifocal Motor Neuropathy (MMN)? *If YES, go to 32. If NO, go to 34.*

32) Does the patient have multi-focal weakness? *If YES, go to 33. If NO, refer to Medical Director.*

33) Is the diagnosis of MMN supported by nerve conduction studies showing focal demyelination and conduction block in motor nerves and normal sensory nerves, and do these findings rule out other conditions that may not respond to IVIG treatment? *If YES, go to 34. If NO, refer to Medical Director.*

34) Has baseline strength/weakness been documented using an objective clinical measuring tool (such as INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin)? *If YES, approve for 1 month. If NO, refer to Medical Director.*

35) Does the patient have a diagnosis of pediatric HIV (age less than 13 years) requiring bacterial control or prevention? *If YES, approve for 3 months. If NO, go to 36.*

36) Does the patient have a diagnosis of Myasthenia Gravis? *If YES, go to 37. If NO, go to 39.*

37) Does the patient have an acute exacerbation resulting in impending myasthenia crisis (such as respiratory compromise, acute respiratory failure, and/or bulbar compromise), or does the patient require thymectomy, or does the patient have refractory myasthenia gravis unresponsive to conventional immunosuppressive therapy alone (such as corticosteroids, azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.)? (Must attach documentation including medications tried, doses, dates, and response to therapy). *If YES, go to 38. If NO, refer to Medical Director.*

38) Will the patient be continued on therapy with corticosteroids or other immunosuppressants (such as azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.) while being treated with IVIG, or does the patient require thymectomy? *If YES, approve for 1 month. If NO, refer to Medical Director.*

39) Does the patient have an acute exacerbation of Relapsing Remitting Multiple Sclerosis (RRMS)? (Must attach documentation of diagnosis). *If YES, go to 40. If NO, go to 41.*

40) Has the patient been unresponsive or intolerant to steroids and first-line treatments (such as Glatopa, Gilenya, Tecfidera, Aubagio, Avonex, Copaxone)? (Must attach medical records including baseline exam and most recent imaging results). *If YES, approve for 3 months. If NO, refer to Medical Director.*

41) Does the patient have a diagnosis of Dermatomyositis/Polymyositis confirmed by muscle biopsy? (Must attach results). *If YES, go to 42. If NO, go to 47.*

42) Does the patient have severe active disease? *If YES, go to 43. If NO, refer to Medical Director.*

43) Does the patient have proximal weakness in all upper and/or lower limbs? *If YES, go to 44. If NO, refer to Medical Director.*

44) Has the patient failed a trial of corticosteroids and at least two other immunosuppressants (such as azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.)? (Must attach documentation including medications tried, doses, dates of therapy, and response to therapy). *If YES, go to 45. If NO, refer to Medical Director.*

45) Will the patient be continued on combination therapy with corticosteroids or other immunosuppressants (such as azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.)? *If YES, go to 46. If NO, refer to Medical Director.*

46) Has the patient's baseline been documented on physical exam? (Must attach documentation). *If YES, approve for 3 months. If NO, refer to Medical Director.*

47) Does the patient have a solid organ transplant (kidney, liver, lung, heart, or pancreas), bone marrow transplant, or does the patient require treatment for allosensitization in preparation for a solid organ transplant? *If YES, go to 48. If NO, go to 49.*

48) Is IVIG being requested for: 1) suppression of panel reactive anti-human leukocyte antigen (HLA) antibodies prior to transplantation; or 2) treatment of antibody-mediated rejection of solid organ transplant; or 3) prevention or treatment of viral infections (such as Parvo B-19 virus or Polyoma BK virus). *If YES, approve for 3 months. If NO, refer to Medical Director.*

49) Does the patient have a diagnosis of Stiff-Person Syndrome? *If YES, go to 50. If NO, go to 53.*

50) Does the patient have anti-glutamic acid decarboxylase (GAD) antibodies? (Must attach documentation.) *If YES, go to 51. If NO, refer to Medical Director.*

51) Has the patient failed at least 2 of the following treatments: benzodiazepines, baclofen, gabapentin, valproate, tiagabine, or levetiracetam? (Must attach documentation including medications tried, doses, dates of therapy, and response to therapy). *If YES, got to 52. If NO, refer to Medical Director.*

52) Has the patient's baseline been documented on physical exam? (Must attach documentation.) *If YES, approve for 3 months. If NO, refer to Medical Director.*

