Corporate Medical Policy: Immunoglobulin Therapy

Restricted Product(s):

- Asceniv™ intravenous (IV) immune globulin for administration by a healthcare professional
- Bivigam® intravenous (IV) immune globulin for administration by a healthcare professional
- Carimune® NF intravenous (IV) immune globulin for administration by a healthcare professional
- Flebogamma® intravenous (IV) immune globulin for administration by a healthcare professional
- Gammagard® S/D intravenous (IV) immune globulin for administration by a healthcare professional
- Gammaplex® intravenous (IV) immune globulin for administration by a healthcare professional
- *Octagam® intravenous (IV) immune globulin for administration by a healthcare professional
- Panzyga® intravenous (IV) immune globulin for administration by a healthcare professional
- *Privigen® intravenous (IV) immune globulin for administration by a healthcare professional
- *Gamunex-C® intravenous (IV) or subcutaneous (SC) immune globulin for administration by a healthcare professional
- *Gammaked™ intravenous (IV) or subcutaneous (SC) immune globulin for administration by a healthcare professional
- *Gammagard™Liquid intravenous (IV) or subcutaneous (SC) immune globulin for administration by a healthcare professional
- Cutaquig™ subcutaneous (SC) immune globulin for administration by a healthcare professional
- Cuvitru™ subcutaneous (SC) immune globulin for administration by a healthcare professional
- **Hizentra® subcutaneous (SC) immune globulin for administration by a healthcare professional
- HyQvia™ subcutaneous (SC) immune globulin for administration by a healthcare professional
- **Xembify™ subcutaneous (SC) immune globulin for administration by a healthcare professional

***preferred intravenous immune globulin (IVIG) agents**
****preferred subcutaneous immune globulin (SCIG) agents**

FDA Approved Use:

- Asceniv
  - For treatment of primary humoral immunodeficiency (PI) in adults and adolescents (12 to 17 years of age)
- Bivigam
  - For treatment of primary humoral immunodeficiency (PI)
- Carimune NF

  - For treatment of primary immunodeficiencies (PID)
  - For treatment of idiopathic thrombocytopenic purpura (ITP)
- Flebogamma
  - For treatment of primary humoral immunodeficiency (PI)
  - For treatment of chronic immune thrombocytopenic purpura (ITP)
- Gammagard S/D
  - For treatment of primary immunodeficiency (PID) in patients 2 years of age and older
  - For prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia (CLL)
  - For treatment of chronic idiopathic thrombocytopenic purpura (ITP)
  - For treatment of Kawasaki syndrome
- Gammaplex
  - For treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older
  - For treatment of chronic immune thrombocytopenic purpura (ITP) in adults
- Octagam
  - For treatment of primary immunodeficiencies (PID)
  - For treatment of chronic immune thrombocytopenic purpura (ITP) in adults
- Panzyga
  - For treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older
  - For treatment of chronic immune thrombocytopenia (ITP) in adults
  - For treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adults
- Privigen
  - For treatment of primary humoral immunodeficiency (PI)
  - For treatment of chronic immune thrombocytopenic purpura (ITP) in patients 15 years of age and older
  - For treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adults
- Gamunex-C
  - For treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older
  - For treatment of idiopathic thrombocytopenic purpura (ITP) in adults and children
  - For treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adults
    - Limitations of use: Maintenance therapy in CIDP has not been studied beyond 6 months
- Gammaked
  - For treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older
  - For treatment of idiopathic thrombocytopenic purpura (ITP) in adults and children

  - For treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adults
- Gammagard Liquid
  - For treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older
  - For maintenance treatment of multifocal motor neuropathy (MMN) in adults
- Cutaquig
  - For treatment of primary humoral immunodeficiency (PI) in adults and pediatric patients 2 years of age and older
- Cuvitru
  - For treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older
- Hizentra
  - For treatment of primary immunodeficiency (PI) in patients 2 years of age and older
  - For maintenance treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) in adults
- HyQvia
  - For treatment of primary immunodeficiency (PI) in adults
  - Limitations of use: Safety and efficacy has not been established for chronic use in conditions other than PI
- Xembify
  - For treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Intravenous immunoglobulin (IVIG) may be considered medically necessary when the following criteria are met:

