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## SPECIALTY GUIDELINE MANAGEMENT

### Subcutaneous Immune Globulin (SCIG): Hizentra®, HyQvia®, Cutaquig®, Cuvitru™ and Xembify®

#### POLICY

##### I. INDICATIONS

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

##### A. FDA-Approved Indications

1. Cutaquig (Immune Globulin Subcutaneous [Human] - hipp, 16.5% Solution)  
Cutaquig is indicated as replacement therapy for primary humoral immunodeficiency (PI) in adults.
2. Cuvitru (Immune Globulin Subcutaneous [Human], 20% Solution)  
Cuvitru is indicated as replacement therapy for primary humoral immunodeficiency in adult and pediatric patients two years of age and older.
3. Hizentra (Immune Globulin Subcutaneous [Human], 20% Liquid)
  - a. Hizentra is indicated as replacement therapy for primary humoral immunodeficiency in adults and pediatric patients 2 years of age and older.
  - b. Hizentra is indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment.  
*Limitations of Use:*  
Hizentra maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Maintenance therapy beyond these periods should be individualized based upon the patient's response and need for continued therapy.
4. HyQvia (Immune Globulin Infusion 10% [Human] with Recombinant Human Hyaluronidase)  
HyQvia is indicated for the treatment of primary immunodeficiency in adults.  
*Limitation of Use:* Safety and efficacy of chronic use of recombinant human hyaluronidase in HyQvia have not been established in conditions other than primary immunodeficiency.
5. Xembify (Immune Globulin Subcutaneous [Human] – klhw, 20% Solution)  
Xembify is indicated for treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older.

##### B. Compendial Uses

1. Idiopathic thrombocytopenic purpura (ITP)
2. Multifocal motor neuropathy
3. Kawasaki syndrome
4. B-cell chronic lymphocytic leukemia (CLL)
5. Prophylaxis of bacterial infections in pediatric human immunodeficiency virus (HIV) infection
6. Prophylaxis of bacterial infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
7. Dermatomyositis
8. Polymyositis

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9. Myasthenia gravis
10. Guillain-Barré syndrome
11. Lambert-Eaton myasthenic syndrome
12. Fetal/neonatal alloimmune thrombocytopenia
13. Parvovirus B19-induced pure red cell aplasia
14. Stiff-person syndrome
15. Management of immune checkpoint inhibitor-related nervous system adverse events
16. Acquired red cell aplasia
17. Acute disseminated encephalomyelitis
18. Autoimmune mucocutaneous blistering diseases
19. Autoimmune hemolytic anemia
20. Autoimmune neutropenia
21. Birdshot retinochoroidopathy
22. BK virus associated nephropathy
23. Churg-Strauss Syndrome
24. Enteroviral meningoencephalitis
25. Hematophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
26. Hemolytic disease of newborn
27. HIV-associated thrombocytopenia
28. Hyperimmunoblobulinemia E Syndrome
29. Hypogammaglobulinemia from chimeric antigen receptor T (CAR-T) therapy
30. Multiple myeloma
31. Neonatal hemochromatosis, prophylaxis
32. Opsoclonus-myooclonus
33. Paraneoplastic opsonus-myooclonus ataxia associated with neuroblastoma
34. Post-transfusion purpura
35. Rasmussen encephalitis
36. Renal transplantation from a live donor with ABO incompatibility or positive cross match
37. Secondary immunosuppression associated with major surgery, hematological malignancy, major burns, and collagen-vascular diseases
38. Solid organ transplantation, for allosensitized members
39. Toxic epidermal necrolysis and Stevens-Johnson syndrome
40. Toxic shock syndrome
41. Systemic lupus erythematosus (SLE)
42. Toxic necrotizing fasciitis due to group A streptococcus

All other indications are considered experimental/investigational and are not a covered benefit.