53) Has the member had an Allogeneic Bone Marrow Transplant (BMT) or Stem Cell Transplant and is requiring prevention for acute Graft-Versus-Host-Disease (aGvHD) or infection? *If YES, go to 54. If NO, go to 55.*

54) Was the BMT allogenic? *If YES, go to 55. If NO, refer to Medical Director.*

55) Was the transplant less than 100 days ago? *If YES, go to 56. If NO, refer to Medical Director.*

56) Is the patient's IgG level less than 400 mg/dL? (Must attach documentation). *If YES, approve for 3 months. If NO, refer to Medical Director.*

57) Does the member have a diagnosis of pediatric Kawasaki's disease and also requiring prevention of coronary artery aneurysms associated Kawasaki's disease? (Must attach documentation of diagnosis). *If YES, approve for 1 month up to a total dose of 4 g per kg. If NO, go to 56.*

58) Does the patient have a diagnosis of Fetal Alloimmune Thrombocytopenia (FAIT)? *If YES, go to 57. If NO, go to 60.*

59) Does the patient have a history of one of the following: previous FAIT pregnancy, family history of the disease, or does screening reveal platelet alloantibodies? *If YES, approve until expected delivery date (not eligible for renewal). If NO, refer to Medical Director.*

60) Does the patient have a diagnosis of Neonatal Alloimmune Thrombocytopenia? *If YES, approve for 1 month (not eligible for renewal). If NO, go to 61.*

61) Does the patient have a diagnosis of Auto-immune Mucocutaneous Blistering disease? *If YES, go to 62. If NO, go to 68.*

62) Has the patient been diagnosed with one of the following: pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucus membrane pemphigoid (or cicatricial pemphigoid), epidermolysis bullosa aquisita, pemphigus gestationis (or herpes gestationis), or linear IgA dermatosis? *If YES, go to 63. If NO, refer to Medical Director.*

63) Does the patient have severe disease that is extensive and debilitating? *If YES, go to 64. If NO, refer to Medical Director.*

64) Has the diagnosis been confirmed by biopsy? (Must attach results). *If YES, go to 65. If NO, refer to Medical Director.*

65) Is the patient's disease progressive? *If YES, go to 66. If NO, refer to Medical Director.*

66) Is the patient's disease refractory to a trial of conventional therapy with corticosteroids and concurrent immunosuppressive treatment (such as azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.)? (Must attach documentation including medications tried, doses, dates of therapy, and response to therapy). *If YES, go to 67. If NO, refer to Medical Director.*

67) Does the patient have a baseline physical exam? *If YES, approve for 3 months. If NO, refer to Medical Director.*

68) Does the patient have a diagnosis of Acquired Immune Deficiency secondary to Chronic Lymphocytic Leukemia or Multiple Myeloma? *If YES, go to 69. If NO, go to 74.*

69) Is the patient's IgG level less than 200 mg/dL? *If YES, approve for 3 months. If NO, go to 70.*

70) Does the patient have a history of multiple hard to treat infections (such as recurrent otitis media, bronchtiectasis, recurrent infections requiring intravenous antibiotics, multiple antibiotic hypersensitivities, chronic or recurrent sinusitis? *If YES, go to 71. If NO, refer to Medical Director.*

71) Does a patient have a deficiency in producing antibodies in response to vaccination? *If YES, go to 72. If NO, refer to Medical Director.*

72) Were titers drawn before challenging with vaccination? *If YES, go to 73. If NO, refer to Medical Director.*

73) Were titers drawn between 4 and 8 weeks of vaccination? *If YES, approve for 3 months. If NO, refer to Medical Director.*

74) Does the patient have a diagnosis of Toxic Shock Syndrome? (Must attach documentation). *If YES, approve for 1 month (not eligible for renewal). If no, refer to Medical Director.*

RENEWAL CRITERIA

1) Does a patient have an absence of unacceptable toxicity (such as acute kidney injury, thrombosis, hemolysis, hypersensitivity, pulmonary adverse reactions, volume overload) from the drug? *If YES, go to 2. If NO, refer to Medical Director.*

2) Have the BUN and serum creatinine been obtained within the last 6 months, and have the concentration and rate of infusion been adjusted accordingly? *If YES, go to 3. If NO, refer to Medical Director.*

