Immune globulin, subcutaneous **(Cutaquig® 16.5%, Cuvitru® 20%, Gammagard® 10%, Gammaked®, Gamunex-C® 10%, Hizentra® 20%, HyQvia® 10%, Xembify® 20%)**	**Place of Service** **Home Infusion Administration** **Outpatient Facility Infusion Administration** **Infusion Center Administration** **HCPCS** **J1551** Cutaquig® per 100 mg **J1555** Cuvitru® per 100 mg **J1558** Xembify® per 100 mg **J1559** Hizentra® per 100 mg **J1561** Gammaked® per 500 mg **J1561** Gamunex-C® per 500 mg **J1569** Gammagard® liquid per 500 mg **J1575** HyQvia® per 100 mg

Condition listed in policy (*see criteria for details*)

- Chronic inflammatory demyelinating polyneuropathy (CIDP) and variants
- Primary immunodeficiency disorders

AHFS therapeutic class: Serums

Mechanism of action: Immune globulin is a sterile, nonpyrogenic solution of globulins containing many antibodies normally present in adult human blood.

(1) Special Instructions and Pertinent Information

Covered under the Medical Benefit, please submit clinical information for prior authorization review via fax.

(2) Prior Authorization/Medical Review is required for the following condition(s)

All requests for subcutaneous immune globulin must be sent for clinical review and receive authorization prior to drug administration or claim payment.

Chronic inflammatory demyelinating polyneuropathy (CIDP) and variants

1. Diagnosis of one of the following:
   a. Typical chronic inflammatory demyelinating polyneuropathy (CIDP)
   b. Multifocal acquired demyelinating polyneuropathy
   c. Pure sensory chronic inflammatory demyelinating polyneuropathy
   d. Distal chronic inflammatory demyelinating polyneuropathy
   e. Focal chronic inflammatory demyelinating polyneuropathy
   f. Motor chronic inflammatory demyelinating polyneuropathy

   AND
2. Diagnosis by a neurologist, **AND**
3. Electrodiagnostic testing (nerve conduction studies) shows definite CIDP OR nerve conduction studies show possible CIDP AND 2 of the following to confirm the diagnosis: CSF examination, nerve biopsy, MRI, ultrasound, **AND**
4. Motor or sensory dysfunction of more than 1 limb developing over at least 2 months, **AND**
5. Absent or reduced tendon reflexes in affected limbs or gait ataxia, **AND**
6. Patient has been stabilized with IVIG and is switching for maintenance therapy

Covered Doses

Maintenance:
0.2 g/kg to 0.4 g/kg SC infusion per week beginning one week after last IVIG infusion

Coverage Period

Maintenance:
Cover yearly based on continued response to treatment [e.g. control of symptoms (weakness, sensory loss, imbalance, pain), and/or improvement or maintenance of functional ability).]
ICD-10: G61.81

Primary immunodeficiency disorders

1. Diagnosis of ONE of the following primary immunodeficiency disorders
    a. Common variable hypogammaglobulinemia
    b. Congenital agammaglobulinemia (e.g., X-linked agammaglobulinemia, BTK deficiency)
    c. Ectodermodysplasia with immunodeficiency (IKBKG: Inhibitor of kB kinase g chain, NEMO (nuclear factor kB essential modulator) deficiency, IKBA/IKBKB GOF mutation)
    d. Variable immunodeficiency with hyper-IgM (e.g., AID deficiency, UNG deficiency, INO90 deficiency, MSH6 deficiency)
    e. WHIM: Warts, hypogammaglobulinemia, immunodeficiency, myelokathexis
    f. Severe combined immunodeficiency (SCID)
    g. Wiskott-Aldrich Syndrome
    h. Combined immunodeficiency (CID) [e.g., IL21 deficiency, Wiskott-Aldrich Syndrome, WIP deficiency, Arp2/3-mediated filament branching defect, RIDDLE (Radiosensitivity, Immune Deficiency, Dysmorphic features, Learning difficulties) syndrome, ICF (immunodeficiency with centromeric instability and facial anomalies), FILS syndrome, Ligase I deficiency, MYSM1 deficiency, Roifman syndrome, Tricho-Hepato-Enteric Syndrome (THES), Wiedemann-Steiner syndrome]
    i. Di George's syndrome
    j. Hyper IgE syndrome (e.g., IL6 receptor deficiency)
    k. AIPS-Caspase 8
    l. CD70 deficiency, CD20 deficiency, SAP deficiency (XLP1), X-linked magnesium EBV and neoplasia (XMEN)
    m. P14/LAMTOR2 deficiency
    n. PLAID (PLCγ2 associated antibody deficiency and immune dysregulation)
    o. GOOD syndrome

AND

2. One of the following:
    a. IgG <200 mg/dL, OR
    b. All or the following:
        i. Member has a history of recurrent bacterial infections, AND
        ii. Inability to respond to IgG antibody production after antigenic challenge against diphtheria and tetanus toxoids or pneumococcal polysaccharide vaccine, AND
        iii. Decreased IgG concentrations (<500mg/dL or below normal as defined by testing laboratory) documented on two or more occasions OR diagnosed by an allergist or immunologist if IgG concentrations are not decreased (>500mg/d or normal as defined by the testing laboratory)

Covered Doses

Gamunex-C®, Gammagard®, Gammaked® (10% immune globulin):

- Previous IVIG dose x 1.37, then divide this dose into weekly doses (e.g., if patient was administered IVIG every three weeks, divide dose by three).