## II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

- A. Primary immunodeficiency
  1. Diagnostic test results (when applicable)
    - a. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
    - b. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination *Streptococcus pneumoniae* antibody titers)
    - c. Pertinent genetic or molecular testing in members with a known genetic disorder
    - d. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry
  2. IgG trough level for those continuing with IVIG therapy
- B. Myasthenia gravis

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1. Clinical records describing standard treatments tried and failed
- C. Secondary hypogammaglobulinemia (CLL, HIV, BMT/HSCT recipients, surgery, malignancy, burns, collagen-vascular disease)
  1. Copy of laboratory report with pre-treatment serum IgG level (when applicable)
- D. Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)
  1. Pre-treatment electrodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS])
  2. For CIDP, pre-treatment cerebrospinal fluid (CSF) analysis (when available)
- E. Dermatomyositis and polymyositis
  1. Pre-treatment electrodiagnostic studies (EMG/NCS)
  2. Pre-treatment muscle biopsy report (when available)
  3. Clinical records describing standard treatments tried and failed
- F. Lambert-Eaton Myasthenic Syndrome (LEMS)
  1. Neurophysiology studies (e.g., electromyography) (when applicable)
  2. A positive anti- P/Q type voltage-gated calcium channel antibody test (when applicable)
- G. Idiopathic thrombocytopenic purpura
  1. Laboratory report with pre-treatment/current platelet count
  2. Chronic/persistent ITP: copy of medical records supporting trial and failure with corticosteroid or anti-D therapy (unless contraindicated)
- H. Parvovirus B19-indicated Pure Red Cell Aplasia (PRCA)
  1. Copy of test result confirming presence of parvovirus B19
- I. Stiff-person syndrome
  1. Anti-glutamic acid decarboxylase (GAD) antibody testing results
  2. Clinical records describing standard treatments tried and failed
- J. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus
  1. Documented presence of fasciitis (when applicable)
  2. Microbiological data (culture or Gram stain)

### III. CRITERIA FOR INITIAL APPROVAL

#### A. Primary Immunodeficiency

Initial authorization of 6 months may be granted for members with any of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, 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 (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
  - c. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
3. Common variable immunodeficiency (CVID)
  - a. Age 4 years or older
  - b. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy)
  - c. Pretreatment IgG level < 500 mg/dL or  $\geq 2$  SD below the mean for age
  - d. History of recurrent bacterial infections

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- e. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
- 4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency
  - a. History of recurrent bacterial infections
  - b. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
  - c. Any of the following pre-treatment laboratory findings:
    - i. Hypogammaglobulinemia: IgG < 500 mg/dL or  $\geq 2$  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  $\geq 2$  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.

Re-authorization of 6 months may be granted when the following criteria are met:

- 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).

#### **B. Myasthenia Gravis**

- 1. Authorization of 1 month may be granted to members who are prescribed IVIG for worsening weakness, acute exacerbation, or in preparation for surgery.
  - a. Worsening weakness includes 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
  - b. Pre-operative management (eg, prior to thymectomy)
- 2. Authorization of 6 months may be granted to members with refractory myasthenia gravis who have tried and failed 2 or more of standard therapies (eg, corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, rituximab).

#### **C. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)**

- 1. Initial authorization of 3 months may be granted when the following criteria are met:
  - a. Disease course is progressive or relapsing/remitting for 2 months or longer
  - b. Moderate to severe functional disability
  - c. The diagnosis was confirmed by electrodiagnostic studies and the evaluation of cerebrospinal fluid (CSF)
- 2. Re-authorization of 6 months may be granted when the following criteria are met:
  - a. Significant improvement in disability and maintenance of improvement since initiation of IVIG therapy
  - b. IVIG is being used at the lowest effective dose and frequency

#### **D. Dermatomyositis or Polymyositis**

- 1. Initial authorization of 3 months may be granted when the following criteria are met:
  - a. Member has at least 4 of the following:
    - i. Proximal muscle weakness (upper or lower extremity and trunk)
    - ii. Elevated serum creatine kinase (CK) or aldolase level