3) Does the patient have a diagnosis of PID? *If YES, go to 4. If NO, go to 5.*

4) Has the patient responded to therapy by having a decrease in the frequency of infection or a decrease in the severity of infection? *If YES, approve for 1 year. If NO, refer to Medical Director.*

5) Does the patient have a diagnosis of Chronic Immune Thrombocytopenia or ITP? *If YES, go to 6. If NO, go to 7.*

6) Has the patient responded to therapy as indicated by the achievement and maintenance of a platelet count of at least 30 x 10^9/L and a greater than two-fold increase in platelet count from baseline measured on two occasions seven days apart and the absence of bleeding. *If YES, approve for 1 year. If NO, refer to Medical Director.*

7) Does the patient have diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy? *If YES, go to 8. If NO, go to 9.*

8) Has the patient demonstrated clinical response to therapy based on an objective clinical measuring tool (such as INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin)? *If YES, approve for 1 year. If NO, refer to Medical Director.*

9) Does the patient have a diagnosis of Multifocal Motor Neuropathy? *If YES, go to 10. If NO, go to 11.*

10) Has the patient demonstrated clinical response to therapy based on an objective clinical measuring tool (such as INCAT, Medical Research Council (MRC) muscle strength, 6-MWT, Rankin, Modified Rankin)? *If YES, approve for 1 year. If NO, refer to Medical Director.*

11) Does the patient have a diagnosis of pediatric HIV requiring continued bacterial control or at an increased risk of infection requiring prevention? *If YES, go to 12. If NO, go to 13.*

12) Has the disease responded as evidenced by a decrease in the frequency of infection or by a decrease in the severity of infection? *If YES, approve to 12 months. If NO, refer to Medical Director.*

13) Does the patient have a diagnosis of Dermatomyositis/Polymyositis? *If YES, go to 14. If NO, go to 15.*

14) Has the patient had a significant improvement from baseline on physical exam? *If YES, approve for 6 months. If NO, refer to Medical Director.*

15) Does the patient have a transplanted solid organ (kidney, liver, lung, heart, pancreas) or complications of bone marrow transplant and is at a continued increased risk of infection? Or is the IVIG requested for use in combination with steroids and/or Rituximab for the treatment of chronic antibody-mediated solid organ transplant rejection? *If YES, go to 16. If NO, go to 17*.

16) Has the patient responded to treatment as evidenced by a decrease in the frequency of infection of by a decrease in the severity of infection, or by the improvement of the graft function, and/or reduction in donor-specific antibody (DSA)? *If YES, approve for 1 year. If NO, refer to Medical Director.*

17) Does the patient have a diagnosis of Stiff-person Syndrome? *If YES, go to 18. If NO, go to 19.*

18) Has the patient had an improvement of symptoms from baseline? (Must attach documentation). *If YES, approve for 1 year. If NO, refer to Medical Director.*

19) Has the patient had an Allogeneic Bone Marrow or Stem Cell Transplant? *If YES, go to 20. If NO, go to 22.*

20) Is the patient's IgG less than 400 mg/dL? (Must attach documentation). *If YES, go to 21. If NO, refer to Medical Director.*

21) Was the transplant less than 360 days post-allogeneic bone marrow transplant? *If YES, approve for up to 360 days post-allogeneic bone marrow transplant. If NO, refer to Medical Director.*

22) Doe the patient have a diagnosis of Auto-Immune Mucocutaneous Blistering Disease? *If YES, go to 23. If NO, go to 24.*

23) Has the patient had a documented improvement from baseline? (Must attach documentation). *If YES, approve for 6 months. If NO, refer to Medical Director.*

24) Does the patient have a diagnosis of Acquired Immune Deficiency secondary to Chronic Lymphocytic Leukemia or Multiple Myeloma and at a continued increased risk of infection requiring continued treatment? *If YES, go to 25. If NO, refer to Medical Director.*

25) Has the patient responded to therapy as evidenced by either a decrease in the frequency of infection or a decrease in the severity of infection? *If YES, approve for 6 months. If NO, go to 26.*

26) Does the patient have a diagnosis of Relapsing Remitting Multiple Sclerosis having tolerated and responded well to IVIG treatment? (Must attach documentation). *If YES, approve for 6 months. If NO, go to 27.*