1. The patient has a diagnosis of **primary immunodeficiency [medical record documentation required]**, **and** the diagnosis has been confirmed by presence of ONE of the following **[medical record documentation required]**:
   a. Agammaglobulinemia, defined as a total IgG less than 200 mg/dL at baseline prior to immune globulin therapy; **OR**
   b. Absence of B lymphocytes; **OR**
   c. ALL of the following:
      i. ONE of the following:
         1. The patient has selective IgG subclass deficiency, defined as deficiency of 1 or more IgG subclasses (e.g., IgG1, IgG2, IgG3, or IgG4) at least two standard deviations (SD) below the age-adjusted mean, assessed on 2 separate occasions during infection free period **[medical record documentation required]**; **OR**

2. The patient has specific antibody deficiency (SAD) with normal levels of both immunoglobulin and total IgG subclasses **[medical record documentation required]**; **OR**
3. The patient has persistent hypogammaglobulinemia, defined as total IgG level less than 400 mg/dL or below the lower limit of normal (i.e., at least two SD below the age-adjusted mean) at baseline prior to immune globulin therapy **[medical record documentation required]**; **OR**
4. The patient has another primary immunodeficiency (e.g., congenital agammaglobulinemia, hypogammaglobulinemia, common variable immunodeficiency, severe combined immunodeficiency, Wiskott-Aldrich syndrome, X-linked agammaglobulinemia, X-linked hyperimmunoglobulinemia M syndrome, ataxia telangiectasia) **[medical record documentation required]**; **AND**

ii. The patient has a lack of response or inability to mount an adequate antibody response to protein and/or polysaccharide antigens (e.g., inability to make IgG antibody against either diphtheria and tetanus toxoids, or pneumococcal polysaccharide vaccine, or both) **[medical record documentation required]**; **AND**

iii. The patient has evidence of recurrent, persistent, severe, difficult-to-treat infections despite aggressive prophylactic management and treatment with antibiotics **[medical record documentation required]**; **OR**

2. The requested agent will be used for the **prevention of bacterial infection in HIV-infected children [medical record documentation required]**; **AND**
   a. The patient is less than 13 years old; **AND**
   b. The patient has hypogammaglobulinemia, defined as total IgG level less than 400 mg/dL or below the lower limit of normal (i.e., at least two standard deviations below the age-adjusted mean) at baseline prior to immune globulin therapy **[medical record documentation required]**; **OR**
3. The patient has a diagnosis of **human parvovirus B19-associated severe anemia [medical record documentation required]**; **OR**
4. The patient has a diagnosis of **toxic shock syndrome [medical record documentation required]**; **OR**
5. The patient has a diagnosis of **chronic lymphocytic leukemia (CLL) [medical record documentation required]**; **AND**
   a. The patient has hypogammaglobulinemia, defined as total IgG level less than 400 mg/dL or below the lower limit of normal (i.e., at least two standard deviations below the age-adjusted mean) at baseline prior to immune globulin therapy **[medical record documentation required]**; **AND**
   b. The patient has a history of recurrent, persistent bacterial infections requiring antibiotics and/or hospitalization **[medical record documentation required]**; **OR**
6. The patient has a diagnosis of **multiple myeloma [medical record documentation required]**; **AND**
   a. The patient has a history of recurrent, persistent, life-threatening bacterial infections requiring antibiotics and/or hospitalization **[medical record documentation required]**; **OR**
7. The patient has another **B-cell lymphoproliferative disease**, including acute lymphoblastic leukemia (ALL) and/or B-cell lymphomas **[medical record documentation required]**; **AND**

