

PHARMACY POLICY STATEMENT

Georgia Medicaid

DRUG NAME	Immune globulin: <u>Intravenous</u> : Bivigam, Carimune NF, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Privigen, and Thymoglobulin <u>Subcutaneous</u> : Cuvitru, Hizentra, and HyQvia
BILLING CODE	J1556-Bivigam; J1566-Carimune NF; J1572-Flebogamma DIF; J1569-Gammagard Liquid; J1566-Gammagard S/D; J1561-Gammaked; J1557-Gammaplex; J1561-Gamunex-C; J1568-Octagam; J1459-Privigen; J7511-Thymoglobulin; J3590-Cuvitru; J1559-Hizentra; J1575-HyQvia
BENEFIT TYPE	Medical
SITE OF SERVICE ALLOWED	Outpatient/Office/Home
COVERAGE REQUIREMENTS	Prior Authorization Required QUANTITY LIMIT – N/A
LIST OF DIAGNOSES CONSIDERED NOT MEDICALLY NECESSARY	Click Here

Immune Globulin (intravenous [IVIG]: Bivigam, Carimune NF, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Privigen and Thymoglobulin; subcutaneous [SCIG]: Cuvitru, Hizentra and HyQvia) is a product that will only be considered for coverage under the **medical** benefit when the following criteria are met:

Members must be clinically diagnosed with one of the following disease states and meet their individual criteria as stated. Limitations: SCIG are only indicated for primary humoral immunodeficiency.

AUTOIMMUNE BULLOUS DISEASE

For **initial** authorization:

1. Member has contraindications to, failure of (refractory to), or significant side effects from systemic corticosteroids or immunosuppressive treatment (e.g., azathioprine, cyclophosphamide, mycophenolate mofetil); AND
2. Member has dermatologic condition, as indicated by **one** or more of the following:
 - a) Bullous pemphigoid;
 - b) Epidermolysis bullosa acquisita;
 - c) Linear IgA bullous dermatosis;
 - d) Mucous membrane (cicatrical) pemphigoid;
 - e) Pemphigoid gestationis;
 - f) Pemphigus foliaceus;
 - g) Pemphigus vulgaris.
3. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease; AND

2. Documentation of titration to the minimum dose and frequency needed to maintain a sustained clinical effect is provided with chart notes.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

For **initial** authorization:

1. IVIG is prescribed for prophylaxis of bacterial infections; AND
2. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization, AND
3. Member has a pretreatment serum IgG level <500 mg/dL (Copy of laboratory report with pre-treatment serum IgG level must be provided with chart notes).
4. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 6 months.

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)

For **initial** authorization:

1. Member has moderate to severe functional disability; AND
2. Electrodiagnostic studies are consistent with multifocal demyelinating abnormalities (Pre-treatment electrodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS] provided with chart notes); AND
3. Member has elevated CSF protein (Pre-treatment cerebrospinal fluid (CSF) analysis when available).
4. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 3 months.

For **reauthorization**:

1. Member has significant improvement in disability and maintenance of improvement since initiation of IVIG therapy; AND
2. In those who are clinically stable and receiving long-term treatment (i.e., more than 1 year), the dose has been tapered and/or treatment withdrawn to determine whether continued treatment is necessary; AND
3. IVIG is being used at the lowest effective dose and frequency.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

DERMATOMYOSITIS OR POLYMYOSITIS

For **initial** authorization:

1. Diagnosis established by clinical features (e.g., proximal weakness, rash), elevated muscle enzyme levels, electrodiagnostic studies (EMG/NCS), and muscle biopsy (when available); supportive diagnostic tests include autoantibody testing and muscle imaging (e.g., MRI), AND
2. Standard first-line treatments (corticosteroids or immunosuppressants) have been tried but were unsuccessful or not tolerated; OR

3. Member is unable to receive standard first-line therapy because of a contraindication or other clinical reason.
4. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 3 months.