27) Does the patient have a diagnosis of refractory myasthenia gravis? *If YES, go to 28. If NO, refer to Medical Director.*

28) Has the patient failed conventional immunosuppressive therapy alone (such as corticosteroids, azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide, etc.)? Or does the patient have contraindications or intolerance to conventional immunosuppressive therapy? (Must attach documentation including medications tried, doses, dates, and response to therapy, or documentation showing that the above medications are contraindicated). *If YES, approve for 3 months. If NO, refer to Medical Director.*

DOSAGE AND ADMINISTRATION

Dosing Recommendations:

- Patient's dose should be reduced to the lowest necessary to maintain benefit for their condition.
- Patients who have tolerated dose reduction and continue to show sustained improvement should have had a trial of treatment discontinuation, with the following exceptions:
  - PID would be excluded from a trial of discontinuation
  - HIV-infected children should show satisfactory control of the underlying disease (e.g. undetectable viral load, CD4 counts elevated above 200 or >15% [ages 9 months-5years] on antiretroviral therapy, etc.]
  - Solid organ transplant, CLL, and MM patients should not be at an increased risk of infection

- Dosing should be calculated using adjusted body weight if one or more of the following criteria are met:
  - Patient's body mass index (BMI) is 30 kg/m2 or more; OR
  - Patient's actual body weight is 20% higher than his or her ideal body weight (IBW)
- Use the following dosing formulas to calculate the adjusted body weight (round dose to nearest 5 gram increment in adult patients):
  - BMI = 703 x (weight in pounds/height in inches2)
  - IBW (kg) for males = 50+ [2.3 (height in inches -60)]
  - IBW (kg) for females = IBW + 0.5 (actual body weight – IBW)
- This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.
- Dose by indication:
  - Auto-immune blistering diseases: Up to 2 g/kg divided over 5 days in a 28-day cycle
  - Bone Marrow or Stem Cell Transplant: 500 mg/kg once weekly x 90 days, then 500 mg/kg every 3 to 4 weeks for up to 360 days post-transplant
  - CIDP: 2 g/kg divided over 2-5 days initially, then 1 g/kg administered in 1-2 infusions every 21 days
  - CLL/MM: 400 mg/kg every 3 to 4 weeks
  - Complications of transplanted solid organ (kidney, liver, lung, heart, pancreas): 2 g/kg divided over 5 days in a 28-day cycle
  - Dermatomyositis/Polymyositis: 2 g/kg divided over 2 to 5 days in a 28-day cycle
  - FAIT: 1 g/kg/week until delivery
  - Guillain-Barre: 2 g/kg divided over 5 days x 1 course
  - ITP: 2 g/kg divided over 5 days or 1 g/kg once daily for 2 consecutive days in a 28-day cycle
  - Kawasaki's Disease (pediatric patients) 1 g/kg to 2 g/kg x 1 course
  - Multifocal Motor Neuropathy: Up to 2 g/kg divided over 5 days in a 28-day cycle
  - Myasthenia Gravis: 1-2 g/kg divided as either 0.5 g/kg daily x 2 days or 0.4 g/kg daily x 5 days x 1 course
  - Neonatal Alloimmune Thrombocytopenia: 1 g/kg x 1 dose may be repeated once if needed.
  - Pediatric HIV: 400 mg/kg every 2 to 4 weeks
  - PID: 200 to 800 mg/kg every 21 to 28 days
  - Stiff Person: 2 g/kg divided over 5 days in a 28-day cycle
  - Toxic shock syndrome: 2 g/kg divided over 5 days x 1 course

RISK FACTORS/SIDE EFFECTS

IgA deficient patients with antibodies to IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions. Hyperproteinemia, increased serum viscosity, and hyponatremia may occur. Aseptic meningitis syndrome (AMS) may occur, especially with high doses or rapid infusion. Hemolysis that is either intravascular or due to enhanced red blood cell sequestration may occur. Risk factors include high doses and non-O blood group. Closely monitor patients for hemolysis and hemolytic anemia. Elevations of systolic and diastolic blood pressure (including cases of hypertensive urgency) have been observed during/shortly following Privigen infusion. These blood pressure elevations were resolved or significantly improved within hours with either observation alone or changes in oral anti-hypertensive therapy. Check patients for a history of hypertension and monitor blood pressure during and following Privigen infusion. Products are made from human blood and may contain infectious agents, e.g., viruses, the variant Creutzfeldt Jakob disease [vCJD]

agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. Antithymocyte globulins can cause anaphylaxis when injected intravenously.