   a. The patient has treatment-related hypogammaglobulinemia, defined as total IgG level less than 400 mg/dL or below the lower limit of normal (i.e., at least two standard deviations below the age-adjusted mean) at baseline prior to immune globulin therapy **[medical record documentation required]**; **OR**
8. The patient has a diagnosis of a **severe, progressive autoimmune mucocutaneous blistering disease**, including pemphigus, pemphigoid, pemphigus vulgaris, pemphigus foliaceus **[medical record documentation required]**; **AND**
   a. The patient has tried and had an inadequate response to conventional therapy (e.g., corticosteroids, azathioprine, cyclophosphamide) for treatment of this indication **[medical record documentation required]**; **OR**
   b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL conventional therapy used in the treatment of autoimmune mucocutaneous blistering diseases **[medical record documentation required]**; **OR**
9. The patient has a diagnosis of **acute, severe idiopathic thrombocytopenic purpura (ITP) [medical record documentation required]**; **AND**
   a. The patient has acute disease with presence of ONE of the following **[medical record documentation required]**:
      i. Major bleeding (e.g., life-threatening bleeding and/or clinically important mucocutaneous bleeding); **OR**
      ii. Severe thrombocytopenia and at high risk for bleeding complications; **OR**
      iii. Severe thrombocytopenia and a slow or inadequate response to corticosteroids; **OR**
      iv. Severe thrombocytopenia and a predictable risk of bleeding in the future (e.g., a procedure or surgery with a high bleeding risk); **AND**
   b. The patient has presence of symptoms associated with ITP **[medical record documentation required]**; **AND**
   c. The patient has persistent thrombocytopenia (i.e., platelets < 20,000/µL [adult] or 30,000/µL [child]) despite treatment with corticosteroids and splenectomy **[medical record documentation required]**; **OR**
   d. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to corticosteroids used for the treatment of ITP **[medical record documentation required]**; **OR**
10. The patient has a diagnosis of **chronic idiopathic thrombocytopenia purpura [medical record documentation required]**; **AND**
   a. The patient has disease duration of at least 6 months **[medical record documentation required]**; **AND**
   b. The patient has presence of symptoms associated with ITP **[medical record documentation required]**; **AND**
   c. The patient has persistent thrombocytopenia (i.e., platelets < 20,000/µL [adult] or < 30,000/µL [child]) despite treatment with corticosteroids and splenectomy **[medical record documentation required]**; **OR**
   d. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to corticosteroids used for the treatment of ITP **[medical record documentation required]**; **OR**
11. The patient has a diagnosis of **Guillain-Barre syndrome [medical record documentation required]**; **AND**
   a. The requested agent will be used as an equivalent alternative to plasma exchange **[medical record documentation required]**; **OR**
12. The patient has a diagnosis of **Kawasaki syndrome [medical record documentation required]**; **OR**

13. The patient has a diagnosis of **granulomatosis with polyangiitis (also known as Wegener granulomatosis) [medical record documentation required]**; **OR**
14. The patient has a diagnosis of **chronic inflammatory demyelinating polyneuropathy (CIDP) [medical record documentation required]**; **AND**
    a. The patient has progressive symptoms present for at least 2 months **[medical record documentation required]**; **AND**
    b. The patient has progressive or relapsing motor sensory impairment of more than one limb **[medical record documentation required]**; **AND**
    c. The patient has electrodiagnostic findings indicating at least ONE of the following are present **[medical record documentation required]**:
        i. Motor distal latency prolongation in 2 nerves; **OR**
        ii. Reduction of motor conduction velocity in 2 nerves; **OR**
        iii. Prolongation of F-wave latency in 2 nerves; **OR**
        iv. Absence of F-waves in at least 1 nerve; **OR**
        v. Partial motor conduction block of at least 1 motor nerve; **OR**
        vi. Abnormal temporal dispersion in at least 2 nerves; **OR**
        vii. Distal CMAP duration increase in at least 1 nerve; **OR**
15. The patient has a diagnosis of **multifocal motor neuropathy [medical record documentation required]**; **AND**
    a. The diagnosis has been confirmed by ALL of the following **[medical record documentation required]**:
        i. Weakness with slowly progressive or stepwise progressive course over at least 1 month; **AND**
        ii. Asymmetric involvement of two or more nerves; **AND**
        iii. Absence of motor neuron signs and bulbar signs; **OR**
16. The patient has a diagnosis of **Eaton-Lambert myasthenic syndrome [medical record documentation required]**; **AND**
    a. The patient has tried and had an inadequate response to an anticholinesterase agent and/or corticosteroid **[medical record documentation required]**; **OR**
    b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL anticholinesterase agents and corticosteroids used in the treatment of Eaton-Lambert myasthenic syndrome **[medical record documentation required]**; **OR**
17. The patient has a diagnosis of **neuromyelitis optica [medical record documentation required]**; **AND**
    a. The patient has a contraindication or lack of response to first-line treatment **[medical record documentation required]**; **AND**
    b. The requested agent will be used as an alternative treatment; **OR**
18. The patient has a diagnosis of **severe, refractory myasthenia gravis [medical record documentation required]**; **AND**
    a. The patient has chronic debilitating disease despite treatment with cholinesterase inhibitors **[medical record documentation required]**; **OR**

   b. The patient has experienced complications from or trial and failure of corticosteroids and/or azathioprine **[medical record documentation required]**; **OR**