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- iii. Muscle pain on grasping or spontaneous pain
  - iv. Myogenic changes on EMG (short-duration, polyphasic motor unit potentials with spontaneous fibrillation potentials)
  - v. Positive anti-Jo-1 (histadyl tRNA synthetase) antibody
  - vi. Non-destructive arthritis or arthralgias
  - vii. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated ESR of more than 20 mm/h by the Westergren method,
  - viii. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen), and
  - b. Standard first-line treatments (corticosteroids) and second-line treatments (immunosuppressants) have been tried but were unsuccessful or not tolerated, or
  - c. Member is unable to receive standard first-line and second-line therapy because of a contraindication or other clinical reason.
2. Re-authorization of 6 months may be granted when the following criterion is met:
- a. Significant improvement in disability and maintenance of improvement since initiation of IVIG therapy

**E. Idiopathic Thrombocytopenic Purpura (Immune Thrombocytopenia)**

- 1. Newly diagnosed ITP (diagnosed within the past 3 months) or initial therapy: authorization of 1 month may be granted when the following criteria are met
  - 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 B), or
    - iii. Rapid increase in platelets is required\* (eg, surgery or procedure)
  - b. Adults (≥ 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 (≥ 3 months from diagnosis) or ITP unresponsive to first-line therapy: authorization of 6 months may be granted when the following criteria are met:
  - 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: authorization of 6 months may be granted when either of the following criteria is met:
  - 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.

\* The member's risk factor(s) for bleeding (see Appendix B) or reason requiring a rapid increase in platelets must be provided.

**F. B-cell Chronic Lymphocytic Leukemia (CLL)**

- 1. Initial authorization of 6 months may be granted when the following criteria are met:
  - a. IVIG is prescribed for prophylaxis of bacterial infections.

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- b. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization.
- c. Member has a pretreatment serum IgG level <500 mg/dL.
- 2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

**G. Prophylaxis of Bacterial Infections in HIV-Infected Pediatric Patients**

- 1. Initial authorization of 6 months may be granted to pediatric members with HIV infection when any of the following criteria are met:
  - a. IVIG is prescribed for primary prophylaxis of bacterial infections and pretreatment serum IgG < 400 mg/dL, or
  - b. IVIG is prescribed for secondary prophylaxis of bacterial infections for members with a history of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period), or
  - c. Member has failed to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine, or
  - d. Member lives in an area where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live, or
  - e. Member has been exposed to measles and request is for a single dose, or
  - f. Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy
- 2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

**H. Prophylaxis of Bacterial Infections in BMT/HSCT Recipients**

- 1. Initial authorization of 6 months may be granted to members who are BMT/HSCT recipients when the following criteria are met:
  - a. IVIG is prescribed for prophylaxis of bacterial infections.
  - b. Either of the following:
    - i. IVIG is requested within the first 100 days post-transplant.
    - ii. Member has a pretreatment serum IgG < 400 mg/dL.
- 2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

**I. Multifocal Motor Neuropathy (MMN)**

- 1. Initial authorization of 3 months may be granted when the following criteria are met:
  - a. Member experienced progressive, multifocal, asymmetrical weakness without objective sensory loss in 2 or more nerves for at least 1 month
  - b. The diagnosis was confirmed by electrodiagnostic studies
- 2. Re-authorization of 6 months may be granted when significant improvement in disability and maintenance of improvement have occurred since initiation of IVIG therapy

**J. Guillain-Barre Syndrome (GBS)**

Authorization of 2 months total may be granted for GBS when the following criteria are met:

- 1. Member has severe disease with significant weakness (eg inability to stand or walk without aid, respiratory weakness)
- 2. Onset of neurologic symptoms occurred less than 4 weeks from the anticipated start of therapy