BLACK BOX WARNING

Thrombosis, renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with intravenous immune globulin.

MONITORING

Monitor renal function, including blood urea nitrogen and serum creatinine, and urine output in patients at risk of developing acute renal failure. Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).

CODING

Note: The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that may be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT Code	Description
N/A	

HCPCS Code	Description
J1459	Injection, immune globulin (Privigen), intravenous, non-lyophilized (e.g. liquid), 500 mg
J1554	Injection, immune globulin (asceniv), 500 mg
J1556	Injection, immune globulin (Bivigam), 500 mg
J1557	Injection, immune globulin (Gammaplex), intravenous, non-lyophilized (e.g. liquid), 500 mg
J1561	Injection, immune globulin, (Gamunex-C/Gammaked), non-lyophilized (e.g. liquid), 500 mg
J1568	Injection, immune globulin, (Octagam), intravenous, non-lyophilized (e.g. liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard liquid), intravenous, non-lyophilized, (e.g. liquid), 500 mg
J1572	Injection, immune globulin, (Flebogamma/Flebogamma Dif), intravenous, non-lyophilized (e.g. liquid), 500 mg

S9338	Home infusion therapy, immunotherapy, administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

ICD 10 Code	Description
N/A	

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Effective Date
2021 Annual review. Primary inherited immunodeficiency (PID) broken out into multiple sections. Additional specialists added. J1554 added to coding table.	C	7/1/2021
2020 Annual policy review. Updated policy language to include additional prior authorization criteria.	B	8/1/2020
2019 Annual policy review. Coding table added. No changes to policy language.	A	7/15/2018
New Policy	A	7/15/2018

REFERENCES

1) Atgam® [prescribing information]. Pharmacia & Upjohn, Co. 2015 Apr.
2) Bivigam® [prescribing information Derivation and validation of diagnostic criteria for chronic inflammatory demyelinating polyneuropathy]. Biotest Pharmaceuticals Corporation. 2013 Oct.
3) Carimune® [prescribing information]. CSL Behring, LLC. 2016 Nov.
4) Flebogamma® [prescribing information]. Institute Grifols, SA. 2018 Mar.
5) Gammagard Liquid® [prescribing information]. Baxalta US, Inc. 2016 Jun.
6) Gammagard.
7) Gammaked® [prescribing information]. Kedrion Biopharma. 2016 Sept.

8) Gammaplex® [prescribing information]. Bio Products Laboratory, Ltd.

9) Gamunex-C® [prescribing information]. Grifols Therapeutics, Inc. 2017 Mar.

10) Octagam® [prescribing information]. Octapharma USA Inc. 2013 Oct.

11) Privigen® [prescribing information]. CSL Behring, LLC. 2017 Sept.

12) Thymoglobulin® [prescribing information]. Genzyme Corporation. 2017 Apr.

13) Skeie GO, Apostolski S, Evoli A, et al. Guidelines for the treatment of autoimmune neuromuscular transmission disorders. Eur J Neurol. 2010;17(7):893-902.

14) The NCCN Clinical Practice Guidelines in Oncology® Non-Hodgkin's Lymphomas (Version 3.2016).

15) Van den Bergh PY, Hadden RD, Bouche P, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies [trunc]. Eur J Neurol 2010 Mar;17(3):356-63.

16) Patwa HS, Chaudhry V, Katzberg H, et al. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2012 Mar 27;78(13):1009-15.

17) French CIDP Study Group. Recommendations on diagnostic strategies for chronic inflammatory demyelinating polyradiculoneuropathy. J Neurol Neurosurg Psychiatry 2008; 79: 115–118.

18) Donofrio PD, Berger A, Brannagan TH, et al. Consensus statement: The use of intravenous immunoglobulin in the treatment of neuromuscular conditions report of the AANEM ad hoc committee. Muscle Nerve. 2009;40:890-900.

19) Feasby T, Banwell B, Benstead T, et al. Guidelines on the use of intravenous immune globulin for neurologic conditions. Transfus Med Rev. 2007;21(2 suppl 1):S57-107.