19. The requested agent will be used for treatment of a **myasthenic exacerbation** (i.e., an acute episode of respiratory muscle weakness) **[medical record documentation required]**; **AND**
    a. The patient has a contraindication to treatment with plasma exchange **[medical record documentation required]**; **OR**
20. The patient has a diagnosis of **dermatomyositis or polymyositis [medical record documentation required]**; **AND**
    a. The patient's disease is refractory to treatment with corticosteroids **[medical record documentation required]**; **AND**
    b. The patient will be using the requested agent in combination with other immunosuppressive agents; **OR**
21. The patient has a diagnosis of **warm antibody hemolytic anemia [medical record documentation required]**; **AND**
    a. The patient is refractory to prednisone AND splenectomy **[medical record documentation required]**; **OR**
22. The patient has a diagnosis of **antiphospholipid syndrome [medical record documentation required]**; **OR**
23. The patient has a diagnosis of **autoimmune encephalitis (AE)**, including but not limited to antibody-mediated AE **[medical record documentation required]**; **AND**
    a. The patient has tried and had an inadequate response to a glucocorticoid **[medical record documentation required]**; **OR**
    b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to all glucocorticoids **[medical record documentation required]**; **OR**
24. The patient has a diagnosis of **neonatal alloimmune thrombocytopenia [medical record documentation required]**; **OR**
25. The patient has a diagnosis of **hemolytic disease of the fetus and newborn** (i.e., erythroblastosis fetalis) **[medical record documentation required]**; **OR**
26. The requested agent will be used in the **transplant setting** for one of the following circumstances:
    a. The patient is a recipient of a hematopoietic cell transplantation **[medical record documentation required]**; **AND**
        i. The patient is at least 180 days post-transplantation; **AND**
        ii. The patient has a total IgG level less than 400 mg/dL **[medical record documentation required]**; **AND**
        iii. The requested agent will be used for prevention of infection (NOTE: For IVIG requests within 180 days post-transplantation date, please refer to internal protocol found within Blue Cross NC Clinical Transplant Process Guidelines); **OR**
    b. Prior to solid organ transplant as treatment for patients at high risk of antibody-mediated rejection including highly allo-sensitized patients and those receiving an ABO incompatible organ **[medical record documentation required]**; **OR**
    c. For the treatment of solid organ transplant antibody-mediated rejection **[medical record documentation required]**; **OR**
27. The patient has a diagnosis of **stiff person syndrome [medical record documentation required]**; **AND**
    a. The patient is not controlled by other therapies used in the treatment of stiff person syndrome **[medical record documentation required]**; **OR**
28. The patient has another diagnosis that is an FDA approved indication for the requested agent **[medical record documentation required]**; **OR**

29. The patient has another diagnosis that is an indication supported by compendia (AHFS, NCCN 1 or 2a recommended indication, or DrugDex level of evidence 1 or 2A) for the requested agent **[medical record documentation required]**; **AND**
30. The patient does NOT have selective immunoglobulin A (IgA) deficiency with known antibody against IgA; **AND**
31. The requested agent will NOT be used to treat relapsing-remitting multiple sclerosis; **AND**
32. The patient does NOT have any FDA labeled contraindications to the requested agent; **AND**
33. If the requested agent is a non-preferred intravenous immune globulin (IVIG) (e.g., Asceniv, Bivigam, Flebogamma, Gammaplex, Gammagard S/D, Panzyga), ONE of the following:
    a. The patient is currently being treated with the requested agent and has been stable on therapy for at least 180 days; **OR**
    b. The patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed; **OR**
    c. The patient has tried and had an inadequate response to TWO preferred IVIG agents (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) **[medical record documentation required]**; **OR**
    d. The patient has an intolerance or hypersensitivity to TWO preferred IVIG agents (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) that is NOT expected to occur with the requested agent **[medical record documentation required]**; **OR**
    e. The patient has an FDA labeled contraindication to ALL preferred IVIG agents (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) that is NOT expected to occur with the requested agent **[medical record documentation required]**; **OR**
    f. The prescriber has provided documentation in support of the use of the non-preferred IVIG agent over TWO preferred IVIG agents (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) for the requested indication **[medical record documentation required]**; **AND**
34. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
35. For requests for injection or infusion administration of the requested medication in an inpatient or outpatient hospital setting, Site of Care Criteria applies (outlined below)*