**K. Lambert-Eaton Myasthenic Syndrome (LEMS)**

- 1. Initial authorization of 6 months may be granted for LEMS when the following criteria are met:
  - a. Diagnosis has been confirmed by either of the following:
    - i. Neurophysiology studies (e.g., electromyography)

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- ii. A positive anti- P/Q type voltage-gated calcium channel antibody test
    - b. Anticholinesterases (eg pyridostigmine) and amifampridine (eg 3,4-diaminopyridine phosphate, Firdapse) have been tried but were unsuccessful or not tolerated
    - c. Weakness is severe or there is difficulty with venous access for plasmapheresis
  - 2. Re-authorization of 6 months may be granted when member is responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).
- L. Kawasaki Syndrome**  
Authorization of 1 month may be granted for pediatric members with Kawasaki syndrome.
- M. Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)**  
Authorization of 6 months may be granted for treatment of F/NAIT.
- N. Parvovirus B19-induced Pure Red Cell Aplasia (PRCA)**  
Authorization of 6 months may be granted for severe, refractory anemia associated with bone marrow suppression, with parvovirus B19 viremia.
- O. Stiff-person Syndrome**  
Authorization of 6 months may be granted for stiff-person syndrome when the following criteria are met:
- 1. Diagnosis has been confirmed by anti-glutamic acid decarboxylase (GAD) antibody testing
  - 2. Member had an inadequate response to first-line treatment (benzodiazepines and/or baclofen)
- P. Management of immune checkpoint inhibitor-related nervous system adverse events**  
Authorization of 1 month may be granted for management of immune checkpoint-inhibitor toxicities when all of the following criteria are met:
- 1. Member has experienced a moderate or severe adverse event to a PD-1 or PD-L1 inhibitor (eg, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab)
  - 2. The offending medication has been held or discontinued
  - 3. Member experienced one or more of the following nervous system adverse events: pneumonitis, myasthenia gravis, peripheral neuropathy, encephalitis, transverse myelitis, or severe inflammatory arthritis
- Q. Acquired Red Cell Aplasia**  
Authorization of 6 months may be granted for acquired red cell aplasia.
- R. Acute Disseminated Encephalomyelitis**  
Authorization of 6 months may be granted for acute disseminated encephalomyelitis in members who have had an insufficient response to intravenous corticosteroid treatment.
- S. Autoimmune Mucocutaneous Blistering Disease**  
Authorization of 6 months may be granted for autoimmune mucocutaneous blistering disease (includes pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa aquisita) when the following criteria are met:
- 1. Diagnosis has been proven by biopsy and confirmed by pathology report, and
  - 2. Condition is rapidly progressing, extensive or debilitating, and
  - 3. Member has failed or experienced significant complications (eg diabetes, steroid-induced osteoporosis) from standard treatment (corticosteroids, immunosuppressive agents).
- T. Autoimmune Hemolytic Anemia**  
Authorization of 6 months may be granted for warm-type autoimmune hemolytic anemia in members who do not respond or have a contraindication to corticosteroids or splenectomy.