20) Gajdos P, Tranchant C, Clair B, et al; Myasthenia Gravis Clinical Study Group. Treatment of myasthenia gravis exacerbation with intravenous immunoglobulin: a randomized double-blind clinical trial. Arch Neurol. 2005;62(11):1689-1693.

21) Elovaara I, et al. EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases. European Journal of Neurology 2008;15(9):893-908.

22) Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society--first revision. J Peripher Nerv Syst. 2010 Dec;15(4):295-301. doi: 10.1111/j.1529-8027.2010.00290.x.

23) Hahn AF, Bolton CF, Pillay N, et al. Plasma exchange therapy in chronic inflammatory demyelinating polyneuropathy. A double-blind, sham controlled, cross-over study. Brain 1996;119:1055–66.

24) The National Institute of Child Health and Human Developments Intravenous Immunoglobulin Study Group. Intravenous immune globulin for the prevention of bacterial infections in children with symptomatic human immunodeficiency virus infection. N Engl J Med. 1991 Jul 11;325(2):73-80.

25) Silberry GK, Abzug MJ, Nachman, S, et al. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children: Recommendations from the National Institutes of Health, Centers for Disease Control and Prevention, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. J Pediatric Infect Dis Soc. 2013 Nov; 32 Suppl 2: i-KK4.

26) Wolfe GI, Barohn RJ, Foster BM, et al; Myasthenia Gravis-IVIG Study Group. Randomized, controlled trial of intravenous immunoglobulin in myasthenia gravis. Muscle Nerve. 2002;26(4):549-552.

27) Hughes RA, Wijdicks EF, Barohn R, et al; Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2003;61(6):736-740.

28) Hughes RA, Swan AV, Raphael JC, Annane D, van Koningsveld R, van Doorn PA. Immunotherapy for Guillain-Barré syndrome: a systematic review. Brain. 2007;130(pt 9):2245-2257.

29) Bussel, JB et al. Antenatal management of alloimmune thrombocytopenia with Intravenous Immunoglobulin: A randomized trial of low dose steroid to intravenous immunoglobulin. Am J Obstet Gynecol 1996; 174 1414-23.

30) Ratko TA, Burnett DA, The Univ Hospital Consortium Expert Panel for the Off-label Use of Polyvalent Intravenously Administered Immunoglobulin Preparations, et al. Recommendations for the off-label use of intravenously administered immunoglobulin preparations. JAMA 1995; 273:1865-70.

31) Ahmed AR, Spigelman Z, Cavacine LA et al. Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. N Eng J Med 2006; 1772-9.

32) American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004; 114:297-316.

33) Gottstein R, Cooke R. Systematic Review of intravenous immunoglobulin in haemolytic disease of the newborn. Arch Dis Child Fetal Neonatal Ed 2003; 88:F6-10.

34) Anderson D, Ali K, Blanchette V, et al. Guidelines on the use of intravenous immune globulin for hematologic conditions. Transfus Med Rev. 2007;21(2 Suppl 1):S9-56.

35) Orange J, Hossny E, Weiler C, et al. Use of intravenous immunoglobulin in human disease: A review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol 2006;117(4 Suppl): S525-53.

36) Stasi R, Evangelista ML, Stipa E, et al. Idiopathic thrombocytopenic purpura: current concepts in pathophysiology and management. Thrombosis and Haemostasis 2008;99(1):4-13.

37) Amagai M, Ikeda S, Shimizu H, et al. A randomized, double-blind trial of intravenous immunoglobulin for pemphigus. J Am Acad Dermatol 2009; 60:595-602

38) Ahmed AR. Intravenous immunoglobulin therapy in the treatment of patients with pemphigus vulgaris unresponsive to conventional immunosuppressive treatment. J Am Acad Dermatol 2001; 45:679-90.

39) Hughes R, Bensa S, Willison H, Van den Bergh P, Comi G, Illa I, Nobile-Orazio E, van Doorn P, Dalakas M, Bojar M, Swan A; Inflammatory Neuropathy Cause and Treatment (INCAT) Group. Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy. Ann Neurol. 2001 Aug; 50(2):195-201.

40) Zinman L, Ng E, Bril V. IV immunoglobulin in patients with myasthenia gravis: a randomized controlled trial. Neurology. 2007 Mar 13;68(11):837-41.

41) Koski CL, Baumgarten M, Magder LS, et al.. Journal of the Neurological Sciences 2009; 277:1-8.