Subcutaneous immunoglobulin (SCIG) may be considered medically necessary when the following criteria are met:

1. The patient has a diagnosis of **primary immunodeficiency [medical record documentation required]**, **and t**he diagnosis has been confirmed by presence of ONE of the following **[medical record documentation required]**:
    a. Agammaglobulinemia, defined as a total IgG less than 200 mg/dL at baseline prior to immune globulin therapy; **OR**
    b. Absence of B lymphocytes; **OR**
    c. ALL of the following:
        i. ONE of the following:
            1. The patient has selective IgG subclass deficiency, defined as deficiency of 1 or more IgG subclasses (e.g., IgG1, IgG2, IgG3, or IgG4) at least two standard deviations (SD) below the age-adjusted mean, assessed on 2 separate occasions during infection free period **[medical record documentation required]**; **OR**

2. The patient has specific antibody deficiency (SAD) with normal levels of both immunoglobulin and total IgG subclasses **[medical record documentation required]**; **OR**
3. The patient has persistent hypogammaglobulinemia, defined as total IgG level less than 400 mg/dL or below the lower limit of normal (i.e., at least two SD below the age-adjusted mean) at baseline prior to immune globulin therapy **[medical record documentation required]**; **OR**
4. The patient has another primary immunodeficiency (e.g., congenital agammaglobulinemia, hypogammaglobulinemia, common variable immunodeficiency, severe combined immunodeficiency, Wiskott-Aldrich syndrome, X-linked agammaglobulinemia, X-linked hyperimmunoglobulinemia M syndrome, ataxia telangiectasia) **[medical record documentation required]**; **AND**

ii. The patient has a lack of response or inability to mount an adequate antibody response to protein and/or polysaccharide antigens (e.g., inability to make IgG antibody against either diphtheria and tetanus toxoids, or pneumococcal polysaccharide vaccine, or both) **[medical record documentation required]**; **AND**

iii. The patient has evidence of recurrent, persistent, severe, difficult-to-treat infections despite aggressive prophylactic management and treatment with antibiotics **[medical record documentation required]**; **OR**

2. The patient has another diagnosis that is an FDA approved indication for the requested agent **[medical record documentation required]**; **OR**
3. The patient has another diagnosis that is an indication supported by compendia (AHFS, NCCN 1 or 2a recommended indication, or DrugDex level of evidence 1 or 2A) for the requested agent **[medical record documentation required]**; **AND**
4. The requested agent will NOT be used to treat relapsing-remitting multiple sclerosis; **AND**
5. The patient does NOT have selective immunoglobulin A (IgA) deficiency with known antibody against IgA; **AND**
6. The patient does NOT have any FDA labeled contraindications to the requested agent; **AND**
7. ONE of the following:
    a. The patient is currently being treated with the requested agent and has been stable on therapy for at least 180 days; **OR**
    b. The patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed; **OR**
    c. The patient has tried and had an inadequate response to an intravenous immune globulin (IVIG) agent **[medical record documentation required]**; **OR**
    d. The patient has an intolerance or hypersensitivity to an IVIG agent that is NOT expected to occur with the requested agent **[medical record documentation required]**; **OR**
    e. The patient has an FDA labeled contraindication to ALL IVIG agents that is NOT expected to occur with the requested agent **[medical record documentation required]**; **OR**
    f. The prescriber has provided documentation in support of the use of the requested agent over an IVIG agent for the requested indication **[medical record documentation required]**; **AND**
8. ONE of the following:

a. If the requested agent is a non-preferred subcutaneous immune globulin (SCIG) (e.g., Cutaquig, Cuvitru), ONE of the following:
    i. The patient is currently being treated with the requested agent and has been stable on therapy for at least 180 days; **OR**
    ii. The patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed; **OR**
    iii. The patient has tried and had an inadequate response to Hizentra AND Xembify **[medical record documentation required]**; **OR**
    iv. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to BOTH Hizentra and Xembify that is NOT expected to occur with the requested agent **[medical record documentation required]**; **OR**
    v. The prescriber has provided documentation in support of the use of the non-preferred SCIG agent over BOTH Hizentra and Xembify for the requested indication **[medical record documentation required]**; **OR**
b. If the requested agent is HyQvia, ONE of the following:
    i. The patient is currently being treated with the requested agent and has been stable on therapy for at least 180 days; **OR**
    ii. The patient has been treated with the requested agent within the past 180 days AND is at risk if therapy is changed; **OR**
    iii. The patient has tried and had an inadequate response to ONE preferred intravenous immune globulin (IVIG) agent (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) **[medical record documentation required]**; **OR**
    iv. The patient has an intolerance or hypersensitivity to ONE preferred IVIG agent (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) that is not expected to occur with the requested agent **[medical record documentation required]**; **OR**
    v. The patient has an FDA labeled contraindication to ALL preferred IVIG agents (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) that is not expected to occur with the requested agent **[medical record documentation required]**; **OR**
    vi. The prescriber has provided documentation in support of the use of HyQvia over ONE preferred IVIG agent (i.e., Octagam, Gamunex-C, Gammaked, Gammagard, Privigen) for the requested indication **[medical record documentation required]**; **AND**
9. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
10. For requests for injection or infusion administration of the requested medication in an inpatient or outpatient hospital setting, Site of Care Criteria applies (outlined below)*

Duration of Approval:

Asceniv for all indications: 180 days (6 months)
All other IVIG and SCIG products: 365 days (1 year)

**NOTE: For hematopoietic cell transplantation: for IVIG requests within 180 days post-transplantation date, please refer to internal protocol found within Blue Cross NC Clinical Transplant Process Guidelines.

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy; **AND**
3. ONE of the following:
    a. The patient was previously approved for short term use of the requested agent (i.e., 6 months) AND the prescriber has provided documentation supporting continued use of the requested agent **[medical record documentation required]**; **OR**
    b. The patient was previously approved for more than 6 months AND ONE of the following:
        i. The patient has had clinical improvement or disease stabilization (e.g., IgG level has improved from pre-treatment levels with the requested agent, reduction in the number and/or severity of difficult to treat infections, reduction in seizure frequency); **OR**
        ii. The prescriber has provided documentation supporting continued use of the requested agent **[medical record documentation required]**; **AND**
4. The requested agent will NOT be used to treat relapsing-remitting multiple sclerosis; **AND**
5. The patient does NOT have selective immunoglobulin A (IgA) deficiency with known antibody against IgA; **AND**
6. The patient does NOT have any FDA labeled contraindications to the requested agent; **AND**
7. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
8. For requests for injection or infusion administration of the requested medication in an inpatient or outpatient hospital setting, Site of Care Criteria applies (outlined below)*

Duration of Approval:

Asceniv for all indications: 180 days (6 months)
All other IVIG and SCIG products: 365 days (1 year)

**NOTE: For hematopoietic cell transplantation: for IVIG requests within 180 days post-transplantation date, please refer to internal protocol found within Blue Cross NC Clinical Transplant Process Guidelines.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
Asceniv™ intravenous (IV) immune globulin	Primary humoral immunodeficiency (PI) in adults and adolescents (12 to 17 years of age)	Refer to prescribing information for specific dosing	J1554 J1599 90283	9999
Bivigam® intravenous (IV) immune globulin	Primary humoral immunodeficiency (PI)	Refer to prescribing information for specific dosing	J1556 J1599 90283	
Carimune® NF intravenous (IV) immune globulin	Primary immunodeficiencies (PID) Idiopathic thrombocytopenic purpura (ITP)	Refer to prescribing information for specific dosing	J1566 J1599 90283	
Cutaquig® subcutaneous (SC) immune globulin	Primary humoral immunodeficiency (PI) in patients 2 years of age and older	Refer to prescribing information for specific dosing	J1551 90284	
Cuvitru™ subcutaneous (SC) immune globulin	Primary humoral immunodeficiency (PI) in patients 2 years of age and older	Refer to prescribing information for specific dosing	J1555 90284	
Flebogamma® intravenous (IV) immune globulin	PI in patients 2 years of age and older Chronic ITP in patients 2 years of age and older	Refer to prescribing information for specific dosing	J1572 J1599 90283	
Gammagard® S/D intravenous (IV) immune globulin	PID in patients 2 years of age and older Prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated	Refer to prescribing information for specific dosing	J1566 90283	