Cuvitru® (20% immune globulin)

Switching from immune globulin intravenous (human) treatment (IVIG) or adult patients switching from HYQVIA:

- Weekly: Start Cuvitru SC 1 week after the last IVIG or HyQvia SC infusion
- Initial weekly dosing: **1.3** x previous IVIG or HyQvia SC dose (grams)/number of weeks between IVIG or HyQvia SC doses.
- Frequent dosing (2 to 7 times per week): divide the calculated weekly dose by the desired number of times per week.

- Biweekly: multiply the calculated weekly dose by two.

Switching from all other immune globulin subcutaneous (human) treatments (SCIG):

- Weekly: weekly dose (grams) should be the same as the weekly dose of prior SCIG treatment (grams)
- Frequent dosing (2 to 7 times per week): divide the calculated weekly dose by the desired number of times per week
- Biweekly dosing: multiply the calculated weekly dose by two

Hizentra® (20% immune globulin)

- Frequent dosing (2 to 7 times per week): Start Hizentra SC 1 week after the last IVIG or Hizentra/SCIG infusion. Divide the calculated weekly dose by the desired number of times per week.
- Weekly: Start Hizentra SC 1 week after last IVIG infusion.
  Initial weekly dosing: cover up to **1.53** × previous IVIG dose (grams)/number of weeks between IVIG doses.
- Biweekly: Start Hizentra SC 1 or 2 weeks after the last IVIG infusion or 1 week after the last weekly Hizentra SC infusion. Administer twice the calculated weekly dose.
- Doses may be adjusted over time to achieve the desired clinical response and serum IgG levels.

HyQvia® (10% immune globulin with recombinant human hyaluronidase):

- Naïve to IgG treatment or switching from immune globulin subcutaneous (Human):
  - *Initial*: Cover target dose (300 to 600 mg/kg) over a seven-week ramp-up period:
    - Week 1: Up to 75 to 150 mg/kg SC
    - Week 2: Up to 150 to 300 mg/kg SC
    - Week 3: No dose given
    - Week 4: Up to 300 to 600 mg/kg SC
  - *Maintenance dose*: Maintenance dosing beginning at Week 7:
    - Up to 300 to 600 mg/kg SC at 3 to 4-week intervals, after initial ramp-up. *Initial ramp-up occurs over seven weeks to achieve target dose*.
- Switching from IVIG treatment: Cover same dose and frequency as previous intravenous treatment after initial seven-week ramp-up:
  - Week 1: ¼ of target dose given
  - Week 2: ½ of target dose given
  - Week 3: No dose given
  - Week 4: ¾ of target dose given
  - Week 7: Maintenance dosing begins

Cutaquig® (16.5% immune globulin):

Switching from IVIG or SCIG infusion: Ensure that patients have received IVIG or SCIG at regular intervals for at least 3 months. Start Cutaquig treatment one week after the last IVIG/SCIG infusion.

- Switching from IVIG to CUTAQUIG: Establish the initial weekly dose by converting the monthly IVIG dose into an equivalent weekly dose and increasing it using a dose adjustment factor. To calculate the initial weekly dose, divide the monthly IVIG dose in grams by the number of weeks between IVIG infusions and then multiply this value with a Dose Adjustment Factor of 1.40. To convert the dose (in grams) to milliliters (mL), multiply the calculated dose (in grams) by 6.

  Weekly: Start Cutaquig one week after last IVIG infusion

$$\text{Initial weekly dose} = \frac{\text{Previous IVIG dose (in grams)} \times 1.40}{\text{No. of weeks between IVIG doses}}$$

- Switching from other SCIG: Dosing should be the same as for previous SCIG. To convert the dose (in grams) to milliliters (mL), multiply the calculated dose (in grams) by 6.

Xembify® (20% immune globulin):

- Switching from immune globulin intravenous (human), 10% (IVIG) to XEMBIFY: calculate the dose by using a dose adjustment factor (1.37)
- Weekly: Begin Xembify® one week after last IVIG infusion.
- Establish initial weekly dose by converting the monthly (or every 3 weeks) IVIG dose into an equivalent weekly dose and increasing it using a dose adjustment factor (1.37).

$$\text{Initial weekly dose (grams)} = \frac{\text{Prior IVIG dose (in grams)} \times 1.37}{\text{Number of weeks between IVIG doses}}$$

- Frequent dosing (2-7 times per week): Divide the calculated weekly dose by the desired number of times per week.
- Switching from immune globulin subcutaneous (human) treatment (SCIG): Weekly dose (grams) should be the same as the weekly dose of prior SCIG treatment (grams).