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- U. Autoimmune Neutropenia**  
Authorization of 6 months may be granted for autoimmune neutropenia where treatment with G-CSF (granulocyte colony stimulating factor) is not appropriate.
- V. Birdshot Retinochoroidopathy**  
Authorization of 6 months may be granted for birdshot (vitiliginous) retinochoroidopathy that is not responsive to immunosuppressives (eg corticosteroids, cyclosporine).
- W. BK Virus Associated Nephropathy**  
Authorization of 6 months may be granted for BK virus associated nephropathy.
- X. Churg-Strauss Syndrome**  
Authorization of 6 months may be granted for severe, active Churg-Strauss syndrome as adjunctive therapy for members who have experienced failure, intolerance, or are contraindicated to other interventions.
- Y. Enteroviral Meningoencephalitis**  
Authorization of 6 months may be granted for severe cases of enteroviral meningoencephalitis.
- Z. Hematophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS)**  
Authorization of 6 months may be granted for treatment of hypogammaglobulinemia in HLH or MAS when total IgG is less than 400 mg/dL or two standard deviations below the mean for age.
- AA. Hemolytic Disease of Newborn**  
Authorization of 6 months may be granted for isoimmune hemolytic disease in neonates.
- BB. HIV-associated Thrombocytopenia**  
Authorization of 6 months may be granted for HIV-associated thrombocytopenia when the following criteria are met:
  1. Pediatric members with IgG < 400 mg/dL and has one of the following:
    - a. 2 or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent, or
    - b. Received 2 doses or measles vaccine and lives in a region with a high prevalence or measles, or
    - c. HIV-associated thrombocytopenia despite anti-retroviral therapy, or
    - d. Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy, or
    - e. T4 cell count  $\geq 200/\text{mm}^3$
  2. Adult members with significant bleeding, platelet count < 20,000/mcL, and failure of RhIG in Rh-positive patients
- CC. Hyperimmunoglobulinemia E Syndrome**  
Authorization of 6 months may be granted to treat severe eczema in hyperimmunoglobulinemia E syndrome.
- DD. Hypogammaglobulinemia from CAR-T therapy**  
Authorization of 6 months may be granted for members with IgG < 400 mg/dL receiving treatment with CAR-T therapy (tisagenlecleucel [Kymriah] or axicabtagene ciloleucel [Yescarta]).
- EE. Multiple Myeloma**



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Authorization of 6 months may be granted for multiple myeloma in members who have recurrent, serious infections despite the use of prophylactic antibiotics.

**FF. Neonatal Hemochromatosis**

Authorization of 6 months may be granted for prophylaxis in members who are pregnant with a history of pregnancy ending in documented neonatal hemochromatosis.

**GG. Opsoclonus-myooclonus**

Authorization of 6 months may be granted for treatment of either of the following:

1. Paraneoplastic opsoclonus-myooclonus-ataxia associated with neuroblastoma
2. Refractory opsoclonus-myooclonus, as last-resort treatment

**HH. Post-transfusion Purpura**

Authorization of 1 month may be granted for post-transfusion purpura.

**II. Rasmussen Encephalitis**

Authorization of 6 months may be granted for Rasmussen encephalitis in members whose symptoms do not improve with anti-epileptic drugs and corticosteroids.

**JJ. Renal Transplantation**

Authorization of 6 months may be granted for a member undergoing renal transplantation from a live donor with ABO incompatibility or positive cross match.

**KK. Secondary Immunosuppression Associated with Major Surgery, Hematological Malignancy, Major Burns, and Collagen-Vascular Diseases**

Authorization of 6 months may be granted to prevent or modify recurrent bacterial or viral infections in members with secondary immunosuppression (IgG < 400 mg/dL) associated with major surgery, hematological malignancy, extensive burns, or collagen-vascular disease.

**LL. Solid Organ Transplantation**

Authorization of 6 months may be granted for solid organ transplantation for allosensitized members.

**MM. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome**

Authorization of 1 month may be granted for severe cases of toxic epidermal necrolysis or Stevens-Johnson syndrome.

**NN. Toxic Shock Syndrome**

Authorization of 1 month may be granted for staphylococcal or streptococcal toxic shock syndrome when the infection is refractory to several hours of aggressive therapy, an undrainable focus is present, or the member has persistent oliguria with pulmonary edema.

**OO. Systemic Lupus Erythematosus**

Authorization of 6 months may be granted for severe, active SLE in members who have experienced inadequate response, intolerance or have a contraindication to first and second line therapies.

**PP. Toxic Necrotizing Fasciitis Due To Group A Streptococcus**

Authorization of 1 month may be granted for members with fasciitis due to invasive streptococcal infection.