For **reauthorization**:

1. Member has significant improvement in disability and maintenance of improvement since initiation of IVIG therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

FETAL/NEONATAL ALLOIMMUNE THROMBOCYTOPENIA (F/NAIT)

For **initial** authorization:

1. Member is a newborn, and thrombocytopenia persists after transfusion of antigen-negative compatible platelet; OR
2. Member is pregnant and has diagnosis of F/NAIT with **one** or more of the following:
 - a) Family history of disease;
 - b) Platelet alloantibodies found on screening;
 - c) Previously affected pregnancy.
3. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

3. Medication will not be reauthorization for continuous use.

GUILLAIN-BARRE SYNDROME (GBS)

For **initial** authorization:

1. Physical mobility is severely affected such that member requires an aid to walk; AND
2. IVIG therapy will be initiated within 2 weeks of symptom onset.
3. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 2 months.

For **reauthorization**:

1. Medication will not be reauthorization for continuous use.

IDIOPATHIC THROMBOCYTOPENIC PURPURA (IMMUNE THROMBOCYTOPENIA)

For **initial** authorization:

1. Initial therapy (Member diagnosed with ITP within the past 3 months):
 - a) Children (< 18 years of age):
 - i) Significant bleeding symptoms (mucosal bleeding or other moderate/severe bleeding); OR
 - ii) High risk for bleeding* (see Appendix A); OR
 - iii) Rapid increase in platelets is required* (e.g., surgery or procedure);
 - b) Adults (\geq 18 years of age):
 - i) Platelet count < 30,000/mcL; OR
 - ii) Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding or rapid increase in platelets is required*; AND
 - iii) Corticosteroid therapy is contraindicated and IVIG will be used alone or IVIG will be used in combination with corticosteroid therapy.
2. Chronic/persistent ITP (\geq 3 months from diagnosis) or ITP unresponsive to first-line therapy (i.e., corticosteroids):
 - a) Platelet count < 30,000/mcL; OR
 - b) Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding* or rapid increase in platelets is required*; AND
 - c) Relapse after previous response to IVIG or inadequate response/intolerance/contraindication to corticosteroid or anti-D therapy.
3. Adults with refractory ITP after splenectomy:
 - a) Platelet count < 30,000/mcL; OR
 - b) Significant bleeding symptoms.
4. ITP in pregnant women: authorization through delivery may be granted to pregnant women with ITP if any **one** or more of the following:
 - a) Any bleeding during pregnancy;
 - b) Platelet count less than 10,000/mm³ (10x10⁹/L) at any time during pregnancy;
 - c) Platelet count between 10,000/mm³ (10x10⁹/L) and 30,000/mm³ (30x10⁹/L) in second or third trimester.
5. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.
* The member's risk factor(s) for bleeding (see Appendix A) or reason requiring a rapid increase in platelets must be provided.

If member meets all the requirements listed above, the medication will be approved for 1 months for initial therapy, or for 6 months for chronic/persistent ITP or for adults with refractory ITP after splenectomy.

For **reauthorization**:

1. Medication will not be reauthorization for continuous use.

KAWASAKI SYNDROME

For **initial** authorization:

1. Pediatric member with Kawasaki syndrome.
2. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 1 months.

For **reauthorization**:

1. Medication will not be reauthorization for continuous use.

KIDNEY TRANSPLANT

For **initial** authorization:

1. Medication is used for prophylaxis or treatment of acute kidney rejection in conjunction with concomitant immunosuppression (e.g., cyclosporine, mycophenolate mofetil, and corticosteroids).
2. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 12 months.

LAMBERT-EATON MYASTHENIC SYNDROME (LEMS)

For **initial** authorization:

1. Member has diagnosis of LEMS and steroids and other immunosuppressive treatments do not control symptoms.
2. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 12 months.

For **reauthorization**:

1. Member has significant improvement in disability and maintenance of improvement since initiation of IVIG therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

MULTIFOCAL MOTOR NEUROPATHY (MMN)

For **initial** authorization:

1. Member has weakness without objective sensory loss in 2 or more nerves; AND
2. Electrodiagnostic studies (electromyography [EMG]) are consistent with motor conduction block; AND
3. Normal sensory nerve conduction studies provided in chart notes.
4. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 3 months.

For **reauthorization**:

1. Member has significant improvement in disability and maintenance of improvement since initiation of IVIG therapy.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

MYASTHENIA GRAVIS

For **initial** authorization:

1. Member has Neonatal Myasthenia Gravis; OR
 2. Member is adult and has worsening weakness including an increase in any of the following symptoms: diplopia, ptosis, blurred vision, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), difficulty chewing, impaired respiratory status, fatigue, and limb weakness. Acute exacerbations include more severe swallowing difficulties and/or respiratory failure; OR
 3. Member is adult and medication used for pre-operative management (e.g., prior to thymectomy).
 4. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.
- Note: Immune Globulin must not be used for maintenance therapy.