42) Sullivan KM, Storek J, Kopecky KJ, et al. A controlled trial of long-term administration of intravenous immunoglobulin to prevent late infection and chronic graft-vs.-host disease after marrow transplantation: clinical outcome and effect on subsequent immune recovery. Biol Blood Marrow Transplant 1996;2:44-53.

43) Alejandria MM, Lansang MA, Dans LF, Mantaring JB. Intravenous immunoglobulin for treating sepsis and septic shock. Cochrane Database Syst Rev 2002;CD001090.

44) American College of Obstetricians and Gynecologists (ACOG), Committee on Practice Bulletins -- Obstetrics. Thrombocytopenia in pregnancy. ACOG Practice Pattern No. 6. Washington, DC: ACOG; September 1999.

45) Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. MMWR 2000;49(No. RR-10):1-128.

46) Emerson GG, Herndon CN, Sreih AG. Thrombotic complications after intravenous immunoglobulin therapy in two patients. Pharmacotherapy. 2002;22:1638-1641.

47) Department of Health (London). Clinical Guidelines for Immunoglobulin Use: Update to Second Edition. August, 2011.

48) Provan, Drew, et al. “Clinical guidelines for immunoglobulin use.” Department of Health Publication, London (2008).

49) Sussman J, Farrugia ME, Maddison P, et al. Myasthenia gravis: Association of British Neurologists’ management guidelines. Pract Neurol 2015; 15: 199-206.

50) Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis-Executive Summary. Neurology. 2016 Jul 26; 87(4): 419-25.

51) Orange JS, Ballow M, Stiehm, et al. Use and interpretation of diagnostic vaccination in primary immunodeficiency: A working group report of the Basic and Clinical Immunology Interest Section of the American Academy of Allergy, Asthma & Immunology. J Allergy Clin Immunol Vol 130 (3).

52) Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 Evidence-based practice guidelines for immune thrombocytopenia. Blood April 2011; Vol 117 (16).

53) Jeffrey Modell Foundation Medical Advisory Board, 2013. 10 Warning Signs of Primary Immunodeficiency. Jeffrey Modell Foundation, New York, NY.

54) Bonilla FA, Khan DA, Ballas ZK, et al. Practice Parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol 2015 Nov;136(5):1186-205.e1-78.

55) Kuitwaard K, de Gelder J, Tio-Gillen AP, et al. Pharmacokinetics of intravenous immunoglobulin and outcome in Guillain-Barré syndrome. Ann Neurol. 2009;66(5):597.

56) Shehata N, Palda VA, Meyer RM, et al: The use of immunoglobulin therapy for patients undergoing solid organ transplantation: an evidence-based practice guideline. Transfus Med Rev 2010; 24 Suppl 1:S7-S27.

57) Jordan SC, Tyan D, Stablein D, et al: Evaluation of intravenous immunoglobulin as an agent to lower allosensitization and improve transplantation in highly sensitized adult patients with end-stage renal disease: report of the NIH IG02 trial. J Am Soc Nephrol 2004; 15(12):3256-3262.

58) Yuan XP, Wang CX, Gao W, et al: Kidney transplant in highly sensitized patients after desensitization with plasmapheresis and low-dose intravenous immunoglobulin. Exp Clin Transplant 2010; 8(2):130-135.

59) Jordan SC, Quartel AW, Czer LSC, et al: Posttransplant therapy using high-dose human immunoglobulin (intravenous gamma globulin) to control acute humoral rejection in renal and cardiac allograft recipients and potential mechanism of action. Transplantation 1998; 66(6):800-805.

60) Sullivan KM, Kopecky KJ, Jocom J, et al: Immunomodulatory and antimicrobial efficacy of intravenous immunoglobulin in bone marrow transplantation. N Engl J Med 1990; 323:705-712.

61) Bhatti AB, Gazali ZA. Recent Advances and Review on Treatment of Stiff Person Syndrome in Adults and Pediatric Patients. Cureus. 2015 Dec 22;7(12):e427

62) Tanimoto K, Nakano K, Kano S, et al. Classification criteria for polymyositis and dermatomyositis. J Rheumatol. 1995 Apr;22(4):668-74.

63) Kyriakides T, Angelini C, Schaefer J, et al. EFNS guidelines on the diagnostic approach to pauci- or asymptomatic hyperCKemia. Eur J Neurol. 2010 Jun 1;17(6):767-73.