**IV. CONTINUATION OF THERAPY**

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Authorization may be granted for continuation of therapy when either the following criteria is met:

- A. For conditions with reauthorization criteria listed under section III: Members who are currently receiving IVIG therapy must meet the applicable reauthorization criteria for the member's condition.
- B. For all other conditions, all members (including new members) must meet initial authorization criteria.

## V. APPENDICES

### Appendix A: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine

- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

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

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

## VI. REFERENCES

1. Cutaquig [package insert]. Hoboken, NJ: Octapharma USA Inc.; December 2018.
2. Cuvitru [package insert]. Lexington, MA: Baxalta US Inc.; February 2019.
3. Hizentra [package insert]. Kankakee, IL: CSL Behring LLC; March 2018.
4. HyQvia [package insert]. Lexington, MA: Baxalta US Inc.; January 2019.
5. Xembify [package insert]. Research Triangle Park, NC: Grifols Therapeutics LLC; July 2019.
6. Asceniv [package insert]. Boca Raton, FL: ADMA Biologics; April 2019.
7. Bivigam [package insert]. Boca Raton, FL: Biotest Pharmaceuticals Corporation; January 2017.
8. Carimune NF [package insert]. Kankakee, IL: CSL Behring LLC; November 2016.
9. Flebogamma 10% DIF [package insert]. Los Angeles, CA: Grifols Biologicals, Inc.; July 2017.
10. Flebogamma 5% DIF [package insert]. Los Angeles, CA: Grifols Biologicals, Inc.; July 2017.
11. Gammagard Liquid [package insert]. Westlake Village, CA: Baxalta US Inc.; June 2016.
12. Gammagard S/D [package insert]. Lexington, MA: Baxalta US Inc.; August 2017.
13. Gammagard S/D IgA less than 1 mcg/mL [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2016.
14. Gammaked [package insert]. Research Triangle Park, NC: Grifols Therapeutics LLC; June 2018.
15. Gammplex 5% [package insert]. Hertfordshire, United Kingdom: Bio Products Laboratory; December 2016.
16. Gammplex 10% [package insert]. Hertfordshire, United Kingdom: Bio Products Laboratory; April 2018.
17. Gamunex-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; June 2018.
18. Octagam 10% [package insert]. Hoboken, NJ: Octapharma USA, Inc.; April 2015.
19. Octagam 5% [package insert]. Hoboken, NJ: Octapharma USA, Inc.; October 2014.
20. Panzyga [package insert]. Hoboken, NJ: Octapharma USA.; January 2019.
21. Privilgen [package insert]. Kankakee, IL: CSL Behring LLC; September 2017.
22. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at <http://www.micromedexsolutions.com> [available with subscription]. Accessed June 16, 2019.
23. AHFS Drug Information. <http://online.lexi.com/lco>. Accessed June 16, 2019.

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24. Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence by Work Group Report of the American Academy of Allergy, Asthma, and Immunology. *J Allergy Clin Immunol*. 2017;139:S1-46.
25. 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 [https://aidsinfo.nih.gov/contentfiles/lvguidelines/oi\\_guidelines\\_pediatrics.pdf](https://aidsinfo.nih.gov/contentfiles/lvguidelines/oi_guidelines_pediatrics.pdf). Accessed June 18, 2019.
26. 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.
27. 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.
28. 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.
29. 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.
30. 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.
31. 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.
32. 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.
33. 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.
34. 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.
35. 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.
36. Immune Deficiency Foundation. About primary immunodeficiencies. Specific disease types. <http://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/>. Accessed June 12, 2019.
37. European Society for Immunodeficiencies. Diagnostic criteria for PID. <http://esid.org/Working-Parties/Clinical/Resources/Diagnostic-criteria-for-PID2>. Accessed June 12, 2019.
38. 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 June 12, 2019.
39. NCCN Clinical Practice Guidelines in Oncology® Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Version 5.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed June 18, 2019.
40. 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.