	with B-cell chronic lymphocytic leukemia (CLL) Chronic ITP Kawasaki Syndrome		
Gammagard ™ Liquid intravenous (IV) or subcutaneous (SC) immune globulin	PI in patients 2 years of age and older Multifocal motor neuropathy (MMN) in adults	Refer to prescribing information for specific dosing	J1569 90283 90284
Gammaked™ intravenous (IV) or subcutaneous (SC) immune globulin	PI in patients 2 years of age and older ITP in adults and children CIDP in adults	Refer to prescribing information for specific dosing	J1561 J1599 90283 90284
Gammaplex® intravenous (IV) immune globulin	PI in patients 2 years of age and older Chronic ITP in adults	Refer to prescribing information for specific dosing	J1557 J1599 90283
Gamunex-C® intravenous (IV) or subcutaneous (SC) immune globulin	PI in patients 2 years of age and older ITP in adults and children CIDP in adults	Refer to prescribing information for specific dosing	J1561 J1599 90283 90284
Hizentra subcutaneous (SC) immune globulin	PI in patients 2 years of age and older CIDP in adults	Refer to prescribing information for specific dosing	J1559 90284

HyQvia™ subcutaneous (SC) immune globulin	PI in adults Limitation of use: Safety and efficacy of chronic use of HyQvia have not been established in conditions other than PI	Refer to prescribing information for specific dosing	J1575 90284
Octagam® intravenous (IV) immune globulin	PID Chronic ITP in adults	Refer to prescribing information for specific dosing	J1568 J1599 90283
Panzyga® intravenous (IV) immune globulin	PI in patients 2 years of age and older Chronic ITP in adults CIDP in adults	Refer to prescribing information for specific dosing	J1599 90283
Privigen® intravenous (IV) immune globulin	PI Chronic ITP in patients 15 years of age and older CIDP in adults Limitations of Use: Privigen maintenance therapy in CIDP has not been studied beyond 6 months	Refer to prescribing information for specific dosing	J1459 J1599 90283
Xembify™ subcutaneous (SC) immune globulin	PI in patients 2 years of age and older	Refer to prescribing information for specific dosing	J1558 90284

***Maximum units allowed for duration of approval**

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an inpatient setting, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; OR
2. For requests for injection or infusion administration in an outpatient hospital setting, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); OR
    b. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; OR
    c. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; OR
    d. Re-initiation of therapy, defined as ONE of the following:
        i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; OR
        ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; OR
    e. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Dalmau J, Graus F. Antibody-mediated encephalitis. *N Engl J Med*. 2018;378(9):840-851.
2. 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):356-63.
3. Gastaldi M, Thouin A, Vincent A. Antibody-mediated autoimmune encephalopathies and immunotherapies. *Neurotherapeutics*. 2016;13(1):147-62.
4. 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;117:S525-S553.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

October 2022: Coding update: In dosing reference table, removed HCPCS codes J1599 and J1569 for Gammagard SD and removed J1599 from Gammagard Liquid
October 2022: Criteria change: Added requirement of trial and failure of an IVIG product prior to use of a SCIG product unless other criteria are met. Added requirement of trial and failure of two preferred IVIG products prior to use of non-preferred IVIG products unless other criteria are met. Added requirement of trial and failure of Hizentra and Xembify prior to use of non-preferred SCIG products (Cutaquig, Cuvitru), and trial and failure of one preferred IVIG product prior to use of HyQvia unless other criteria are met. Added continuation criteria. **Policy notification given 8/4/2022 for effective date 10/1/2022**.
July 2022: Coding update: Added HCPCS code J1551 to dosing reference table for Cutaquig effective 7/1/2022, deleted C9399, J3490, and J3590 termed 6/30/2022.
April 2022: Criteria change: Added requirement of trial and failure of two preferred IVIG and/or SCIG products prior to use of non-preferred Asceniv unless other criteria are met. Adjusted duration of approval for Asceniv to 6 months for all indications. **Policy notification given 2/3/2022 for effective date 4/4/2022**.
February 2022: Criteria update: Expanded indication for Cutaquig to patients 2 years of age and older per FDA approval update.
June 2021: Criteria change: Added selective IgG subclass deficiency and specific antibody deficiency (SAD) under primary immunodeficiencies for IVIg and SCIg; added age requirement for bacterial infection prevention in HIV-infected children; added requirements for FDA labeled or compendia accepted indication with specific evidence level rating, no FDA labeled contraindications, and maximum units; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.