64) Feliciani C, Joly P, Jonkman MF, et al. Management of bullous pemphigoid: the European Dermatology Forum consensus in collaboration with the European Academy of Dermatology and Venereology. Br J Dermatol. 2015 Apr;172(4):867-77.

65) Hertl M, Jedlickova H, Karpati S, et al. Pemphigus. S2 Guideline for diagnosis and treatment--guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV). J Eur Acad Dermatol Venereol. 2015 Mar;29(3):405-14.

66) Harman KE, Albert S, Black MM; British Association of Dermatologists. Guidelines for the management of pemphigus vulgaris. Br J Dermatol. 2003 Nov;149(5):926-37.

67) Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: A review of evidence. J Allergy Clin Immunol. 2017 Mar;139(3S):S1-S46.

68) Dantal J. Intravenous Immunoglobulins: In-Depth Review of Excipients and Acute Kidney Injury Risk. Am J Nephrol 2013;38:275-284.

69) Cahaba Government Benefit Administrators, LLC. Local Coverage Determination (LCD): Drugs and Biologicals: Immune Globulin Intravenous (IVIg) (L34256). Centers for Medicare & Medicaid Services, Inc. Updated on 09/19/2017 with effective date 10/1/2017. Accessed March 2018.

70) First Coast Service Options, Inc. Local Coverage Determination (LCD): Intravenous Immune Globulin (L34007). Centers for Medicare & Medicaid Services, Inc. Updated on 9/22/2017 with effective date 10/1/2017. Accessed March 2018.

71) Noridian Administrative Services, LLC. Local Coverage Determination (LCD): Immune Globulin Intravenous (IVIg) (L34074; L34314). Centers for Medicare & Medicaid Services, Inc. Updated on 11/12/2016 with effective date 10/1/2016. Accessed March 2018.

72) Novitas Solutions, Inc. Local Coverage Determination (LCD): Intravenous Immune Globulin (IVIG) (L35093). Centers for Medicare & Medicaid Services, Inc. Updated on 9/29/2017 with effective date 10/1/2017. Accessed March 2018.

73) Wisconsin Physicians Service Insurance Corporation. Local Coverage Determination (LCD): Immune Globulins (L34771). Centers for Medicare & Medicaid Services, Inc. Updated on 9/19/2017 with effective date 10/1/2017. Accessed March 2018.

74) CGS, Administrators, LLC. Local Coverage Determination (LCD): Intravenous Immune Globulin (L35891). Centers for Medicare & Medicaid Services, Inc. Updated on 3/30/2017 with effective date 1/1/2017. Accessed March 2018.

75) Palmetto GBA. Local Coverage Determination (LCD): Intravenous Immunoglobulin (IVIG) (L34580). Centers for Medicare & Medicaid Services, Inc. Updated on 9/1/2017 with effective date 10/1/2017. Accessed March 2018.

76) National Coverage Determination (NCD) for Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases (250.3). Centers for Medicare and Medicaid Services, Inc. Updated on 12/01/2015 with effective date 10/1/2015. Accessed March 2018.

77) National Government Services, Inc. Local Coverage Article for Intravenous Immune Globulin (IVIG) - Related to LCD L33394 (A52446). Centers for Medicare & Medicaid Services, Inc. Updated on 9/22/2017 with effective date 10/7/2017. Accessed March 2018.

78) Noridian Healthcare Solutions, LLC. Local Coverage Article for Intravenous Immune Globulin (IVIG)-NCD 250.3 – Related to LCD L34314, L34074 (A54641, A54643). Centers for Medicare & Medicaid Services, Inc. Updated on 1/18/2017 with effective date 11/7/2015. Accessed March 2018.

79) Noridian Healthcare Solutions, LLC. Local Coverage Article: Coverage of Intravenous Immune Globulin for Treatment of Primary Immune Deficiency Diseases in the Home – Medicare Benefit Policy Manual, Chapter 15, (A54660, A54662). Centers for Medicare & Medicaid Services, Inc. Updated 9/4/2015 with effective date 10/1/2015. Accessed March 2018.

80) Lewis RA. (2017). Chronic inflammatory demyelinating polyneuropathy: Etiology, clinical features, and diagnosis. *UpToDate.* Updated on July 18, 2017. Accessed March 2018.