Reference number(s)
2043-A

41. 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.
42. Olney RK, Lewis RA, Putnam TD, Campellone JV. Consensus criteria for the diagnosis of multifocal motor neuropathy. *Muscle Nerve*. 2003;27:117-121.
43. Dalakas M. Inflammatory muscle diseases. *N Engl J Med*. 2015;372(18):1734-1747.
44. 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.
45. 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.
46. 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.
47. NCCN Clinical Practice Guidelines in Oncology® Management of Immunotherapy-Related Toxicities (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. <https://www.nccn.org>. Accessed June 18, 2019.
48. [HIVPeds]Working Group on Antiretroviral Therapy of the National Pediatric HIV Resource Center. Antiretroviral therapy and medical management of pediatric HIV infection. *Pediatrics*. 1998;102:1005-1063.
49. Center for Medicare and Medicaid Services (CMS). Intravenous immune globulin for autoimmune mucocutaneous blistering diseases. Decision Memorandum. CPG-00109N. Baltimore, MD: CMS; January 22, 2002.
50. Sawinski D, Goral S. BK virus infection: An update on diagnosis and treatment. *Nephrol Dial Transplant*. 2015;30(2):209-217.
51. Groh M, Pagnoux C, Baldini C, et al. Eosinophilic granulomatosis with polyangiitis (Churg–Strauss) (EGPA)Consensus Task Force recommendations for evaluation and management. *Eur J Intern Med*. 2015;26(7):545-553.
52. McKinney RE, Katz SL, Wilfert CM. Chronic enteroviral meningoencephalitis in agammaglobulinemic patients. *Rev Infect Dis*. 1987;9(2):334-56.
53. Sen, E.S., Clarke, SL, Ramanan, A.V. Macrophage Activation Syndrome. *Indian J Pediatr*. 2016;83(3): 248-53.
54. Kimata H. High-dose intravenous gammaglobulin treatment of hyperimmunoglobulinemia E syndrome. *J Allergy Clin Immunol*. 1995;95:771-774.
55. Yescarta [package insert]. Santa Monica, CA: Kite Pharma; October 2017.
56. Kymriah [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018.
57. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at <https://www.online.lexi.com> [available with subscription]. Accessed June 19, 2019.
58. Whittington PF, Kelly S. Outcome of pregnancies at risk for neonatal hemochromatosis is improved by treatment with high-dose intravenous immunoglobulin. *Pediatrics*. 2008;121(6):e1615-e1621.
59. Tate ED, Pranzatelli MR, Verhulst SJ, et al. Active comparator-controlled rater-blinded study of corticotropin-based immunotherapies for opsoclonus-myoclonus syndrome. *J Child Neurol*. 2012; 27:875-884.
60. Mutch LS, Johnston DL. Late presentation of opsoclonus-myoclonus-ataxia syndrome in a child with stage 4S neuroblastoma. *J Pediatr Hematol Oncol*. 2005;27(6):341-343.
61. Sonnenday CJ, Ratner LE, Zachary AA, et al. Preemptive therapy with plasmapheresis/intravenous immunoglobulin allows successful live donor renal transplantation in patients with a positive cross-match. *Transplant Proc*. 2002;34(5):1614-1616.
62. Razonable RR, Humar A. Cytomegalovirus in Solid Organ Transplantation. *Am J Transplant*. 2013;13:93-106.
63. Jordan SC, Toyoda M, Kahwaji J, et al. Clinical Aspects of Intravenous Immunoglobulin Use in Solid Organ Transplant Recipients. *Am J Transplant*. 2011;11:196-202

Reference number(s)
2043-A

64. Kimberlin DW, Brady MT, Jackson MA, et al. Staphylococcus aureus. American Academy of Pediatrics. Red Book: 2018 Report of the Committee on Infectious Diseases. 2018:733-746
65. Gordon C, Amisshah-Arthur MB, Gayed M, et al. British Society for Rheumatology guideline on management of systemic lupus erythematosus in adults. *Rheumatology (Oxford)*. 2018;57:e1-45.