If member meets all the requirements listed above, the medication will be approved for 1 month.

For **reauthorization**:

1. Medication will not be reauthorization for continuous use.

PARVOVIRUS B19-INDUCED PURE RED CELL APLASIA (PRCA)

For **initial** authorization:

1. Member has parvovirus B19-induced PRCA.
2. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Medication will not be reauthorization for continuous use.

PRIMARY IMMUNODEFICIENCY

For **initial** authorization:

Member must have **one** of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (e.g., X-linked or autosomal recessive agammaglobulinemia):
 - a) Diagnosis confirmed by genetic or molecular testing; OR
 - b) Pretreatment IgG level < 200 mg/dL; OR
 - c) Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only);
2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency):
 - a) Diagnosis confirmed by genetic or molecular testing (if applicable); AND
 - b) History of recurrent bacterial infections (e.g., pneumonia, otitis media, sinusitis, sepsis, gastrointestinal); AND
 - c) Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix B);
3. Common variable immunodeficiency (CVID):
 - a) Member is 4 years of age or older; AND
 - b) Other causes of immune deficiency have been excluded (e.g., drug induced, genetic disorders, infectious diseases such as HIV, malignancy); AND
 - c) Member's pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age; AND
 - d) Member has a history of recurrent bacterial infections; AND
 - e) Member has impaired antibody response to pneumococcal polysaccharide vaccine documented in chart notes (see Appendix B);
4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency:
 - a) Member has a history of recurrent bacterial infections; AND
 - b) Member has impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix B)
 - c) Member has ANY of the following pre-treatment laboratory findings:
 - i) Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age;
 - ii) Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels;
 - iii) Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels;
 - iv) 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;
 - v) Specific antibody deficiency: normal IgG, IgA and IgM levels.
5. Other predominant antibody deficiency disorders must meet a), b), and c) i) in section 4. above.
6. Other combined immunodeficiency must meet criteria in section 2. above.
7. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.
Note: Gammagard Liquid, Gamunex-C, and Gammaked may be administered intravenously or subcutaneously for primary immunodeficiency.

If member meets all the requirements listed above, the medication will be approved for 12 months.

For **reauthorization**:

1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of IVIG and consider a dose adjustment (when appropriate).

If member meets all the reauthorization requirements above, the medication will be approved for an additional 12 months.

PROPHYLAXIS OF BACTERIAL INFECTIONS IN BMT/HSCT RECIPIENTS

For **initial** authorization:

1. Member is BMT/HSCT recipient; AND
2. IVIG is prescribed for prophylaxis of bacterial infections; AND
3. Either of the following:
 - a) IVIG is requested within the first 100 days post-transplant; OR
 - b) Member has a pretreatment serum IgG < 400 mg/dL.
4. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy and documented in chart notes.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 6 months.

PROPHYLAXIS OF BACTERIAL INFECTIONS IN HIV-INFECTED PEDIATRIC PATIENTS

For **initial** authorization:

1. Member with HIV infection and is 18 years of age or younger; AND
2. IVIG is prescribed for **primary** prophylaxis of bacterial infections and pretreatment serum IgG < 400 mg/dL; OR
3. IVIG is prescribed for **secondary** prophylaxis of bacterial infections with ALL of the following:
 - a) History of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period);
 - b) Member is not able to take combination antiretroviral therapy;
 - c) Antibiotic prophylaxis was tried but was not effective (e.g., trimethoprim-sulfamethoxazole).
4. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy and documented in chart notes.

If member meets all the reauthorization requirements above, the medication will be approved for an additional 6 months.

STIFF-PERSON SYNDROME

For **initial** authorization:

1. Medication is used for treatment of stiff-person syndrome in members who have experienced an inadequate response or intolerance, or have a contraindication to first-line therapy such as a benzodiazepine (e.g., diazepam) and/or baclofen.
2. **Dosage allowed:** Please see dosage and administration information in individual drug package insert.

If member meets all the requirements listed above, the medication will be approved for 6 months.