Non-Discrimination and Accessibility Notice

Discrimination is Against the Law

- Blue Cross and Blue Shield of North Carolina (“Blue Cross NC”) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex.
- Blue Cross NC does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

  Blue Cross NC:

  - Provides free aids and services to people with disabilities to communicate effectively with us, such as:

  - Qualified interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)

- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

- If you need these services, contact Customer Service **1-888-206-4697**, TTY and TDD, call **1-800-442-7028**.

- If you believe that Blue Cross NC has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:
  - Blue Cross NC, PO Box 2291, Durham, NC 27702, Attention: Civil Rights Coordinator- Privacy, Ethics & Corporate Policy Office, Telephone **919-765-1663**, Fax **919-287-5613**, TTY **1-888-291-1783** civilrightscoordinator@bcbsnc.com

- You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, Civil Rights Coordinator - Privacy, Ethics & Corporate Policy Office is available to help you.

- You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at *https://ocrportal.hhs.gov/ocr/portal/lobby.jsf,* or by mail or phone at: U.S. Department of Health and Human Services 200 Independence Avenue, SW Room 509F, HHH Building Washington, D.C. 20201 **1-800-368-1019, 800-537-7697** (TDD). Complaint forms are available at *http://www.hhs.gov/ocr/office/file/index.html*.

- This Notice and/or attachments may have important information about your application or coverage through Blue Cross NC. Look for key dates. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call Customer Service **1-888-206-4697**.

ATTENTION: If you speak another language, language assistance services, free of charge, are available to you. Call 1-888-206-4697 (TTY: 1-800-442-7028).

ATENCIÓN: Si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-888-206-4697 (TTY: 1-800-442-7028).

注意：如果您講廣東話或普通話， 您可以免費獲得語言援助服務。請致電 1-888-206-4697
(TTY：1-800-442-7028）。

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số
1-888-206-4697 (TTY: 1-800-442-7028).

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.
1-888-206-4697 (TTY: 1- 800-442-7028)번으로 전화해 주십시오.

ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1-888-206-4697 (ATS : 1-800-442-7028).

ملحوظة: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم
1-888-206-4697. المبرقة الكاتبة: 1-800-442-7028.

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau
1-888-206-4697 (TTY: 1-800-442-7028).

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-888-206-4697 (телетайп: 1-800-442-7028).

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-888-206-4697 (TTY: 1-800-442-7028).

સુચના: જો તમે ગુજરાતી બોલતા હો, તો નિ:સુલ્કુ ભાષા સહાય સેવાઓ તમારા માટે ઉપલબ્ધ છે. ફોન કરો
1-888-206-4697 (TTY: 1-800-442-7028).

ចំណាំ៖ ប្រសិនបើលោកអ្នកនិយាយជាភាសាខ្មែរ សេវាកម្មជំនួយផ្នែកភាសាមានផ្តល់ជូនសម្រាប់លោកអ្នកដោយមិនគិតថ្លៃ។ សូមទំនាក់ទំនងតាមរយៈលេខ៖ 1-888-206-4697 (TTY: 1-800-442-7028)។

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-888-206-4697 (TTY: 1-800-442-7028).

ध्यान दें: यदि आप हिन्दी बोलते हैं तो आपके लिए मुफ्त में भाषा सहायता सेवाएं उपलब्ध हैं। 1-888-206-4697 (TTY: 1-800-442-7028) पर कॉल करें।

ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-888-206-4697 (TTY: 1-800-442-7028).

注意事項：日本語を話される場合、無料の言語支援をご利用いただけます。1-888-206-4697（TTY: 1-800-442-7028）まで、お電話にてご連絡ください。