Coverage Period

Initial: 6 months
Reauthorization: Annually based upon continued response to treatment

ICD-10:

D80.0, D80.1, D80.3, D80.5, D80.6, D80.7, D81.0-D81.2, D81.6, D81.7, D81.89, D81.9, D82.0, D82.1, D82.3, D82.4, D83.0, D83.1, D83.2, D83.8, D83.9

(3) The following condition(s) DO NOT require Prior Authorization/Preservice

All requests for subcutaneous immune globulin must be sent for clinical review and receive authorization prior to drug administration or claim payment.

(4) This Medication is NOT medically necessary for the following condition(s)

Blue Shield's research indicates there is inadequate clinical evidence to support off-label use of this drug for the following conditions (Health and Safety Code 1367.21):

- The use of subcutaneous immune globulin for indications other than CIPD and variants and the primary immunodeficiencies listed in section (2) are not medically necessary due to a lack of controlled evidence.

Coverage for a Non-FDA approved indication, requires that criteria outlined in Health and Safety Code § 1367.21, including objective evidence of efficacy and safety are met for the proposed indication.

Please refer to the Provider Manual and User Guide for more information.

(5) Additional Information

How supplied:

- Cutaquig®: 1 gm, 1.65 gm, 2 gm, 3.3 gm, 4 gm, 8 gm (single use vials)
- Cuvitru®: 1 gm, 2 gm, 4 gm, 8 gm, 10 gm (single use vials)
- Hizentra®: 1 gm, 2 gm, 4 gm, 10 gm (single use vials)
- Gamunex®-C: 1gm, 2.5 gm, 5 gm, 10 gm, 20 gm, 40 gm (single use bottles)
- Gammagard®: 1 gm, 2.5 gm, 5 gm, 10 gm, 20 gm, 30 gm (single use bottles)
- Gammaked®: 1 gm, 2.5 gm, 5 gm, 10 gm or 20 gm (single use vials)
- HyQvia®: 2.5 gm, 5 gm, 10 gm, 20 gm, 30 gm (dual vial unit of two single use vials containing the labeled amount of functionally active Immune Globulin Infusion 10% (Human) and Recombinant Human Hyaluronidase)
- Xembify®: 1 gm, 2 gm, 4 gm, 10 gm (single use vials)

(6) References

- AHFS®. Available by subscription at http://www.lexi.com
- Bonilla FA, Khan DA, Ballas ZK et al. Practice parameter for the diagnosis and management of primary immunodeficiency. Allergy Clin Immunol 2015; 136(5): 1186-1205;1205 e1-e78.
- Cutaquig® (immune globulin subcutaneous, human) [Prescribing Information]. Paramus, NJ: Octapharma USA, Inc.; 7/2020.
- Cuvitru® (immune globulin subcutaneous, human) [Prescribing information]. Lexington, MA: Baxalta US Inc.; 9/2021.
- DrugDex®. Available by subscription at http://www.micromedexsolutions.com/home/dispatch
- Hizentra® (immune globulin subcutaneous, human) [Prescribing Information]. Kankakee, IL: CSL Behring LLC; 4/2021.
- Gammagard® (immune globulin, human) [Prescribing information]. Lexington, MA: Baxalta US Inc.; 3/2021.
- Gammaked® (immune globulin, human) [Prescribing information]. Fort Lee, NJ: Kedrion Biopharma, Inc.; 1/2021.
- Gamunex-C® (immune globulin, human) [Prescribing information]. Research Triangle Park, NC: Grifols Therapeutics LLC; 1/2020.
- HyQvia® (immune globulin 10% subcutaneous with recombinant human hyaluronidase) [Prescribing information]. Lexington, MA: Baxalta US Inc.; 3/2021.
- Perez EE, Orange JS, Bonilla F et al. Work Group Report of the American Academy of Allergy, Asthma & Immunology: Update on the use of immunoglobulin in human disease: A review of evidence. J Allergy Clin Immunol 2017;139:S1-46.
- Tangye SG, et al. Human Inborn Errors of Immunity: 2019 Update on the Classification from the International Union of Immunological Societies Expert Committee. J Clin Immunol. 2020 Jan;40(1):24-64.
- Van den Bergh PYK, et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force-Second revision. J Peripher Nerv Syst. 2021 Sep;26(3):242-268.
- Xembify® (immune globulin subcutaneous, human) [Prescribing information]. Research Triangle Park, NC: Grifols Therapeutics LLC; 8/2020.

(7) Policy Update

Date of last revision: 3Q2023
Date of next review: 2Q2024
Changes from previous policy version:

- Section (1): Effective 10/30/2023 and after, site of care (SOC) management program will apply to this drug.
  Rationale for medications requiring SOC management: Low to no risk of infusion-related adverse reactions, as reported in the package insert and medical literature

BSC Drug Coverage Criteria to Determine Medical Necessity
Reviewed by P&T Committee