For **reauthorization**:

1. Medication will not be reauthorization for continuous use.

CareSource considers Immune Globulin (intravenous [IVIG]: Bivigam, Carimune NF, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Privigen, Thymoglobulin; subcutaneous [SCIG]: Cuvitru, Hizentra, HyQvia) not medically necessary for the treatment of the following disease states based on a lack of robust clinical controlled trials showing superior efficacy compared to currently available treatments:

Acquired hemophilia	Myocarditis, acute
Adrenoleukodystrophy	Neonatal sepsis, prevention
Alzheimer's disease	Neonatal sepsis, treatment
Amyotrophic lateral sclerosis (ALS)	Ocular myasthenia
Antiphospholipid antibody syndrome (APS) in pregnancy	Paraneoplastic cerebellar degeneration, sensory neuropathy, or encephalopathy
Asthma, non-steroid dependent	Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)
Atopic dermatitis	POEMS syndrome
Autism spectrum disorders	Postinfectious cerebellar ataxia
Autoimmune liver disease	Postoperative sepsis
Autoimmune neutropenia	Pseudomembranous colitis
Campylobacter species-induced enteritis	Respiratory syncytial virus (RSV) lower respiratory tract infection
Cerebral infarctions with antiphospholipid antibodies	Rheumatic fever, acute
Chronic fatigue syndrome	Sjogren's syndrome
Demyelinative brain stem encephalitis	Spontaneous recurrent abortions, prevention
Demyelinating neuropathy associated with monoclonal IgM	Systemic lupus erythematosus
Dilated cardiomyopathy	Urticaria, chronic
HIV infection or prophylaxis	Vasculitides and antineutrophil antibody syndromes
HTLV-1-associated myelopathy	Routine prophylaxis of Measles, Varicella, and Rubella
Idiopathic dysautonomia, acute	Treatment of Measles, Varicella, and Rubella
Inclusion body myositis	
Isolated IgA deficiency	
Isolated IgG4 deficiency	
Lumbosacral or brachial plexitis	

DATE	ACTION/DESCRIPTION
11/15/2017	New policy for Immune Globulin created. Diagnoses associate with impatient life-threatening therapies were removed. Diagnoses of CIDP, Dermatomyositis or Polymyositis, ITP, MMN, Primary Immunodeficiency and Stiff-Person Syndrome got criteria expanded. Diagnosis of Acquired red cell aplasia was revised to PRCA with criteria. Length of coverage and reauthorization length were added.

References:

1. Bivigam [package insert]. Boca Raton, FL: Biotest Pharmaceuticals Corporation; October 2013.
2. Carimune NF [package insert]. Kankakee, IL: CSL Behring LLC; September 2013.
3. Flebogamma 10% DIF [package insert]. Los Angeles, CA: Grifols Biologicals, Inc.; January 2016.
4. Flebogamma 5% DIF [package insert]. Los Angeles, CA: Grifols Biologicals, Inc.; April 2015.
5. Gammagard Liquid [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; April 2014.
6. Gammagard S/D [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; April 2014.
7. Gammagard S/D IgA less than 1 mcg/mL [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; September 2013.
8. Gammaked [package insert]. Fort Lee, NJ: Kedrion Biopharma, Inc.; September 2013.
9. Gammaplex [package insert]. Hertfordshire, United Kingdom: Bio Products Laboratory; July 2015.
10. Gamunex-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; July 2014.
11. Octagam 10% [package insert]. Hoboken, NJ: Octapharma USA, Inc.; April 2015.
12. Octagam 5% [package insert]. Hoboken, NJ: Octapharma USA, Inc.; October 2014.
13. Privigen [package insert]. Kankakee, IL: CSL Behring LLC; November 2013.
14. Cuvitru [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2016.
15. Hizentra [package insert]. Kankakee, IL: CSL Behring LLC; October 2016.
16. HyQvia [package insert]. Westlake Village, CA: Baxter Healthcare Corporation; September 2016.
17. Thymoglobulin [package insert]. Cambridge, MA: Genzyme Corporation; April 2017.
18. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at <http://www.micromedexsolutions.com> [available with subscription]. Accessed November 1, 2017.
19. AHFS Drug Information. <http://online.lexi.com/lco>. Accessed November 1, 2017.
20. Amagai M, Ikeda S, Shimizu H, et al. A randomized double-blind trial of intravenous immunoglobulin for pemphigus. *J Am Acad Dermatol* 2009; 60(4):595-603.
21. Kirtschig G, Middleton P, Bennett C, Murrell DF, Wojnarowska F, Khumalo NP. Interventions for bullous pemphigoid. *Cochrane Database of Systematic Reviews* 2010, Issue 10. Art. No.: CD002292.
22. Orange JS, Hossny EM, Weiler CR, 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;417(4 Suppl):S525-553.
23. Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/oi_guidelines_pediatrics.pdf. Accessed November 8, 2017.
24. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009;15(10):1143-1238.
25. Feasby T, Banwell B, Bernstead T, et al. Guidelines on the use of intravenous immune globulin for neurologic conditions. *Transfus Med Rev.* 2007;21(2):S57-S107.
26. Donofrio PD, Berger A, Brannagan TH 3rd, 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(5):890-900.
27. Elovaara I, Apostolski S, van Doorn P, 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. *Eur J Neurol.* 2008;15(9):893-908.
28. 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;78(13):1009-1015.
29. Anderson D, Kaiser A, Blanchette V, et al. Guidelines on the use of intravenous immune globulin for hematologic conditions. *Transfus Med Rev.* 2007;21(2):S9-S56.
30. Picard C, Al-Herz W, Bousfiha A, et al. Primary immunodeficiency diseases: an update on the classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency. *J Clin Immunol.* 2015; 35(8):696-726.

31. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol*. 2015;136(5):1186-205.e1-78.
32. Orange JS, Ballou M, Stiehm ER, 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 and Immunology. *J Allergy Clin Immunol*. 2012;130:S1-S24.
33. Ameratunga R, Woon ST, Gillis D, Koopmans W, Steele R. New diagnostic criteria for common variable immune deficiency (CVID), which may assist with decisions to treat with intravenous or subcutaneous immunoglobulin. *Clin Exp Immunol*. 2013;174(2):203-11.
34. Immune Deficiency Foundation. About primary immunodeficiencies. Specific disease types. <http://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/>. Accessed November 8, 2017.
35. Immune Deficiency Foundation. Diagnostic and Clinical Care Guidelines for Primary Immunodeficiency Diseases. 3rd edition. Towson, MD: Immune Deficiency Foundation; 2015. <http://primaryimmune.org/wp-content/uploads/2015/03/2015-Diagnostic-and-Clinical-Care-Guidelines-for-PI.pdf>. Accessed November 8, 2017.
36. The NCCN Clinical Practice Guidelines in Oncology® B-cell Lymphomas (Version 2.2017). © 2017 National Comprehensive Cancer Network, Inc. <http://www.nccn.org>. Accessed November 8, 2017.
37. 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 and the Peripheral Nerve Society - first revision. *Eur J Neurol*. 2010;17(3):356-363.
38. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Societies guideline on management of multifocal motor neuropathy. *J Peripher Nerv Syst*. 2010;15:295-301.
39. Olney RK, Lewis RA, Putnam TD, Campellone JV. Consensus criteria for the diagnosis of multifocal motor neuropathy. *Muscle Nerve*. 2003;27:117-121.
40. Dalakas M. Inflammatory muscle diseases. *N Engl J Med*. 2015;372(18):1734-1747.
41. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood*. 2011;117(16):4190-4207.
42. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood*. 2010;115(2):168-186.
43. Shearer WT, Dunn E, Notarangelo LD, et al. Establishing diagnostic criteria for severe combined immunodeficiency disease (SCID), leaky SCID, and Omenn syndrome: the Primary Immune Deficiency Treatment Consortium experience. *J Allergy Clin Immunol*. 2014;133(4):1092.

Effective date: 11/29/2017

Revised date: 11/14/2017

APPENDICES

Appendix A: Examples of Risk Factors for Bleeding (not all inclusive)

- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (e.g., peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession or lifestyle predisposes patient to trauma (e.g., construction worker, fireman, professional athlete)

Appendix B: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine

- Age 6 years and older: antibody levels are not ≥ 1.3 mcg/mL for at least 70% of serotypes in the vaccine
- Age 2 to 5 years: antibody levels are not ≥ 1.3 mcg/mL for at least 50% of serotypes in the vaccine
- Not established for children less than 2 years of age